

On-line Table 1: Search syntax

PubMed Search Accessed on November 17, 2018 (71 Articles)	EMBASE Search Accessed on November 17, 2018 (168 Articles)	Scopus Search Accessed on November 17, 2018 (371 Articles)
(((small vessels(Title/Abstract) OR small arteries(Title/Abstract))) AND flow diversion(Title/Abstract)) AND (intracranial aneurysms(Title/Abstract) OR cerebral aneurysms(Title/Abstract))) OR (((intracranial aneurysms(Title/Abstract) OR cerebral aneurysms(Title/Abstract))) AND distal(Title/Abstract)) AND (flow diversion(Title/Abstract) OR flow diverter(Title/Abstract)))	'intracranial aneurysms':ab,ti AND 'flow diverter':ab,ti AND 'distal':ab,ti OR ('intracranial aneurysms':ab,ti AND 'flow diverter':ab,ti AND 'artery':ab,ti)	(intracranial AND aneurysms AND flow AND diversion AND distal) OR (TITLE- ABS-KEY (intracranial AND aneurysms AND small AND vessels AND flow AND diversion))

On-line Table 2: Summary of studies included in meta-analysis

Study Name	Design	No. of Aneurysms Treated by FD	Successful Stent Deployment	Overall Complete Occlusion	Overall Rate of Treatment-Related Complications	Description of Complication	Antiplatelet Therapy (Loading Dose/Maintenance Dose)
Studies reporting MCA location							
Morais et al, 2017 ⁴²	R	8	NA	NA	NA	M2 arterial narrowing (n = 4)	ASA 320 mg/day + CP 300 mg/day 1 day before/ASA 160 mg/day + CP 75 mg/day for 1 yr, then ASA 160 mg/day
Möhlenbruch et al, 2017 ³¹	PMC	18	18/18	9/16	3/18	3 Symptomatic arterial slow flow of covered M2	ASA 100–300 mg/day + CP 75 mg/day 5 days before/ASA 100 mg/day + CP 75 mg/day for 3–6 mo, then ASA 100 mg/day
Bhogal et al, 2017 ²⁹	PMC	13	13/13	11/12	2/13	1 Acute in-stent thrombosis reversed with therapy + 1 ischemic basal ganglia lesion	ASA 100 mg/day + CP 75 mg/day/ASA 100 mg/day + CP 75 mg/day for 1 yr, then ASA 100 mg/day
Iosif et al, 2017 ³⁰	PMC	63	63/63	39/40	5/58	3 Periprocedural and 1 delayed thromboembolism + 1 peri-aneurysmal inflammation	ASA 100 mg/day + CP 75 mg/day/ASA 100 mg/day + CP 75 mg/day
Bhogal et al, 2018 ¹¹	R	15	15/15	11/14	2/15	1 Arterial dissection + 1 ischemic perforator lesion	ASA 100 mg/day + CP 75 mg/day 7 days before/ASA 100 mg/day + CP 75 mg/day for 2 mo, then ASA 100 mg/day
Topcuoglu et al, 2016 ²⁶	R	29	29/29	20/27	5/28	1 Acute thrombosis of covered M2 + 2 M2 narrowing + 1 M2 occlusion + 1 aneurysm rupture + 1 ICH	ASA 300 mg/day + CP 75 mg/day 5–10 days before/ASA 300 mg/day + CP 75 mg/day for 6 mo, then ASA 100 mg/day
Lin et al, 2016 ¹	R	20	19/20	17/19	2/20	1 Ischemic lesion + 1 in-stent delayed occlusion	ASA 300 mg/day + CP 75 mg/day 5 days before/NA
Briganti et al, 2016 ¹²	R	15	NA	12/15	4/14	4 Delayed thromboembolic events	ASA 150 mg/day + CP 75 mg/day 5 days before/ASA 100 mg/day + CP 75 mg/day for 1 yr, then ASA 100 mg/day
Caroff et al, 2016 ¹³	R	15	14/15	9/13	7/14	1 Acute transitory in-stent occlusion + 6 thromboembolic events	ASA 160 mg/day + CP 75 mg/day 7 days before/ASA 100 mg/day + CP 75 mg/day for 3 mo, then ASA 100 mg/day
Gawlitza et al, 2016 ¹⁸	R	12	12/12	4/12	6/12	1 Intraoperative perforation + 5 perforator strokes	ASA 100 mg/day + CP 75 mg/day 7 days before/ASA 100 mg/day + CP 75 mg/day for 4 mo, then ASA 100 mg/day
Yavuz et al, 2014 ²⁷	R	25	23/25	21/25	3/21	1 SAH of unknown origin + 1 acute in-stent thrombosis resolved with therapy + 1 thromboembolism after CP discontinuation	ASA 160 mg/day + CP 75 mg/day 5 days before/ASA 100 mg/day + CP 75 mg/day for 6 mo, then ASA 100 mg/day
Saleme et al, 2014 ⁴	R	19	19/19	NA	NA	NA	NA
Zanaty et al, 2014 ²⁸	R	10	10/10	8/9	3/10	1 Symptomatic occlusion of covered M2 + 2 thromboembolisms after CP discontinuation	ASA 81 mg/day + CP 75 mg/day 10 days before/ASA 81 mg/day + CP 75 mg/day for 6 mo, then ASA 81 mg/day
De Vries et al, 2013 ¹⁷	P	9	9/9	3/5	NA	NA	ASA 80 mg + CP 75 mg 5 days before/ASA 100 mg/day + CP 75 mg/day for 6 mo, then ASA 100 mg/day
Pistocchi et al, 2012 ²³	R	8	8/8	3/5	2/8	1 Intraprocedural arterial perforation + 1 delayed in-stent thrombosis with permanent deficit	ASA 250 mg/day + CP 75 mg/day/ASA 250 mg/day + CP 75 mg/day for 6 mo
Lubicz et al, 2011 ²¹	R	7	7/7	7/8	NA	NA	ASA 300 mg + CP 300 mg 5 days before/ASA 160 mg/day + CP 75 mg/day for 6 mo
Studies reporting AcomA location							
Pistocchi et al, 2012 ²³	R	16	16/16	12/14	1/16	Transient hemiparesis due to slow flow of covered A2	ASA 250 mg/day + CP 75 mg/day/ASA 250 mg/day + CP 75 mg/day for 6 mo
Toma et al, 2013 ²⁵	R	7	7/7	NA	2/7	Acute in-stent thrombosis (n = 2)	ASA 300 mg/day + CP 75 mg/day 3 days before/ASA 300 mg/day + CP 75 mg/day for 3–6 mo, then ASA lifelong
Saleme et al, 2014 ⁴	R	9	9/9	9/9	NA	NA	NA
Gawlitza et al, 2016 ¹⁸	R	5	5/5	5/5	2/5	2 Ischemic lesions due to the coverage of Heubner artery	ASA 100 mg/day + CP 75 mg/day 7 days before/ASA 100 mg/day + CP 75 mg/day for 4 mo, then ASA 100 mg/day
Dabus et al, 2017 ¹⁵	R	13	13/13	11/13	2/13	1 Caudate infarct + 1 ICH	NA
Colby et al, 2017 ¹⁴	R	41	48/50	29/34	4/41	2 Acute in-stent thromboses + 2 ICHs	NA
Möhlenbruch et al, 2017 ³¹	PMC	11	11/11	6/9	0/11	NA	ASA 100–300 mg/day + CP 75 mg/day 5 days before/ASA 100 mg/day + CP 75 mg/day for 3–6 mo, then ASA 100 mg/day
Wakhloo et al, 2015 ³³	PMC	12	NA	8/9	0/12	NA	ASA 81 mg/day + CP 75 mg/day 3 days before/ASA 81 mg/day + CP 75 mg/day for 3 mo, then ASA 81 mg/day
Lin et al, 2017 ²⁰	R	10	10/10	NA	NA	NA	NA

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On-line Table 2: Continued

Study Name	Design	No. of Aneurysms Treated by FD	Successful Stent Deployment	Overall Complete Occlusion	Overall Rate of Treatment-Related Complications	Description of Complication	Antiplatelet Therapy (Loading Dose/Maintenance Dose)
Lin et al (aneurysms retreated) 2018 ¹⁹	R	6	5/6	5/6	0/6	NA	NA
Pierot et al, 2018 ²²	P MC	9	9/9	NA	3/9	1 Thromboembolism + 1 acute in-stent occlusion + 1 intraprocedural perforation	NA
Rautio et al, 2018 ²⁴	R	6	6/6	6/6	0/6	NA	ASA 100 mg/day + CP 75 mg/day 5 days before/ASA 160 mg/day + CP 75 mg/day for 6 mo, then ASA 160 mg/day for 12 mo
Studies reporting DACA location							
Möhlenbruch et al, 2017 ³¹	P MC	13	13/13	10/13	1/13	1 Symptom related to diminished flow of the covered branch	ASA 100–300 mg/day + CP 75 mg/day 5 days before /ASA 100 mg/day + CP 75 mg/day for 3–6 mo, then ASA 100 mg/day
De Macedo et al, 2018 ¹⁶	R	7	7/7	5/7	0/7	NA	ASA 81–325 mg/day + CP 75 mg/day for a minimum of 6 mo
Dabus et al, 2017 ¹⁵	R	6	6/6	3/6	0/6	NA	NA
Lin et al, 2016 ¹	R	5	5/5	5/5	0/5	NA	ASA 300 mg/day + CP 75 mg/day 5 days before/NA
Nossek et al, 2017 ²²	R	5	5/5	5/5	1/5	1 Asymptomatic occlusion of covered branch	ASA 325 mg/day + CP 75 mg/day 5 days before/ASA 300 mg/day + CP 75 mg/day for at least 3 mo
Cagnazzo et al, 2018 ²	R	17	17/17	13/17	3/17	1 Acute in-stent occlusion after discontinuation of AT + 1 subacute reversible in-stent occlusion + 1 thromboembolism	ASA 81 mg/day + CP 75 mg/day 5 days before/ASA 81 mg/day + CP 75 mg/day for 6 mo, then ASA 81 mg/day lifelong

Note:—R indicates retrospective study; P MC, prospective multicentric study; CP, clopidogrel; ASA, acetylsalicylic acid; NA, not available; ICH, intracranial hemorrhage.

On-line Table 3: Quality measure of included studies by the modified Newcastle-Ottawa quality assessment scale^{a,b}

Study Name	Selection				Comparability		Outcome/Exposure			Total
	1)	2)	3)	4)	a) (Not tested)	b)	1)	2)	3)	
MCA location retrospective design (score 0–8)										
Morais et al, 2017 ⁴²	*	*					*			3
Bhogal et al, 2017 ²⁹	*	*				*	*		*	5
Topcuoglu et al, 2016 ²⁶	*	*				*	*		*	5
Lin et al, 2016 ¹	*	*				*	*		*	5
Briganti et al, 2016 ¹²	*	*				*	*		*	5
Caroff et al, 2016 ¹³	*	*				*	*		*	5
Gawlitza et al, 2016 ¹⁸	*	*				*	*		*	5
Yavuz et al, 2014 ²⁷	*	*				*	*		*	5
Saleme et al, 2014 ⁴	*	*					*		*	4
Zanaty et al, 2014 ²⁸	*	*				*	*		*	5
De Vries et al, 2013 ¹⁷	*	*					*		*	4
Pistocchi et al, 2012 ²³	*	*				*	*		*	5
Lubicz et al, 2011 ²¹	*	*					*		*	4
MCA location prospective design (score 0–8)										
Möhlenbruch et al, 2017 ³¹	*		*	*		*	*	*	*	7
Bhogal et al, 2017 ²⁹	*		*	*		*	*	*	*	7
Iosif et al, 2017 ³⁰	*		*	*			*	*	*	6
AcomA location retrospective design (score 0–8)										
Pistocchi et al, 2012 ²³	*	*				*	*		*	5
Toma et al, 2013 ²⁵	*	*				*	*		*	5
Saleme et al, 2014 ⁴	*	*					*		*	4
Gawlitza et al, 2016 ¹⁸	*	*				*	*		*	5
Dabus et al, 2016 ¹⁵	*	*				*	*		*	5
Colby et al, 2017 ¹⁴	*	*				*	*		*	5
Lin et al, 2017 ²⁰	*	*					*		*	4
Lin et al, (aneurysm retreatment) 2018 ¹⁹	*	*					*		*	4
Rautio et al, 2018 ²⁴	*	*					*		*	4
AcomA location prospective design (score 0–8)										
Möhlenbruch et al, 2017 ³¹	*		*	*		*	*	*	*	7
Wakhloo et al, 2015 ³³	*		*	*		*	*	*	*	7
Pierot et al, 2018 ³²	*		*	*		*	*	*	*	7
DACA location retrospective design (score 0–8)										
De Macedo et al, 2018 ¹⁶	*	*				*	*		*	5
Dabus et al, 2017 ¹⁵	*	*				*	*		*	5
Lin et al, 2016 ¹	*	*				*	*		*	5
Nossek et al, 2017 ²²	*	*				*	*		*	5
Cagnazzo et al, 2018 ²	*	*				*	*		*	5
DACA location prospective design (score 0–8)										
Möhlenbruch et al, 2017 ³¹	*		*	*		*	*	*	*	7

^a Newcastle-Ottawa quality-assessment scale for retrospective studies. Studies with ≥ 5 asterisks were considered high-quality.

Selection

1) Is the case definition adequate?

- a) Yes, with independent validation*
- b) Yes, eg. 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.* (these criteria could be modified to indicate specific control for a second important factor)

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On-line Table 3: Continued

Note =

Comparability (point a) was not tested because 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 (eg, surgical records)*
- 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) Less than 20%*
- b) Nonrespondents described
- c) Rate different and no designation.

^b Newcastle-Ottawa quality-assessment scale for prospective studies. Studies with ≥ 5 asterisks were considered high-quality.

Selection

1) Representativeness of the exposed cohort

- a) Truly representative of the average (patients treated with braided stents) in the community*
- b) Somewhat representative of the average (patients treated with braided stents) in the community*
- c) Selected group of users, eg, 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 (eg, surgical records)*
- 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* (these criteria 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 (distal vs proximal location, anterior vs posterior circulation and so forth)

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) to 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

On-line Table 4: Patient population and characteristics of distally located intracranial aneurysms treated with flow diversion

Variables	Raw Nos. (%)	No. of Articles	95% CI
Population characteristics			
Overall patients/aneurysms	484	27	
No. of MCA aneurysms	286	16	
No. of AcomA aneurysms	145	12	
No. of DACA aneurysms	53	6	
Mean/median age (general population) (yr)	54.5/55 (range, 18–82)	24	
Mean/median age (MCA population) (yr)	53/52 (range, 21–82)	12	
Mean/median age (AcomA population) (yr)	56/55 (range, 18–73)	7	
Mean/median age (DACA population) (yr)	57/58 (range, 20–81)	5	
Overall proportion of men	127/350 = 36%	20	31–41
Aneurysm characteristics			
Overall mean aneurysm size	6 mm (median, 5.7 mm; range, 2–21 mm)	24	
Mean MCA aneurysm size	7 mm (median, 6.5 mm; range, 3–21 mm)	11	
Mean AcomA aneurysm size	5.6 mm (median, 5 mm; range, 4–15 mm)	8	
Mean DACA aneurysm size	5.2 mm (median, 5.5 mm; range, 2–12 mm)	5	
Treatment characteristics			
Type of FD/total of FD used			
PED	284/457 = 62%		57–66
FRED	71/457 = 15.5%	24	12–19
Silk	48/457 = 10.5%		8–13
p64	31/457 = 7%		4–9
Surpass	23/457 = 5%		3–7
Radiologic Follow-up (mo)			
Mean	12 (range, 4–28)	27	
Median (IQR)	12.5 (10–12.5)		
Clinical follow-up (mo)			
Mean	13 (range, 6–30)	27	
Median (IQR)	12 (10–14)		

On-line Table 5: Factors related to aneurysm occlusion and treatment-related complications after flow diversion of distally located anterior circulation aneurysms

Variables	Complete/Near-Complete Occlusion (95% CI)	No. of Articles	P Value	Treatment-Related Complications (95% CI)	No. of Articles	P Value
Factors influencing occlusion and complication rate						
Aneurysm size						
Small vs large/giant ^a	104/128 vs 35/44 (0.4–2.3) ($I^2 = 0\%$) OR = 1.02	12	.9	14/94 vs 11/36 (0.1–1.1) ($I^2 = 0\%$) OR = 0.4	13	.04 ^b
Mean aneurysm size	Complete occlusion 6 ± 4.6 mm vs Incomplete occlusion 6.5 ± 6.3 mm	12	.3	Complications 7 ± 4.3 mm vs No complications 4.4 ± 4.5 mm	12	.06 ^b
Mean difference of age among completely occluded vs	54 vs 60 yr Mean difference = 6 (2.5–12.6) ($I^2 = 82\%$)	11	.06 ^b	58.5 vs 60 Mean difference = 1.7 (0.5–6.2) ($I^2 = 0\%$)	13	.09
Incompletely occluded aneurysms	47/59 vs 101/136 (0.5–2.8) ($I^2 = 0\%$) OR = 1.05	10	.4	3/26 vs 12/64 (0.2–9) ($I^2 = 48\%$) OR = 1.99	7	.5
Flow diverter alone	33/37 vs 77/101 (0.5–3.8) ($I^2 = 0\%$) OR = 1.4	15	.5	12/60 vs 16/122 (0.7–3.7) ($I^2 = 0\%$) OR = 1.6	15	.2
Multiple flow diverters	48/60 = 80% (72–90) ($I^2 = 0\%$) vs	6	.5	8/47 = 14% (4–23) ($I^2 = 0\%$) vs	5	.8
Single flow diverter	186/244 = 76% (82–97) ($I^2 = 0\%$)	16	.5	38/222 = 15% (9–22) ($I^2 = 47\%$)	14	
Fusiform/dissecting aneurysms						
Saccular						

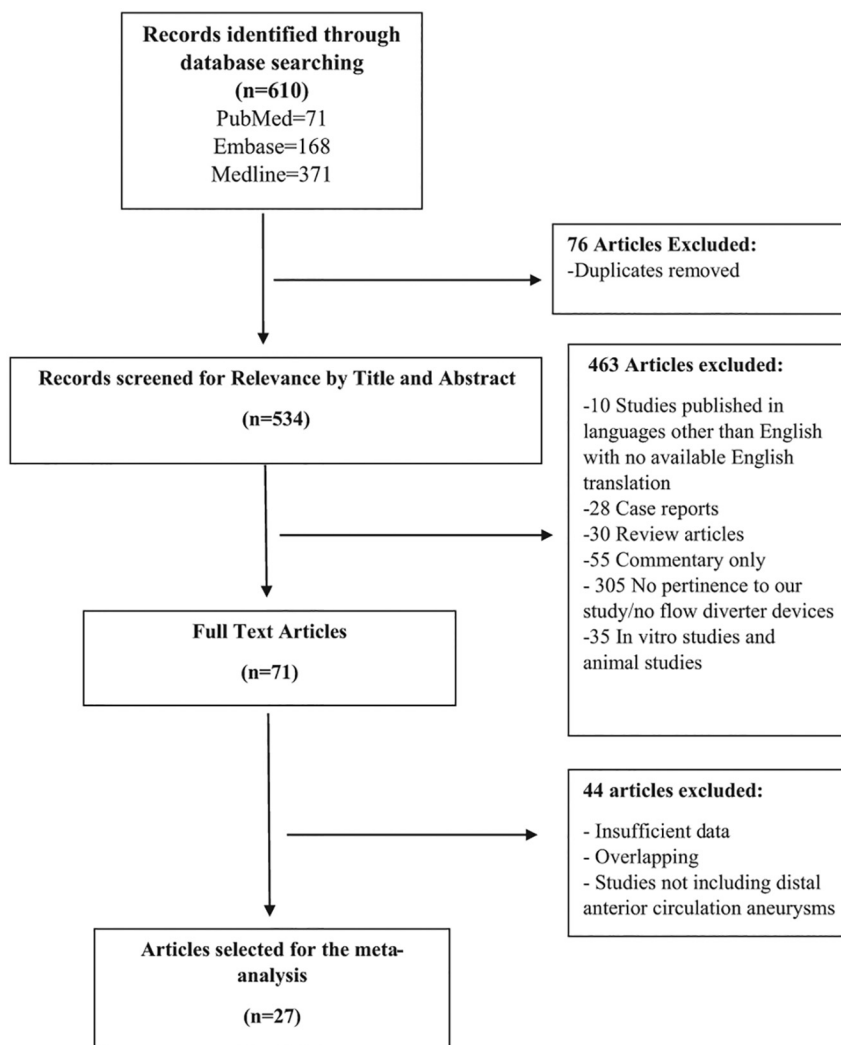
^a Small aneurysms, ≤10 mm; large aneurysms, ≥10 mm; giant aneurysms, ≥25 mm; CI, confidence interval; I^2 , heterogeneity.

^b Significant.

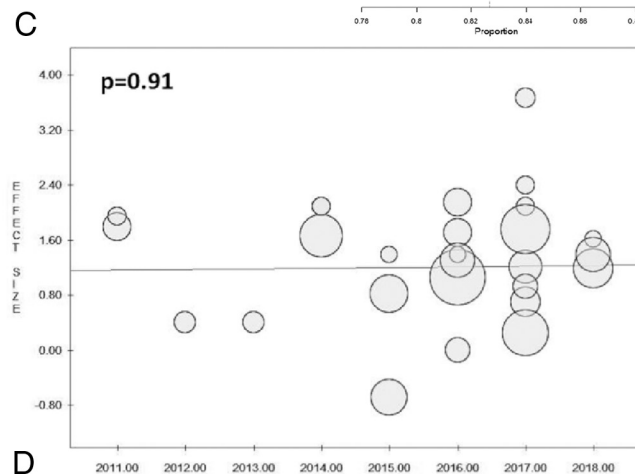
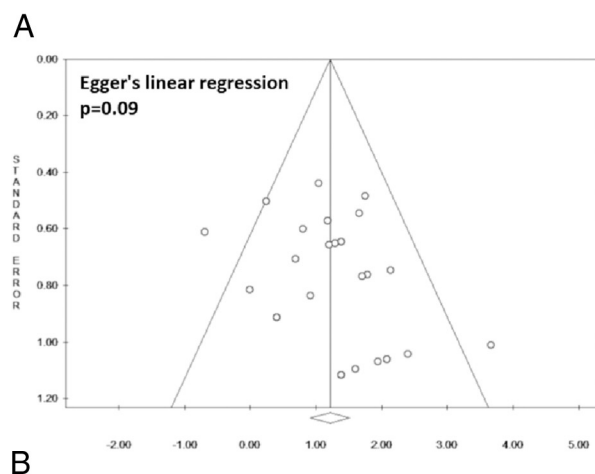
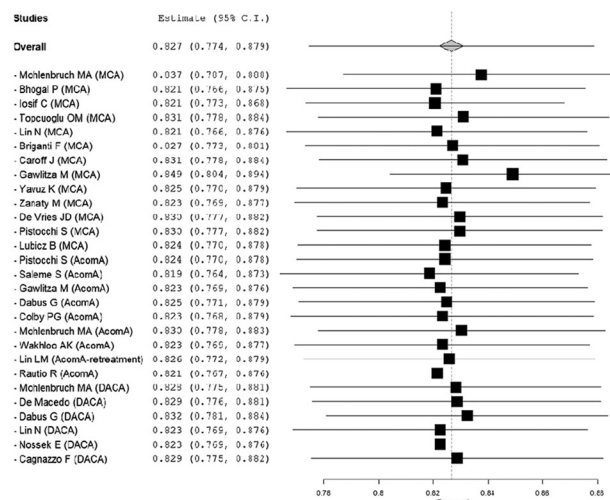
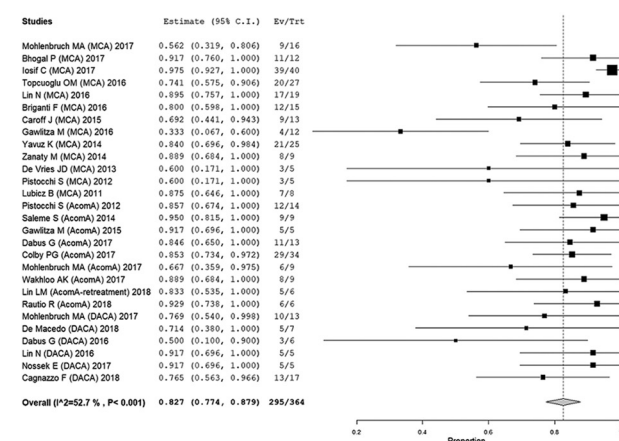
On-line Table 6: Outcome of covered vessels by flow-diverter stents used for the treatment of distally located anterior circulation aneurysms

Variables	Results of Systematic Review and Meta-Analysis	No. of Articles	Statistic (95% CI) (I^2)
Angiographic outcomes and symptoms related to arterial flow changes			
Overall rate of vessel occlusion (late follow-up)	29/283 = 6.3%	22	(3.5–9.1) (I^2 = 4.2%)
Overall rate of arterial narrowing (late follow-up)	69/283 = 23.8%	22	(15.7–32) (I^2 = 80%)
Symptoms related to vessel occlusion	6/269 = 3.5%	21	(1.1–5) (I^2 = 0%)
Symptoms related to arterial narrowing/slow flow	6/245 = 3%	21	(1–4) (I^2 = 0%)
Angiographic outcome of covered vessels by location and device			
Rate of vessel occlusion (MCA location)	22/207 = 7.3%	14	(3.5–11) (I^2 = 15%)
Rate of vessel occlusion (ACA location)	7/76 = 5.5%	8	(1–11) (I^2 = 0%)
Rate of vessel occlusion (PED device)	11/124 = 7.7%	12	(3.2–12) (I^2 = 0%)
Rate of vessel occlusion (other devices)	9/61 = 7%	4	(3.5–10) (I^2 = 0%)

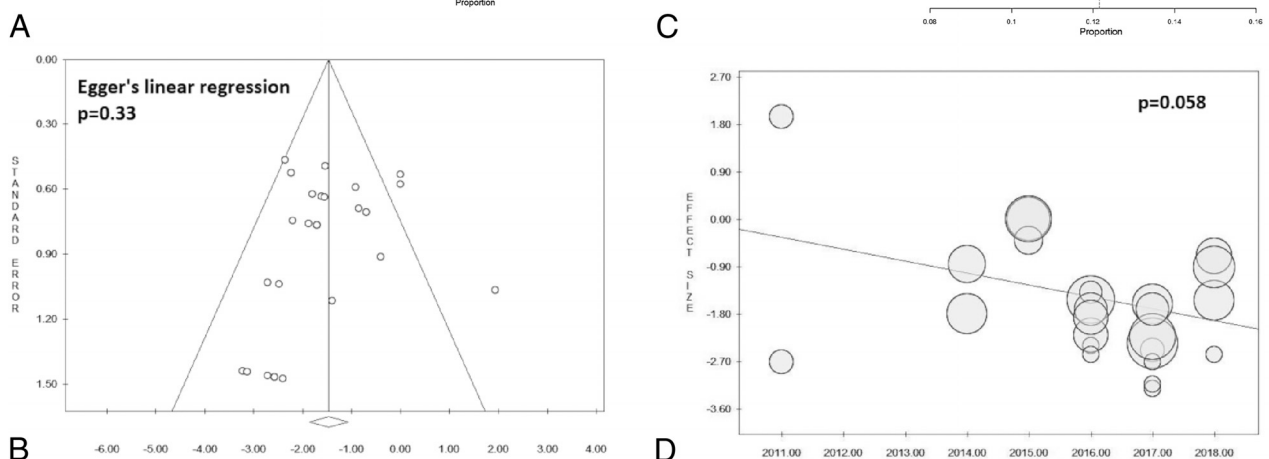
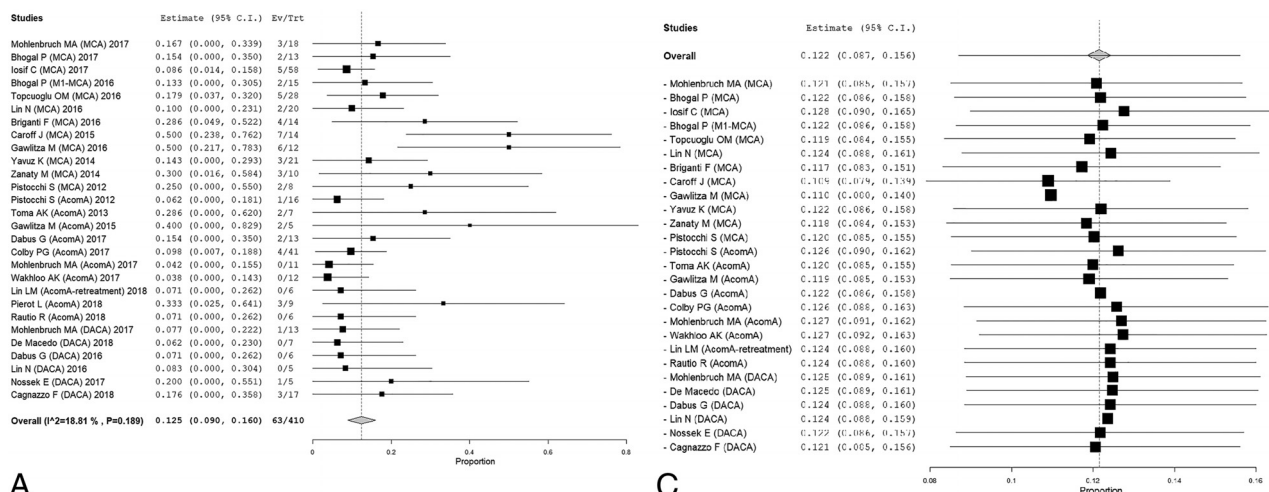
Note:—ACA indicates anterior cerebral artery.



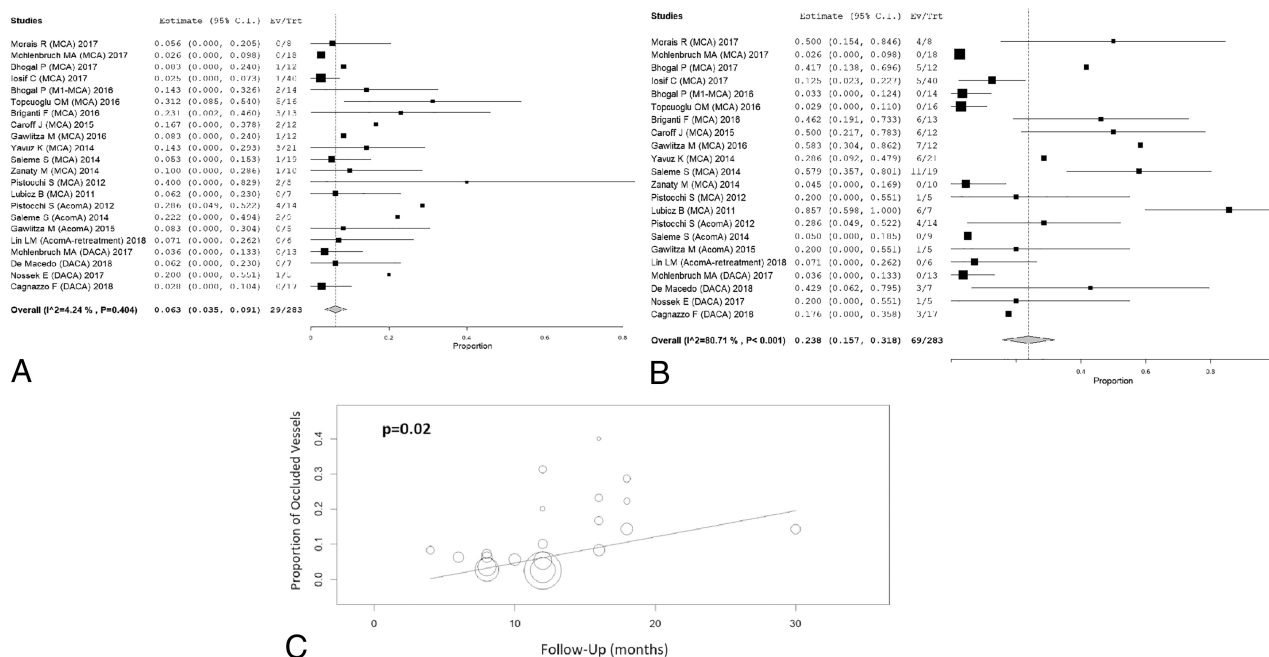
ON-LINE FIG 1. PRISMA diagram detailing the specifics of the systematic literature review.



ON-LINE FIG 2. Forest plot demonstrating the overall rate of aneurysm occlusion (A). The funnel plot (Egger linear regression) excludes publication bias (B). Sensitivity analysis shows that no individual study significantly influenced the reported outcome (C). Meta-regression shows a nonsignificant variation of the effect size (D).



ON-LINE FIG 3. Forest plot demonstrating the overall rate of treatment-related complications (A). The funnel plot (Egger linear regression) excludes publication bias (B). Sensitivity analysis shows that no individual study significantly influenced the reported outcome (C). Meta-regression shows a trend toward lower complications during the analyzed period (D).



ON-LINE FIG 4. Forest plot showing the rate of occlusion (A) and narrowing (B) of jailed arteries. Meta-regression demonstrates a significant association between jailed vessel occlusion and the length of the angiographic follow-up (C).