

On-line Table 1: Search syntax

PubMed Search Accessed on April 3, 2018 (246 Articles)	EMBASE Search Accessed on April 3, 2018 (128 Articles)	MEDLINE Search Accessed on April 3, 2018 (73 Articles)
(((flow-diverter (Title/Abstract) AND ruptured aneurysms (Title/Abstract)) OR (flow-diverter (Title/Abstract) AND ("subarachnoid haemorrhage" (All Fields) OR "subarachnoid hemorrhage" (MeSH Terms) OR ("subarachnoid" (All Fields) AND "hemorrhage" (All Fields)) OR "subarachnoid hemorrhage" (All Fields)))) OR (pipeline (Title/Abstract) AND ruptured aneurysms (Title/Abstract))) OR (flow diversion (Title/Abstract) AND ("rupture"(MeSH Terms) OR "rupture" (All Fields) OR "ruptured"(All Fields)) OR ("subarachnoid haemorrhage" (All Fields) OR "subarachnoid hemorrhage" (MeSH Terms) OR ("subarachnoid" (All Fields) AND "hemorrhage" (All Fields)) OR "subarachnoid hemorrhage" (All Fields))))	('flow diverter':ab,ti AND 'ruptured aneurysms':ab,ti) OR ('flow diverter':ab,ti AND 'subarachnoid hemorrhage':ab,ti) OR ('pipeline embolization device':ab,ti AND 'ruptured intracranial aneurysm':ab,ti) OR ('flow diversion':ab,ti AND ('ruptured intracranial aneurysm':ab,ti OR 'subarachnoid hemorrhage':ab,ti))	(flow diverter and ruptured aneurysms).ab. (flow diverter and subarachnoid hemorrhage).ab. (flow diversion and (ruptured aneurysms or subarachnoid hemorrhage)).ab. (pipeline and subarachnoid hemorrhage).ab.

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

Study Name	Design	No. of Patients Treated with FD in the Acute Phase	Type of AT Therapy (Loading Dose)	AT Maintenance Dose	Overall Complete/Near-Complete Occlusion	Overall Rate of Treatment-Related Complications	Aneurysm Rebleeding	Quality of Studies (NOS)
Kulcsár et al, 2010 ¹⁴	R	3	CP 75 mg + ASA 100 mg 3 days before treatment	CP 75 mg daily (3 mo) + ASA 100 mg daily	3/3	1/3	0/3	4
de Barros Faria et al, 2011 ¹²	R	12	CP 300 mg	CP 75 mg daily (3 mo) + ASA 100 mg daily (for life)	8/12	0/12	0/12	4
McAuliffe and Wenderoth, 2012 ¹⁹	P MC	11	CP 600 mg + ASA 300 mg (3 pts); CP 300 mg + ASA 300 mg (3 pts); CP 450 mg + ASA 150 mg (1 pt); long-term therapy with CP 75 mg + ASA 100 mg (1 pt); CP 75 mg + ASA 150 mg 5–7 days before treatment (3 pts)	CP 75 mg daily (6–12 mo) + ASA 325 mg daily (for life)	8/9	4/11	2/11 (within 72 hr) (fusiform 21 mm + saccular 34 mm)	7
Cruz et al, 2013 ¹¹	R MC	20	CP 600 mg + ASA 325 mg 24 hr before treatment	Dual AT for a minimum 6 mo	15/16	7/20	1/20 (within 24 hr) (saccular giant)	4
Chan et al, 2014 ¹⁰	R	8	CP 300 mg + ASA 325 mg	CP 75 mg daily (3 pts); ASA 80 mg daily + CP 75 mg daily (2 pts); CP 160 mg daily (3 pts)	8/8	1/8	0/8	4
Lin et al, 2015 ¹⁵	R MC	26	CP 600 mg + ASA 650 mg	CP 75 mg daily (3 mo) + ASA 325 mg daily (for life)	21/23	5/26	1 (within 24 hr) (saccular 3 mm)	4
Aydin et al, 2015 ⁷	R	11	CP 600 mg + ASA 650 mg	CP 75 mg daily (6 mo) + ASA 300 mg daily (6 mo, then ASA 100 mg for life)	10/10	1/11	0/11	4
Peschillo et al, 2016 ²²	R	3	CP 600 mg + ASA 500 mg	CP 75 mg daily + ASA 300 mg daily	3/3	3/3	0/3	3
Chalouhi et al, 2015 ⁹	P DB	20	CP 600 mg + ASA 650 mg (15 pts); tirofiban 0.10 mcg/kg/min (5 pts)	CP 75 mg daily + ASA 81 mg daily	12/15	1/20	0/20	4
Möhlenbruch et al, 2015 ²⁰	P	5	Tirofiban infusion	CP 75 mg daily + ASA 100 mg daily	5/5	2/5	0	7
Linfante et al, 2017 ¹⁶	R	10	Dual AT (not specified)	Dual AT (not specified)	9/9	0/10	0/10	4
Duman et al, 2017 ¹³	R	5	CP 600 mg 6 hr before treatment	CP 7 mg daily + ASA 300 mg daily for 1 yr	NA	1/5	0	3
Peschillo et al, 2017 ²³	R	4	CP 450 mg + ASA 500 mg (1 pt); no AT (1 pt); CP 7 mg + ASA 100 mg (2 pts)	CP 75 mg daily + ASA 100 mg daily (6–12 mo)	4/4	1/4	0	
Maus et al, 2018 ¹⁸	R	15	Tirofiban infusion	CP 75 mg daily + ASA 100 mg daily	8/8	3/15	1/15 (within 24 hr) (dissecting 8 mm)	4
Lozupone et al, 2018 ¹⁷	R	17	Abciximab 0.25 mg/kg followed by 12-hr infusion of 0.125 mg/kg/min of abciximab	ASA 100 mg daily (3 mo) + ticlopidine 250 mg × 2 daily (1 mo)	12/15	4/17	0/17	4
Cerejo et al, 2017 ⁸	R	8	CP 600 mg + ASA 650 mg	Dual AT for a minimum 6 mo	5/8	1/8	0/8	4
Yang et al, 2017 ²⁶	R	13	CP 600 mg + ASA 500 mg	Dual AT for a minimum 3 mo, then ASA for 1 yr	10/10	2/13	0/13	4
Ryan et al, 2017 ²⁴	R	13	CP 600 mg + ASA 650 mg	Dual AT	5/12	2/13	0/13	4
Volker et al, 2018 ²⁵	R	10	Tirofiban infusion	CP 75 mg + ASA 100 mg for at least 3 mo	8/10	1/10	0/10	4
Parthasarathy et al, 2018 ²¹	R	9	Prasugrel 50 mg + ASA 75 mg	Prasugrel 10 mg	8/9	2/9	0/9	4

Note:—R indicates retrospective study; P, prospective study; R MC, retrospective multicentric study; P MC, prospective multicentric study; P DB, prospectively maintained database; FD, flow diversion; pt, patient; AT, antiplatelet therapy; NOS, Newcastle Ottawa Scale; NA, not applicable.

On-line Table 3: Quality measure of included studies by the Newcastle-Ottawa Quality Assessment Scale: retrospective design (score 0–9)

Study Name	Selection				Comparability		Exposure			Total
	1	2	3	4	a	b	1	2	3	
Volker et al, 2018 ²⁵	*	*				*	*			4
Lin et al, 2015 ¹⁵	*	*				*	*			4
Kulcsár et al, 2010 ¹⁴	*	*				*	*			4
Cruz et al, 2013 ¹¹	*	*				*	*			4
de Barros Faria et al, 2011 ¹²	*	*				*	*			4
Chan et al, 2014 ¹⁰	*	*				*	*			4
Peschillo et al, 2016 ²²	*	*					*			3
Chalouhi et al, 2015 ⁹	*	*				*	*			4
Maus et al, 2018 ¹⁸	*	*				*	*			4
Lozupone et al, 2018 ¹⁷	*	*				*	*			4
Aydin et al, 2015 ⁷	*	*				*	*			4
Cerejo et al, 2017 ⁸	*	*				*	*			4
Yang et al, 2017 ²⁶	*	*				*	*			4
Yang et al, 2017 ²⁶	*	*				*	*			4
Duman et al, 2017 ¹³	*	*					*			3
Linfante et al, 2017 ¹⁶	*	*				*	*			4
Chalouhi et al, 2015 ⁹	*	*				*	*			4
Parthasarathy et al, 2018 ²¹	*	*				*	*			4

Note:—Asterisks indicate each point of the Newcastle-Ottawa Scale (score 0–9).

On-line Table 4: Quality measure of included studies by the Newcastle-Ottawa Quality Assessment Scale: prospective design/cohort (score 0–9)

Study Name	Selection				Comparability		Outcome			Total
	1	2	3	4	a	b	1	2	3	
McAuliffe and Wenderoth, 2012 ¹⁹	*		*	*		*	*	*	*	7
Möhlenbruch et al, 2015 ²⁰	*		*	*		*	*	*	*	7

Note:—Asterisks indicate each point of the Newcastle-Ottawa Scale (score 0–9).

On-line Table 5: Patient population and characteristics of acutely ruptured intracranial aneurysms treated with flow-diverter stents

Variables	Raw Numbers (%)	No. of Articles	95% CI
Population characteristics			
No. of patients	223	20	
Mean/median age (yr)	53.3/53 (5–80)	20	
Proportion of males	141/213 = 66%	18	59–72
Aneurysm characteristics and SAH grade			
Aneurysm morphology			
Saccular	42/223 = 18.8%	9	14–24
Dissecting/fusiform	77/223 = 34.5%	11	28–40
Blister	104/223 = 46.6%	13	40–53
Aneurysm location			
Anterior circulation	150/223 = 67%		60–73
Posterior circulation	73/223 = 33%	20	26–39
Mean aneurysm size (mm)	5.6 (median = 4, IQR = 2–7, range = 2–16)	20	
SAH grade (Hunt and Hess)			
1	24/82 = 29.3%	7	20–39
2	29/82 = 35.4%		25–46
3	14/82 = 17%		10–26
4	11/82 = 13.4%		7–22
5	4/82 = 4.8%		1.5–12
SAH grade (Fisher grade)			
1	9/88 = 10.2%	9	5.2–18
2	19/88 = 21.5%		14–31
3	21/88 = 23.8%		16–33
4	39/88 = 44.3%		34–54
SAH grade (WFNS grade)			
I	44/104 = 42.3%	9	33–51
II	21/104 = 20%		13–28
III	11/104 = 10.6%		6–18
IV	15/104 = 14.4%		8.8–22
V	13/104 = 12.5%		7–20
Treatment characteristics			
Mean/median time between SAH and FD	6.7/4 (days) IQR = 3–9.6	15	
Type of FD device/total of FDs used			
PED	236/274 = 86%	20	81–89
Silk	29/274 = 10.6%		7.5–14
FRED	8/274 = 3%		1.4–5
Surpass	1/274 = 0.4%		0.1–2.2
No. of patients treated with multiple FDs	47/187 = 25%	18	19–31
No. of patients treated with FD + coiling	40/211 = 19%	19	14–25
Radiologic follow-up (mo)	Mean = 9.6, range = 2–30 Median = 7.5, IQR = 6–12	19	
Clinical follow-up (mo)	Mean = 9.2, range = 3–24 Median = 8.7, IQR = 6–12	19	

Note:—WFNS indicates World Federation of Neurosurgical Societies; FD, flow diversion; PED, Pipeline Embolization Device.

On-line Table 6: Treatment-related outcomes after flow diversion of acutely ruptured intracranial aneurysms

Variables	Results of Meta-Analysis	No. of Articles	Statistic (95% CI) (I^2)
Angiographic outcomes			
Long-term aneurysm occlusion rate	162/189 = 88.9%	19	(84.2–93.5) (I^2 = 20.9%)
Saccular	20/25 = 79%	7	(64–93) (I^2 = 0%)
Dissecting/fusiform	51/58 = 89%	10	(82–96) (I^2 = 0%)
Blister	76/89 = 88%	13	(81–95) (I^2 = 26%)
Immediate aneurysm occlusion rate	29/86 = 32%	13	(15.4–48) (I^2 = 79.6%)
Saccular	2/7 = 28%	3	(3–50) (I^2 = 0%)
Dissecting/fusiform	10/25 = 45%	3	(18–91) (I^2 = 90%)
Blister	17/54 = 35%	7	(14–56) (I^2 = 77%)
Treatment-related complications and clinical outcomes			
Overall treatment-related complications	42/223 = 17.8%	20	(11–24) (I^2 = 52.6%)
Saccular	7/31 = 23%	8	(11–49) (I^2 = 43%)
Dissecting/fusiform	11/69 = 13%	10	(5–20) (I^2 = 9%)
Blister	16/97 = 18%	13	(8–27) (I^2 = 50%)
Periprocedural/early complications (within 30 days)	37/223 = 16%	20	(10–22) (I^2 = 47%)
Delayed complications (after 30 days)	5/223 = 3%	20	(0.9–6) (I^2 = 37.7%)
Transient complications	28/223 = 9%	20	(4–11) (I^2 = 0%)
Permanent complications	16/223 = 7%	20	(4–11) (I^2 = 0%)
Treatment-related mortality	6/223 = 4.5%	20	(2–7) (I^2 = 0%)
Overall rate of good neurologic outcome	169/210 = 83%	20	(76–89) (I^2 = 0%)
Type of complications			
Thromboembolic complications	26/223 = 8%	20	(4.4–11) (I^2 = 22%)
Saccular	4/31 = 9.9%	8	(0.5–19) (I^2 = 0%)
Dissecting/fusiform	6/69 = 8.3%	10	(2–14) (I^2 = 0%)
Blister	12/97 = 10.2%	13	(4.5–16) (I^2 = 0%)
Hemorrhagic complications	16/223 = 7%	20	(3.5–10) (I^2 = 0%)
Saccular	3/31 = 12%	8	(2–22) (I^2 = 0%)
Dissecting/fusiform	5/69 = 7.5%	10	(2–13) (I^2 = 0%)
Blister	3/84 = 6%	13	(12–10) (I^2 = 0%)
Acute in-stent thrombosis	6/223 = 4%	20	(1.6–6) (I^2 = 0%)
Rebleeding rate after treatment ^a	5/223 = 4%	20	(1.8–7) (I^2 = 0%)
Rebleeding among anterior circulation	4/150 = 4.6%	17	(1.3–7.4) (I^2 = 0%)
Rebleeding among posterior circulation	1/73 = 3%	13	(1.7–12) (I^2 = 0%)

^a Rebleeding occurred among 1 fusiform (21 mm) aneurysm, 2 saccular giant aneurysms, 1 small (3 mm) aneurysm, and 1 medium-sized (8 mm) aneurysm.

On-line Table 7: Factors related to aneurysm occlusion and treatment-related complications after flow diversion of ruptured intracranial aneurysms^a

Variables	Complete/Near-Complete Occlusion	No. of Articles	P Value	Treatment-Related Complications	No. of Articles	P Value
Aneurysm-related factors						
Anterior circulation	102/123 = 83% (75–91) (I ² = 53%)	18		18/149 = 11.7% (7–16) (I ² = 0%)	20	
Vs			.27			.004 ^b
Posterior circulation	57/63 = 89% (82–96) (I ² = 0%)	13		16/72 = 27% (14–40) (I ² = 66%)	13	
Proximal location	120/136 = 89% (84–94) (I ² = 0%)	19		29/149 = 14.8% (8–21) (I ² = 43%)	14	
Vs			.28			.88
Distal location	41/48 = 83% (74–93) (I ² = 0%)	10		9/56 = 14% (5–23) (I ² = 12%)	10	
Small, medium-sized saccular aneurysms	25/31 = 83% (66–98) (I ² = 34%)	5		7/38 = 18% (5–30) (I ² = 0%)	6	
Vs			.6			.9
Large-giant saccular aneurysms	21/24 = 88% (77–95) (I ² = 0%)	4		7/32 = 19% (6–32) (I ² = 0%)	5	
Patient-related factors						
Younger than 60 yr	105/120 = 90% (85–95) (I ² = 0%)	17		29/142 = 19% (11–18) (I ² = 50%)	18	
Vs			.01 ^b			.1
Older than 60 yr	43/52 = 76% (64–88) (I ² = 49%)	17		10/53 = 19% (10–27) (I ² = 0%)	17	
Low SAH grade	70/80 = 89% (82–95) (I ² = 0%)	13		17/91 = 16% (9–23) (I ² = 0%)	14	
Vs			.2			.5
High SAH grade	62/76 = 83% (74–91) (I ² = 25%)	14		10/53 = 12% (10–27) (I ² = 0%)	15	
Treatment-related factors						
Flow-diverter alone	104/113 = 90% (88–96) (I ² = 0%)	14		24/127 = 19% (10–28) (I ² = 52%)	16	
Vs			.12			.3
Flow-diverter plus coiling	19/25 = 81% (64–93) (I ² = 0%)	6		17/103 = 14% (7–19) (I ² = 0%)	16	
Single flow diverter	107/127 = 86% (79–93) (I ² = 36%)	16		20/141 = 10% (5–15) (I ² = 0%)	16	
Vs			.61			.004 ^b
Multiple flow diverters	42/50 = 83% (74–91) (I ² = 0%)	14		14/52 = 26% (14–45) (I ² = 59%)	12	

^a Data in parentheses are I² and confidence interval.

^b Significant.

On-line Table 8: Relationship between timing of flow diversion (within 72 hr vs later than 72 hr) and treatment-related outcomes^a

Angiographic and Clinical Outcomes	FD Within 72 Hr	No. of Articles	FD Between 72 Hr and 30 Days	No. of Articles	P Value
Overall complete/near-complete aneurysm occlusion	50/61 = 85% (7–93) (I ² = 0%)	14	64/70 = 89% (8–9.5) (I ² = 0%)	14	.49
Overall complication rate	16/81 = 18.6% (10–26) (I ² = 0%)	15	15/79 = 16% (8–23) (I ² = 0%)	14	.66
Ischemic complications	8/81 = 10% (4–16) (I ² = 0%)	15	12/79 = 14% (7–21) (I ² = 0%)	14	.43
Hemorrhagic complications	8/81 = 10% (5–18) (I ² = 0%)	15	3/79 = 4% (2–13) (I ² = 0%)	14	.13
Aneurysm rebleeding after treatment	3/81 = 4% (2–10) (I ² = 0%)	15	1/79 = 1.2% (0.8–5) (I ² = 0%)	14	.26

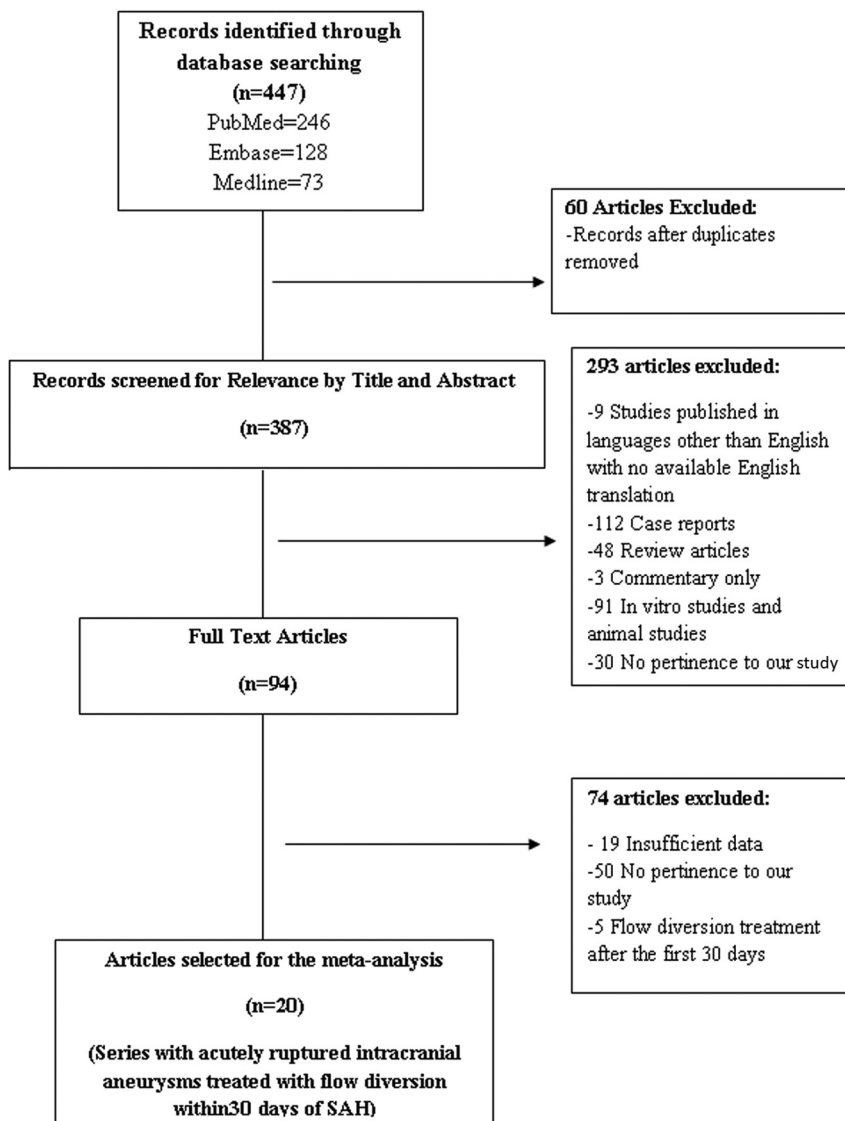
Note:—FD indicates flow diversion.

^a Data in parentheses are I² and confidence interval.

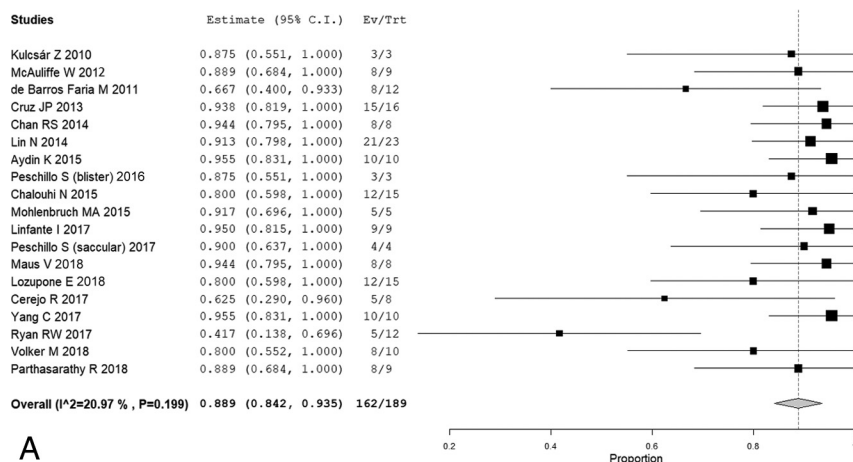
On-line Table 9: Association between antiplatelet therapy and treatment-related outcomes after flow diversion of ruptured intracranial aneurysms

Type of AT (Loading Dose/Maintenance Dose)	Complete/Near-Complete Occlusion (95% CI)	Treatment-Related Complications (95% CI)	Aneurysm Rebleeding (95% CI)	No. of Articles
L = CP 300–600 mg + ASA 300–650 mg	84/99 = 85%	25/128 = 19.5%	4/128 = 3%	13
M = CP 75 mg + ASA 80–300 mg daily	(76–90)	(13–27)	(0.9–8)	
L = tirofiban (infusion)	21/23 = 91%	6/35 = 17%	1/35 = 2.8%	4
M = CP 75 mg + ASA 80–100 mg daily	(72–98)	(7–33)	(0.1–15)	
L = prasugrel 50 mg + ASA 75 mg	8/9 = 89%	2/9 = 22%	0/9	1
M = prasugrel 10 mg daily	(54–95)	(6–55)		
L = abciximab 0.25 mg/kg followed by infusion of 0.125 μ g/kg/min (12 hr)	12/15 = 80%	4/17 = 23%	0/17	1
M = ASA 100 mg daily + ticlopidine 250 mg $\times$ 2 daily	(54–93)	(9–47)		

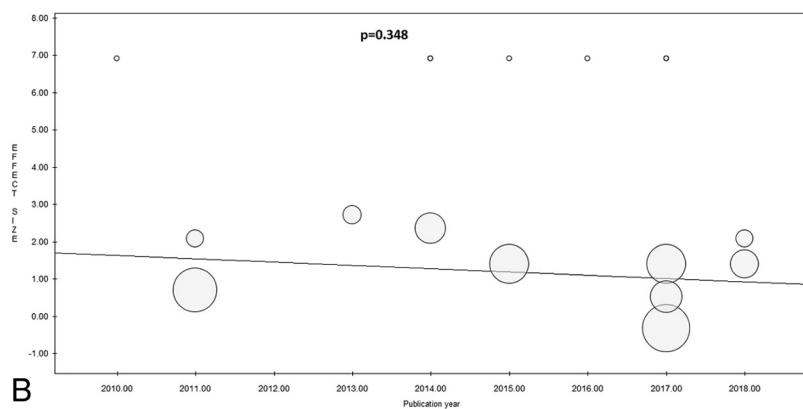
Note:—M indicates maintaining; L, loading; AT, antiplatelet therapy.



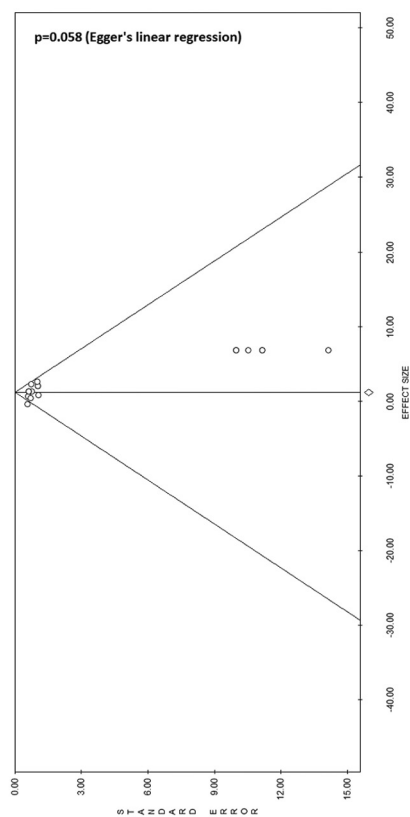
ON-LINE FIG 1. PRISMA diagram detailing the specifics of the systematic literature review and meta-analysis.



A

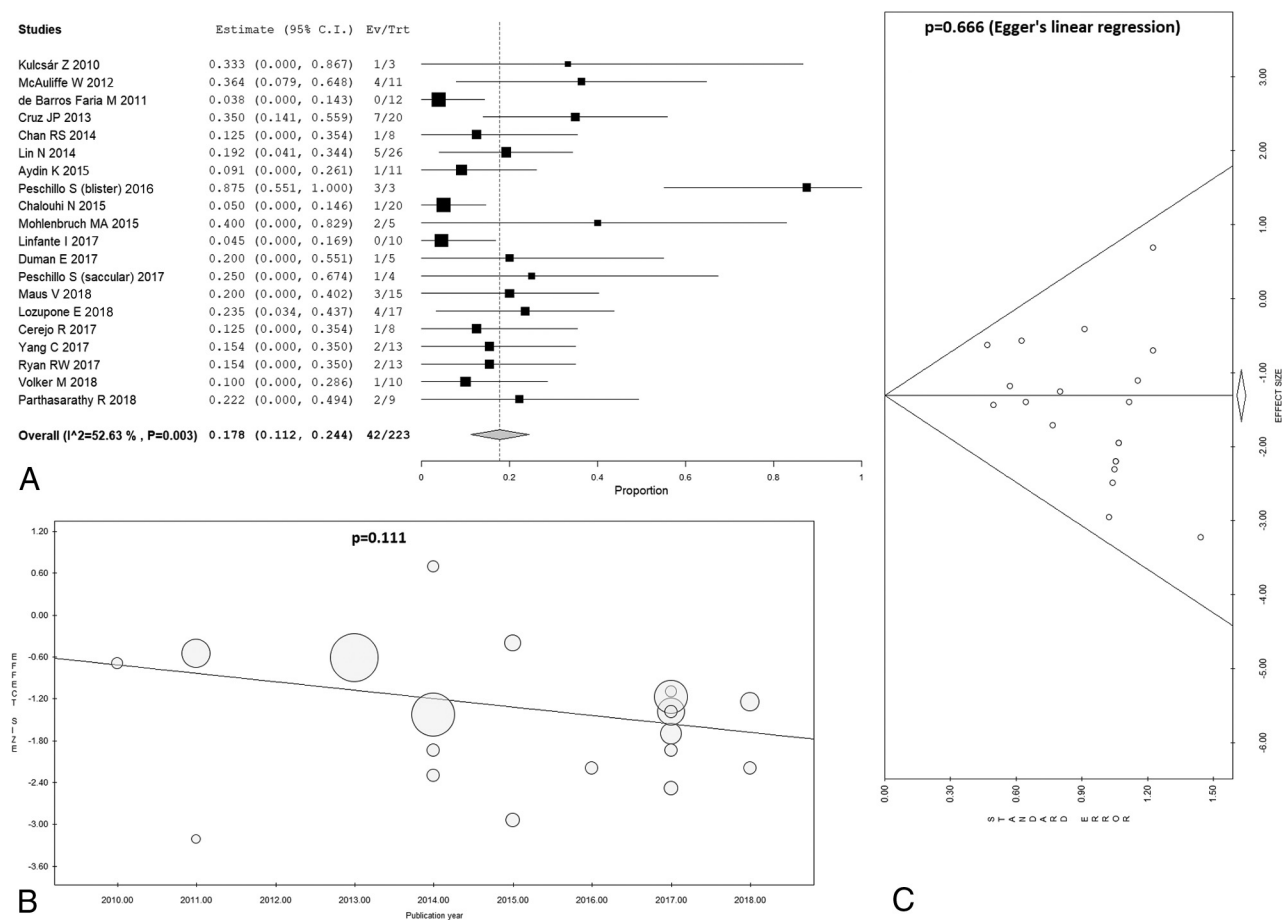


B



C

ON-LINE FIG 2. Forest plot demonstrates the overall rate of occlusion of ruptured aneurysms after flow diversion (A). Meta-regression shows a nonsignificant variation of the effect size during the analyzed period (B). The funnel plot followed by the Egger linear regression test excludes publication bias (C).



ON-LINE FIG 3. Forest plot demonstrates the overall rate of treatment-related complications after flow diversion of ruptured aneurysms (A). Meta-regression shows a nonsignificant variation of the effect size during the analyzed period (B). The funnel plot followed by the Egger linear regression test excludes publication bias (C).