On-line Table 1: Search syntax

PubMed Search Accessed on October 20, 2018 (24 Studies)	EMBASE Search Accessed on October 20, 2018 (37 Studies)
((Prasugrel(Title/Abstract) AND intracranial aneurysms(Title/Abstract)) OR (Prasugrel(Title/Abstract) AND endovascular(Title/Abstract))) OR ((prasugrel(Title/Abstract) AND clopidogrel(Title/Abstract)) AND aneurysms(Title/Abstract))	'prasugrel':ti,ab,kw AND 'intracranial aneurysm':ti,ab,kw OR ('prasugrel':ti,ab,kw AND 'endovascular':ti,ab,kw) OR ('prasugrel':ti,ab,kw AND 'clopidogrel':ti,ab,kw AND 'aneurysms':ti,ab,kw)

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

Study Name	Design	No. Pts/No. of Aneurysms (PS Group)	No. Pts/No. of Aneurysms (CP Group)	PS Loading Dose	CP Loading Dose	PS Maintenance Dose	CP Maintenance Dose	Overall Complications (PS Group)	Overall Complications (CP Group)	Quality of Studies (NOS)
Akbari et al, 2013[7]	R	31/31	55/55	PS 60 mg 1 day before + ASA 325 mg	CP 75 mg + ASA 325 mg 7 days before	PS 10 mg/day	CP 75 mg/day + ASA 325 mg/day	7/31 (6 ICH +1 thromboembolism)	2/55 (2 ICHs)	6
Stetler et al, 2013[12]	R	16/16	NA	PS 40 mg 1 day before	NA	PS 5–10 mg /day	NA	1/16 (Retroperitoneal hematoma)	NA	3
Ha et al, 2016[14]	R	98/116	96/106	PS 20 mg 1 day before + PS 5 mg the morning of the procedure	CP 300 mg 1 day before + CP 75 mg the morning of the procedure	PS 5 mg/day for 3 mo, after ASA lifelong	CP 75 mg/day + ASA 100 mg/day for at least 3 mo	1/116 (Aneurysm perforation)	1/106 (Aneurysm perforation)	6
Kim et al, 2017[9]	P	118/118	183/183	PS 30 mg 1 day before	CP 75 mg, CP + ASA 100 mg 5 days before	PS 5–10 mg/day	CP 75 mg/day + ASA 100 mg/day for at least 3 mo	7/118 (2 Thrombo-embolisms +5 ICHs)	24/183 (16 Thrombo-embolisms +8 ICHs)	8
Sedat et al, 2017[10]	R	100/100	100/100	PS 60 mg 1 day before	CP 75 mg + ASA 75 mg 7 days before	PS 10 mg/day for 6 mo	CP 75 mg/day + ASA 75 mg/day for at least 6 mo	18/100 (1 Aneurysm perforation +3 ICHs + 2 groin hematomas + 12 thrombo-embolisms)	21/100 (1 Aneurysm perforation +1 ICH + 2 groin hematomas + 17 thrombo-embolisms)	6
Lee et al, 2018[13]	R	24/24	NA	PS 20 mg 1 day before	NA	PS 5 mg/day	NA	0/24	NA	3
Cho et al, 2018[8]	R	225/277	186/228	PS 20 mg 1 day before	CP 300 mg 1 day before	PS 5 mg/day for 3 mo, after ASA lifelong	CP 75 mg/day + ASA 100 mg/day (or triple AT) for at least 3 mo, after ASA lifelong	2/277 (1 Thrombo-embolism +1 ICH)	10/228 (7 Thrombo-embolisms +3 ICHs)	6

Note:—NOS indicates the Newcastle-Ottawa Quality Assessment Scale; R, retrospective study; P, prospective study; Pts, patients; ICH, intracerebral hemorrhage; NA, not available.

On-line Table 3: Quality measure of included retrospective studies by the Newcastle-Ottawa Quality Assessment Scale[a]

	Selection				Comparability		Exposure			
Study Name	1	2	3	4	a	b	1	2	3	Total
Akbari et al, 2013[7]	*	*		*	*		*	*		6
Stetler et al, 2013[12]	*	*					*			3
Ha et al, 2016[14]	*	*		*	*		*	*		6
Sedat et al, 2017[10]	*	*		*	*		*	*		6
Lee et al, 2018[13]	*	*					*			3
Cho et al, 2018[8]	*	*		*	*		*	*		6

[a] Score 0–9. "High-quality" indicates studies with ≥6 asterisks. Each asterisk indicates 1 point of the scale. a) Comparability (point A) was tested comparing treatment-related outcomes among the prasugrel and clopidogrel groups. b) Comparability (point B) was tested comparing the secondary outcomes (type of complications, aneurysm occlusion, platelet inhibition value) among patients treated with prasugrel vs clopidogrel.

On-line Table 4: Quality measure of included prospective study by the Newcastle-Ottawa Quality Assessment Scale[a]

	Selection				Comparability		Outcome			
Study Name	1	2	3	4	a	b	1	2	3	Total
Kim et al, 2017[9]	*	*	*	*	*		*	*	*	8

[a] Score 0–9. "High-quality" indicates studies with ≥6 asterisks. Each asterisk indicates 1 point of the scale. a) Comparability (point A) was tested comparing treatment-related outcomes among the prasugrel and clopidogrel groups. b) Comparability (point B) was tested comparing the secondary outcomes (type of complications, aneurysm occlusion, platelet inhibition value) among patients treated with prasugrel vs clopidogrel.

On-line Table 5: Characteristics of patients with intracranial aneurysms treated endovascularly: comparison between antiplatelet therapy with prasugrel and clopidogrel

Variables	Patients under Prasugrel (95% CI)	Patients under Clopidogrel (95% CI)	*P* Value
Total No. of studies	*7*	*5*	
No. of patients	612	620	
No. of aneurysms/procedures	682	672	
Mean age (range) (yr)	57, 20–70	56, 19–73	.3
Men/overall population	342/612 = 56% (51–59)	283/620 = 45.6% (41–49)	.001[a]
Aneurysm location			
Anterior circulation	557/641 = 87% (84–89)	456/571 = 82% (78–85)	.01[a]
Posterior circulation	84/641 = 13% (10–15)	99/571 = 18% (14–21)	.01[a]
Mean aneurysm size (mm)	7 (3–21)	8 (3–23)	.2
Type of treatment			
Coiling/BAC	245/672 = 36.4% (32–40)	259/571 = 45.3% (41–49)	.002[a]
SAC/FD	427/672 = 63.6% (58–67)	312/571 = 54.7% (50–58)	.001[a]
Radiologic follow-up (mo)			
Median	12	12	
IQR	(12–24)	(12–22)	
Mean	14	13	
Clinical follow-up (mo)			
Median	14	14	
IQR	(11–23)	(13–24)	
Mean	15	14	

Note:—BAC indicates balloon-assisted coiling; SAC, stent-assisted coiling; FD, flow diverter; IQR, interquartile range.
[a] Significant.

On-line Table 6: Hemorrhagic complication rate after low-dose and high-dose prasugrel

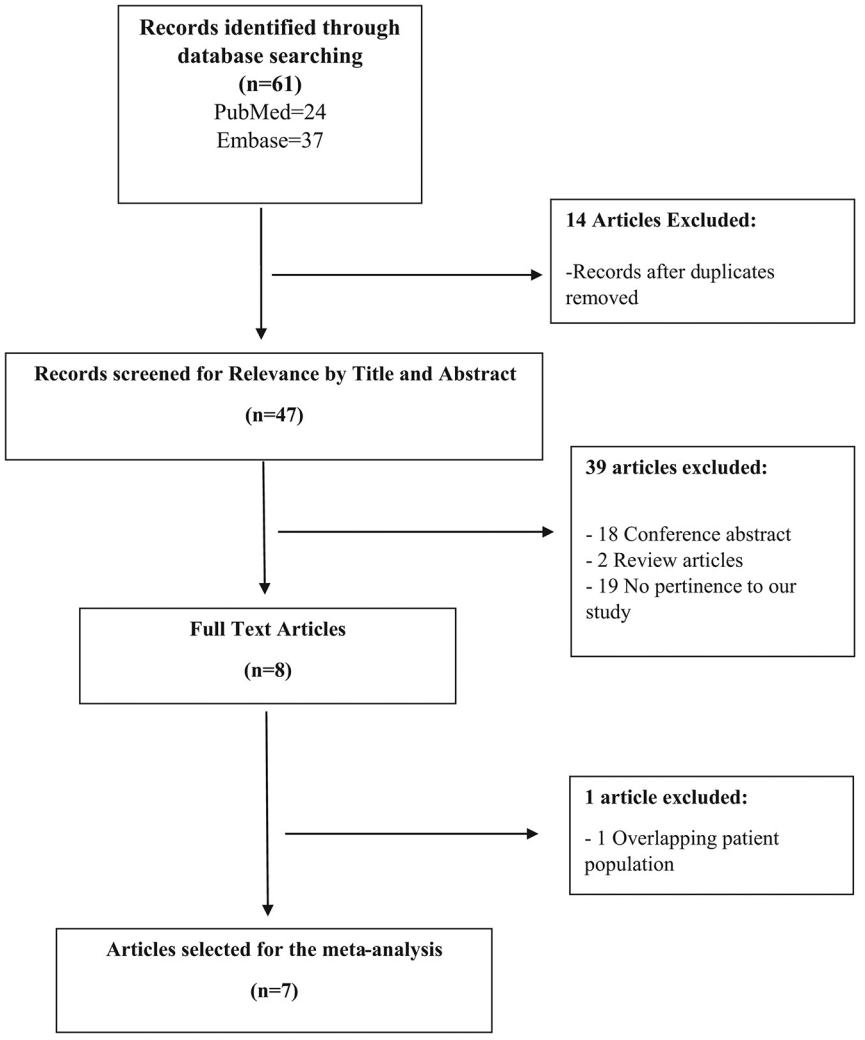
Periprocedural Outcomes Related to the Dose of PS[a]	PS 20 mg 1 Day before Treatment (Low-Dose)	PS 40–60 mg 1 Day before Treatment (High-Dose)[b]	*P* Value
Intraprocedural/very early hemorrhagic complications (95% CI) (I^2)	5/535 = 0.6% (0.1–1.6) (I^2 = 0%) (4 articles)	13/147 = 9.3% (0.2–18) (I^2 = 60%) (3 articles)	.001[c]
Delayed outcomes related to the dose of PS[a]	**PS 5 mg/day after treatment (low-dose)**	**PS 10 mg/day after treatment (high-dose)**	***P* Value**
Delayed hemorrhagic complications (95% CI) (I^2)	0/433 = 0% (4 articles)	2/249 = 0.9%[d] (0.3–2) (I^2 = 0%) (3 articles)	.001[c]

[a] Complication rates were pooled using meta-analysis of proportion.
[b] In 1 study, patients were treated with ASA, 325 mg, + PS, 60 mg, 1 day before treatment.
[c] Significant.
[d] Two cases of groin hematoma.

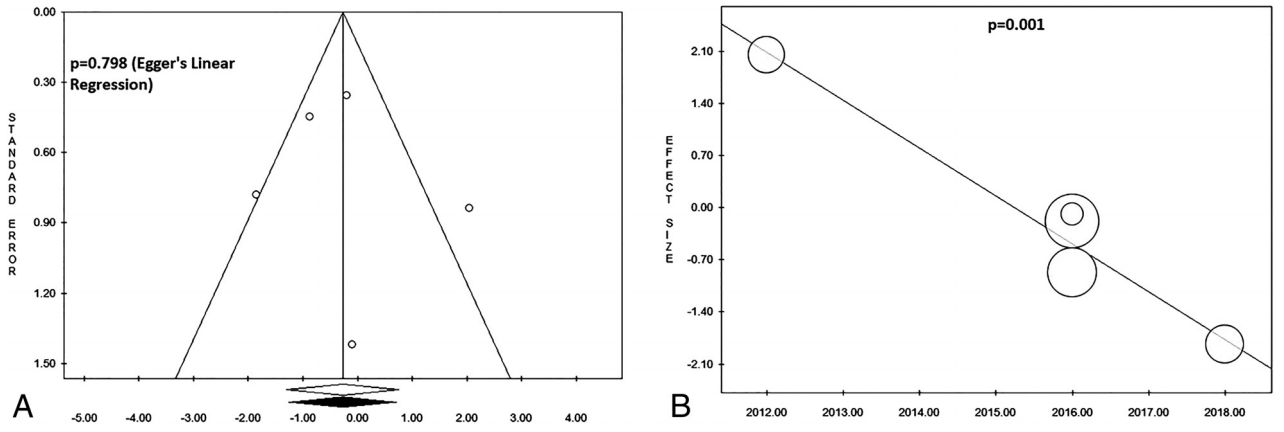
On-line Table 7: Relationship between type of treatment and complication rates among prasugrel and clopidogrel groups

	PS			CP		
Outcomes[a]	Overall Complications	Ischemic Complications	Hemorrhagic Complications	Overall Complications	Ischemic Complications	Hemorrhagic Complications
FD + SAC	25/254 = 7% (2–13) (I^2 = 70%) (5 articles)	16/254 = 4.5% (1–9) (I^2 = 60%) (5 articles)	9/254 = 2.5% (0.5–4) (I^2 = 0%) (5 articles)	28/265 = 10% (3–20) (I^2 = 90%) (3 articles)	23/265 = 7% (2–14) (I^2 = 88%) (3 articles)	5/265 = 2% (1–4) (I^2 = 40%) (3 articles)
BAC/coiling	3/281 = 1.1% (0.5–13) (I^2 = 0%) (4 articles)	2/281 = 0.6% (0.1–12) (I^2 = 0%) (4 articles)	2/281 = 0.6% (0.1–12) (I^2 = 0%) (4 articles)	5/247 = 2% (0.1–4) (I^2 = 0%) (2 articles)	4/247 = 1.5% (0.01–3) (I^2 = 0%) (2 articles)	1/247 = 0.5% (0.01–2) (I^2 = 0%) (2 articles)

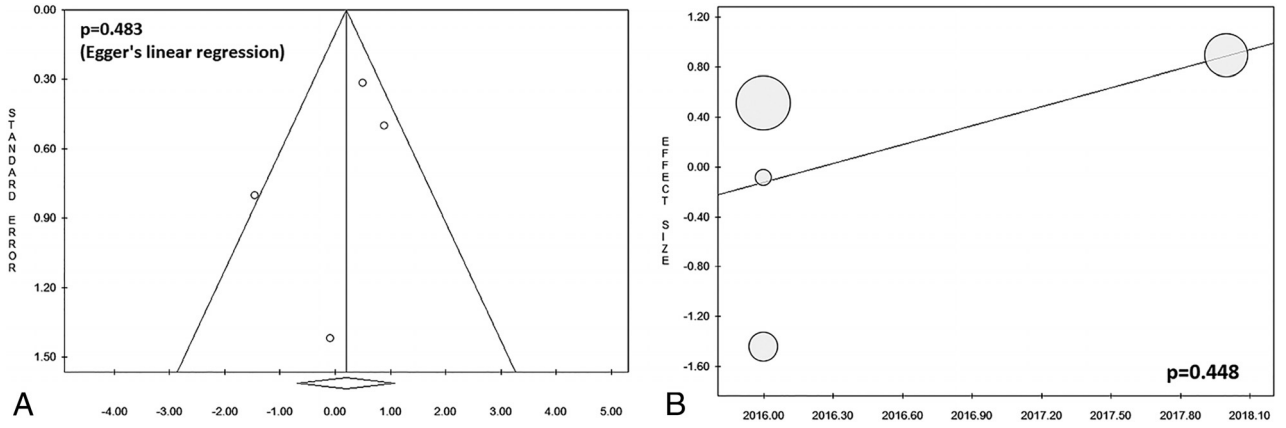
Note:—BAC indicates balloon-assisted coiling; SAC, stent-assisted coiling; FD, flow diverter.
[a] Complication rates were pooled using meta-analysis of proportion.



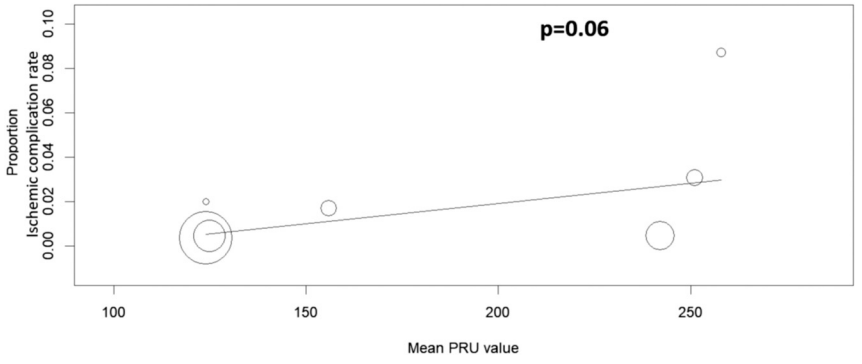
ON-LINE FIG 1. PRISMA diagram detailing the specifics of the systematic literature review.



ON-LINE FIG 2. Overall effect of prasugrel versus clopidogrel on the treatment-related complication rate. The funnel plot followed by the Egger linear regression test excludes publication bias (*A*). Meta-regression shows a significant variation of the effect size (*B*) during the investigated years.



ON-LINE FIG 3. When we excluded the study of Akbari et al[7] from the sensitivity analysis, the funnel plot followed by the Egger linear regression test excludes publication bias (*A*) and the meta-regression shows a nonsignificant variation of the effect size (*B*).



ON-LINE FIG 4. Meta-regression showing a significant decrease of the ischemic complication rate in relation to the mean PRU value.