Perioperative Antiplatelet Therapy In Patients With Drug-Eluting Stent Undergoing Noncardiac SURgEry

ASSURE-DES Randomized Trial

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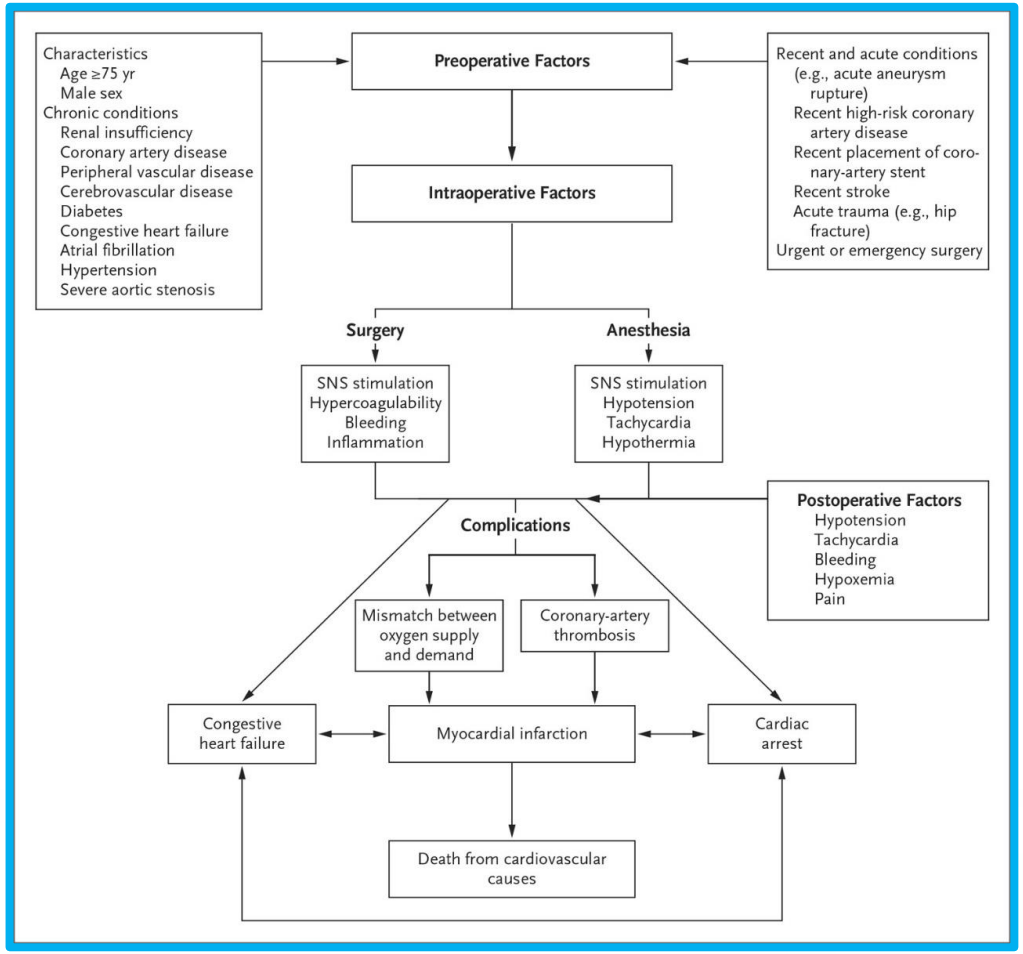
Preoperative, Intraoperative, and Postoperative Factors Associated with Perioperative Cardiac Complications in Patients Undergoing Major Noncardiac Surgery



N Engl J Med 2015;373:2258-69

Non-Cardiac Surgery and Cardiac Events

Catheterization and Cardiovascular Interventions 65:516–519 (2005)

Late Thrombosis of Sirolimus-Eluting Stents Following Noncardiac Surgery

Mithal Nasser, MD, Michael Kapeliovich, MD, and Walter Markiewicz,* MD, FACC

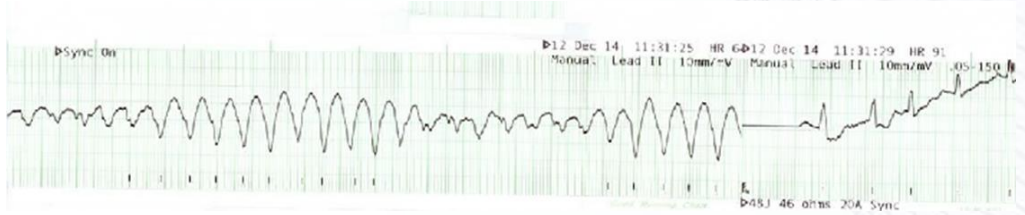
We describe two patients with in-stent thrombosis occurring 4 and 21 months after implantation of sirolimus-eluting stents. Both cases occurred following noncardiac surgery. In both cases, aspirin had been stopped prior to surgery. Both patient sustained a severe myocardial infarction; one died. The occurrence of late thrombosis of sirolimus-eluting stents is of concern.

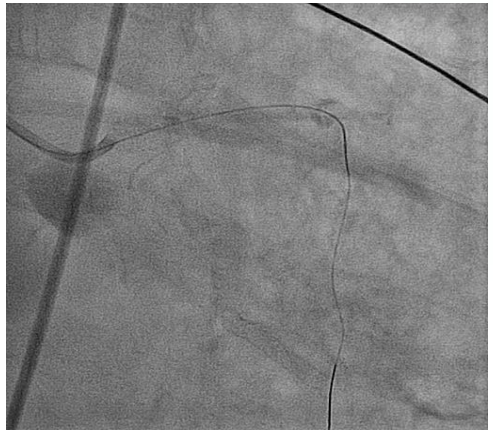
Key words: acute thrombosis; stent; drug-eluting stent; percutaneous coronary intervention; complication; myocardial infarction

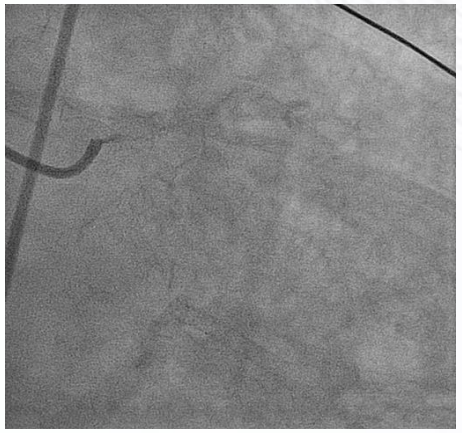
INTRODUCTION

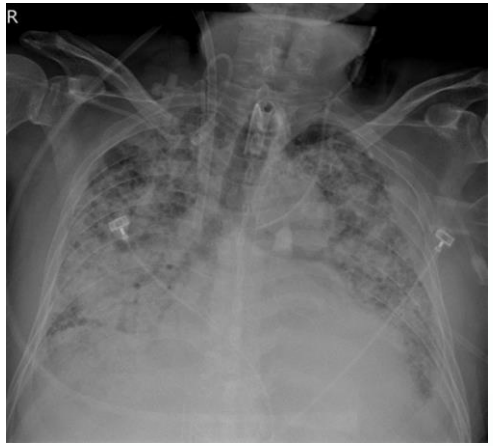
Stent thrombosis is a feared complication of percutaneous coronary interventions [1,2]. Overall incidence following bare stent implantation is < 1–2% when

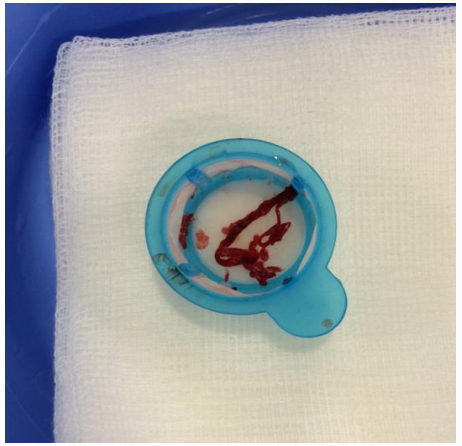
underwent an excision biopsy of an enlarged right supraclavicular node under general anesthesia. The procedure lasted ~ 40 min and was uneventful. Aspirin had been stopped 10 days earlier. Two hours following the procedure, the patient complained of





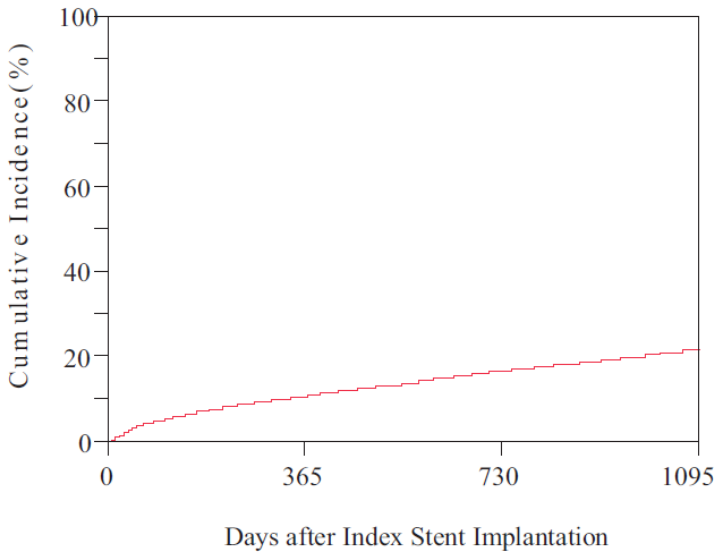






How Many Patients with DES Need Non-Cardiac Surgery ?

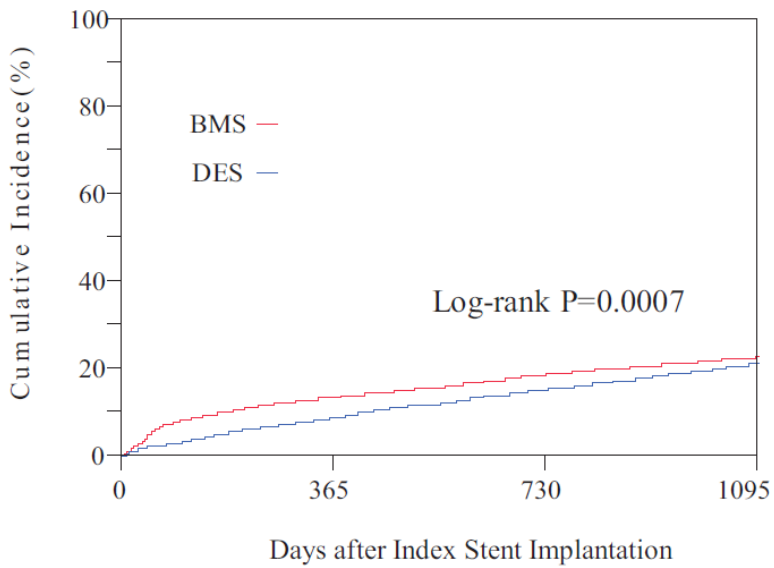
A



	Baseline	42 Days	1 Year	2 Years	3 Years
Incidence		3.0%	11%	17%	22%
Number of events		355	1253	1878	2218
				7317	3673

10% at 1 Year
20% at 3 Year

B



	Baseline	42 Days	1 year	2 years	3 years
BMS					
Incidence		4.4%	13%	19%	23%
Number of events		227	682	914	1034
Number of patients at risk	5405	4933	4205	3105	1666
DES					
Incidence		1.9%	9%	15%	21%
Number of events		128	575	914	1034
Number of patients at risk	6802	6550	5845	4212	2007

Circ Cardiovasc Interv. 2012;5:237-246

2016 ACC/AHA Focused Update

COR	LOE	Recommendations
I		Elective noncardiac surgery should be delayed 30 days after BMS implantation and optimally 6 months after DES implantation (101-103,143-146).
I	C-EO	In patients treated with DAPT after coronary stent implantation who must undergo surgical procedures that mandate the discontinuation of $P2Y_{12}$ inhibitor therapy, it is recommended that aspirin be continued if possible and the $P2Y_{12}$ platelet receptor inhibitor be restarted as soon as possible after surgery.
IIa	C-EO	When noncardiac surgery is required in patients currently taking a $P2Y_{12}$ inhibitor, a consensus decision among treating clinicians as to the relative risks of surgery and discontinuation or continuation of antiplatelet therapy can be useful.
IIb	C-EO	Elective noncardiac surgery after DES implantation in patients for whom $P2Y_{12}$ inhibitor therapy will need to be discontinued may be considered after 3 months if the risk of further delay of surgery is greater than the expected risks of stent thrombosis.
III: Harm	B-NR	Elective noncardiac surgery should not be performed within 30 days after BMS implantation or within 3 months after DES implantation in patients in whom DAPT will need to be discontinued perioperatively (101-103,143-146).

2014 ESC/ESA Guidelines

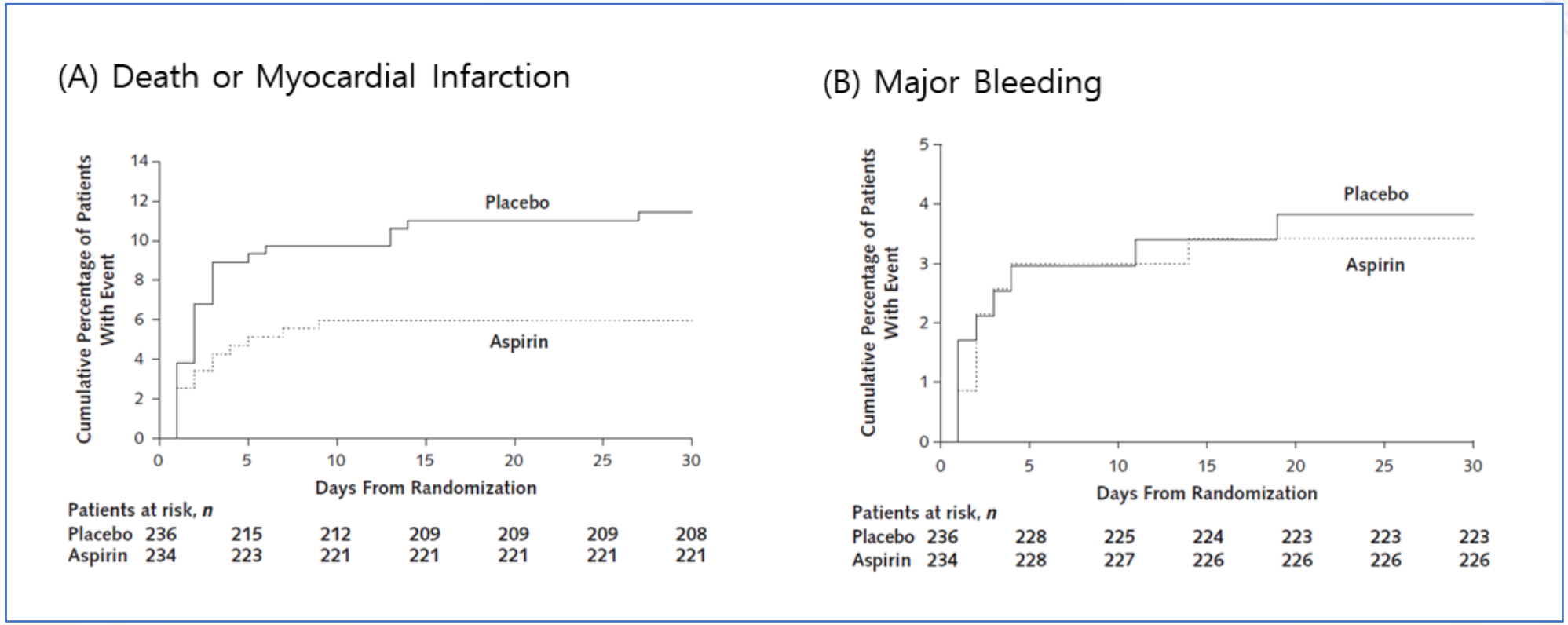
Independently of the timeframe between DES implantation and surgery, single anti-platelet therapy (preferably with aspirin) should be continued.

2022 ESC Guidelines

Recommendations	Class[a]	Level[b]
It is recommended to delay elective NCS until 6 months after elective PCI and 12 months after an ACS.[264,271]	I	A
After elective PCI, it is recommended to delay time-sensitive NCS until a minimum of 1 month of DAPT treatment has been given.[266,271,288,289]	I	B
In patients with a recent PCI scheduled for NCS, it is recommended that management of antiplatelet therapy is discussed between the surgeon, anaesthesiologist, and cardiologist.	I	C
In high-risk patients with a recent PCI (e.g. STEMI patients or high-risk NSTE-ACS patients), a DAPT duration of at least 3 months should be considered before time-sensitive NCS.	IIa	C
Continuation of medication		
In patients with a previous PCI, it is recommended to continue aspirin peri-operatively if the bleeding risk allows.[244]	I	B

Recommended time interval for drug interruption before NCS		
If interruption of $P2Y_{12}$ inhibitor is indicated, it is recommended to withhold ticagrelor for 3–5 days, clopidogrel for 5 days, and prasugrel for 7 days prior to NCS.[262–264]	I	B
For patients undergoing high bleeding risk surgery (e.g. intracranial, spinal neurosurgery, or vitreoretinal eye surgery), it is recommended to interrupt aspirin for at least 7 days pre-operatively.	I	C
In patients without a history of PCI, interruption of aspirin at least 3 days before NCS may be considered if the bleeding risk outweighs the ischaemic risk, to reduce the risk of bleeding.[243]	IIb	B
Resumption of medication		
If antiplatelet therapy has been interrupted before a surgical procedure, it is recommended to restart therapy as soon as possible (within 48 h) post-surgery, according to interdisciplinary risk assessment.	I	C

Subgroup: POISE-2

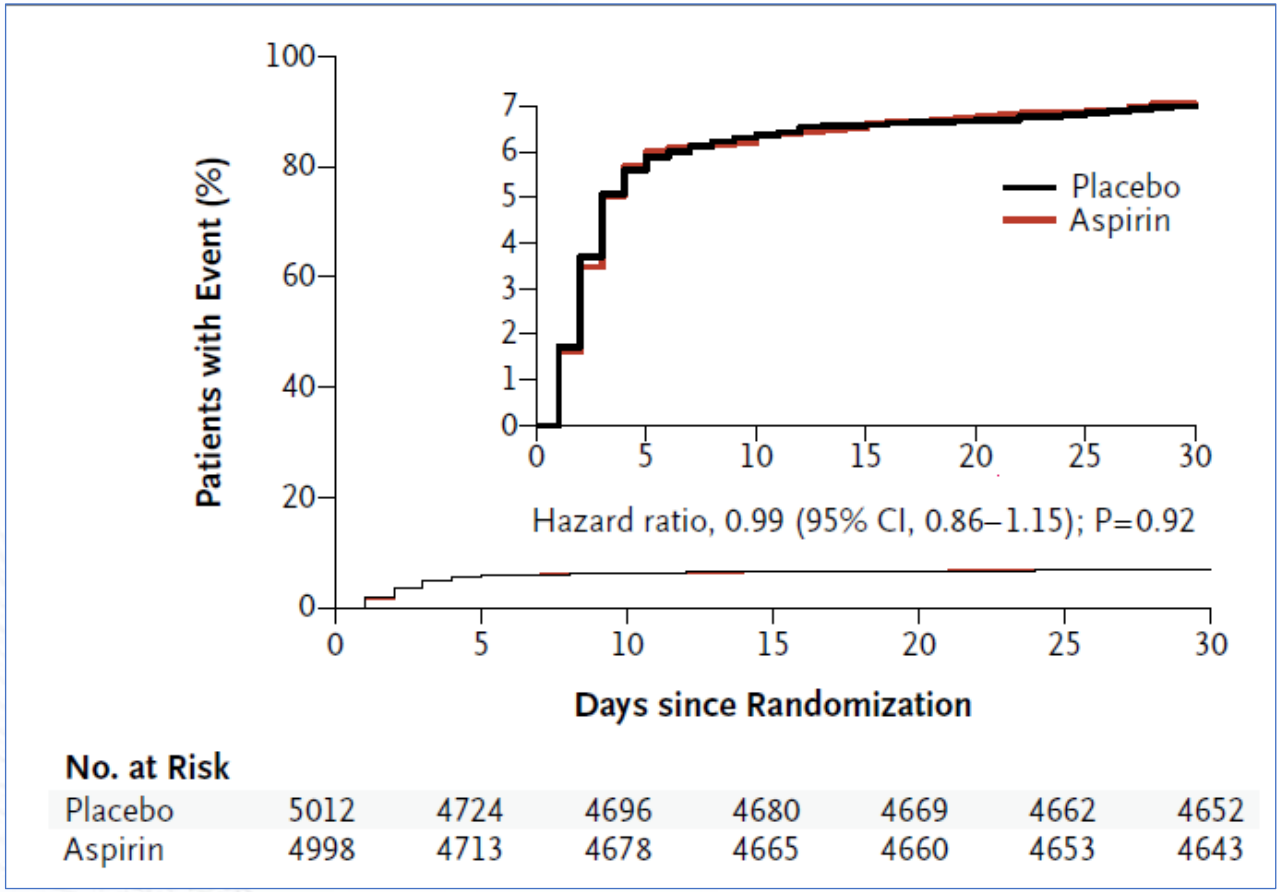


Death	0.9% vs. 1.3%
Non Fatal MI	5.1% vs. 11.0%

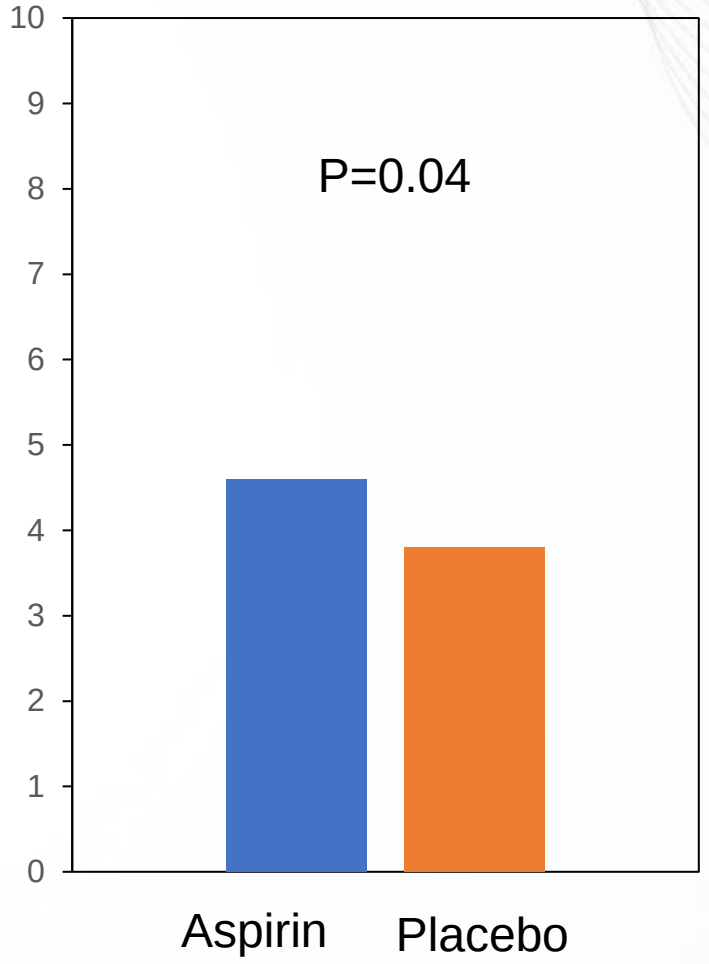
Ann Intern Med. 2018;168:237-244.

POISE-2: Aspirin in NCS

Death and Non Fatal MI

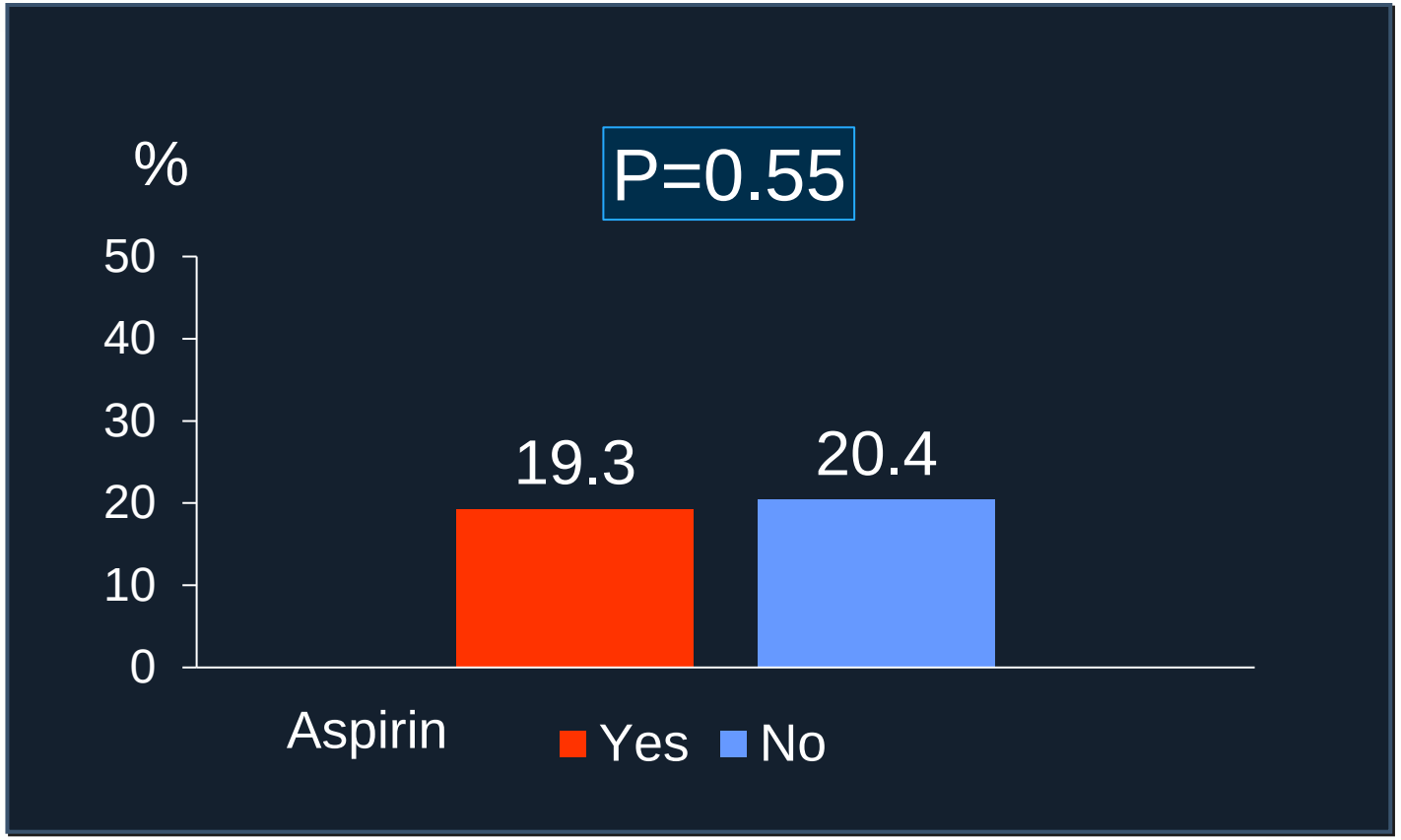


Major Bleeding



N Engl J Med 2014;370:1494-503.

ATACAS: Aspirin in CABG

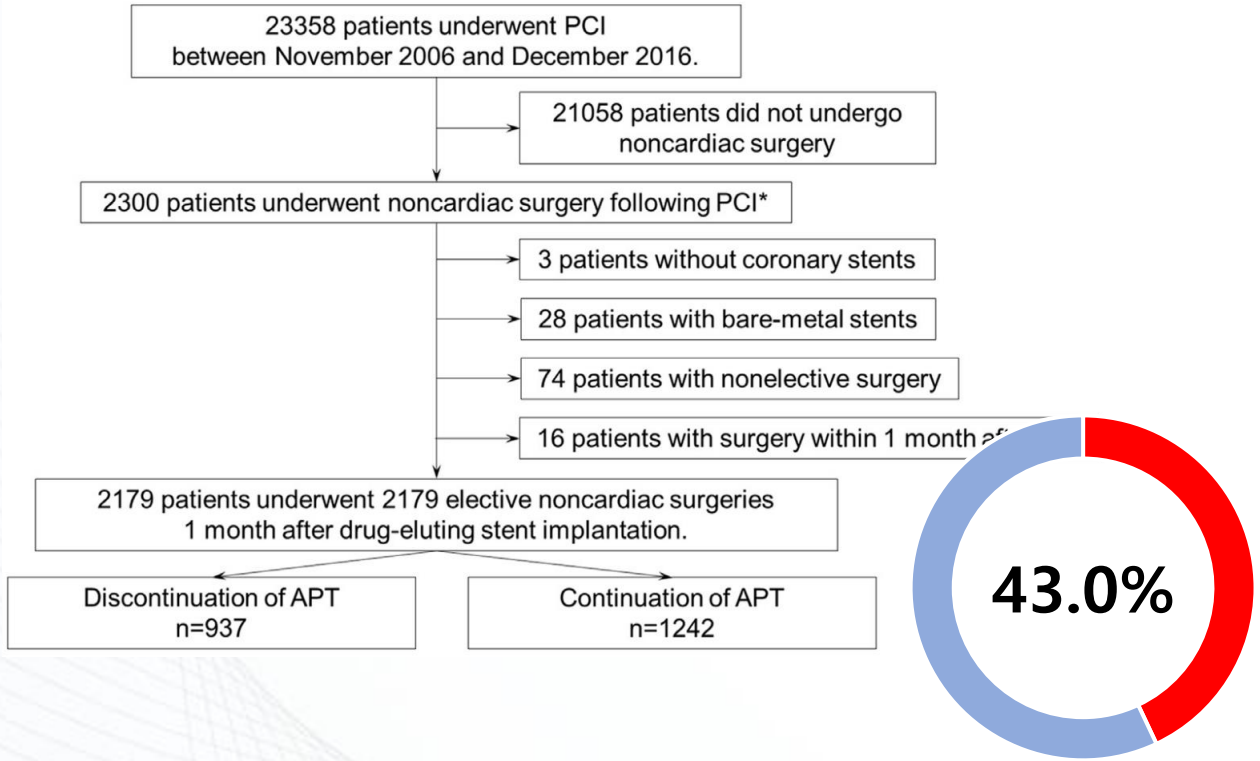


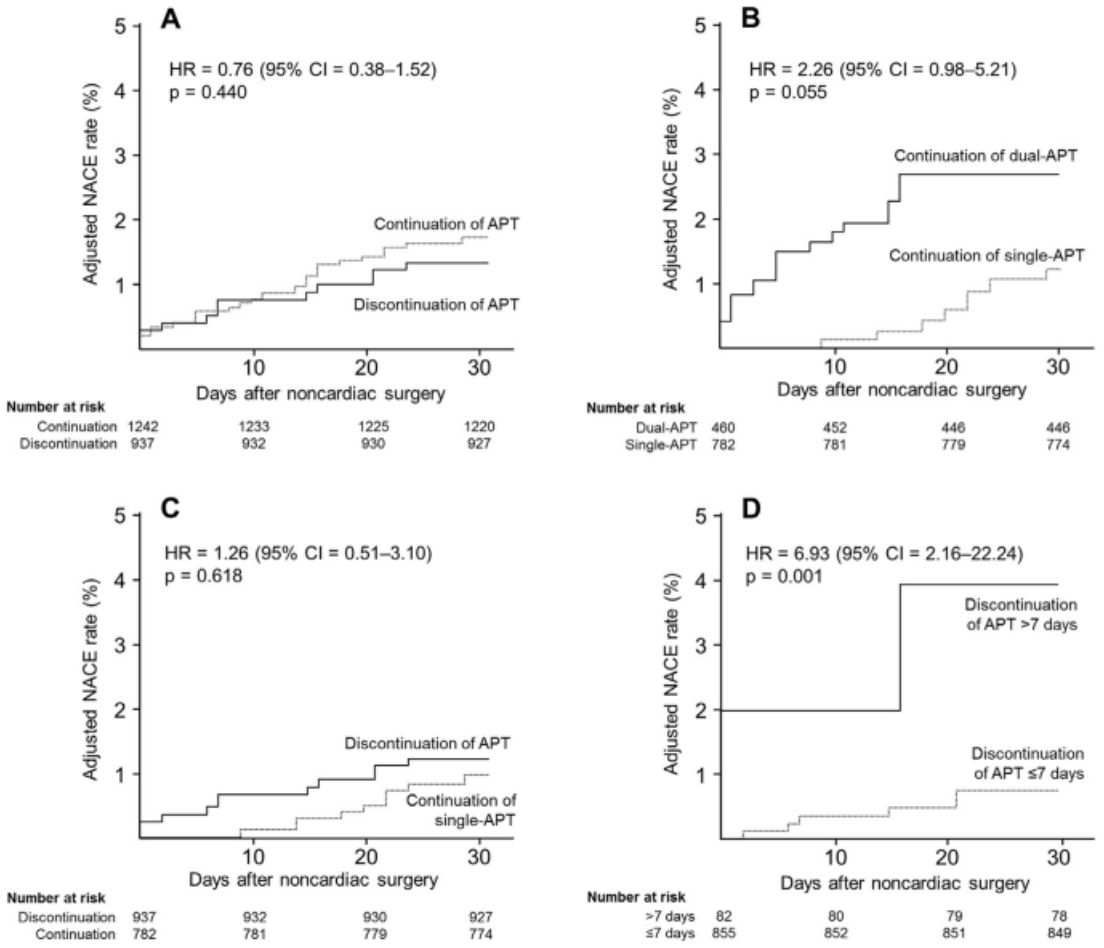
Among patients undergoing coronary artery surgery, the administration of preoperative aspirin resulted in ***neither a lower risk of death or thrombotic complications nor a higher risk of bleeding than that with placebo***.

N Engl J Med 2016;374:728-37.

Severance Cardiovascular Hospital Registry

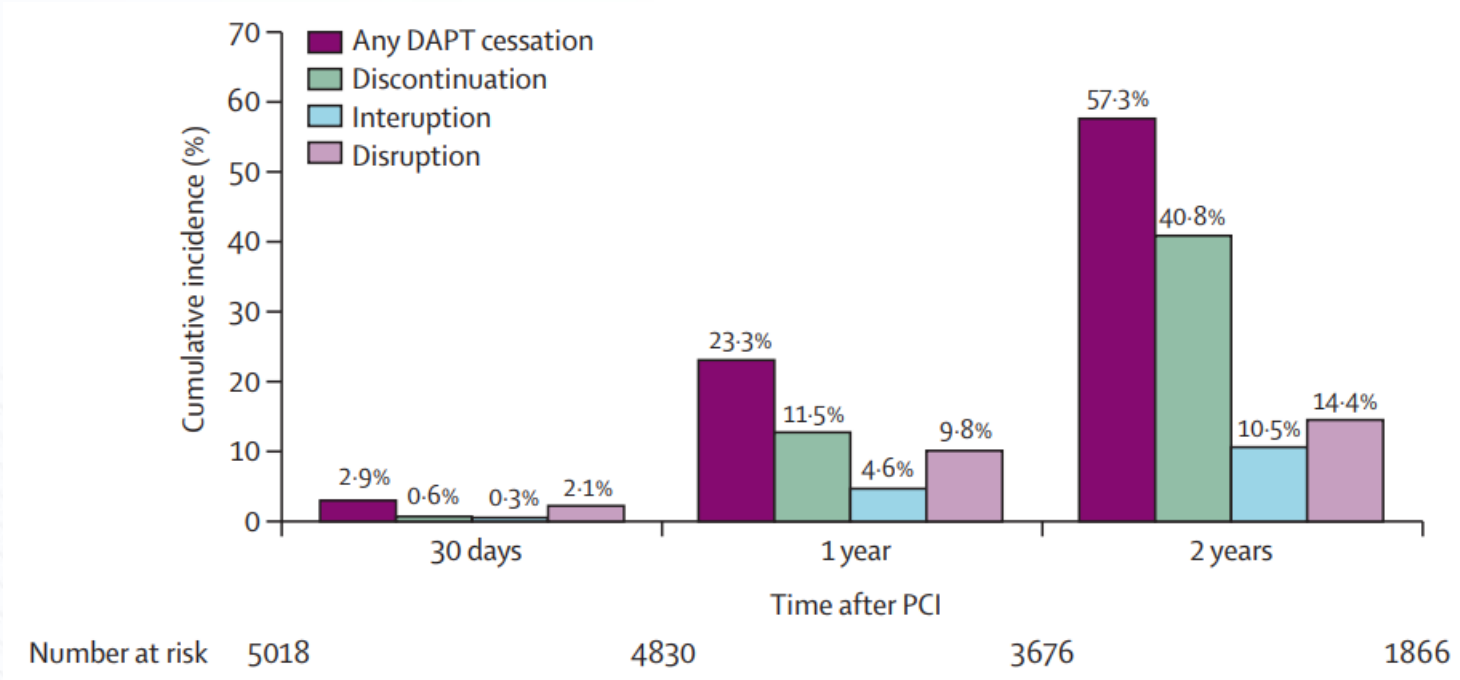
Anti-Platelet Discontinuation





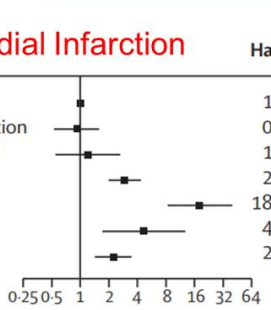
Am J Cardiol. 2019 May 1;123(9):1414-1421

PARIS Registry



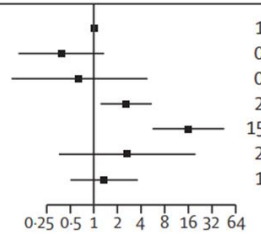
Myocardial Infarction

	Hazard ratio (95% CI)	p value	Observed	Expected
On-DAPT	1·00 (Ref)		116	116·0
Discontinuation	0·92 (0·53–1·58)	0·748	18	19·7
Interruption	1·20 (0·55–2·63)	0·647	7	5·8
Disruption	2·95 (1·99–4·38)	<0·0001	39	13·2
0–7 days	18·25 (8·34–39·95)	<0·0001	7	0·4
8–30 days	4·69 (1·71–12·83)	0·003	4	0·9
>30 days	2·22 (1·42–3·46)	<0·0001	28	12·6



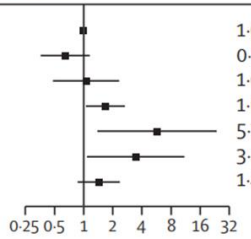
Stent Thrombosis

	Hazard ratio (95% CI)	p value	Observed	Expected
On-DAPT	1·00 (Ref)		57	57·0
Discontinuation	0·39 (0·11–1·35)	0·137	3	7·7
Interruption	0·64 (0·09–4·82)	0·664	1	1·6
Disruption	2·58 (1·22–5·46)	0·013	10	3·9
0–7 days	15·94 (5·57–45·58)	<0·0001	4	0·3
8–30 days	2·68 (0·36–19·68)	0·334	1	0·4
>30 days	1·35 (0·50–3·64)	0·551	5	3·7



Cardiac Death

	Hazard ratio (95% CI)	p value	Observed	Expected
On-DAPT	1·00 (Ref)		100	100·0
Discontinuation	0·64 (0·36–1·16)	0·141	15	23·3
Interruption	1·06 (0·48–2·34)	0·885	7	6·6
Disruption	1·68 (1·05–2·67)	0·029	26	15·5
0–7 days	5·73 (1·39–23·62)	0·016	2	0·3
8–30 days	3·44 (1·08–10·98)	0·037	3	0·9
>30 days	1·44 (0·87–2·38)	0·161	21	14·6



Lancet. 2013 Nov 23;382(9906):1714-22

Antiplatelet Cessation vs. Maintenance: Summary of Studies

2007년-2019년

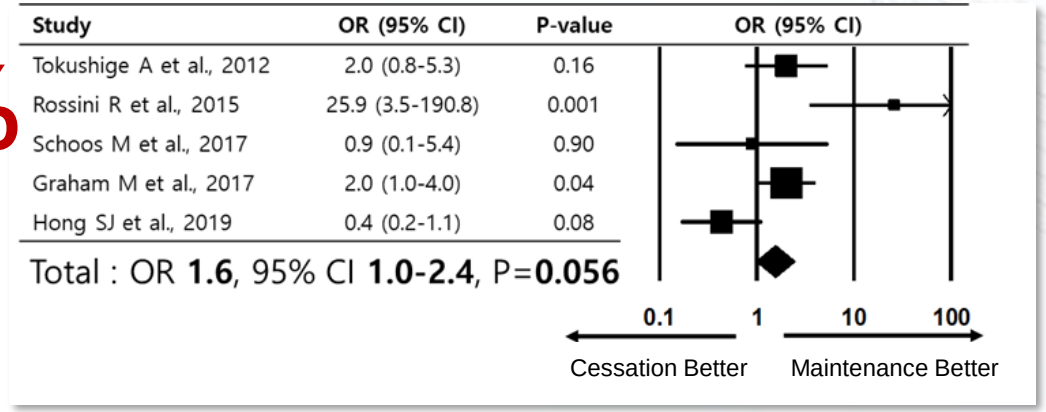
5 Observational Study and **4880 Patients**

- **Maintenance (N=2144)『Cessation (N=2736)』**

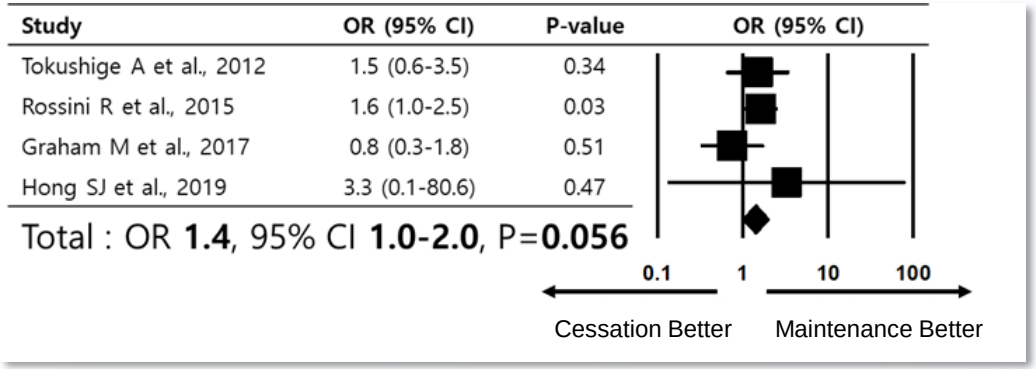
Stop Rate: 56%

연구자/발표년도	허혈성 사건	중단군	유지군	출혈성 사건	중단군	유지군
Schoos M et al. 2017	MI	2/254	3/340	N/A	N/A	N/A
Tokushige A et al. 2012	Death, MI or Stroke	26/1088	5/416	GUSTO moderate or severe Bleeding	27/1044	7/403
Graham M et al. 2017	Death or MI	27/236	14/234	POISE-2 Major or Life-threatening Bleeding	10/236	13/234
Rossini R et al. 2015	Cardiac death, MI, or Stroke	30/371	1/295	BARC 3 Bleeding	65/371	34/295
Hong SJ et al. 2019	Death, MI, or Stent thrombosis	6/787	15/859	ISTH Major Bleeding	1/787	0/859

Ischemic Events



Bleeding Events



A US National, Retrospective Cohort Study (N=41 989)

	No. (%)			*P* Value
	Overall	MACE	No MACE	
Antiplatelet medication prior to surgery				
Dual	328 (57.8)	170 (59.9)	158 (55.6)	.43
Single	206 (36.3)	100 (35.2)	106 (37.3)	
None	34 (6.0)	14 (4.9)	20 (7.0)	
Antiplatelet management at surgery				
Dual therapy				
All therapy continued	216 (65.9)	114 (67.1)	102 (64.6)	.82
Clopidogrel held	36 (11.0)	16 (9.4)	20 (12.7)	
Aspirin held	14 (4.3)	7 (4.1)	7 (4.4)	
All therapy held	62 (18.9)	33 (19.4)	29 (18.4)	
Aspirin only				
Continued	143 (82.7)	70 (87.5)	73 (78.5)	.12
Held	30 (17.3)	10 (12.5)	20 (21.5)	
Clopidogrel only				
Continued	22 (66.7)	12 (60.0)	10 (77.0)	.31
Held	11 (33.3)	8 (40.0)	3 (23.1)	
Antiplatelet cessation >5 d, all held				
Yes	137 (24.1)	65 (22.9)	72 (25.4)	.49
No	431 (75.9)	219 (77.1)	212 (74.7)	

JAMA. 2013;310(14):1462-1472

ASSURE DES Randomized Trial

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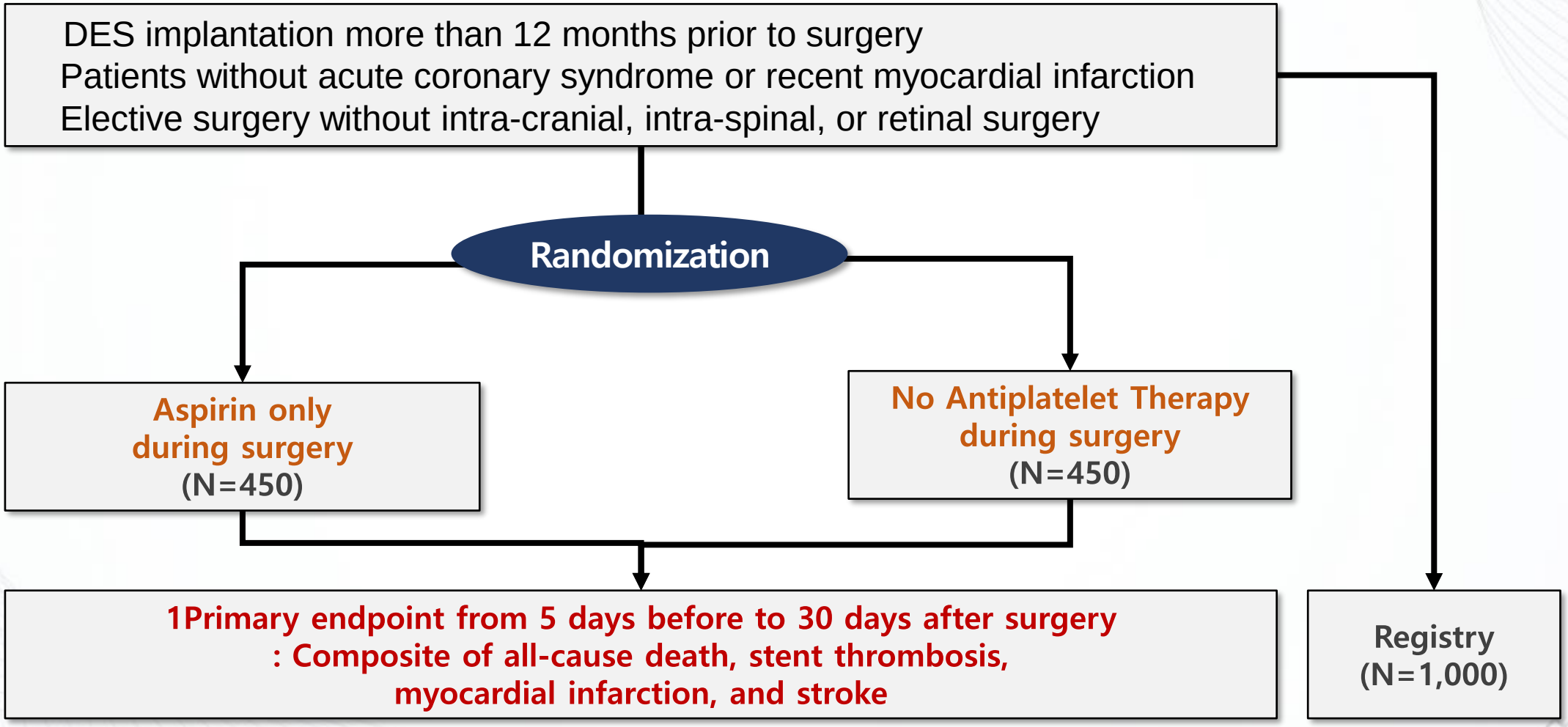


ASSURE DES Randomized Trial

Objectives

- This trial compared the clinical efficacy and safety of antiplatelet therapy in patients undergoing non-cardiac surgery for more than 12 months after PCI with DES.
- This trial compared outcome of discontinued antiplatelet treatment group and aspirin-alone treatment group.

Primary endpoint

- The Composite of Death, Stent Thrombosis, MI, Stroke (5 days before and 30 days after Non-cardiac Surgery)

ASSURE DES Randomized Trial

Inclusion Criteria

1) Men and women aged 19 years or more
2) Patients who implanted ≥ 1 coronary drug-eluting stents
3) Patients scheduled for surgery at more than 12 months after PCI
4) Patients scheduled for elective non-cardiac surgery under general anesthesia

Exclusion Criteria

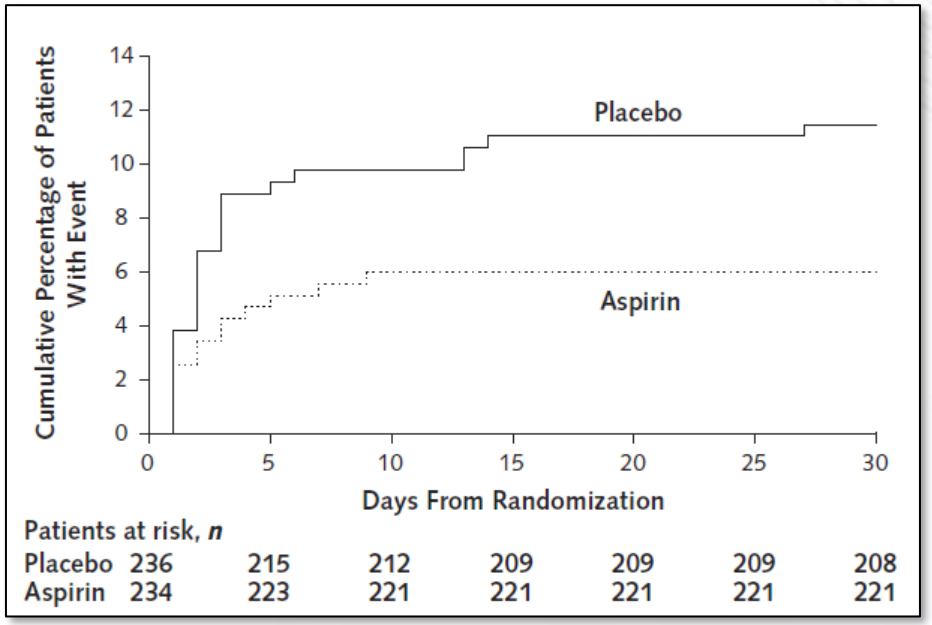
1) Patient who currently have ACS or MI within 1 month
2) Patient with dyspnea (NYHA III~IV) due to severe LV dysfunction (EF ≤30%) or severe VHD
3) Patient who have Intolerance for aspirin
4) Patient who need for anticoagulation therapy
5) Emergent operation
6) Cardiac surgery
7) High bleeding risk op. (Intra-cranial, Intra-spinal, Retinal surgery)
8) Pregnant and/or lactating women

ASSURE DES Randomized Trial

Sample Size

▶ Based on the results of the study in the POISE-2 trial, the primary endpoints of each treatment group were estimated. We will randomize 900 patients over 12 months after coronary stenting by 1:1 fashion, a) aspirin-alone treatment, b) discontinuation of antiplatelet agents. The assumed primary endpoint event rate was assumed 6.0% in aspirin-only therapy group and 11.5% in antiplatelet therapy discontinuation group. We estimated that enrollment of 900 patients would provide the study with 80% power to establish superiority of aspirin-only therapy in primary end point at 30 days, at a two-side type I error rate of 0.05.

POISE-2 (Ann Intern Med. 2018;168:237-244)



ASSURE DES Randomized Trial

TRIAL PROCEDURES AND FOLLOW-UP

- Patients are randomized to Aspirin-alone or Non-Antiplatelet group.
- Aspirin-alone group takes only aspirin from 5 days before surgery.
- Patients on a single P2Y12 inhibitor change to aspirin from 5d before operation.
- Patients on DAPT change to single aspirin from 5 days before operation.
- DAPT is resumed postoperatively as soon as possible (if possible, POD #2)
- Non-antiplatelet group discontinue all antiplatelet agent from 5 days before op. Antiplatelet agent is resumed as soon as possible after op.
- All patients are followed up by OPD visits or telephone at 30 day after surgery.

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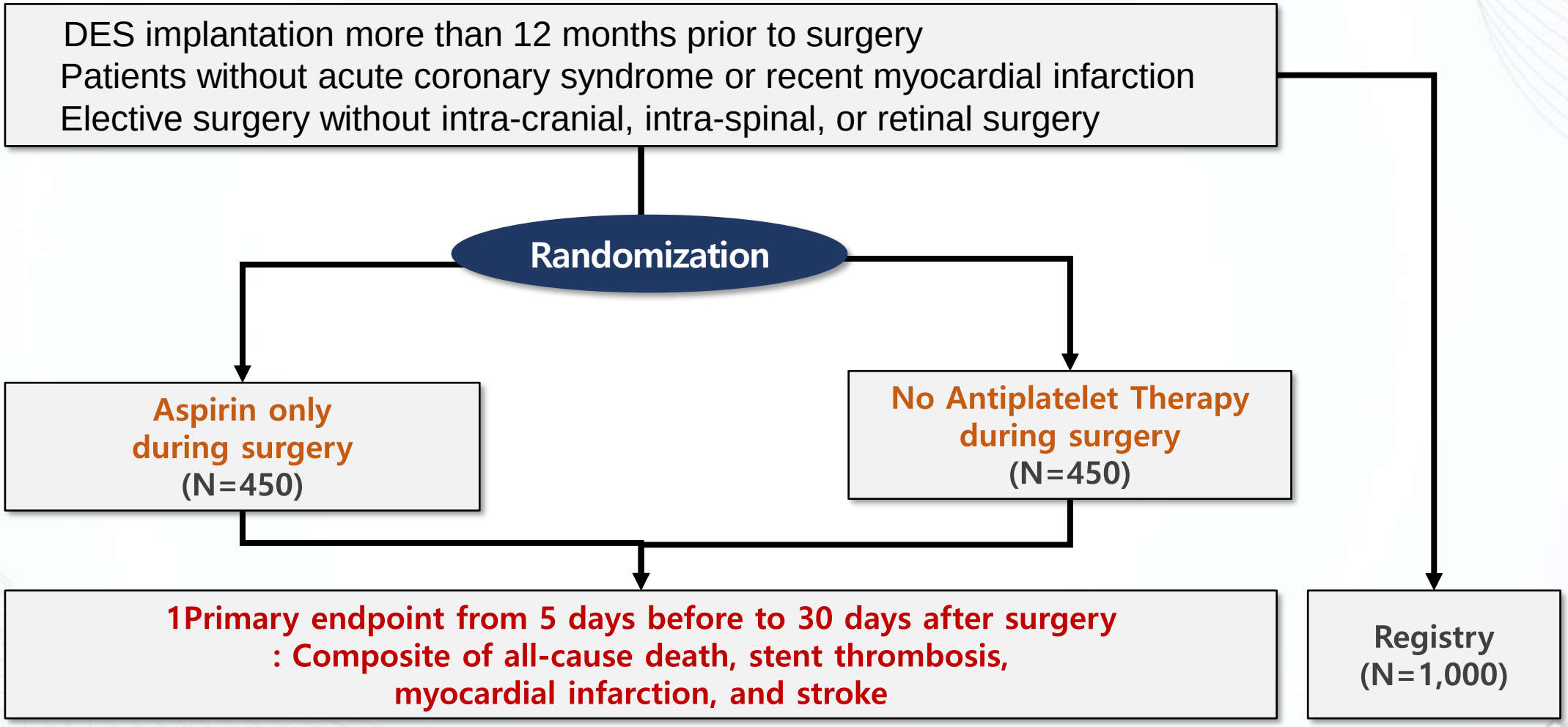

Current Status

Summary

- The ASSURE-DES trial is a prospective, multicenter, and randomized study to compare the safety and efficacy of aspirin cessation or not in perioperative period of non-cardiac surgery in patient who have undergone PCI with DES for more than 12 months.
- It may help to determine optimal antiplatelet therapy in patient who underwent PCI with DES before non-cardiac surgery.