

Perioperative Antiplatelet Therapy

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62/M, 2년 6개월전 pLAD 병변에 대하여 스텐트
시술받음

건강검진위해 개원외과에서 위식도 내시경과
대장내시경 검사 예약

근처 개원내과에 아스피린과 클로피도그렐 중단여부
문의후 7일간 항혈소판 복용중단하고 검사 받음

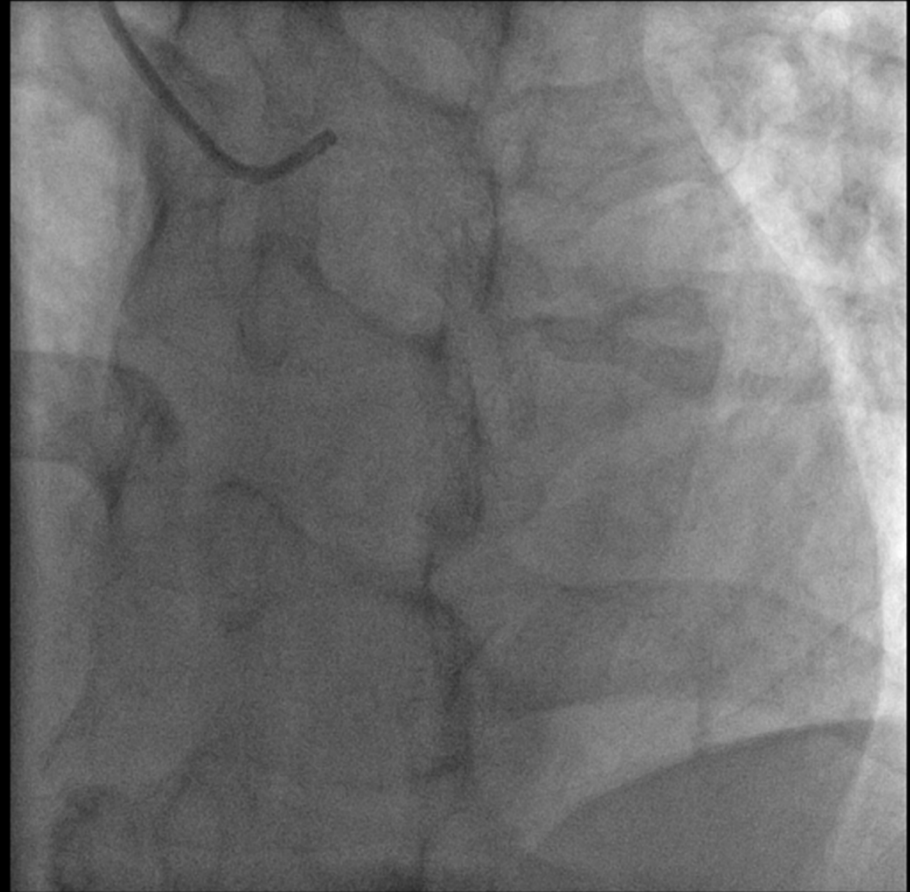
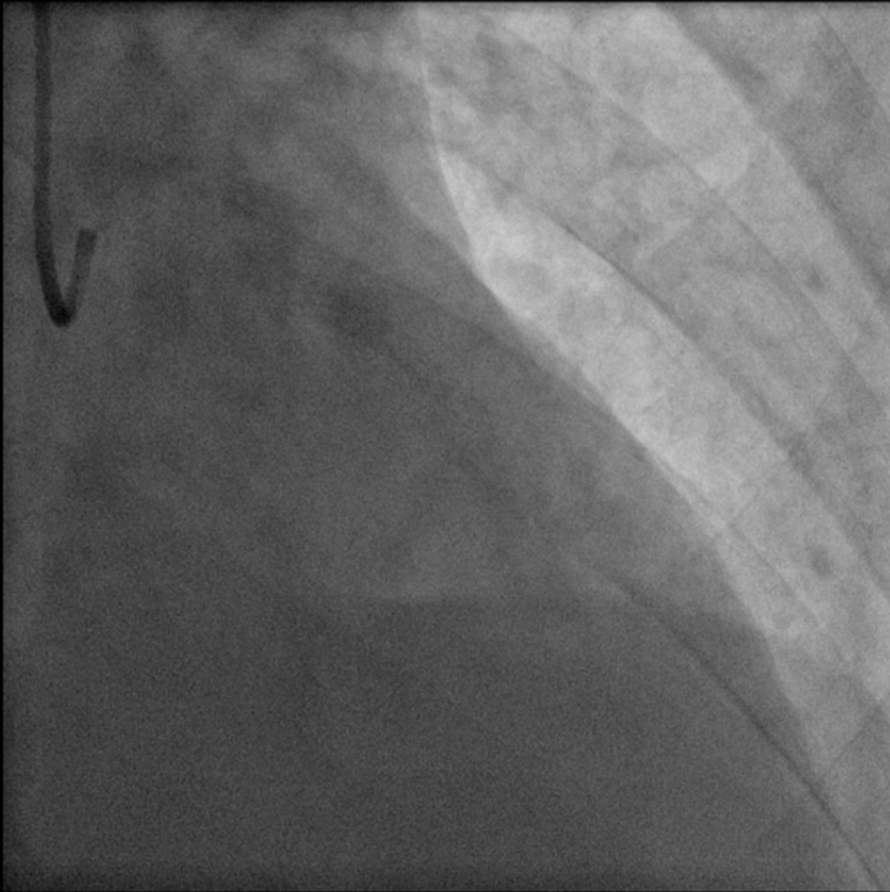
검사후 다음날 집에서 sudden death 상태로 발견됨

47/M, 3년 전 mLAD PCI (Cypher ?)

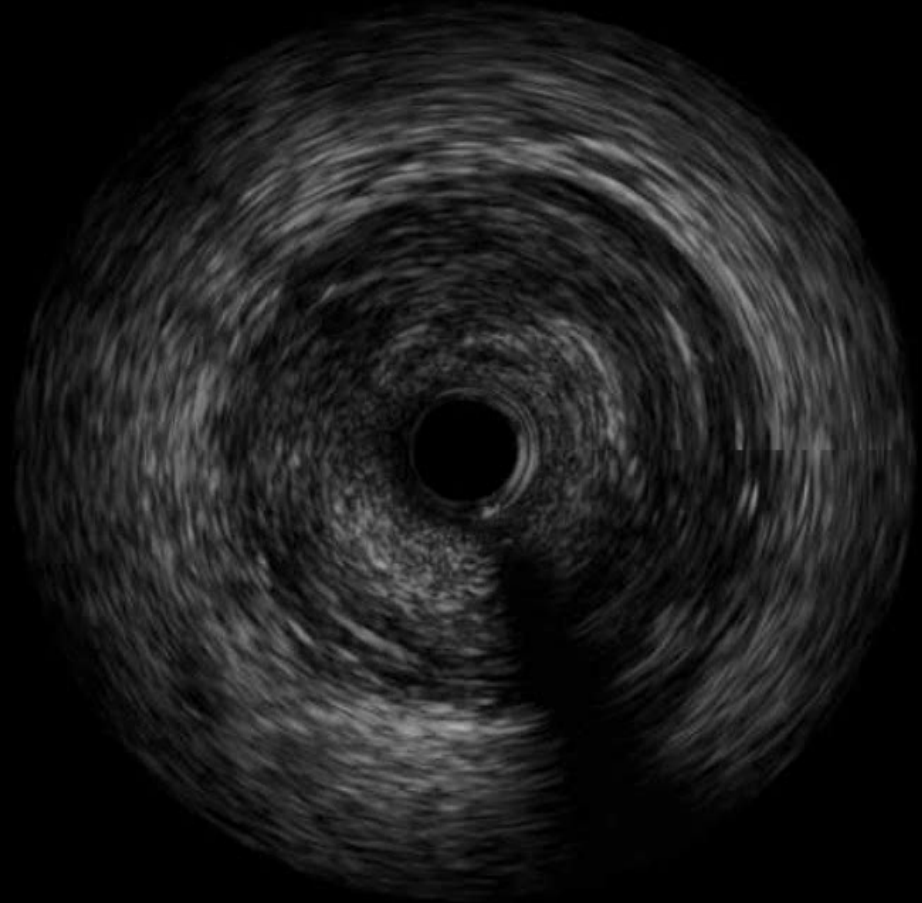
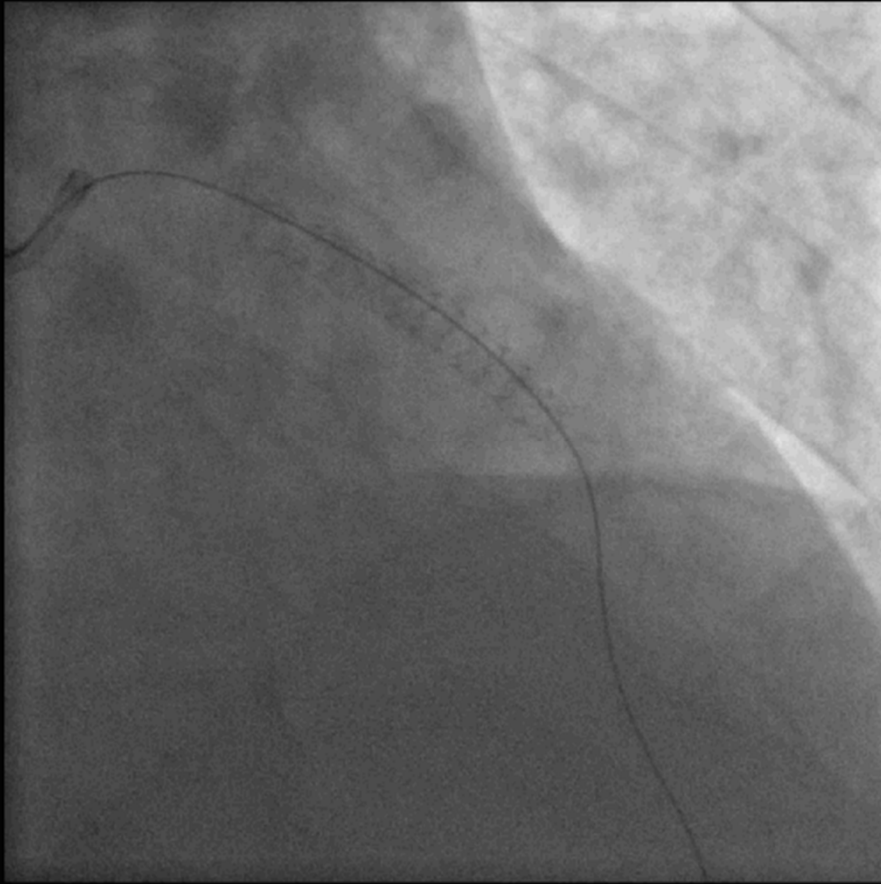
On aspirin & clopidogrel

One week ago, DAPT withdrawal due to travel

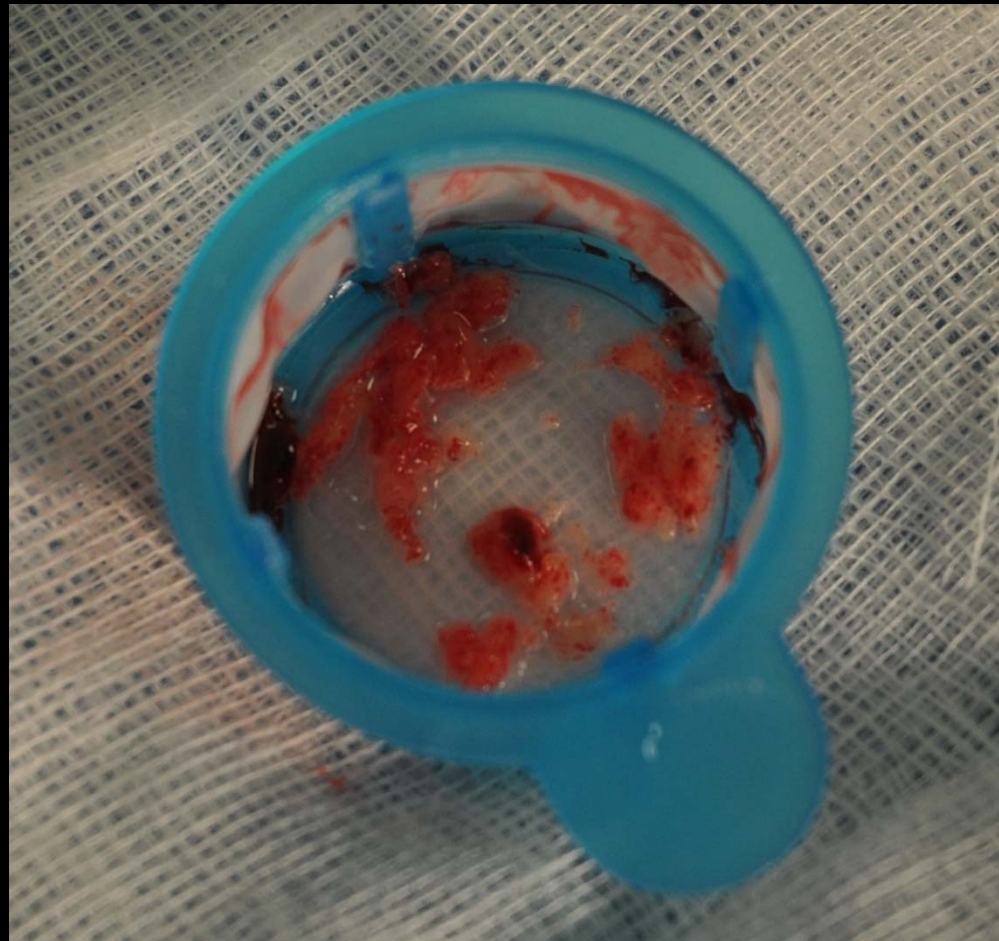
Sudden chest pain



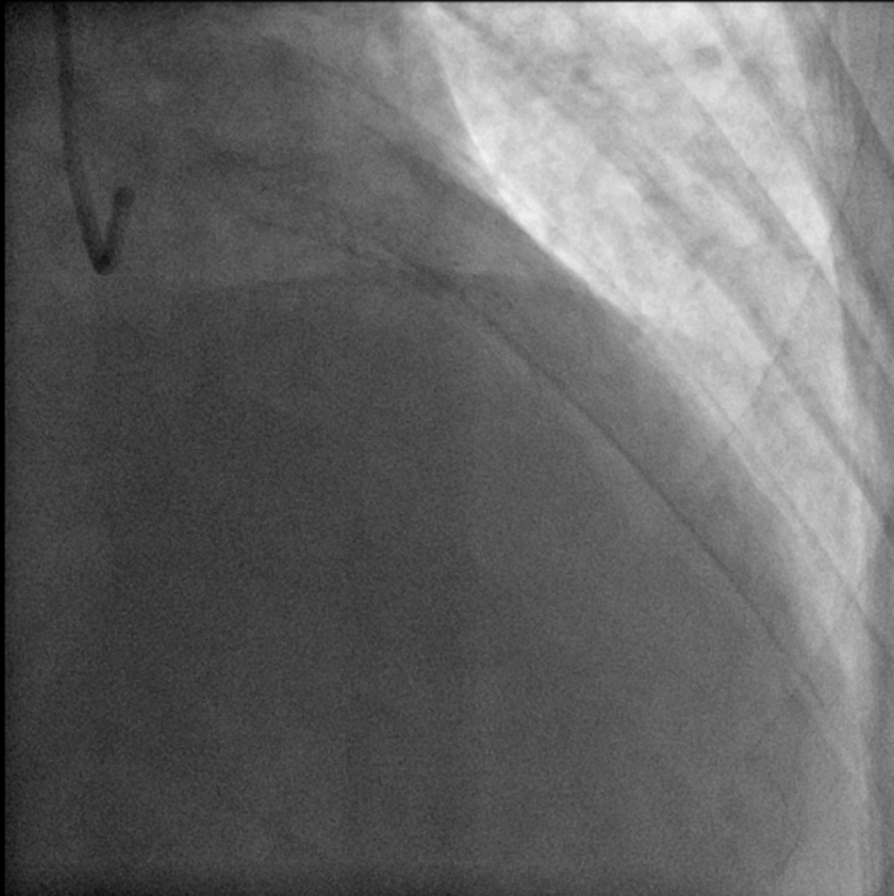
After thrombus aspiration & ballooning



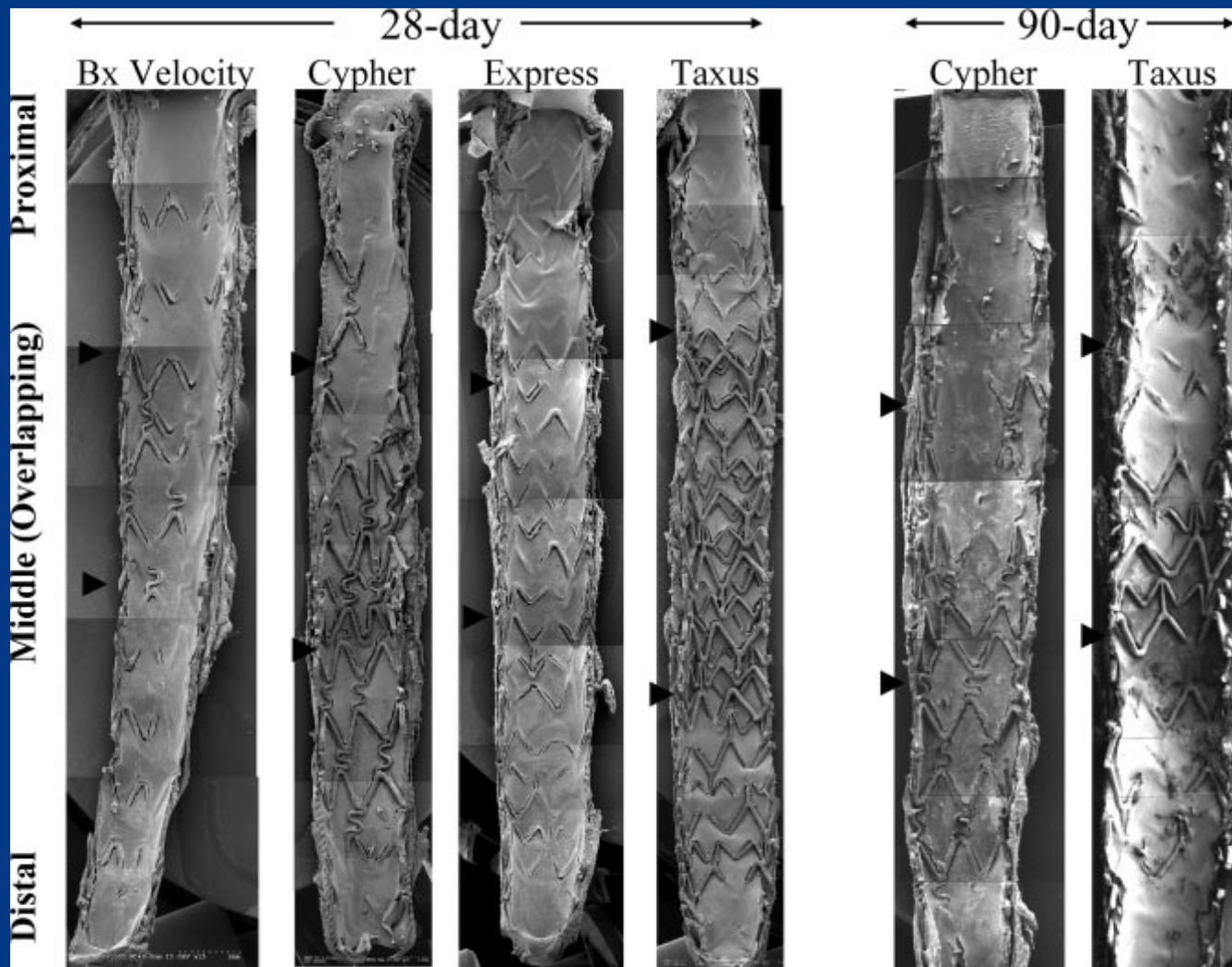
Manual thrombectomy



Resolute Integrity 3.0*12 mm + Voyage 4.5*8 mm



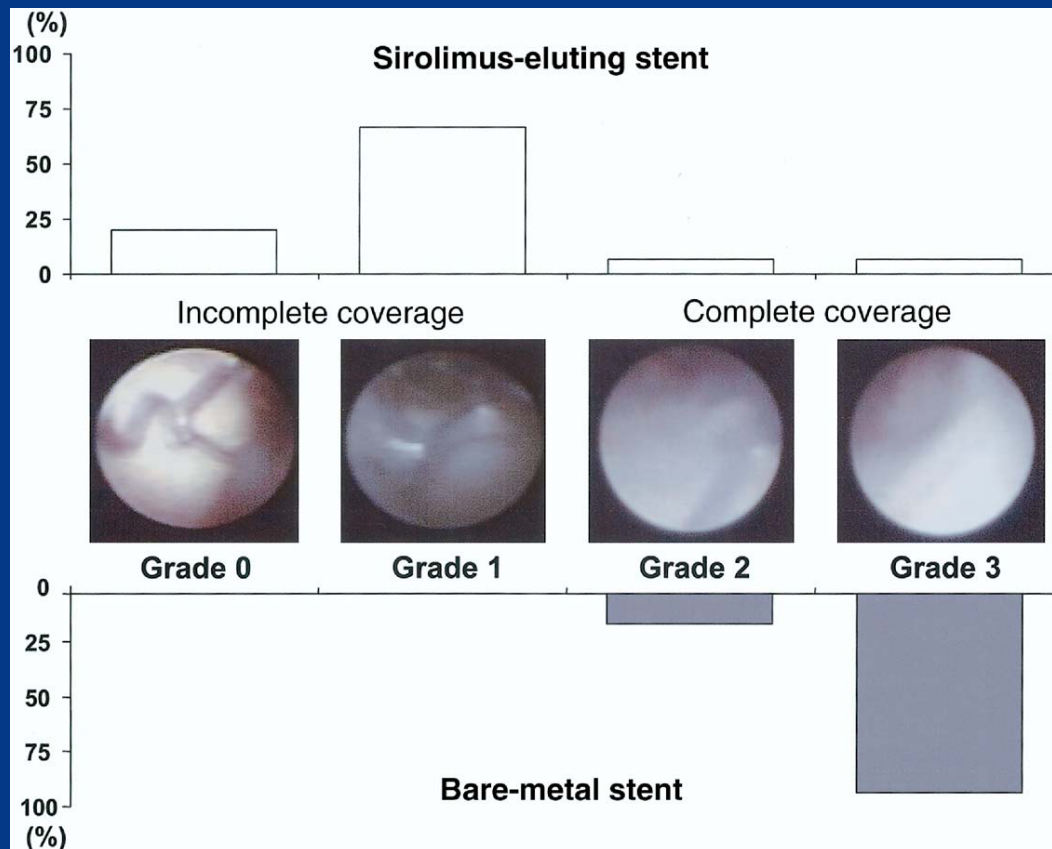
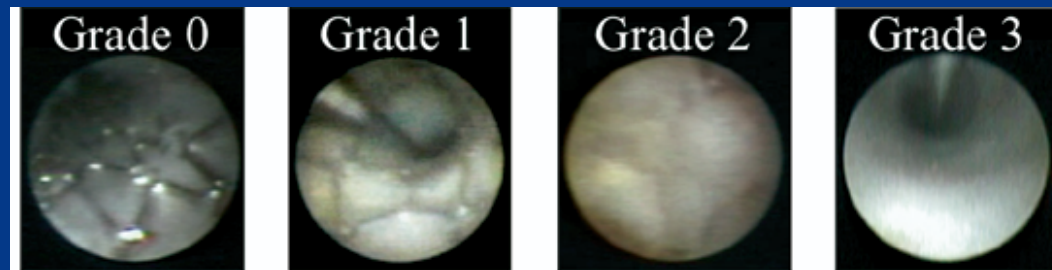
DES : double edge sword
delayed & defective neoendothelialization
Late or very late stent thrombosis



Finn AV, et al. Arterioscler Thromb Vasc Biol 2007;27:1500-10

Angioscopy (8 months after) in stable angina

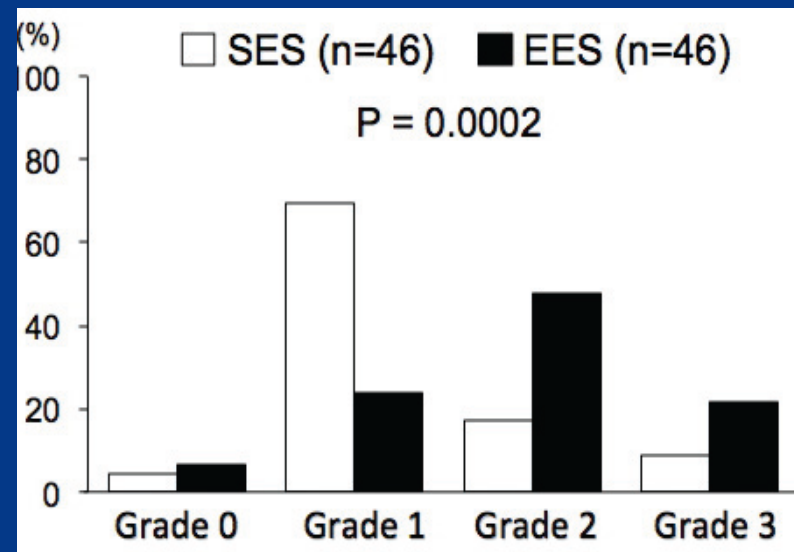
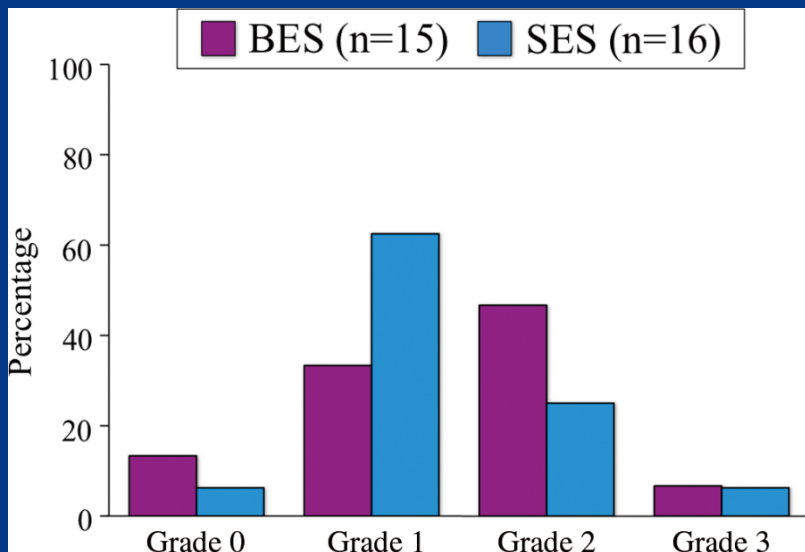
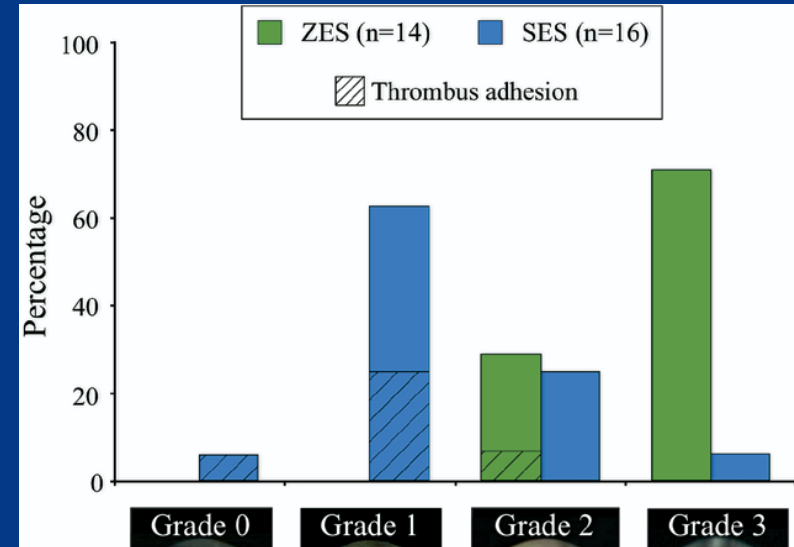
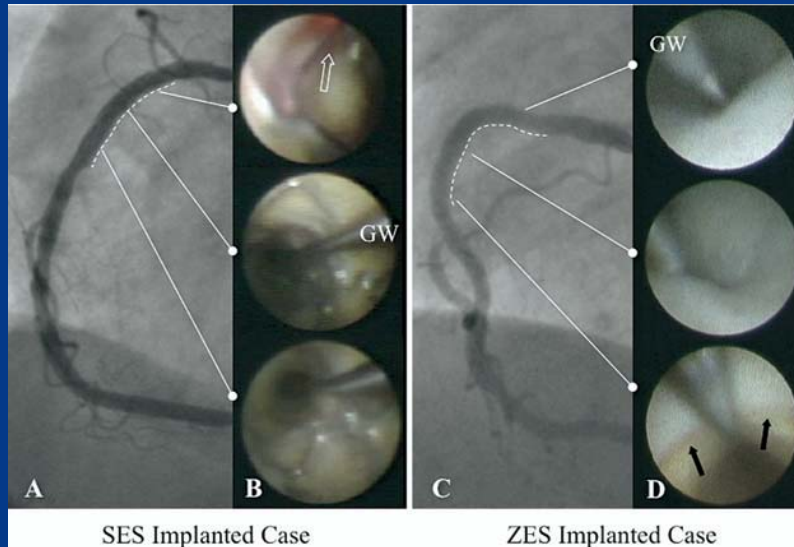
Neointimal coverage



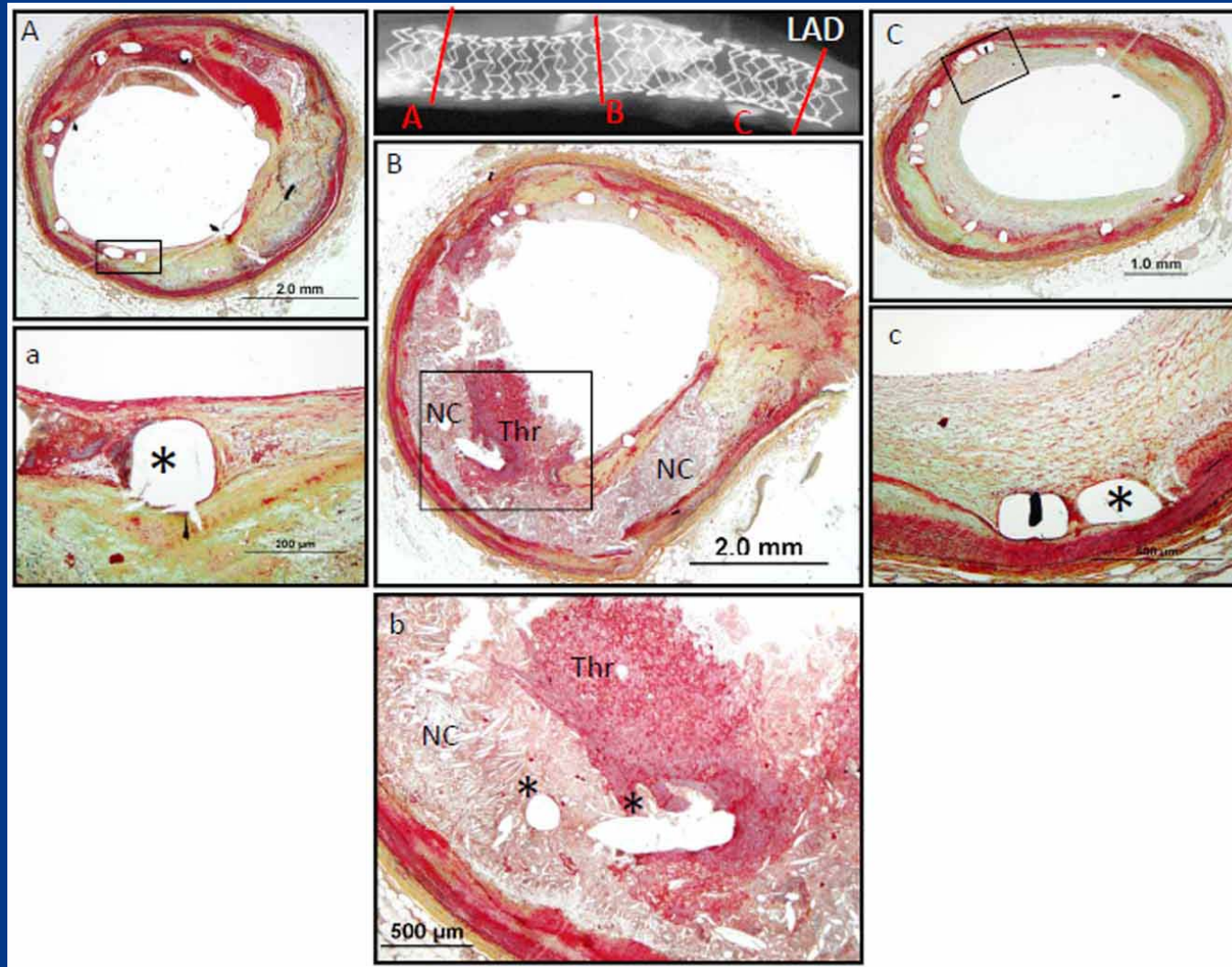
Kotani J et al, J Am Coll Cardiol 2006;47:2108-11

Angioscopy (9 months after) in stable angina

Neointimal coverage of 2nd generation DES



VLST : Delayed Endothelialization 9 months after PES in AMI

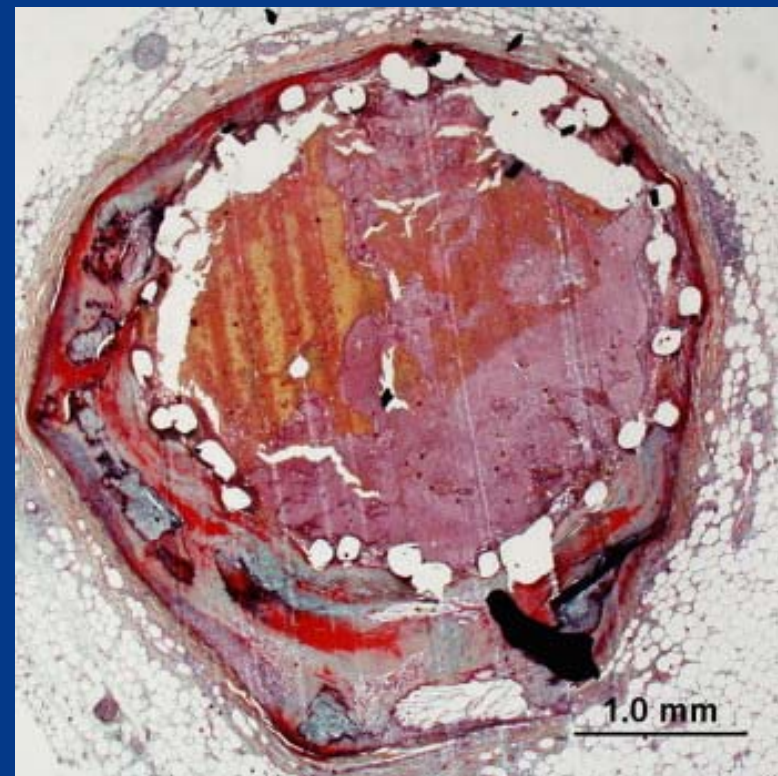


Nakazawa G et al, Circulation 2008;118:11138

Late or Very late stent thrombosis after DES

- Defective neointimal coverage
- Discontinuation of DAPT

**Defective endothelialization
when meet with
anti-plateletes skipping**



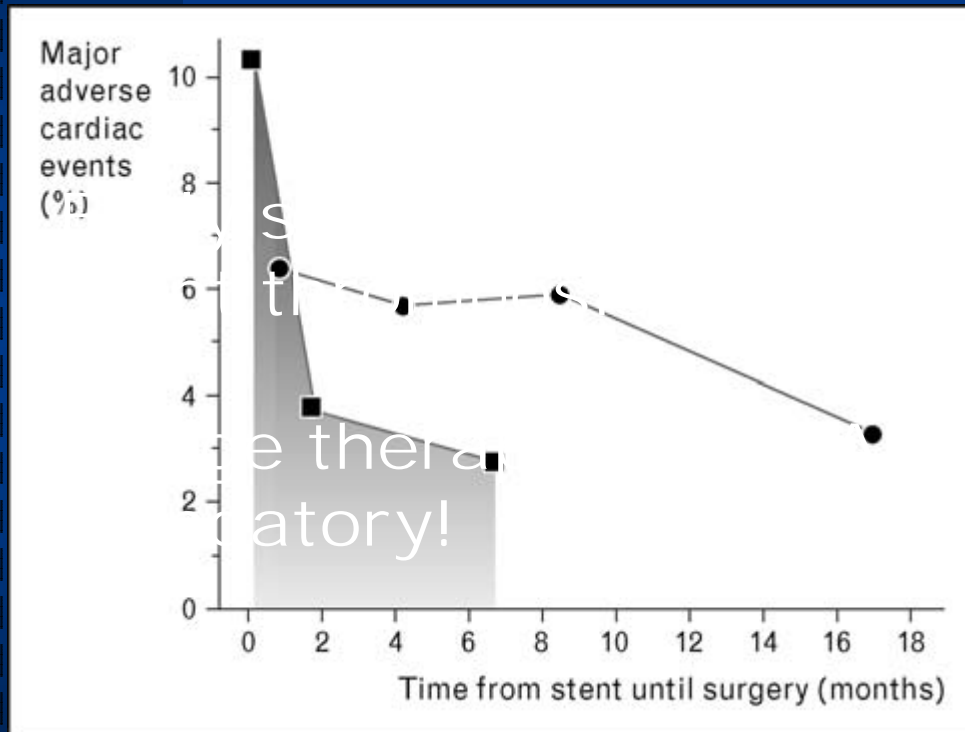
Antiplatelets in Perioperative Period



1. What consider before antiplatelet decision?
 - How long after PCI : 6 month vs 1 year post-DES?
 - How many risk factors for stent thrombosis
 - Bleeding risk in noncardiac surgery
2. Cataract, dental extraction, endoscopic biopsy?
3. Safe in late-generation DES?

When is appropriate time of surgery after DES?

6 month vs 1 year after



Anesthesiology 2007

	Late surgery (n=162)	Early surgery (n=30)
No MACE	161 (99.4%)	26 (86.7%)
MACE	1 (0.6%)	4 (13.3%)

	Continued DAPT (n=17)	Discontinued DAPT (n=13)
No MACE	17 (100%)	9 (69.3%)
MACE	0 (0%)	4 (30.7%)

J Am Coll Cardiol 2007

How many risk factors for stent thrombosis?

1. Premature discontinuation of antiplatelet therapy
2. Renal failure
3. Diabetes
4. Acute coronary syndrome
5. Low ejection fraction
6. Bifurcated lesions
7. Stent underexpansion and malapposition
8. Stent length
9. SES (possibly)

JAMA 2005, J Am Coll Cardiol 2007, Circulation 2006, 2007

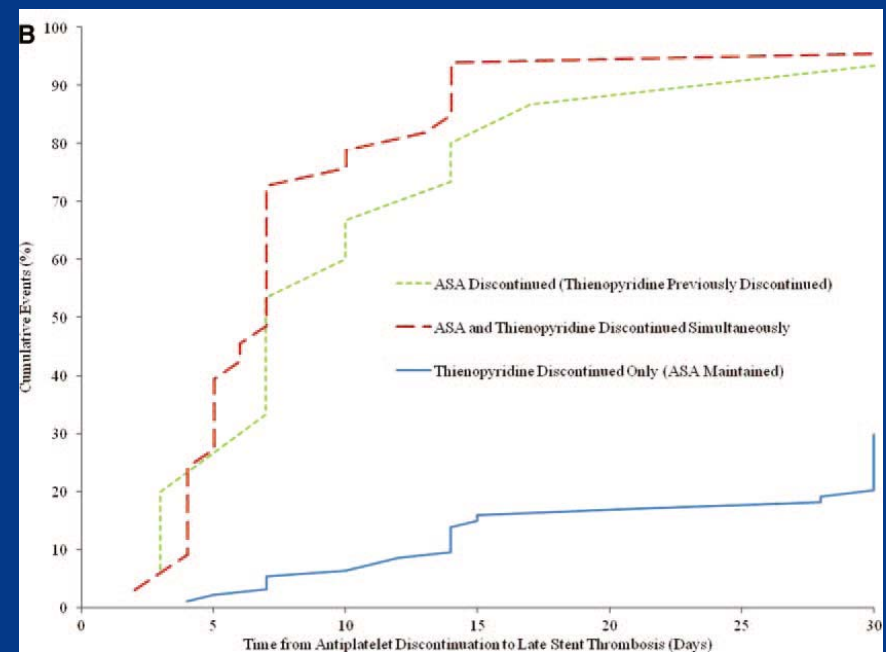
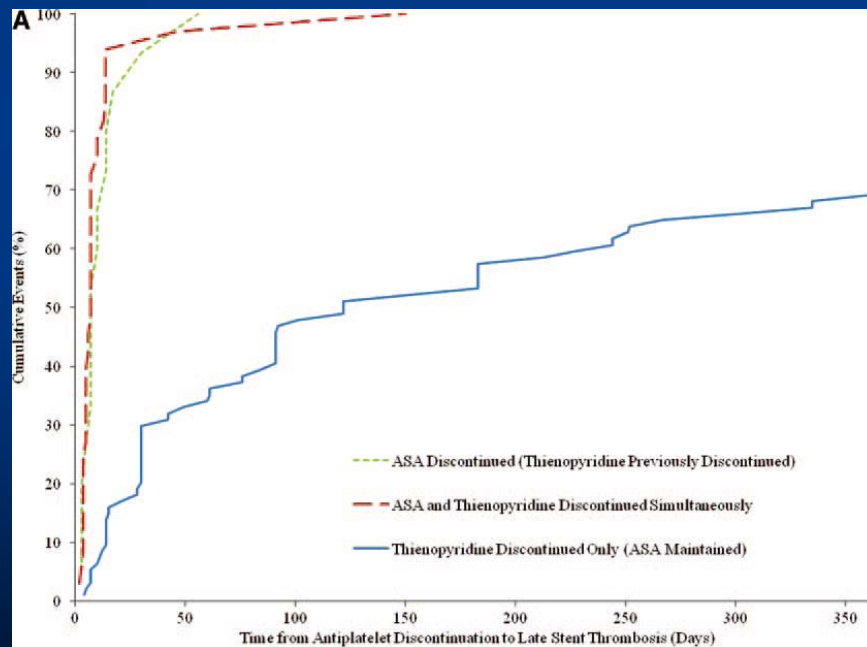
Bleeding risk in noncardiac surgery

Low	Intermediate	High
Endoscopy Dental extraction Eye ant. Chamber op	Visceral surgery	Intracranial neurosurgery
Plastic surgery Minor orthopedic & otolaryngology surgery	Major orthopedic & otolaryngology op	Spinal canal surgery
Peripheral surgery Biopsy		Eye post. Chamber surgery

Chassot PG et al, Br J Anaesth 2007;99:316-28

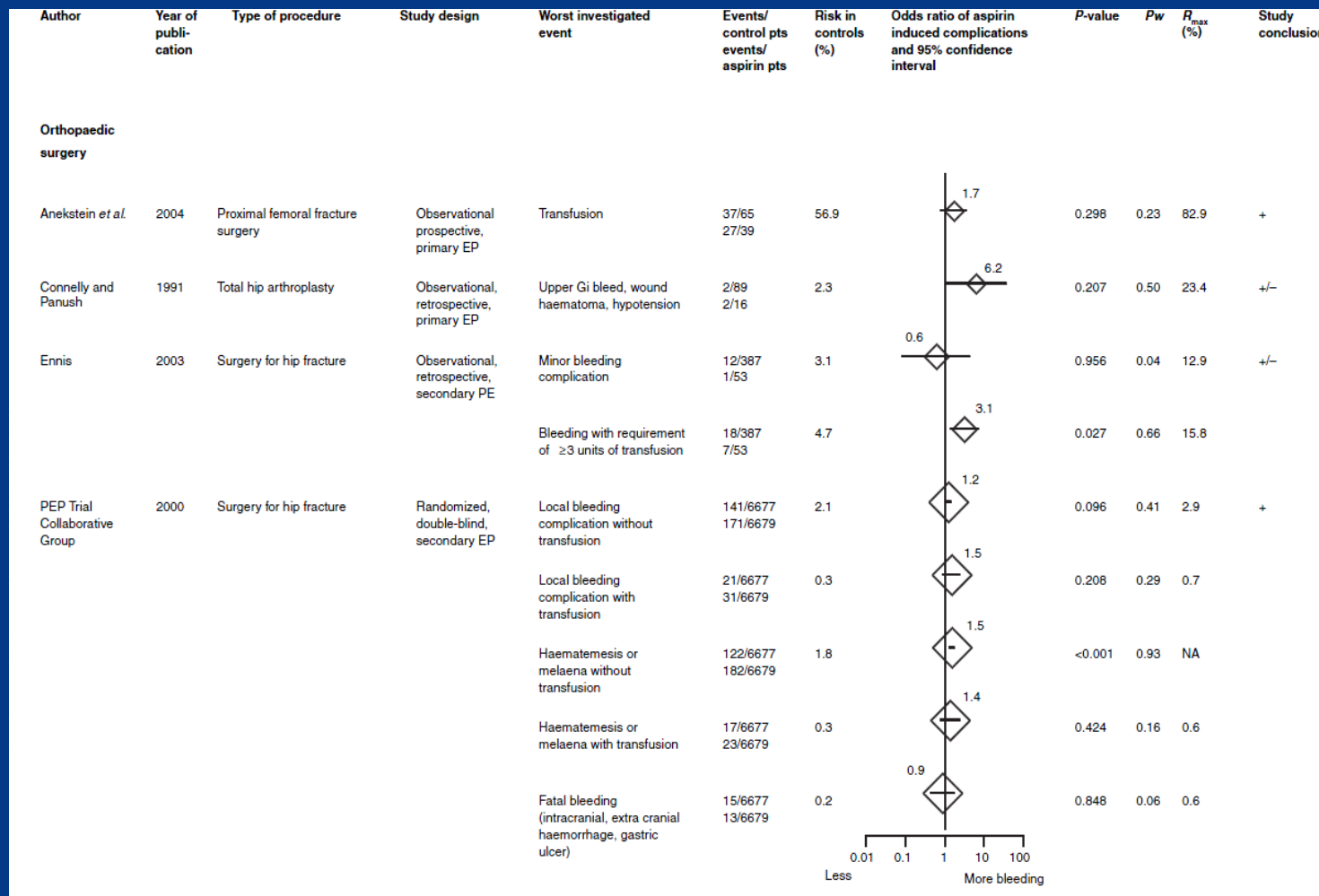
Safety of short-term discontinuation of antiplatelet therapy in SES+PES era

Situation	Simultaneous stop of ASA & CLOPD	ASA stop in ASA only medication	Only CLOPD stop in DAPT medication
Median time to LST	7 days	7 days	122 days



Eisenberg MJ et al, Circulation 2009;119:1634-42

Effect of preoperative aspirin use in intermediate bleeding risk surgery



Burger W *et al*, *J Intern Med* 2005;257:399-414

Effect of preoperative aspirin use in off-pump CABG

	Aspirin (n=170)	No aspirin (n=170)	P
Mortality (%)	1.2	1.8	0.65
Blood loss in ICU (mL)	845	777	0.26
Reop for bleeding (%)	3.5	3.5	0.99
GI bleeding (%)	1.2	1.2	0.99

Srinivasan AK et al, Ann Thorac Surg 2003;76:41-5

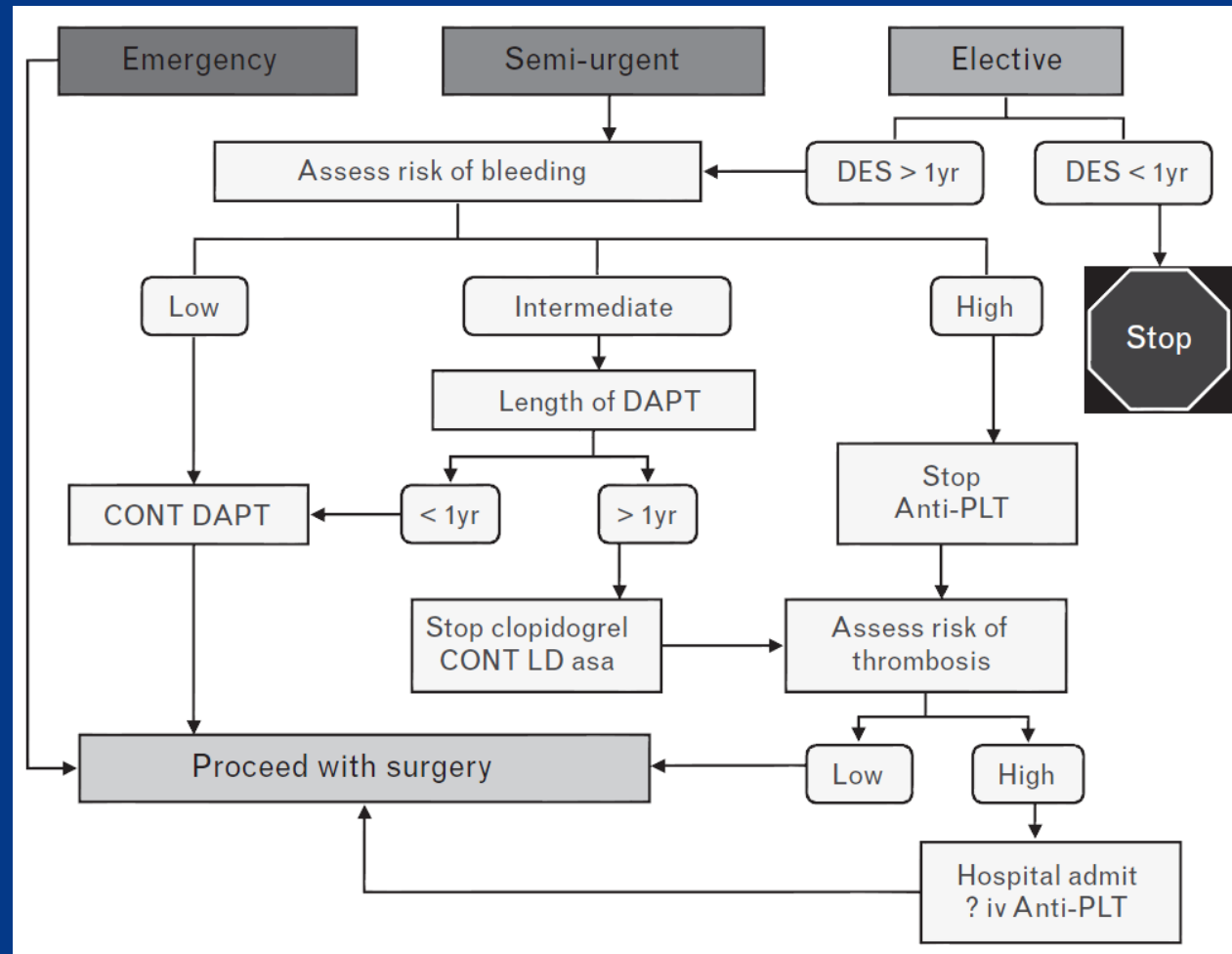
Effect of preoperative aspirin use in low to intermediate bleeding risk surgery

1. Aspirin continuation → more bleeding by a factor of 1.5

2. **Increased risk of perioperative hemorrhage with antiplatelet agents is not necessarily associated with increased morbidity, mortality or surgical outcome**

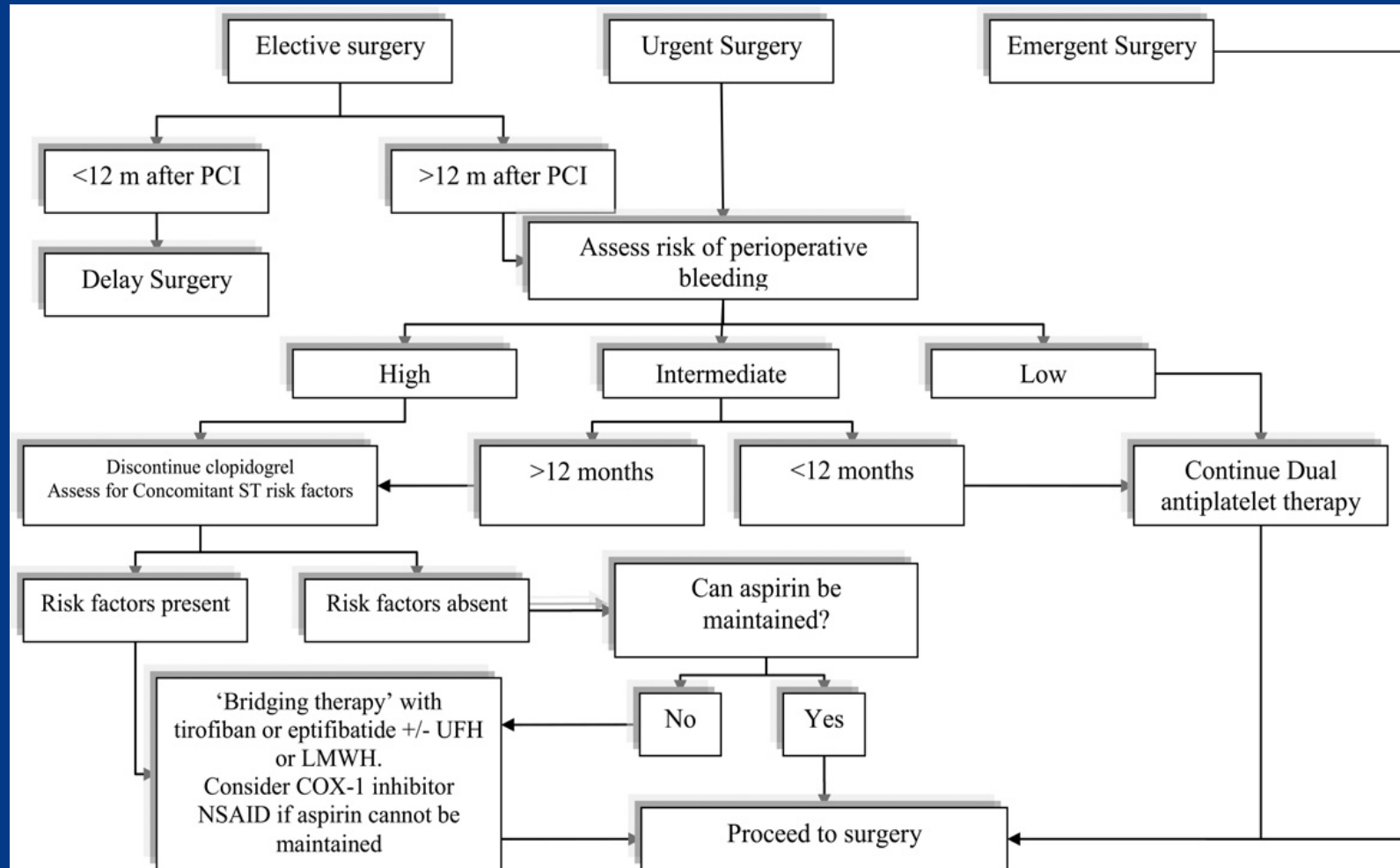
3. Withdrawal of aspirin → higher incidence of cardiovascular events

Algorithm of perioperative Management of patients with DES



Dalal AR et al, Can J Anaesth 2006;53:1230-43

Algorithm of perioperative Management of patients with DES



Abualsaud AO et al, J Am Coll Cardiol Intv 2010;3:131-42

Endoscopy & antiplatelet agents

European Society of GI endoscopy guideline

	Endoscopy with low bleeding risk	Endoscopy with high bleeding risk
Low thrombotic risk* <ul style="list-style-type: none"> - Coronary DES >12 months previously - Bare metal coronary stents inserted >6 weeks previously without associated risk factors† - Stroke without cardiac failure >6 weeks previously 	Maintain APA therapy	<ul style="list-style-type: none"> - Stop aspirin 5 days only for EUS-FNA of cysts, EMR and ESD, ampullary resection and endoscopic sphincterotomy with large-balloon papillary dilation for biliary stone extraction - In patients taking a thienopyridine alone, it is recommended to substitute aspirin‡
High thrombotic risk* <ul style="list-style-type: none"> - Coronary DES inserted ≤12 months previously - Bare metal coronary stents inserted ≤6 weeks previously or >6 weeks with associated risk factors† - Stroke ≤6 weeks previously 	Maintain dual APA therapy	<ul style="list-style-type: none"> - Delay endoscopy and/or consult cardiologist to discuss temporary cessation of thienopyridine: <ul style="list-style-type: none"> - clopidogrel, 5 days - prasugrel, 7 days - Aspirin should be maintained in all cases

Boustiere C et al, Endoscopy 2011;43:445-8

Endoscopy & antiplatelet agents

European Society of GI endoscopy guideline

Bleeding risk	Endoscopic procedure	Continuation of aspirin?	Continuation of clopidogrel or prasugrel?
Low risk	EGD and colonoscopy +/- biopsy	Yes	Yes
	EUS without FNA	Yes	Yes
	Colonic polypectomy < 1 cm	Yes	No*
	Dilation of digestive stenoses	Yes	No
	EUS-FNA of solid masses	Yes	No
	Digestive stenting	Yes	No
	ERCP with stent placement or papillary balloon dilation without endoscopic sphincterotomy	Yes	Yes
	Argon plasma coagulation	Yes	No†
	High risk	EMR, ESD and ampullary resection	No
Endoscopic sphincterotomy		Yes	No
Endoscopic sphincterotomy + large-balloon papillary dilation		No	No
Colonic polypectomy > 1 cm		Yes	No*
EUS-FNA of cystic lesions		No	No
Percutaneous endoscopic gastrostomy		Yes	n. a.
Esophageal variceal band ligation		Yes	No

Boustiere C et al, Endoscopy 2011;43:445-8

Cataract & antiplatelet agents

Complication	Maintenance N=273	Discontinuation N=285	p Value
Hemorrhagic			
Subconjunctival Hemorrhage	47(16.1)	31(10.8)	0.0309
Microscopic Hyphema 1d post-op	8(2.9)	5(1.8)	0.3572
Dot Retinal Hemorrhage	3(1.1)	2(0.7)	0.6187
Non-hemorrhagic, Intraoperative			
Early Perforation	2(0.7)	3(1.1)	0.6884
Posterior Capsule Rupture	4(1.5)	3(1.1)	0.6616
Vitreous Loss	3(1.1)	3(1.1)	0.9578

Kobayashi H, J Cataract Refract Surg 2010;36:1115-9

Dental extraction & antiplatelet agents

Complications	DES on DAPT (N=100)	Control group without APT (N=100)	P
Excessive Intra-extractive blood loss	2(2)	1(1)	0.36
Transfusion	0(0)	0(0)	-
Re-hospitalization	0(0)	0(0)	-

Park MW et al, Clin Cardiol (In press)

Perioperative Antiplatelet Therapy

American college of chest physicians
: evidence-based clinical practice guidelines

In patients who are receiving ASA for the **secondary prevention of cardiovascular disease** and are having **minor dental or dermatologic procedures or cataract surgery**, we suggest **continuing ASA around the time of the procedure** *instead of* stopping ASA 7 to 10 days before the procedure (Grade 2C)

Douketis JD et al, Chest 2012;141:e326s-350s

Perioperative Antiplatelet Therapy

American college of chest physicians
: evidence-based clinical practice guidelines

In patients with a coronary stent who are receiving **dual antiplatelet therapy and require surgery**, we recommend deferring surgery for at least **6 weeks after placement of a bare-metal stent and for at least 6 months after placement of a drug-eluting stent** *instead of* undertaking surgery within these time periods (Grade 1C).

In patients who **require surgery within 6 weeks** of placement of a bare-metal stent or within 6 months of placement of a drug-eluting stent, we suggest **continuing dual antiplatelet therapy around the time of surgery** *instead of* stopping dual antiplatelet therapy 7 to 10 days before surgery (Grade 2C).

Douketis JD et al, Chest 2012;141:e326s-350s

Resuming clopidogrel

Clopidogrel should be restarted once the risk of bleeding has been diminished (ideally within the first 24h) with a **loading dose of 300 mg to 600 mg.**

Kaluza GL et al, J Am Coll Cardiol 2000;35:1288-94

Bridging therapy with heparin

- **ST is a platelet-mediated process**
- **Hypercoagulability after abrupt cessation of UFH**
- **Heparin was not effective in preventing ST in the early days of BMS**

Serruys PW et al. N Engl J Med 1994;331:489-95

Bridging antiplatelet therapy with cangrelor in patients undergoing cardiac surgery

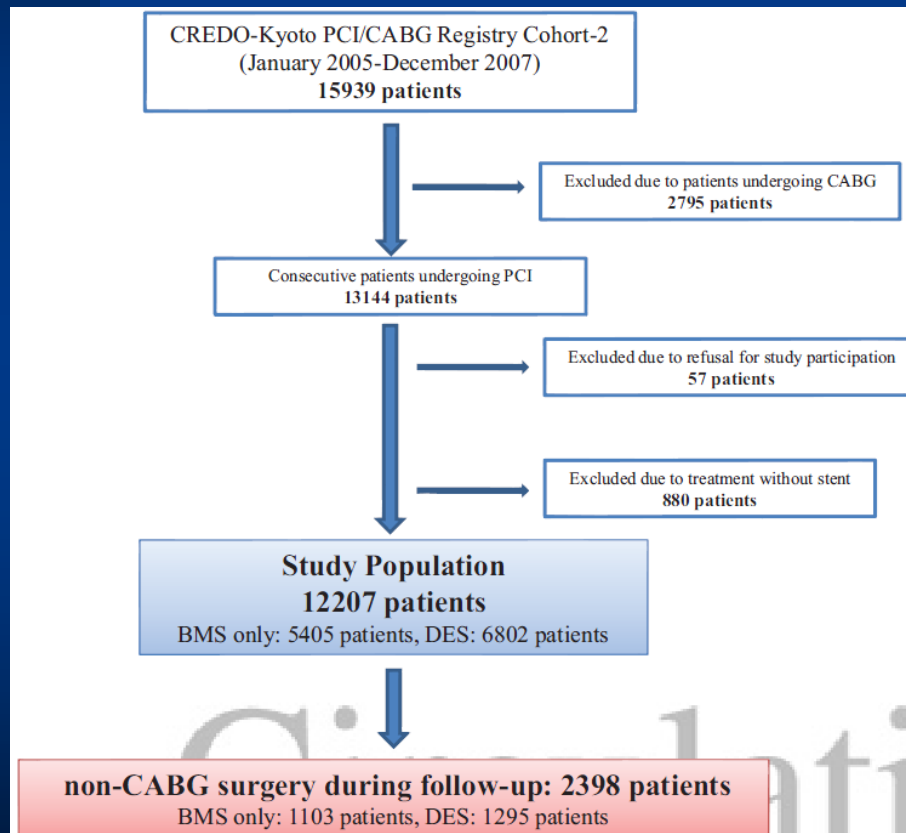
Excessive Bleeding, Primary Safety End Point, During the CABG Surgery and Through Hospital Discharge	No. of Patients/Total (%)		Relative Risk (95% CI)	P Value
	Cangrelor (n = 106)	Placebo (n = 101)		
Protocol defined	12/102 (11.8)	10/96 (10.4)	1.1 (0.5-2.5)	.76
Surgical reexploration	2/102 (2.0)	2/96 (2.1)	0.9 (0.1-6.5)	.95
24-h chest tube output, >1.5 L	8/102 (7.8)	5/96 (5.2)	1.5 (0.5-4.4)	.46
Incidence of PRBC transfusions >4 units	6/102 (5.9)	8/96 (8.3)	0.7 (0.3-2.0)	.50
BARC -defined	10/102 (9.8)	10/96 (10.4)	0.9 (0.4-2.2)	.89
Fatal bleeding	0/102 (0.0)	0/96 (0.0)	NA	NA
Perioperative intracranial bleeding within 48 h	0/102 (0.0)	0/96 (0.0)	NA	NA
Reoperation following closure of sternotomy for the purpose of controlling bleeding	2/102 (2.0)	2/96 (2.1)	0.9 (0.1-6.5)	.95
Transfusion of ≥5 units of whole blood or PRBC within a 48-h period	7/102 (6.9)	8/96 (8.3)	0.8 (0.3-2.2)	.70
Chest tube output ≥2 L within a 24-h period	3/102 (2.9)	4/96 (4.2)	0.7 (0.2-3.1)	.64

Bridging therapy

- **High bleeding risk surgery**
 - Intracranial surgery
 - Medullary or spinal canal surgery
 - Post chamber surgery
- **Hybrid CABG in the setting of ACS**
- **Surgery done less than 6 months**

Asian Data on surgery & APT

Credo-Kyoto PCI/CABG registry

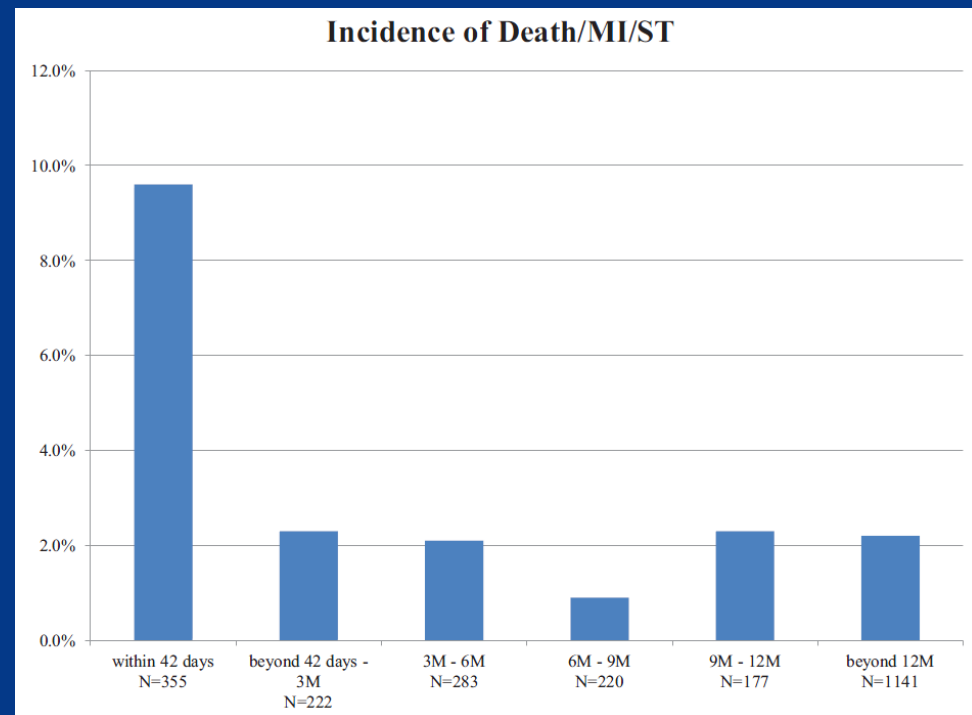
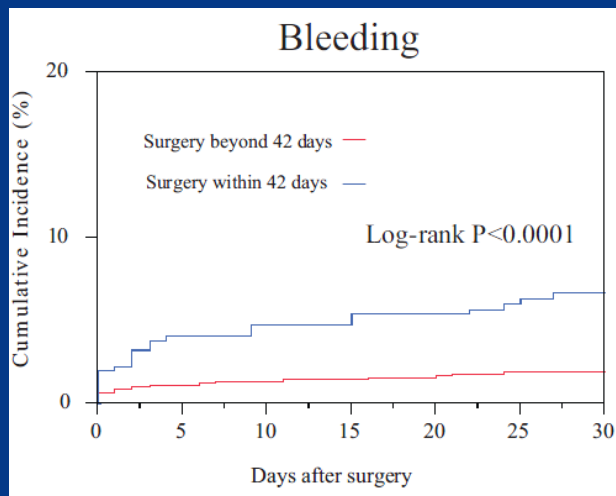
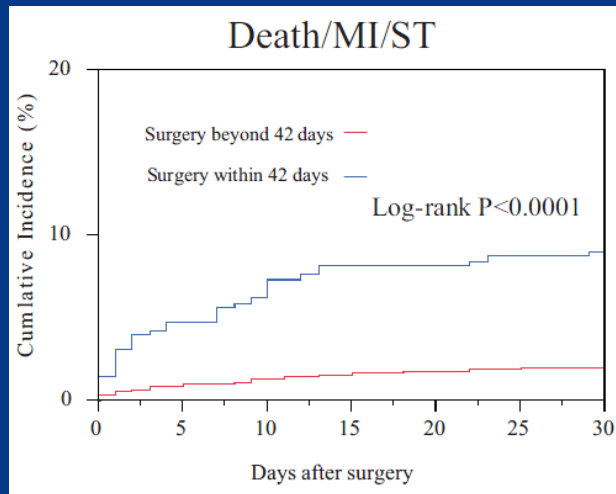


Surgical Fields	No. of Patients (%)	BMS	DES
All	2398	1103	1295
Vascular surgery	370 (15%)	207 (19%)	163 (13%)
Abdominal surgery	352 (15%)	157 (14%)	195 (15%)
Ophthalmic surgery	291 (12%)	91 (8.3%)	200 (15%)
Gastrointestinal endoscopic procedures	276 (12%)	118 (11%)	158 (12%)
Oral and maxillofacial surgery	214 (8.9%)	81 (7.3%)	133 (10%)
Orthopedic surgery	212 (8.8%)	85 (7.7%)	127 (9.8%)
Pacemaker implantation	152 (6.3%)	75 (6.8%)	77 (5.9%)
Urologic surgery	115 (4.8%)	55 (5.0%)	60 (4.6%)
Respiratory surgery	110 (4.6%)	69 (6.3%)	41 (3.2%)
Cardiac surgery	84 (3.5%)	52 (4.7%)	32 (2.5%)
Neurosurgery	56 (2.3%)	24 (2.2%)	32 (2.5%)
Dermatologic surgery	53 (2.2%)	23 (2.1%)	30 (2.3%)
Otorhinolaryngological surgery	51 (2.1%)	31 (2.8%)	20 (1.5%)
Mammary surgery	21 (0.9%)	13 (1.2%)	8 (0.6%)
Gynecological surgery	17 (0.7%)	8 (0.7%)	9 (0.7%)
Others	19 (0.8%)	11 (1.0%)	8 (0.6%)
Unknown	5 (0.2%)	3 (0.3%)	2 (0.2%)

Tokushige A et al. Circ Cardiovasc Interv 2012 (In press)

Asian Data on surgery & APT

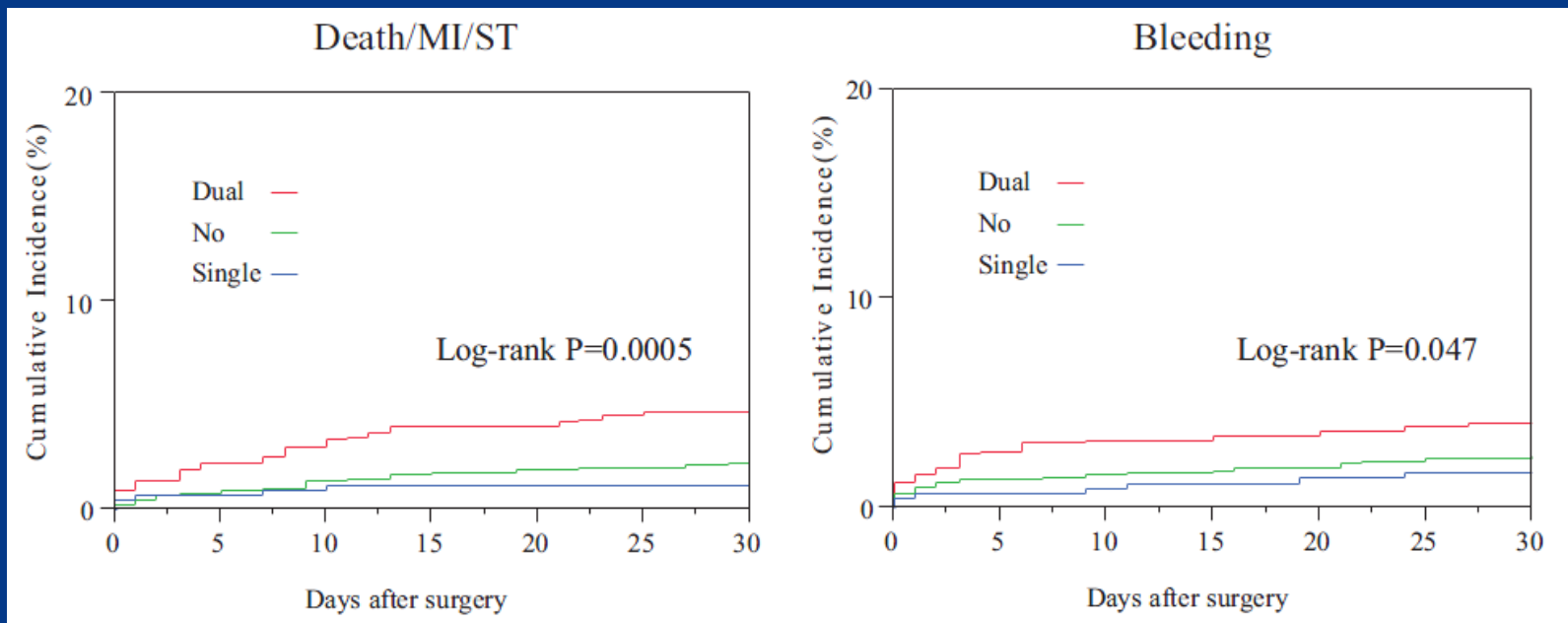
Credo-Kyoto PCI/CABG registry



Tokushige A et al. Circ Cardiovasc Interv 2012 (In press)

Asian Data on surgery & APT

Credo-Kyoto PCI/CABG registry



Tokushige A et al. Circ Cardiovasc Interv 2012 (In press)

Take-home messages

- **Surgery should be postponed at least 6 months after coronary stenting**
- **Except high bleeding risk surgery, aspirin should be maintained in all surgeries/procedures.**
- **Bridging therapy with cangrelor or new antiplatelet agents will be a safer prescription than heparin in high-risk patients who discontinued DAPT.**

Thank you for your attention!