Interruption of DAPT Due to Need For Surgery

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 - Intellectual property: HygeiaTel



Perioperative DAPT: Setting the Stage

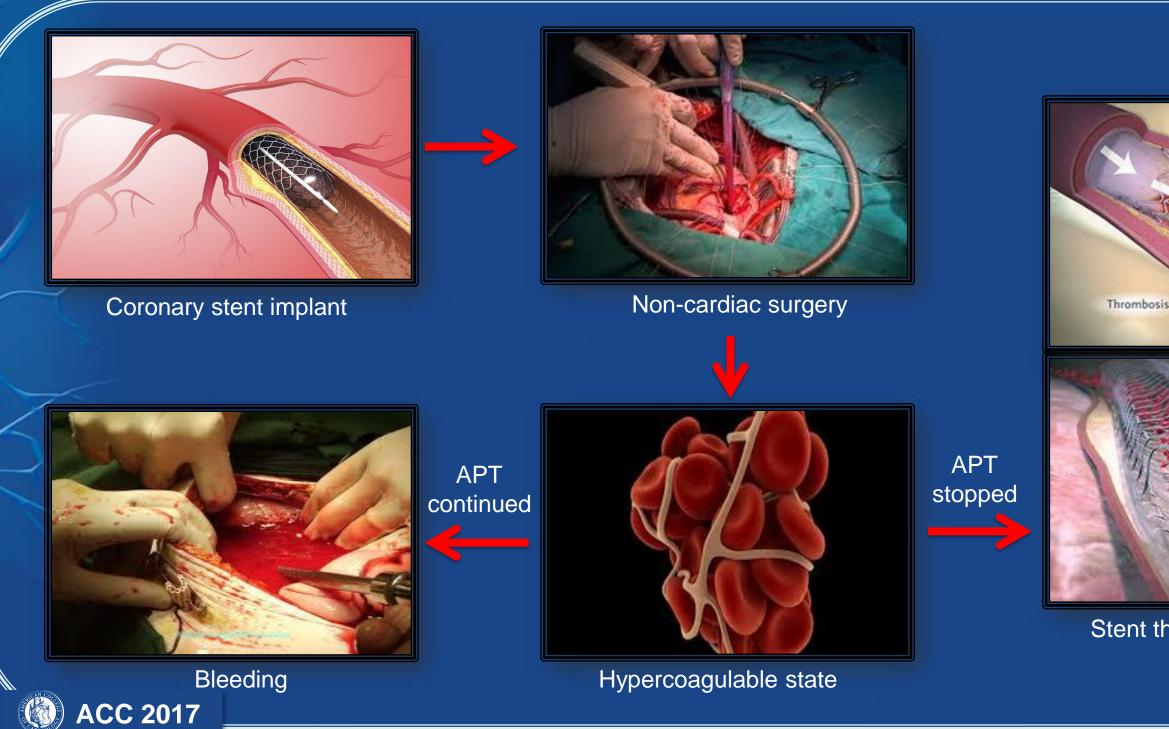
- 5-12% patients post-PCI with DES require non-cardiac surgery procedures (NCS) over an ensuing 12-month period
 - Peri-operative dual anti-platelet therapy (DAPT) \uparrow bleeding & its interruption is associated with a heightened risk of ischemic complications
 - Spectrum of peri-operative complications post-PCI inextricably related to: indication for PCI, timing of surgery, anti-platelet therapy (APT) status, PCI factors (DES, complexity, h/o ST etc) & risk of surgery-ischemic/hemorrhagic

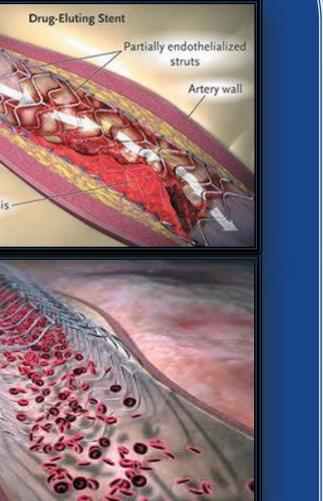


J Am Coll Cardiol 2016;67: 1038–49



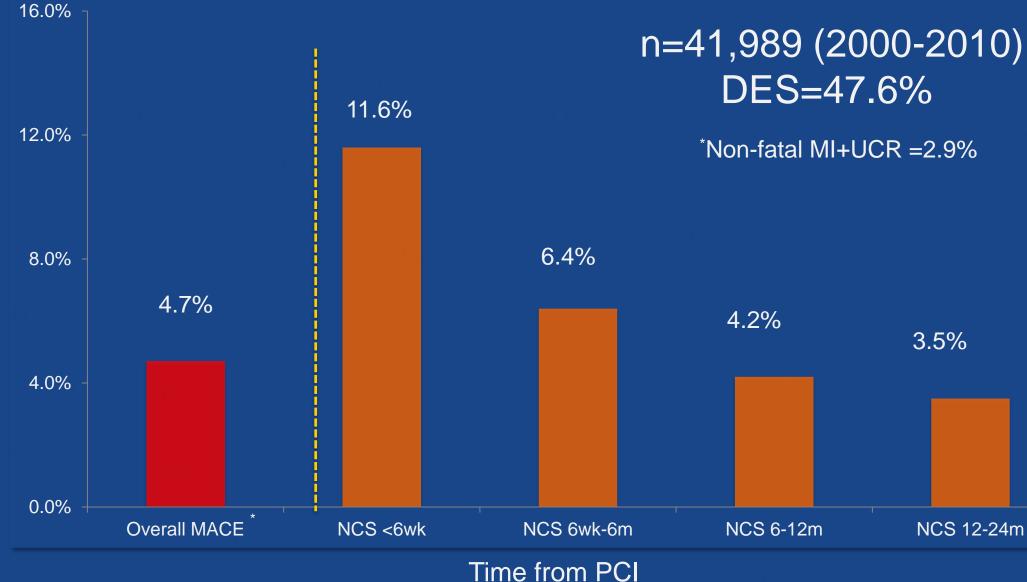
Antiplatelet Therapy Considerations in Post-PCI Patients During Non-Cardiac Surgery





Stent thrombosis & ischemic complications

MACE*: Early Surgery After Stenting Carries Higher Risk Of Ischemic Events





*MACE: 30-day all-cause mortality, MI, & urgent cardiac revascularization (UCR) 95% CI: 4.5-4.9



Hawn et al. JAMA 2013

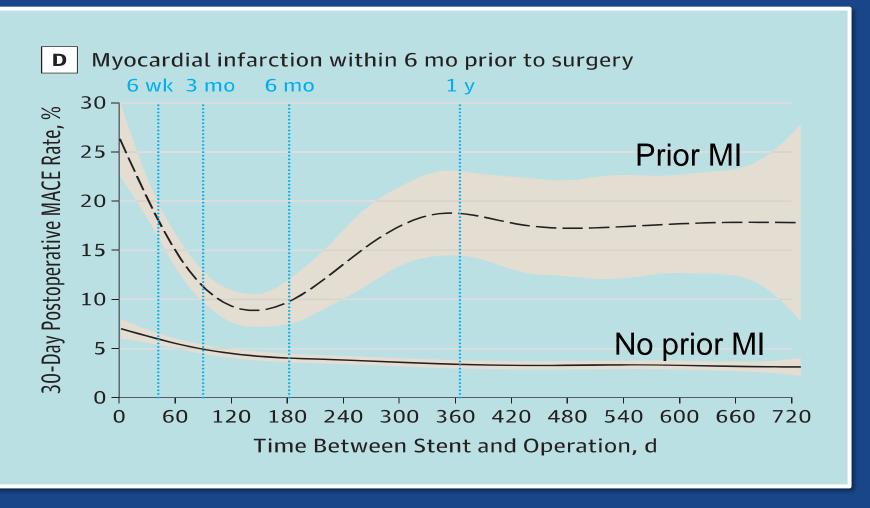
Underlying Ischemic Risk Key Driver of MACE **Following NCS**

Predictors of MACE:

- Timing of NCS
- Non-elective surgery
- **Prior MI**
- Cardiac risk index

Did not predict MACE:

- **Preoperative APT**
- **Cessation of DAPT**
- Stent type
- Type of surgery



Most perioperative ischemic complications driven by non-stented vessel MI & urgent coronary revascularization, *not ST*



*30-day all-cause mortality, MI, & cardiac revascularization

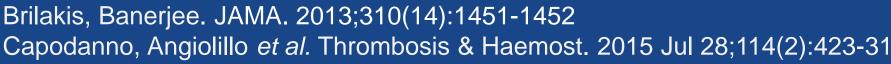


Hawn et al. JAMA 2013

Peri-operative Antiplatelet Therapy Bridge

Options:

- Continue low-dose aspirin through the peri-operative period
- $ASA + P2Y_{12}$ continuation associated with higher bleeding complications
- Peri-operative UF heparin or LMW heparin not acceptable: associated with $\uparrow \uparrow$ MACE
- Short-active (reversible) IV antiplatelet agents: appropriate as peri-operative bridge (tirofiban, eptifibatide, cangrelor)







Determination of Thrombotic Risk

Low Risk (<1%)*	Intermediate Risk (1- 5%)*	High (>5
 >4 weeks after PCI with POBA >6 months after PCI with BMS >12 months after PCI with DES 	 >2 weeks ≤4 weeks after PCI with POBA >1 month ≤6 months after PCI with BMS >6 month ≤12 months after PCI with DES >12 months after complex PCI with DES (long stents, multiple stents, overlapping, small vessels, bifurcations, left main, last remaining vessel) 	≤2 weeks after PCI ≤1 month after PCI ≤6 months after PCI ≤12 months after co ≤6 months after PCI Previous ST

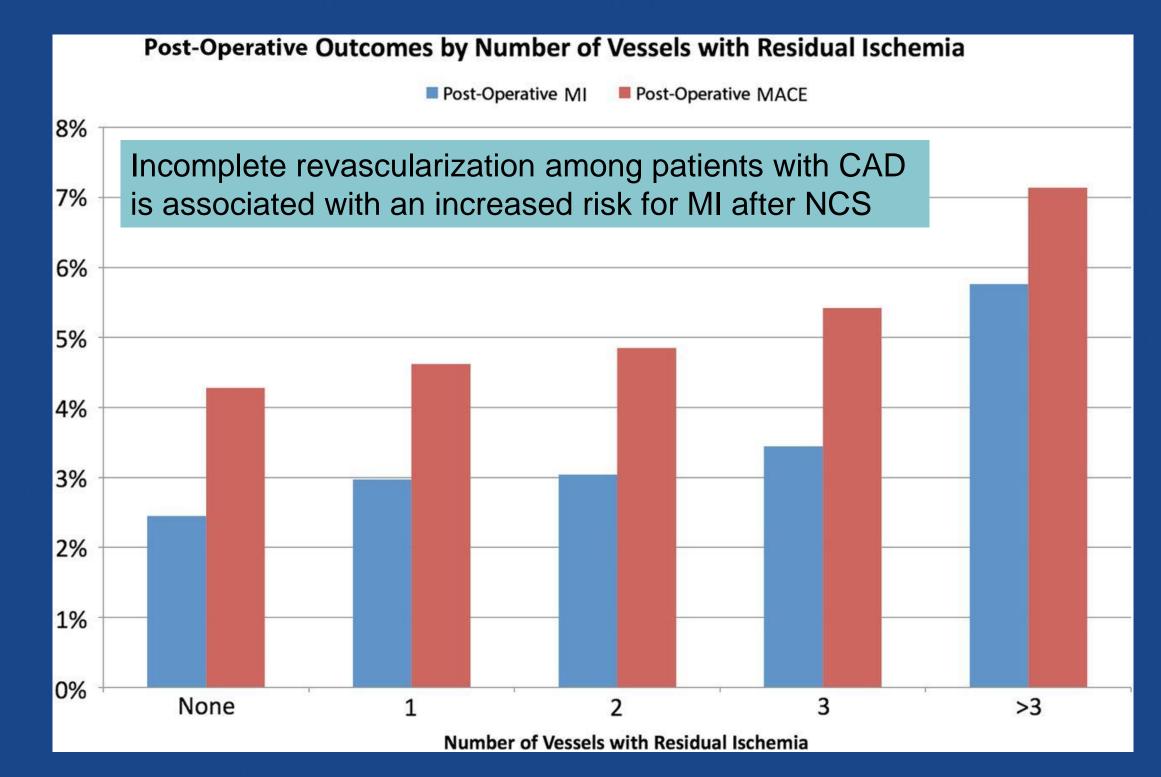
*30-day ischemic event rates of cardiovascular death and MI; PCI: percutaneous coronary intervention; POBA: plain old balloon angioplasty; BMS: bare metal stent; DES; drug-eluting stent; MI: myocardial infarction; ST: stent thrombosis



2014 ESC/ESA Guidelines on non-cardiac surgery Eur Heart J, 35 (2014), pp. 2383–2431

h Risk 5%)* I with POBA I with BMS CI with DES complex PCI with DES CI for MI

Incomplete Coronary Revasc. & Perioperative Ischemia



Armstrong et al. **JACC 2017**

ACC 2017

Determination of Hemorrhagic Risk of Non-cardiac and Cardiac Surgeries

Low Risk

Intermediate Risk



General, Orthopedic and Urologic Surgeries

Hernioplasty, plastic surgery of incisional hernias, cholecystectomy, appendectomy, colectomy, gastric resection, intestinal resection, breast surgery, hand surgery, arthroscopy, cystoscopy and uretroscopy

Vascular Surgery

Carotid endarterectomy, bypass or endarterectomy of lower extremity, EVAR, TEVAR, limb amputations

Cardiac Surgery

Hemorrhoidectomy, splenectomy, gastrectomy, bariatric surgery, rectal resection, thyroidectomy, prosthetic shoulder, knee, foot and major spine surgery, prostate biopsy, orchiectomy

Hepatic resection, duodenocefalopancreasectomy, hip, major pelvic and proximal femur fracture surgery, nephrectomy, cystectomy, TIRP, TURBT, prostatectomy

Open abdominal aorta surgery

Open thoracic and thoracoabdominal surgery

Mini-thoracotomy, TAVR (apical approach), OPCAB, CABG, valve replacement

Reintervention, endocarditis, CABG in PCI failure, aortic dissections



Rossini et al. EuroIntervention, 2014. 10(1): p. 38-46

High Risk

		ssment of	Thrombot	ic & Hemor	rk		
Ris	SK	Thrombotic Risk					
	×		Low	Intermediate			
	rhagic risk	Low	ASA, P2Y ₁₂ interruption 5d, resume 24-72h	Postpone; ASA, P2Y ₁₂ interruption 5d, resume 24-72h	P F		
Z	mor	Intermediate	ASA, P2Y ₁₂ interruption 5d, resume 24-72h	Postpone; ASA, P2Y ₁₂ interruption 5d, resume 24-72h	IV		
	Ĩ	High	ASA, P2Y ₁₂ interruption 5d, resume 24-72h	Postpone; ASA, P2Y ₁₂ interruption 5d, resume 24-72h	IV		



Rossini R *et al.* Eurointervention 2014; 10:38-46; *Angiolillo et al. JAMA, 2012. 307(3): p. 265-74



High

Postpone; ASA, P2Y₁₂ continue

APT Bridging

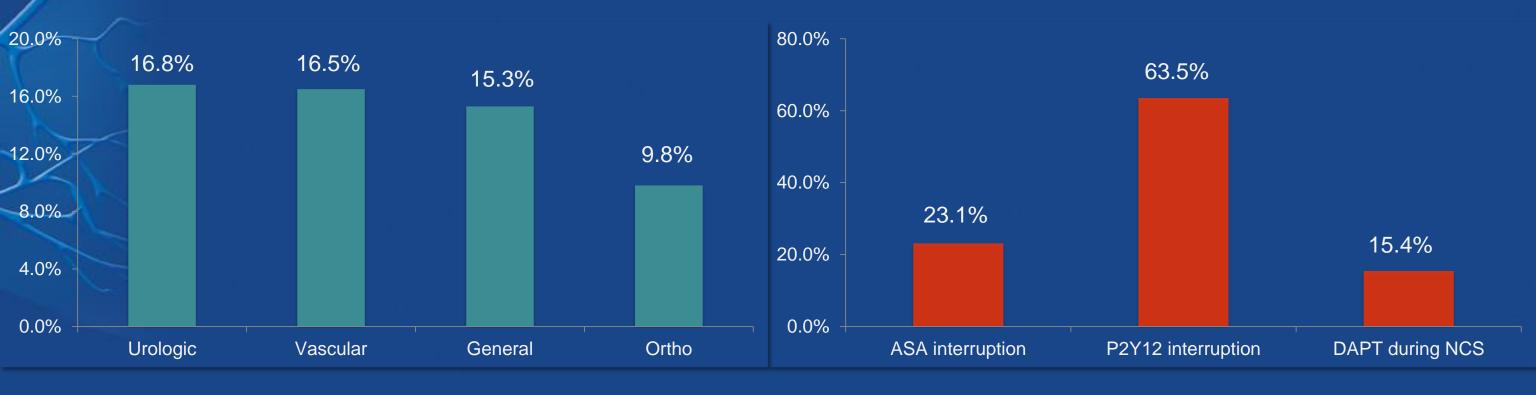
APT Bridging

Surgery After Stenting (SAS) Registry*: Variability In Management

Prospective, June 2013-Dec 2014: n=1137; 18 centers

Top four NCS

Perioperative DAPT management



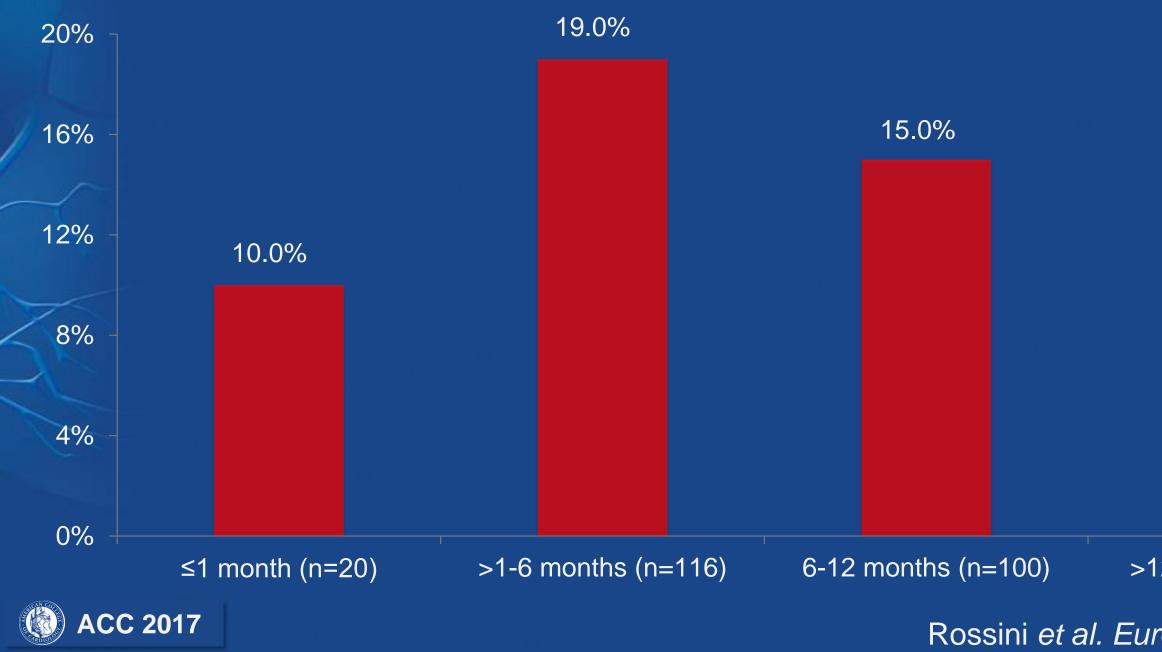


Rossini *et al. CCI* 2017





IV Bridging Based On Time Interval From Stenting **To Surgery**



Rossini et al. Euro PCR 2015; CCI 2017

>12 months (n=846)





Prospective SAS Registry Results

	Outcomes	Event Rates		1-month I	MACE 8	& BA
	In-hospital NACE (Ischemic events + BARC 3-5 bleed)	12.7%	20% -	MAC	E 📕 B	BARC (
	30d-MACE; ST	3.5%; 0.2%	16% -		16%	
2	30d-BARC ≥3 bleeding	11.3%	- 12% 8% -	10%		
1 1	30d-MACE in high thrombotic, intermediate-high bleeding risk group	3.0%	4% -	5%	5%	3%
	DAPT or P2Y12 inhibitor during surgery n predictor of MACE; ASA ↑ bleeds	ot an independent	- 0% -	≤1m (n=20)	<1-6m (n=116)	6- (n=

predictor of MACE; ASA \uparrow bleeds

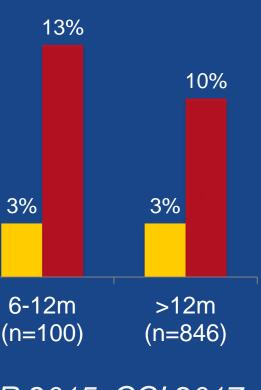
Rossini et al. Euro PCR 2015; CCI 2017





ARC 3-5 Bleed

3-5 bleed



Vorapaxar in ACS Patients Undergoing Surgery

	ACS	Vorapaxar	Placebo	р	-		30-da	ay Clin	ical
	eoperative enopyridine	89%	86%	0.036	6% -		Vorapaxar	(n=1171)	
Stu he	udy drug Id	23%	20%	0.102	4% -	3.9% 3.4%		3.4%	
Su	rgery ≤6m	50%	47%	0.165	2% -			2.8%	
	edian time to rgery	13d	15d	0.431			1.2% 1.0%		0.3%
PCI	=70%; DES=40%;				- 0% +	Primary ischemic	CV death	MI	ST

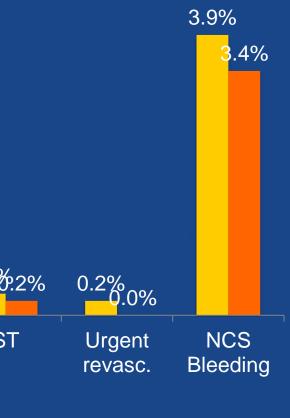
endpoint





Outcomes

Placebo (n=1031)



Diepen et al. JAHA 2015

Frequency of Complications with Bridging Therapy

Meta-analysis of 8 published studies between 2002-2013; n=280

30d-Outcomes	Pooled estimate rate (%)	
ST	1.3%	
Major bleeding	7.4%	
Any bleeding	20.6%	
Transfusion	13.9%	
Death	3.5%	
MI	1.6%	
MACE*	4.6%	

*MACE= death, MI, UCR

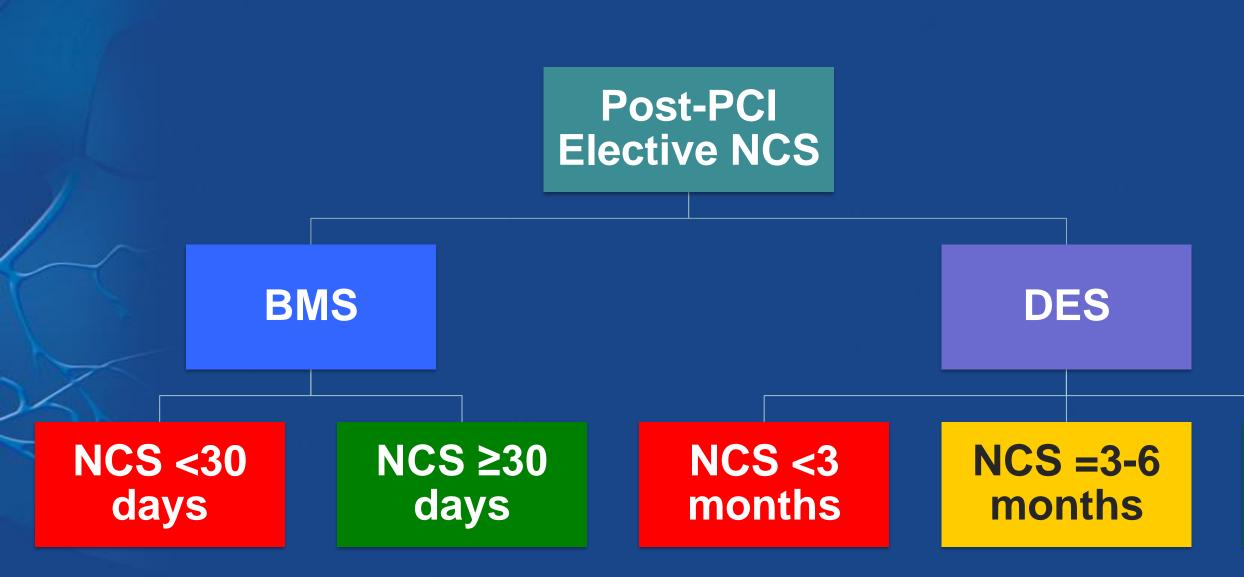
ACC 2017

Warshauer, Brilakis, Banerjee. Cath. Card. interventions 2015



95% Cl	
0.3-3.0	
2.8-14.1	
4.8-43.2	
1.0-38.2	
1.7-5.9	
0.3-3.6	
2.5-7.3	

Guideline Recommendations On Timing of Non-cardiac Surgery Post-PCI





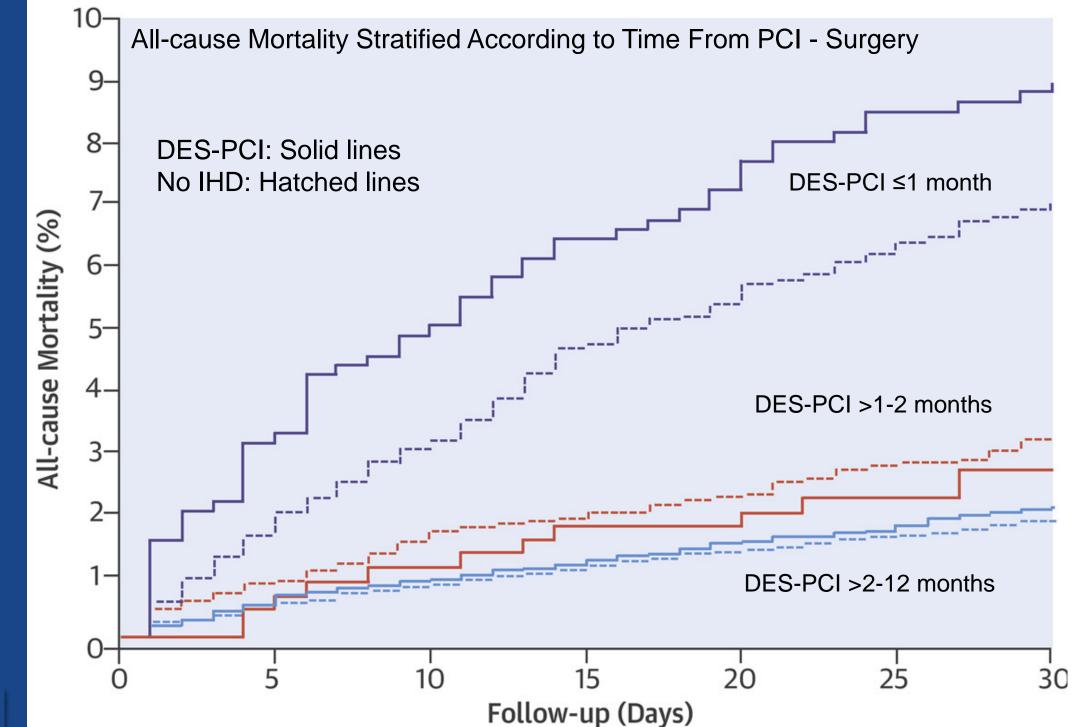
Levine et al. Circulation. 2016;134:e123–e155

I IIa IIb III

ACC/AHA Guidelines

NCS >6 months

Western Denmark Heart Registry & Danish National Patient Register



Egholm et al. JACC Volume 68, Issue 24, 2016, 2622–2632



Western Denmark Heart Registry & Danish National Patient Register

- Surgery in patients treated with DES-PCI is associated with an increased 30-day risk of MI
- Surgery among DES-PCI-treated patients did not increase 30day all-cause mortality
 - Beyond the first month after DES-PCI, these patients had same perioperative risk as surgery in patients without IHD
- Surgery after DES-PCI might be performed earlier without an increased risk



Options For Managing Perioperative DAPT

	Thrombotic Risk					
		Low	Intermediate			
agic ris	Low	ASA, P2Y ₁₂ interruption 5d, resume 24-72h	Postpone; ASA, P2Y ₁₂ interruption 5d, resume 24-72h	P F		
Hemorrhagic risk	Intermediate	ASA, P2Y ₁₂ interruption 5d, resume 24-72h	Postpone; ASA, P2Y ₁₂ interruption 5d, resume 24-72h	IV		
	High	ASA, P2Y ₁₂ interruption 5d, resume 24-72h	Postpone; ASA, P2Y ₁₂ interruption 5d, resume 24-72h	IV		





High

Postpone; ASA, P2Y₁₂ continue

Management of Peri-operative DAPT Post-PCI

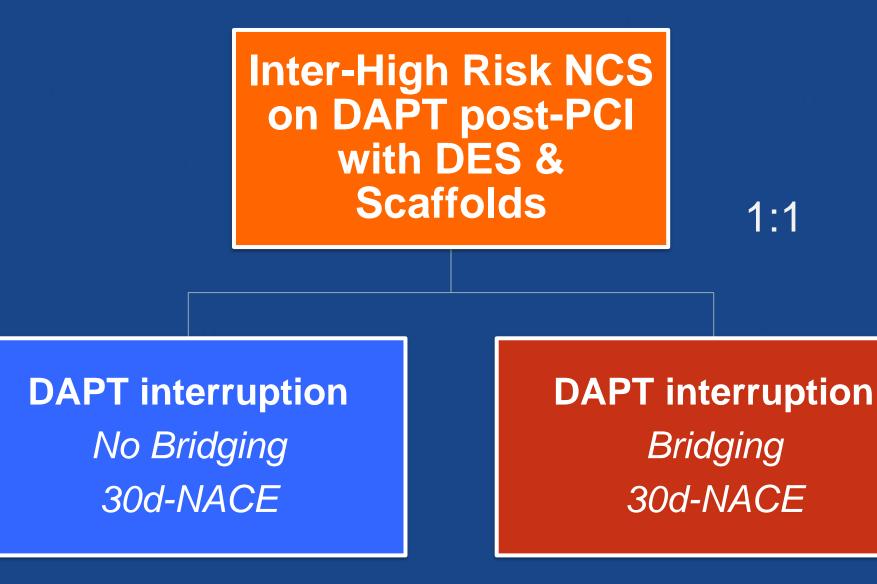
- Millions of patients worldwide affected by DAPT interruption for NCS
- Improved stent safety \rightarrow shorter DAPT durations, however timing of surgery from PCI (esp. post-MI) is an important determinant of perioperative ischemic events
- Proportion of patients undergoing early surgery post-DES implants is expected to increase with shorter DAPT requirements following elective PCI
- Benefit of bridging unclear, scientific equipoise, significant provider & patient uncertainty





'To Bridge or Not to Bridge'

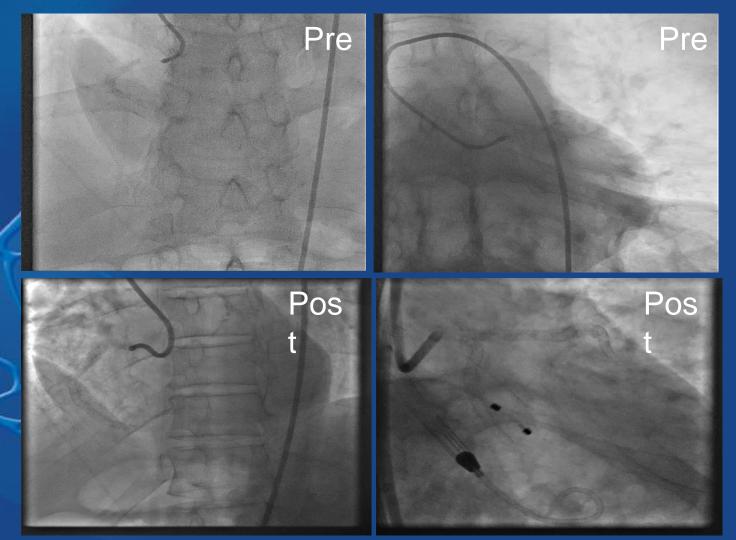
Proposed <u>Management of Antiplatelet Regimen During Noncardiac Surgery (MARS) Trial</u>







Clinical Case Presentation



Discharged on Ticagrelor & ASA 81 mg



76 y male is referred for cor. angio/PCI. He is dyspneic; low-grade fever. PMH: HTN, CKD4. Smoker (steroids), right total hip replacement (THR) ~2m ago. EKG: S. tach; peak troponin 9.0 ng/mL; ECHO: LVEF=35%, inf-lat. HK, PASP=70 mm Hg. Readmitted on 45 day post-PCI: rt. hip pain, fever/rigor fatigue. CT & ortho eval.: possible rt. deep joint infection; surgical debridement recommended. Peri-operative DAPT management options:

- 1. Delay orthopedic revision by at least 3m
- 2. Operate on ASA + Ticagrelor
- 3. Hold Ticagrelor (5d), cont. ASA + Tirofiban bridge
- 4. Hold Ticagrelor (5d), cont. ASA
- 5. None of the above (or other options)