

# Considering DAPT in Difficult Cases

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CHAPTER

# Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
■ Grant/Research Support	None
■ Consulting Fees/Honoraria	Volcano-Philips
■ Major Stock Shareholder/Equity	Technology Solutions Group
■ Royalty Income	None
■ Ownership/Founder	Technology Solutions Group, BioInfo Accelerator Fund
■ Intellectual Property Rights	None
■ Other Financial Benefit	None

# DAPT (Dual AntiPlatelet Therapy)

- Foundations for DAPT therapy
- Importance with drug eluting stents (DES)
- Difficult patient subsets
  - Those who also need antithrombin therapy, or oral anticoagulants (OAC)
  - Those who need surgery early after initiation
  - Those who develop serious bleeding
  - Those who develop stent thrombosis on DAPT
- Recommendations for general internists

# Why DAPT?

- Original stents placed in early 1990's without intravascular imaging and at low balloon pressure, usually for "bail out" indications
  - Required extensive anticoagulation to prevent thrombosis (coumadin, dextran, ASA, heparin, dipyridamole). 5-7 days in hospital
- In mid 90's intravascular imaging showed marked stent under-expansion.
  - Columbo et al used higher pressure, better expansion and a new antiplatelet P2Y<sub>12</sub> inhibitor: ticlopidine.
  - No need for antithrombins or OAC: DAPT was born!



# DAPT and DES

- In early 2000's DES developed to combat restenosis
- Initial concern was on cost and proper allocation of these stents
- But then.....
  - Excessive rates of stent thrombosis led to work wide "crisis" regarding how long DAPT was needed
  - DAPT "education" efforts spread to all medical fields

# Late thrombosis in drug-eluting coronary stents after discontinuation of antiplatelet therapy

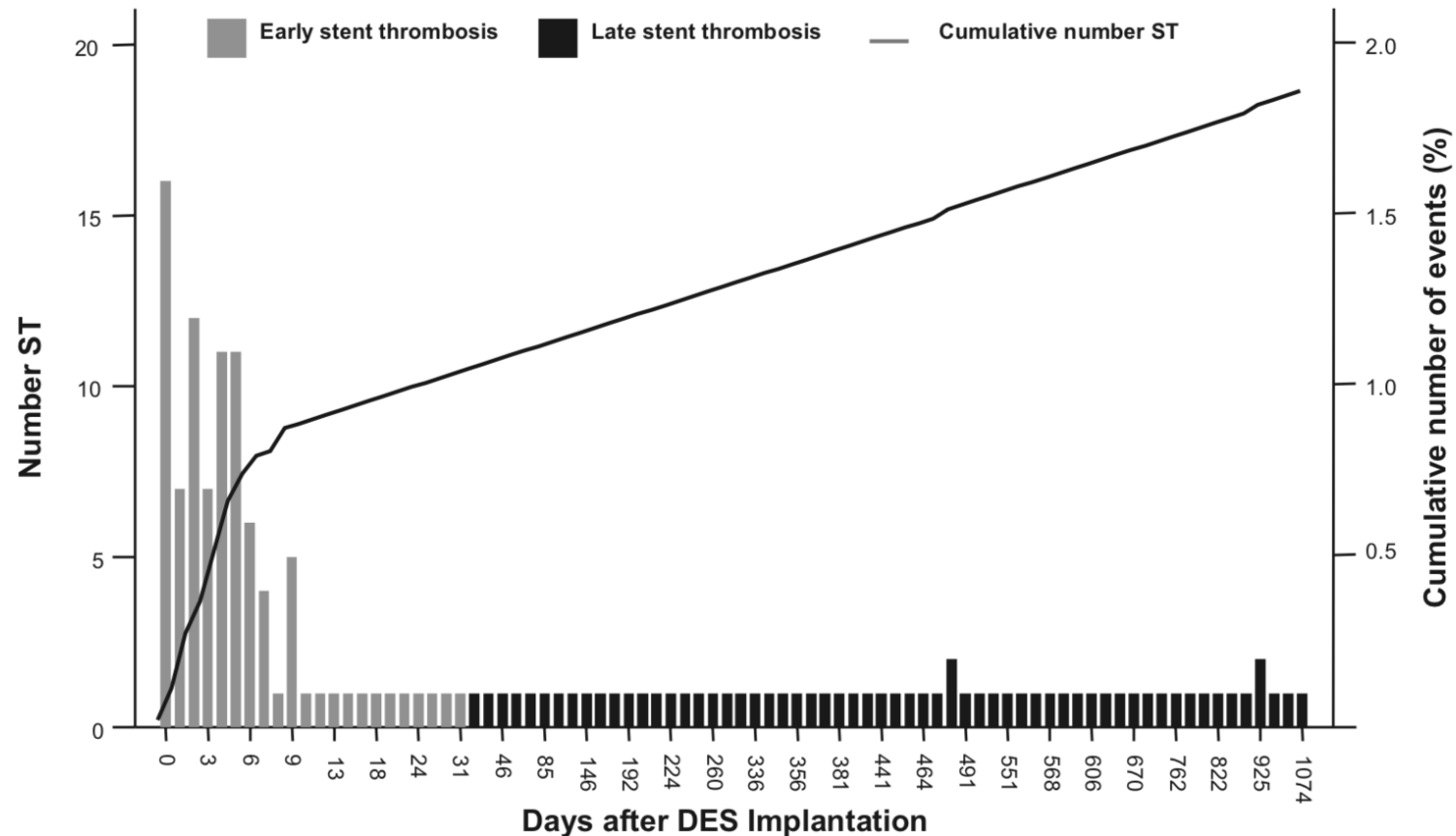
Eugène P McFadden, Eugenio Stabile, Evelyn Regar, Edouard Cheneau, Andrew T L Ong, Timothy Kinnaird, William O Suddath, Neil J Weissman, Rebecca Torguson, Kenneth M Kent, August D Pichard, Lowell F Satler, Ron Waksman, Patrick W Serruys

Although the safety profiles of coronary stents eluting sirolimus or paclitaxel do not seem to differ from those of bare metal stents in the short-to-medium term, concern has arisen about the potential for late stent thromboses related to delayed endothelialisation of the stent struts. We report four cases of angiographically-confirmed stent thrombosis that occurred late after elective implantation of polymer-based paclitaxel-eluting (343 and 442 days) or sirolimus-eluting (335 and 375 days) stents, and resulted in myocardial infarction. All cases arose soon after antiplatelet therapy was interrupted. If confirmed in systematic long-term follow-up studies, our findings have potentially serious clinical implications.

Lancet 2004; 364:1519-21

# A new issue with DES: Late thrombosis

1956 *Circulation* October 23, 2007

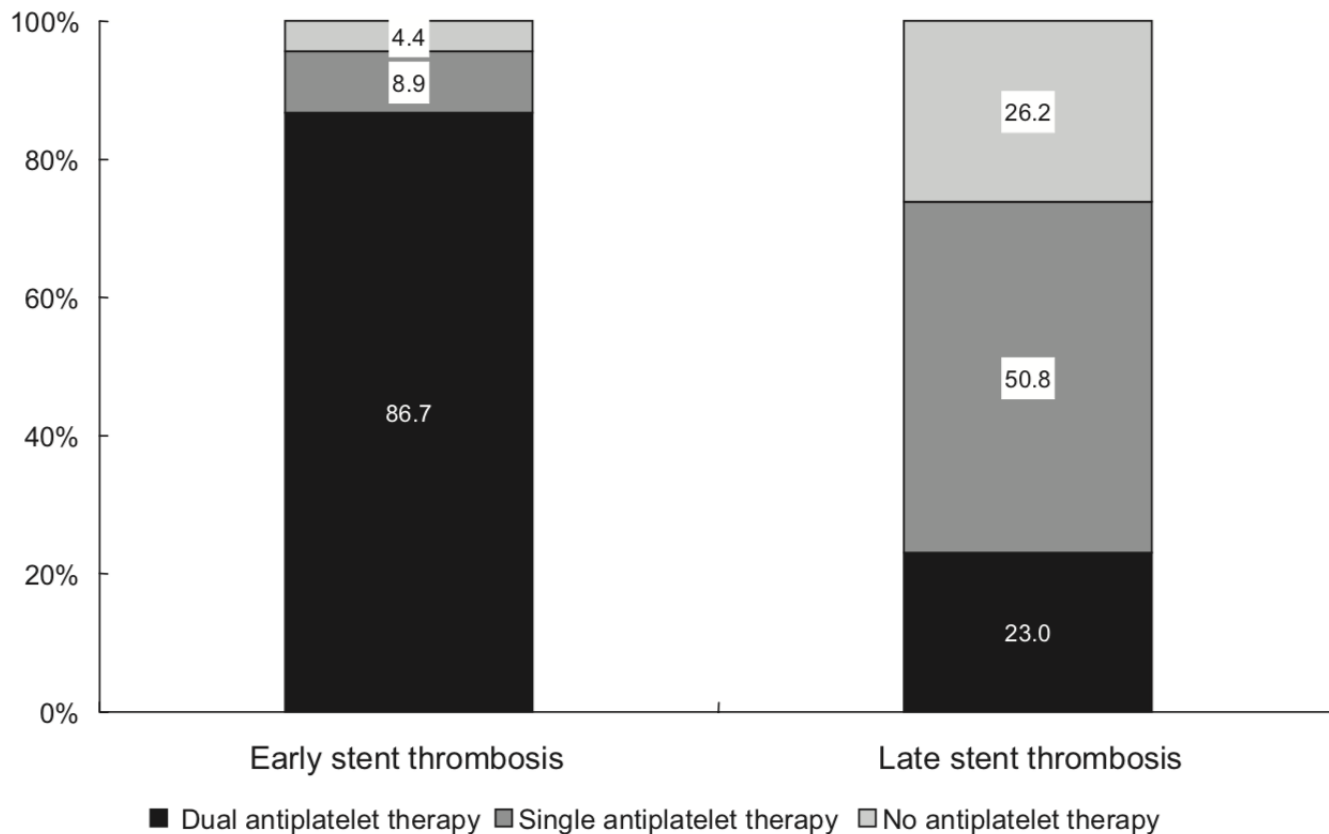


**Figure 5.** Frequency distribution over time of ST in 152 of 8146 consecutive DES patients. Early ST cases are gray (91 patients); late ST cases (61 patients) are black. The line shows the cumulative number of events over time. Reproduced from Daemen et al,<sup>11</sup> copyright © 2007, with permission from Elsevier.

*Circulation*. 2007;116:1952-1965

# Most Late ST patients NOT on DAPT

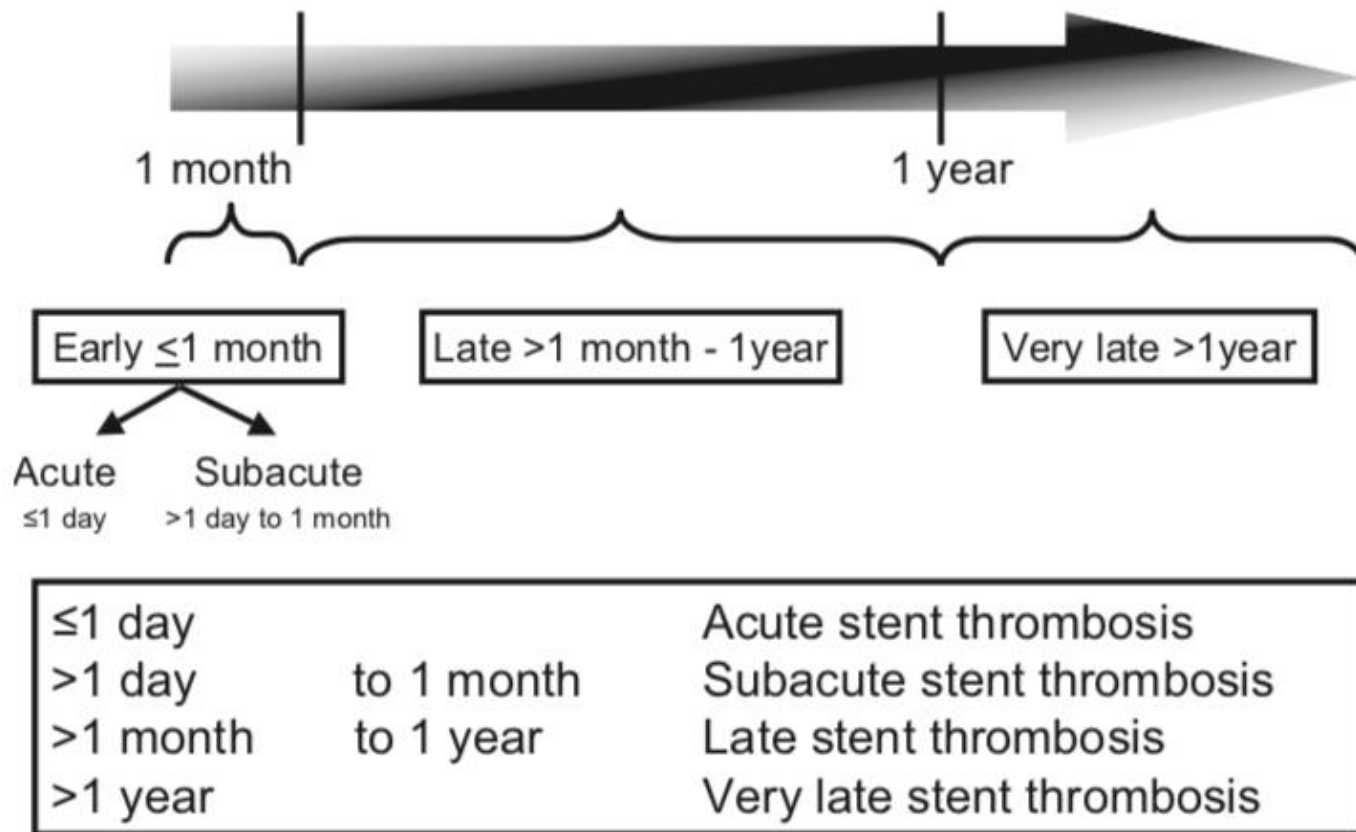
1958    *Circulation*    October 23, 2007



**Figure 7.** Antiplatelet treatment at the time of DES thrombosis in 152 patients. Proportion of patients with early (left column; 91 patients) and late (right column; 61 patients) ST, respectively, treated with dual, single, or no antiplatelet therapy. Data from Daemen et al.<sup>11</sup>

*Circulation.* 2007;116:1952-1965

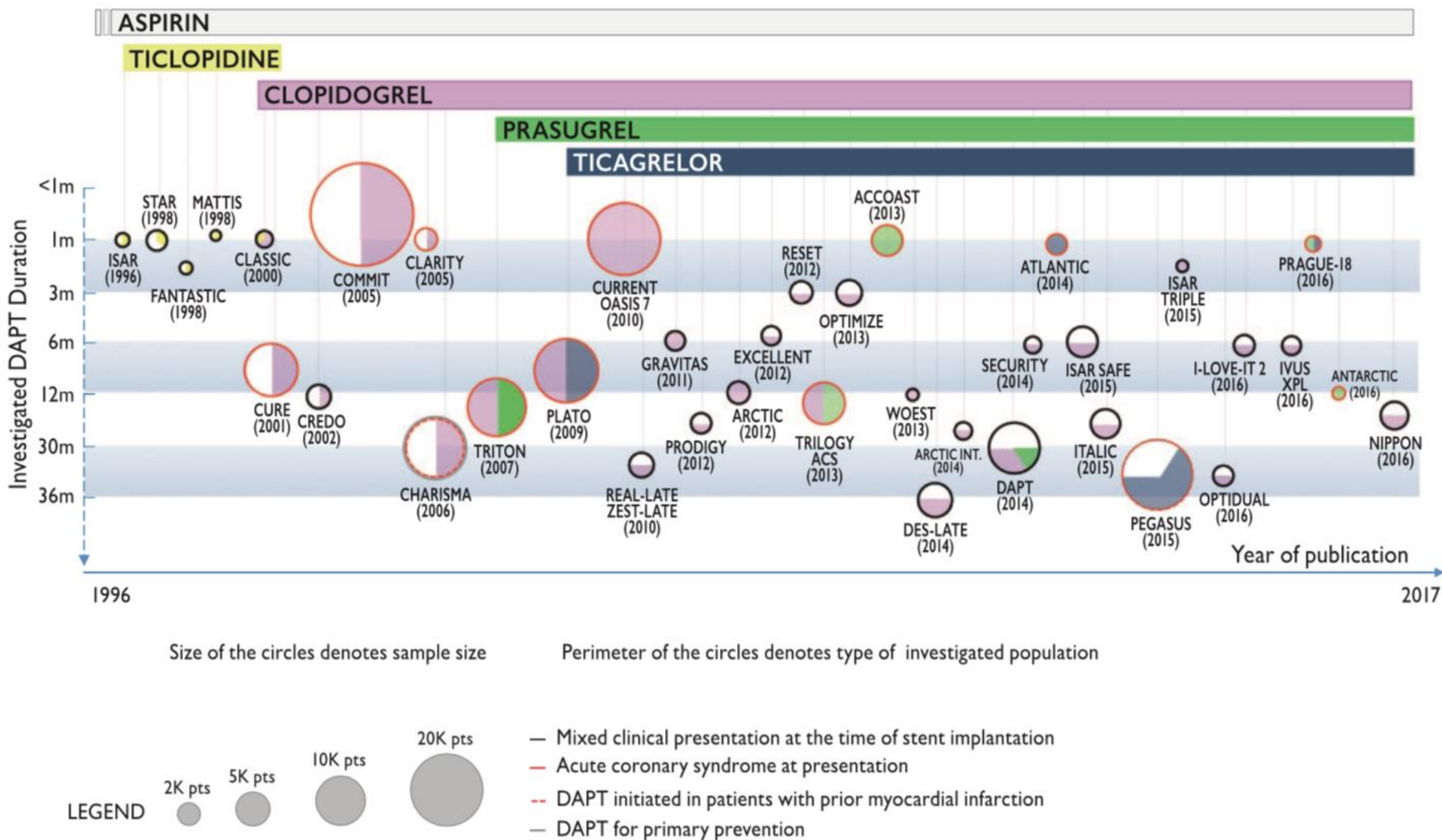
# Time Frame of Stent Thrombosis



*Circulation.* 2007;116:1952-1965

# Further P2Y<sub>12</sub> development

- Clopidogrel: better than Ticlopidine with fewer side effects
- Ticagrelor: better than Clopidogrel
- Prasugrel: better than Clopidogrel
- Cangrelor: iv and ultrashort acting





**ACC/AHA FOCUSED UPDATE**

# 2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease



A Report of the American College of Cardiology/American Heart Association  
Task Force on Clinical Practice Guidelines

An Update of the 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention,  
2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery, 2012 ACC/AHA/ACP/AATS/  
PCNA/SCAI/STS Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart  
Disease, 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction,  
2014 AHA/ACC Guideline for the Management of Patients With Non-ST-Elevation Acute Coronary  
Syndromes, and 2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and  
Management of Patients Undergoing Noncardiac Surgery



European Society  
of Cardiology

European Heart Journal (2018) **39**, 213–254  
doi:10.1093/eurheartj/ehx419

**ESC GUIDELINES**

# **2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS**

**The Task Force for dual antiplatelet therapy in coronary artery disease of the European Society of Cardiology (ESC) and of the European Association for Cardio-Thoracic Surgery (EACTS)**

**Authors/Task Force Members: Marco Valgimigli\* (Chairperson) (Switzerland), Héctor Bueno (Spain), Robert A. Byrne (Germany), Jean-Philippe Collet (France), Francesco Costa (Italy), Anders Jeppsson<sup>1</sup> (Sweden), Peter Jüni (Canada), Adnan Kastrati (Germany), Philippe Kolh (Belgium), Laura Mauri (USA), Gilles Montalescot (France), Franz-Josef Neumann (Germany), Mate Petricevic<sup>1</sup> (Croatia), Marco Roffi (Switzerland), Philippe Gabriel Steg (France), Stephan Windecker (Switzerland), and Jose Luis Zamorano (Spain)**



Canadian Journal of Cardiology 34 (2018) 214–233

## Society Guidelines

# 2018 Canadian Cardiovascular Society/Canadian Association of Interventional Cardiology Focused Update of the Guidelines for the Use of Antiplatelet Therapy

Shamir R. Mehta, MD, MSc (co-chair),<sup>a</sup> Kevin R. Bainey, MD,<sup>b</sup> Warren J. Cantor, MD,<sup>c</sup>  
Marie Lordkipanidzé, BPharm, PhD,<sup>d</sup> Guillaume Marquis-Gravel, MD,<sup>d</sup>  
Simon D. Robinson, MBChB, MD,<sup>e</sup> Matthew Sibbald, MD, PhD,<sup>a</sup> Derek Y. So, MD,<sup>f</sup>  
Graham C. Wong, MD, MPH,<sup>g</sup> Joseph G. Abunassar, MD,<sup>f</sup> Margaret L. Ackman, PharmD,<sup>b</sup>  
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Sean van Diepen, MD,<sup>b</sup> Subodh Verma, MD,<sup>k</sup> G.B. John Mancini, MD,<sup>g</sup> John A. Cairns, MD,<sup>g</sup>  
and Jean-François Tanguay, MD (co-chair);<sup>d</sup> and members of the Secondary Panel

# General considerations

- Balancing thrombotic events with bleeding events
- Liberal use of risk estimating scores
- All aspirin doses are 81mg
- Choice of P2Y<sub>12</sub> depends on the balance
  - Clopidogrel less effect on platelets
  - Ticagrelor more effect on platelets
  - Prasugrel more effect, but risk in prior CVA
- Clinical syndrome class effect: Stable (SIHD) or acute coronary syndrome (STEMI, NSTEMI)

# Risk Estimators

- Precise DAPT: “balanced score” for duration of DAPT only
- CHA<sub>2</sub>DS<sub>2</sub>-VASc : “thrombosis score” for afib
- HAS-BLED: “bleeding score” for OAC

# “Balanced” Risk Scores: DAPT duration

	PRECISE-DAPT score <sup>18</sup>
Time of use	At the time of coronary stenting
DAPT duration strategies assessed	Short DAPT (3–6 months) vs. Standard/long DAPT (12–24 months)
Score calculation <sup>a</sup>	<div> <div>HB</div> <div> <math>\geq 12</math> 11-5 11 10-5 <math>\leq 10</math> </div> </div> <div> <div>WBC</div> <div> <math>\leq 5</math> 8 10 12 14 16 18 <math>\geq 20</math> </div> </div> <div> <div>Age</div> <div> <math>\leq 50</math> 60 70 80 <math>\geq 90</math> </div> </div> <div> <div>CrCl</div> <div> <math>\geq 100</math> 80 60 40 20 0 </div> </div> <div> <div>Prior Bleeding</div> <div> No Yes </div> </div> <div> <div>Score Points</div> <div> 0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 </div> </div>
Score range	0 to 100 points
Decision making cut-off suggested	Score $\geq 25 \rightarrow$ Short DAPT Score $< 25 \rightarrow$ Standard/long DAPT
Calculator	<a href="http://www.precisedaptscore.com">www.precisedaptscore.com</a>

**Table 3. Published risk assessment tools for determining duration of DAPT**

Score name	Online calculator	Patient population	Score description
PRECISE-DAPT <sup>22</sup>	<a href="http://www.precisedaptscore.com/predapt/index.html">www.precisedaptscore.com/predapt/index.html</a>	PCI with or without ACS	Estimates 1-year rates of ischemic and bleeding events for patients treated with PCI. Patients with PRECISE-DAPT score > 25 have higher predicted rates of bleeding events and similar rates of ischemic events with shortened DAPT (3-6 months vs 12-24 months)
CALIBER <sup>17</sup>	<a href="https://farr-data-lab.shinyapps.io/caliber-prolonged_dapt_benefits_harms_risks">https://farr-data-lab.shinyapps.io/caliber-prolonged_dapt_benefits_harms_risks</a>	Patients surviving 1 year after MI including those treated with or without PCI	Estimates ischemic and bleeding events 2-6 years after MI with and without prolonged DAPT
DAPT <sup>19</sup>	<a href="http://tools.acc.org/DAPTriskapp/#!/content/calculator">http://tools.acc.org/DAPTriskapp/#!/content/calculator</a>	Patients 1 year after PCI without bleeding or ischemic events	Estimates the net benefit between ischemic and bleeding events with prolonged DAPT. Patients with DAPT score $\geq 2$ had fewer ischemic and bleeding events with prolonged DAPT (>12 months)



# Thrombosis risk score for afib: CHA<sub>2</sub>DS<sub>2</sub>-VASc

(b) Risk factor-based approach expressed as a point based scoring system, with the acronym CHA <sub>2</sub> DS <sub>2</sub> -VASc (Note: maximum score is 9 since age may contribute 0, 1, or 2 points)	
Risk factor	Score
Congestive heart failure/LV dysfunction	1
Hypertension	1
Age $\geq 75$	2
Diabetes mellitus	1
Stroke/TIA/thrombo-embolism	2
Vascular disease <sup>a</sup>	1
Age 65–74	1
Sex category (i.e. female sex)	1
Maximum score	9

a = Prior myocardial infarction, peripheral artery disease, aortic plaque.

# Bleeding Risk Scores: HAS-BLED

## HAS-BLED score

Condition	Points
<b>H</b> - Hypertension	1
<b>A</b> - Abnormal renal or liver function (1 point each)	1 or 2
<b>S</b> - Stroke	1
<b>B</b> - Bleeding	1
<b>L</b> - Labile INRs	1
<b>E</b> - Elderly (> 65 years)	1
<b>D</b> - Drugs or alcohol (1 point each)	1 or 2

HAS-BLED score	Bleeds per 100 patient-years
0	1.13
1	1.02
2	1.88
3	3.74
4	8.70
5	12.5

Note: HAS-BLED has been validated for warfarin, but not for the new anticoagulants.

# Smartphone calculator apps:



Qx Calculate



Precise DAPT



SCAI AUC Tools

**CHA<sub>2</sub>DS<sub>2</sub>-VASc**

**HAS-BLED**

# Balancing Ischemia vs. Bleeding

**Table 1.** High-risk clinical and angiographic events

Feature
Clinical <sup>14</sup>
Before myocardial infarction or troponin-
Diabetes mellitus treated with oral hypog
Chronic kidney disease (creatinine cleara
Previous stent thrombosis
Current smoker
Angiographic
Multiple stents ( $\geq 3$ stents implanted, $\geq$
biodegradable vascular scaffold
Long lesion length ( $>60$ mm total stent length) <sup>15</sup>
Complex lesions (bifurcation treated with 2 stents, stenting of chronic
occlusion) <sup>15</sup>
Left main or proximal LAD stenting <sup>16</sup>
Multivessel PCI <sup>17</sup>
LAD, left anterior descending artery; PCI, percutaneous coronary intervention.

**Table 5** High-risk features of stent-driven recurrent ischaemic events

• Prior stent thrombosis on adequate antiplatelet therapy
• Stenting of the last remaining patent coronary artery
• Diffuse multivessel disease especially in diabetic patients
• Chronic kidney disease (i.e. creatinine clearance $<60$ mL/min)
• At least three stents implanted
• At least three lesions treated
• Bifurcation with two stents implanted
• Total stent length $>60$ mm
• Treatment of a chronic total occlusion

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Eur Heart J 2018;39:213-254

# Balancing Ischemia vs. Bleeding

**Table 2. Factors associated with increased bleeding risk**

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Need for OAC in addition to DAPT
Advanced age (older than 75 years)
Frailty
Anemia with hemoglobin < 110 g/L
Chronic renal failure (creatinine clearance < 40 mL/min)
Low body weight (<60 kg)
Hospitalization for bleeding within past year
Previous stroke/intracranial bleed
Regular need for NSAIDs or prednisone

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DAPT, dual antiplatelet therapy; NSAIDs, nonsteroidal anti-inflammatory drugs; OAC, oral anticoagulation.

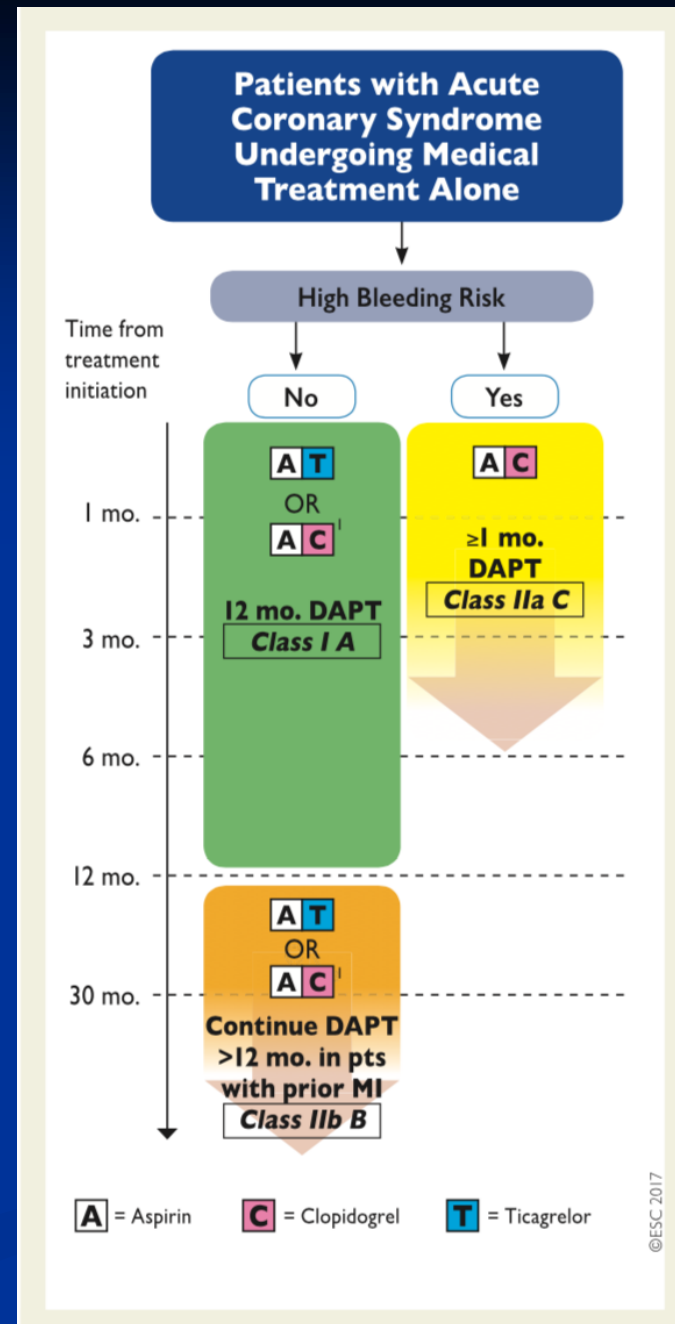
**TABLE 4****Clinical and Procedural Factors Associated With Increased Ischemic Risk (Including Stent Thrombosis) or Increased Bleeding Risk (62-70)**

<b>Increased Ischemic Risk/Risk of Stent Thrombosis (may favor longer-duration DAPT)</b>	<b>Increased Bleeding Risk (may favor shorter-duration DAPT)</b>
<b>Increased ischemic risk</b>	History of prior bleeding
Advanced age	Oral anticoagulant therapy
ACS presentation	Female sex
Multiple prior MIs	Advanced age
Extensive CAD	Low body weight
Diabetes mellitus	CKD
CKD	Diabetes mellitus
<b>Increased risk of stent thrombosis</b>	Anemia
ACS presentation	Chronic steroid or NSAID therapy
Diabetes mellitus	
Left ventricular ejection fraction <40%	
First-generation drug-eluting stent	
Stent undersizing	
Stent underdeployment	
Small stent diameter	
Greater stent length	
Bifurcation stents	
In-stent restenosis	

ACS indicates acute coronary syndrome; CAD, coronary artery disease; CKD, chronic kidney disease; DAPT, dual antiplatelet therapy; MI, myocardial infarction; and NSAID, nonsteroidal anti-inflammatory drug.

# Medical treatment: NO stent

12 months DAPT  
Unless high bleeding risk (HBR)



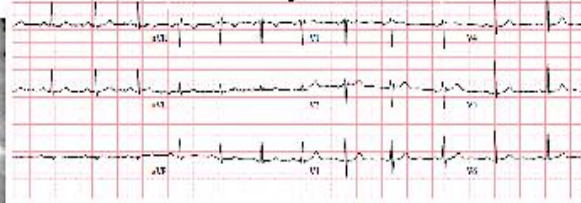


# Simple Stent Case: STEMI

February 5, 2017 @ 18:22



January 2, 2017



Total Occlusion of  
LAD

Interventional wire  
& balloon  
established flow

DES to the LAD

## PCI for STEMI or NSTEMI/ACS

### DAPT for 1 year

ASA 81 mg OD +  
Ticagrelor 90 mg BID **or** Prasugrel 10 mg OD  
preferred over  
Clopidogrel 75 mg OD

### At 1 year, determine bleeding risk

Not at high risk of bleeding<sup>1</sup>

### Continue DAPT for up to 3 years

ASA 81 mg OD +  
Ticagrelor 60 mg BID **or**  
Clopidogrel 75 mg OD<sup>2</sup>

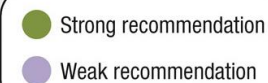
High risk of bleeding<sup>1</sup>

### SAPT

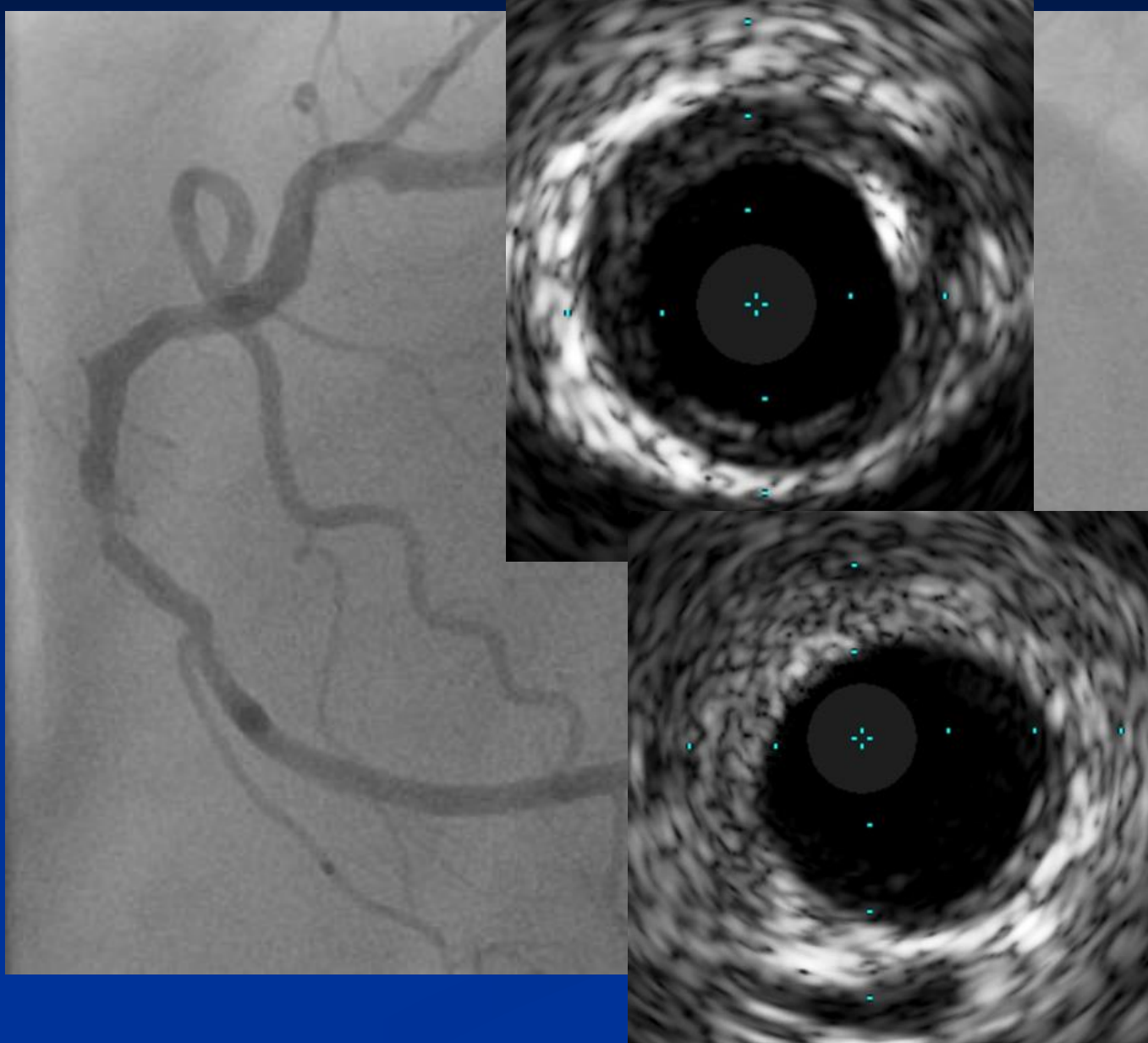
ASA 81 mg OD  
**or**  
Clopidogrel 75 mg OD

<sup>1</sup> Factors associated with increased bleeding risk include: need for OAC in addition to DAPT, advanced age (> 75 years), frailty, anemia with hemoglobin < 110 g/dL, chronic renal failure (creatinine clearance < 40 mL/min), low body weight (< 60 kg), hospitalization for bleeding within last year, prior stroke/intracranial bleed, regular need for NSAIDs or prednisone

<sup>2</sup> Instead of ticagrelor or clopidogrel, prasugrel 5-10 mg daily is also an option (weak recommendation)

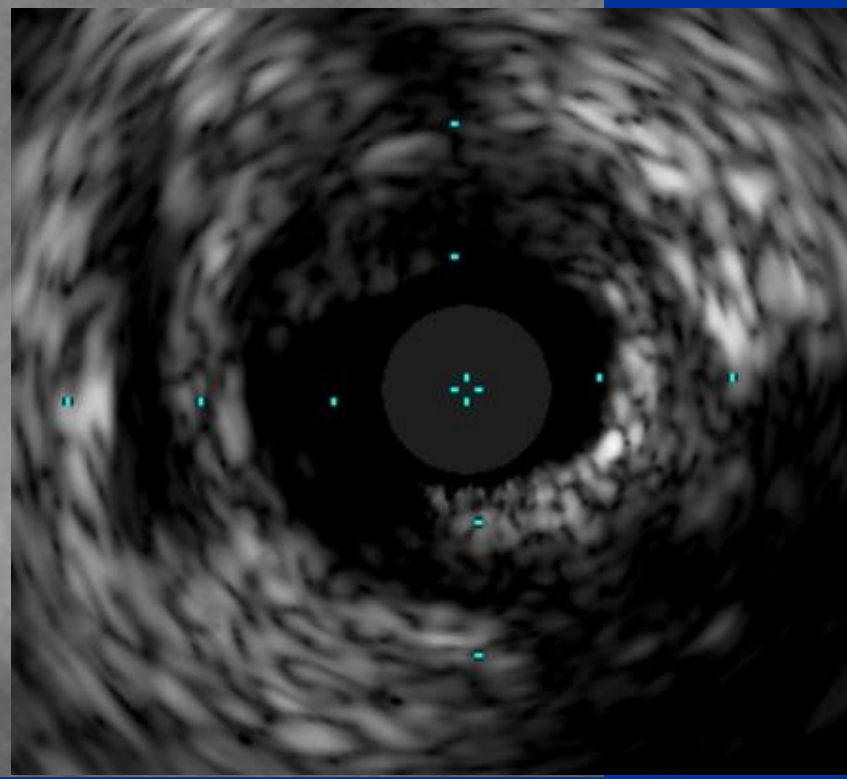
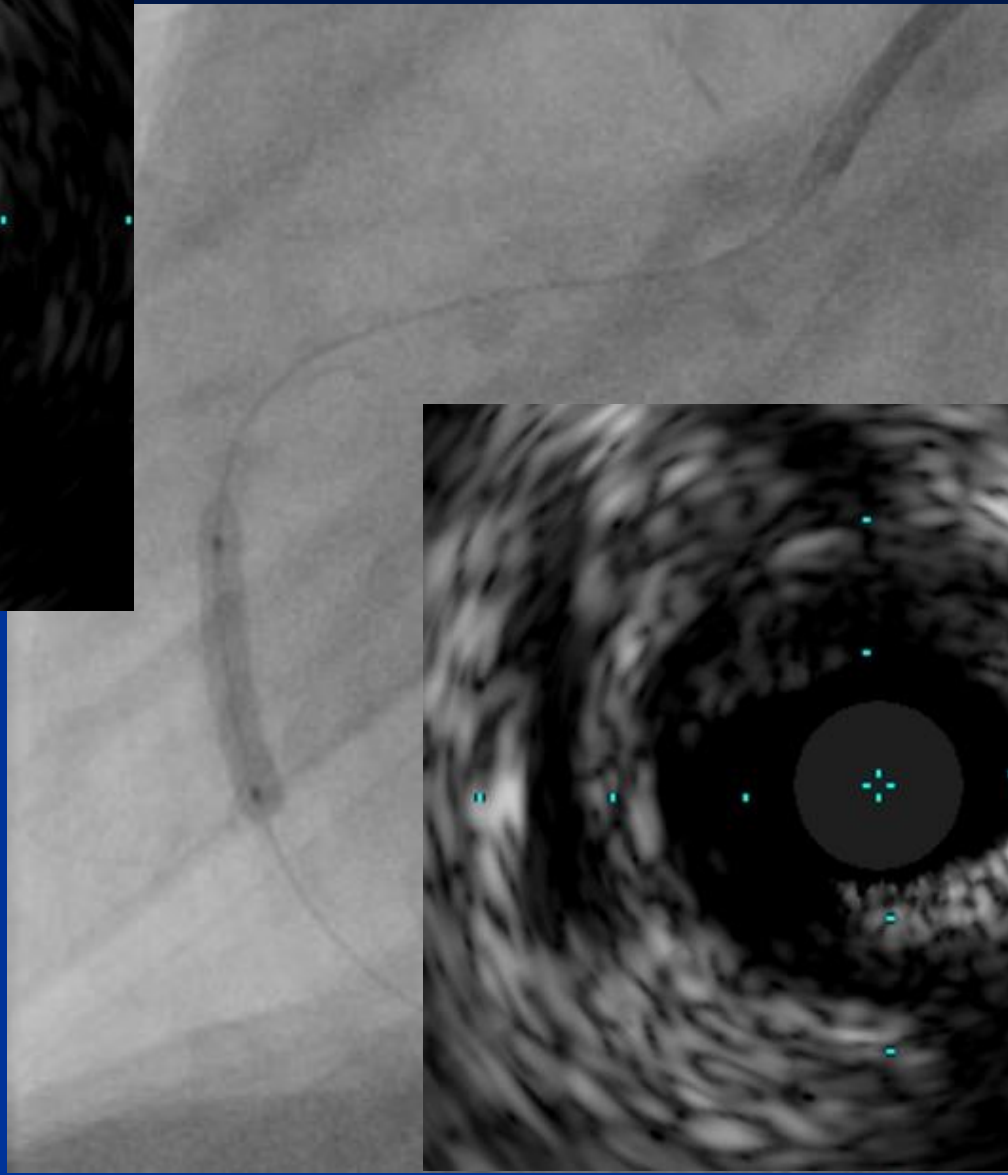
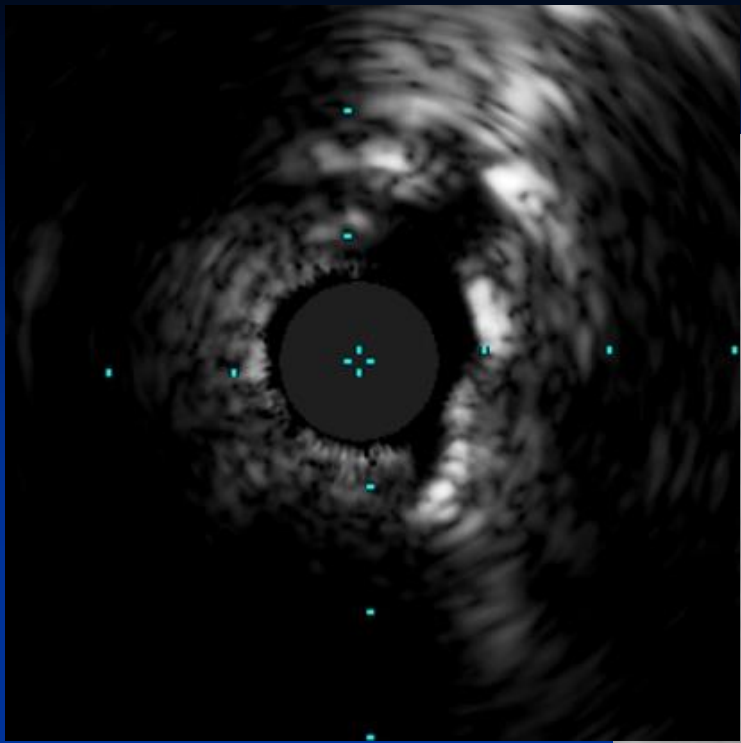


# Elective PCI: some nuances



IVUS  
will not  
pass  
lesion

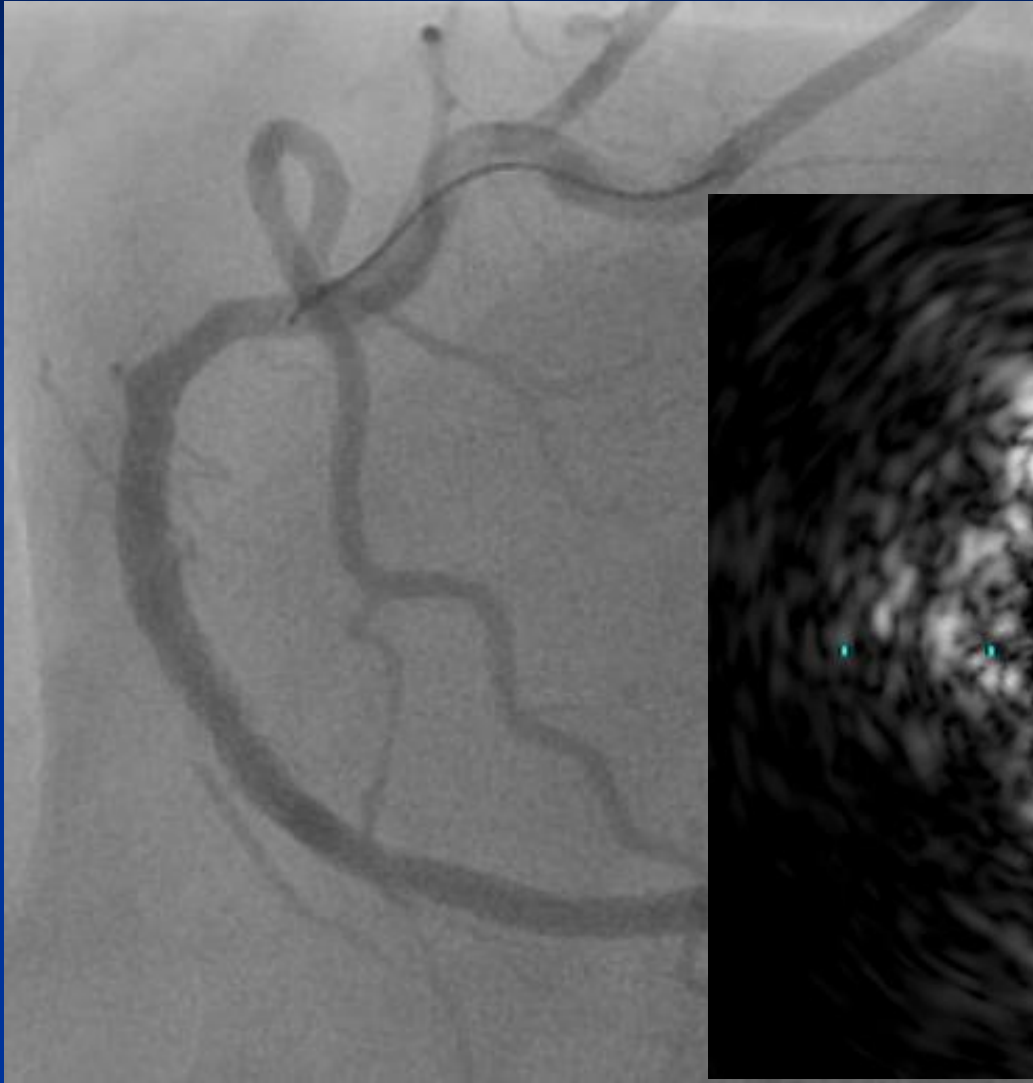
Reference  
diameter:  
2.9mm



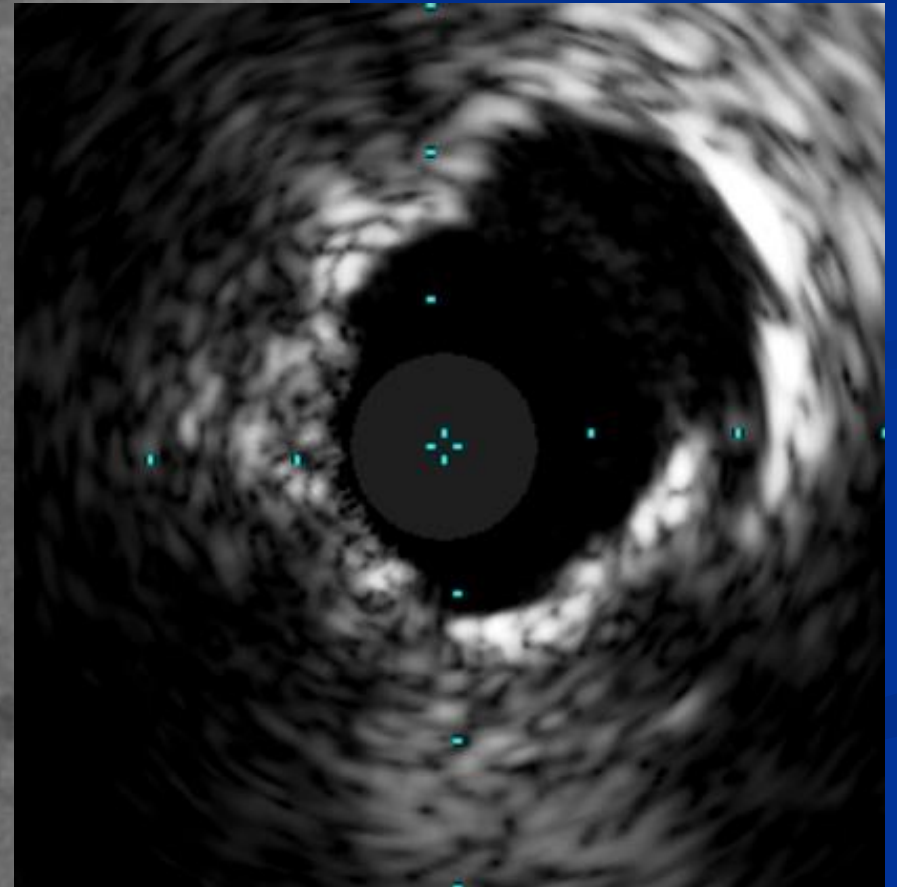
Pre-dilate with 3.0  
noncompliant  
balloon, then re-  
check IVUS:  
dissections seen

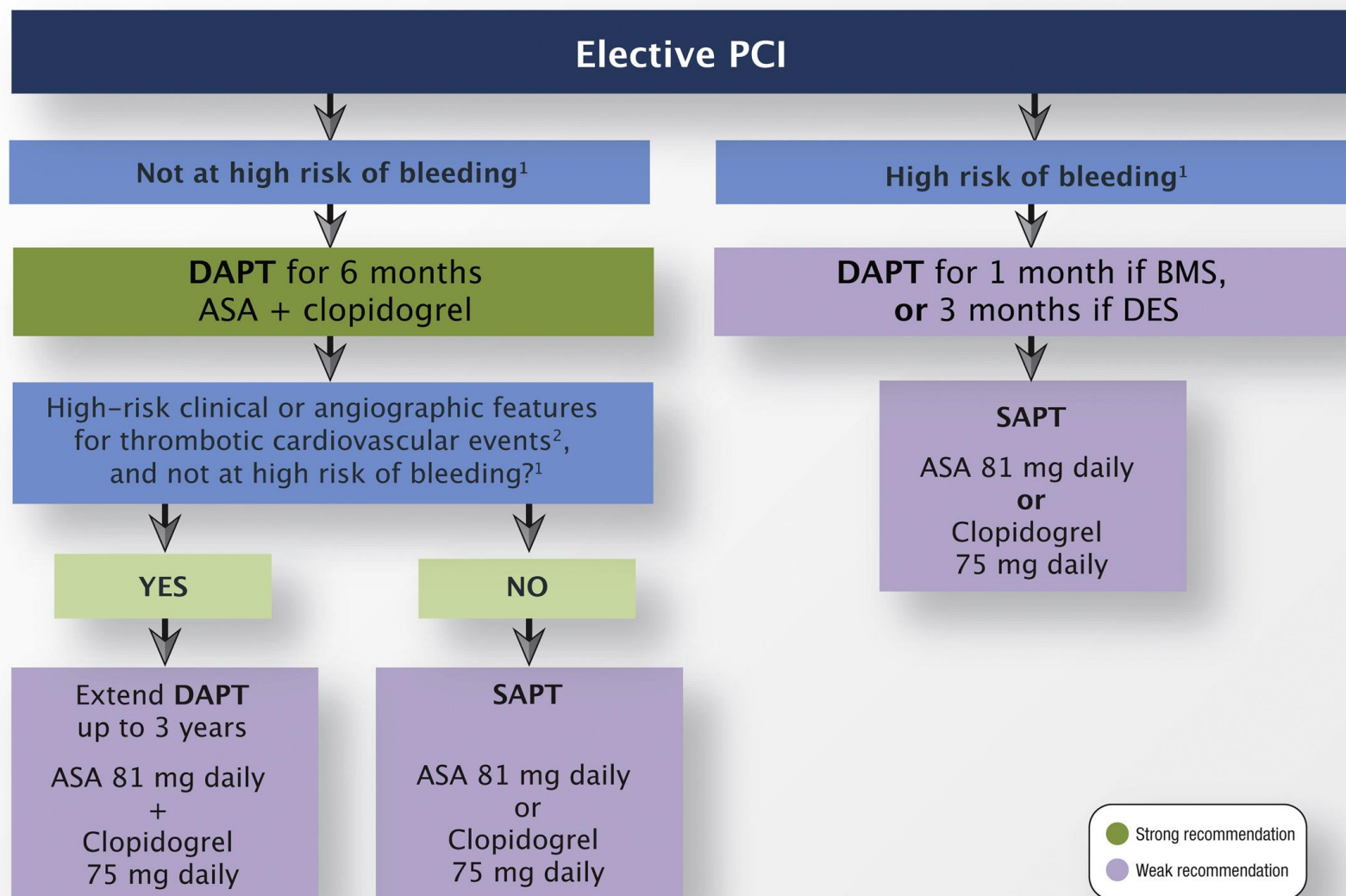


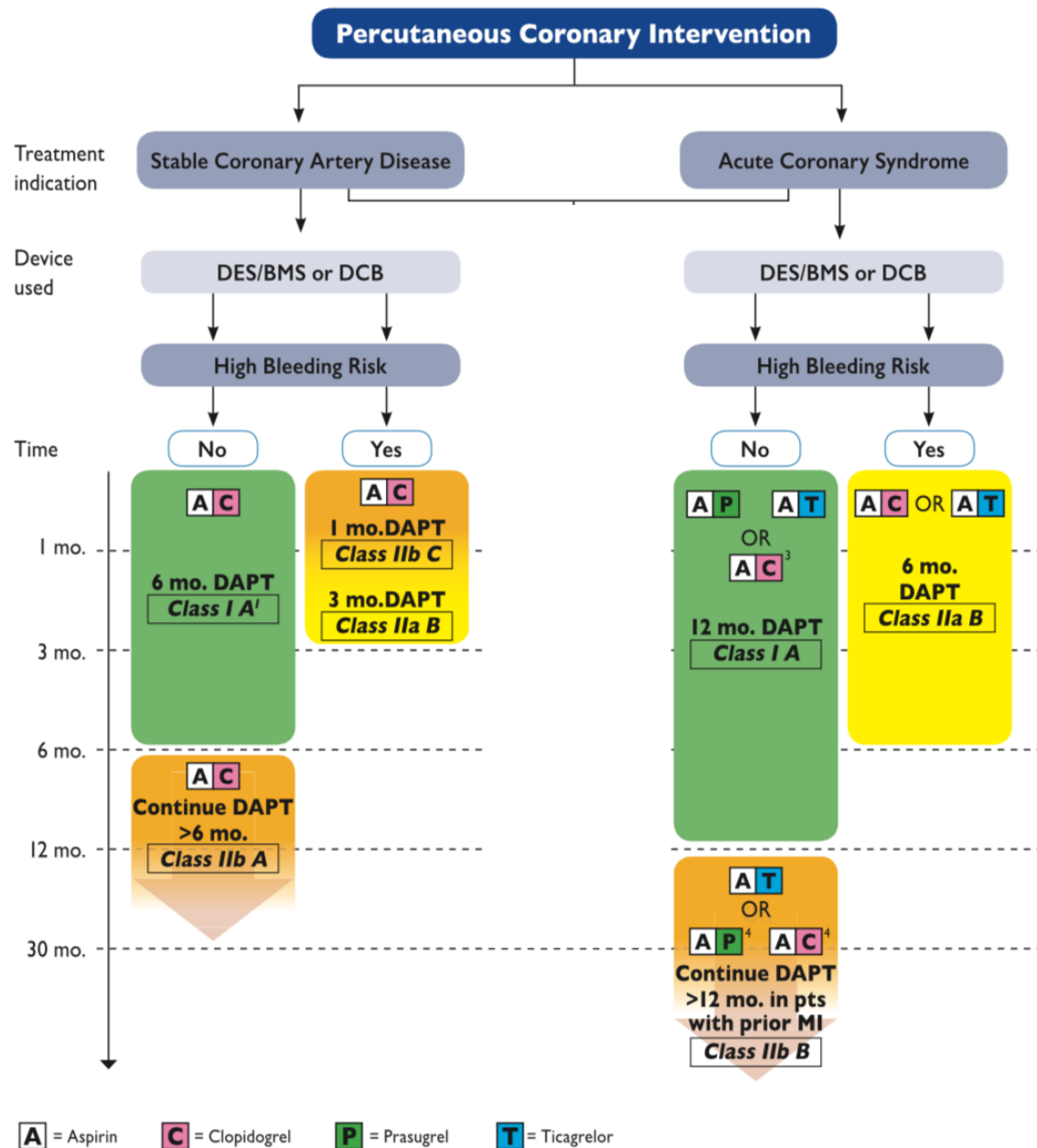
# After 3.5mm post-dilation @ 26 atm



6.2 mm<sup>2</sup>









# Acute anterior STEMI

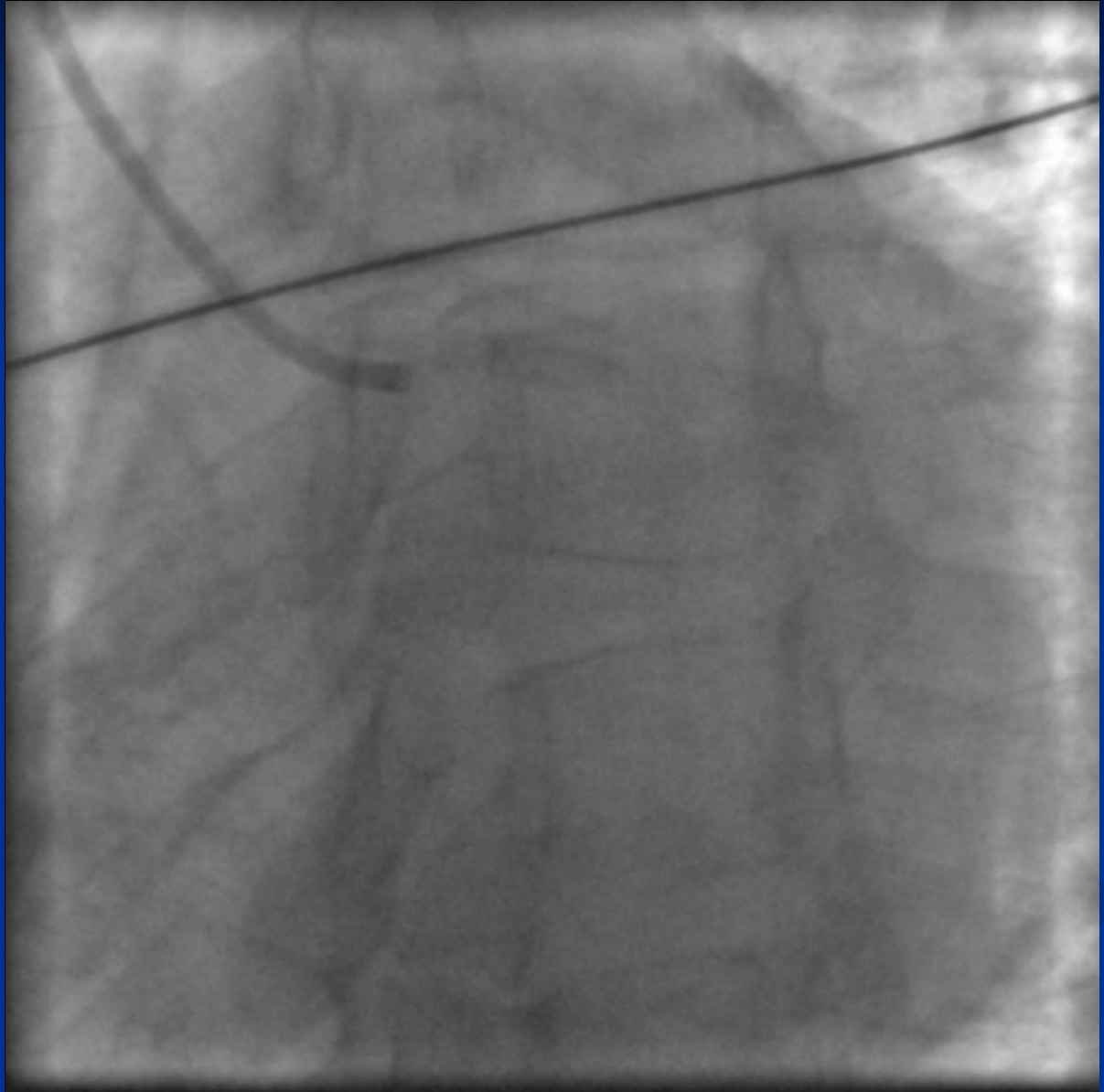
In ED:

ASA 325

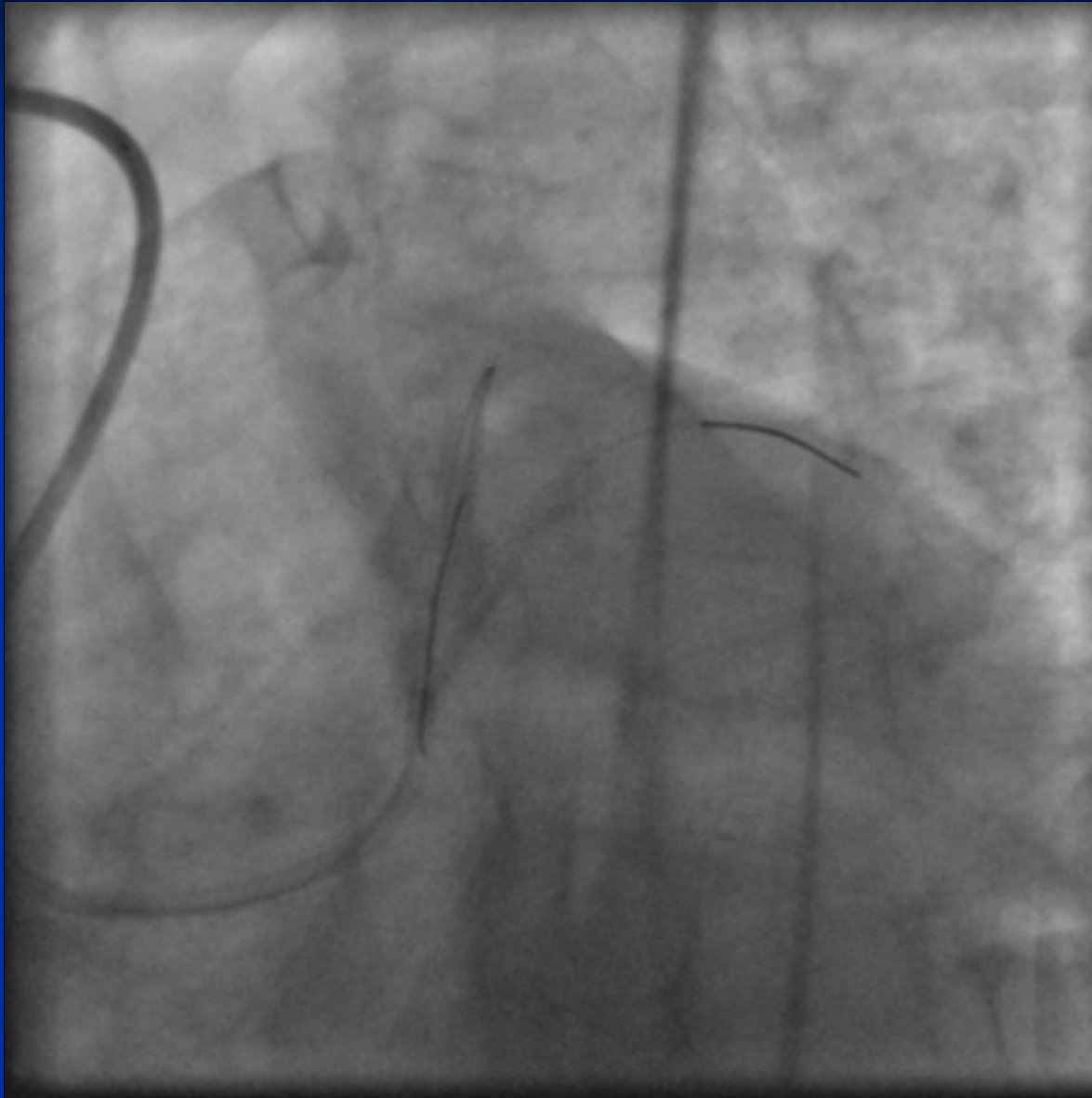
Ticagrelor 180 mg

In Lab:

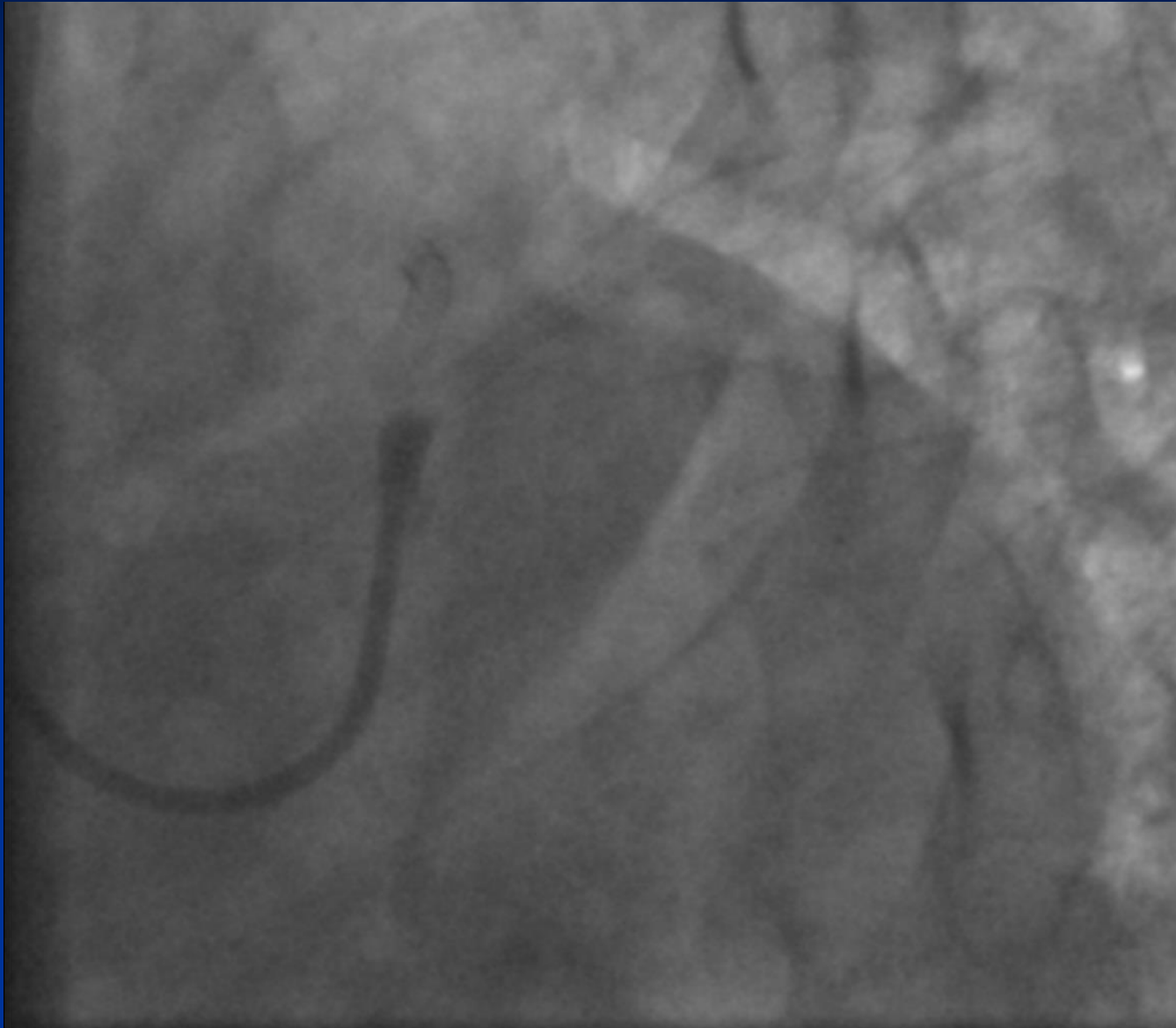
Bivaliruden



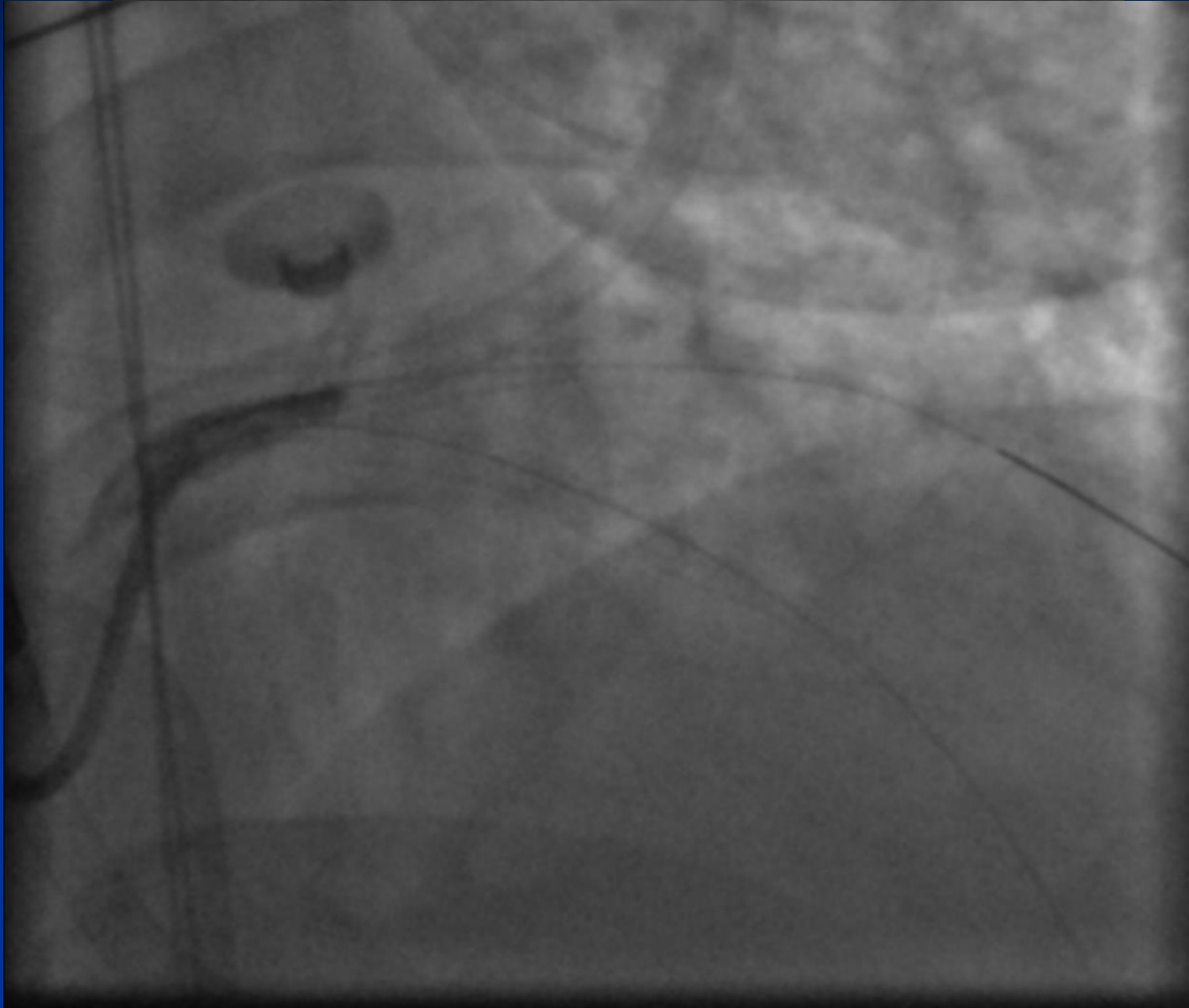
**After DES to LAD and also of non-culprit D1**



**Four hours later: recurrent pain and shock**

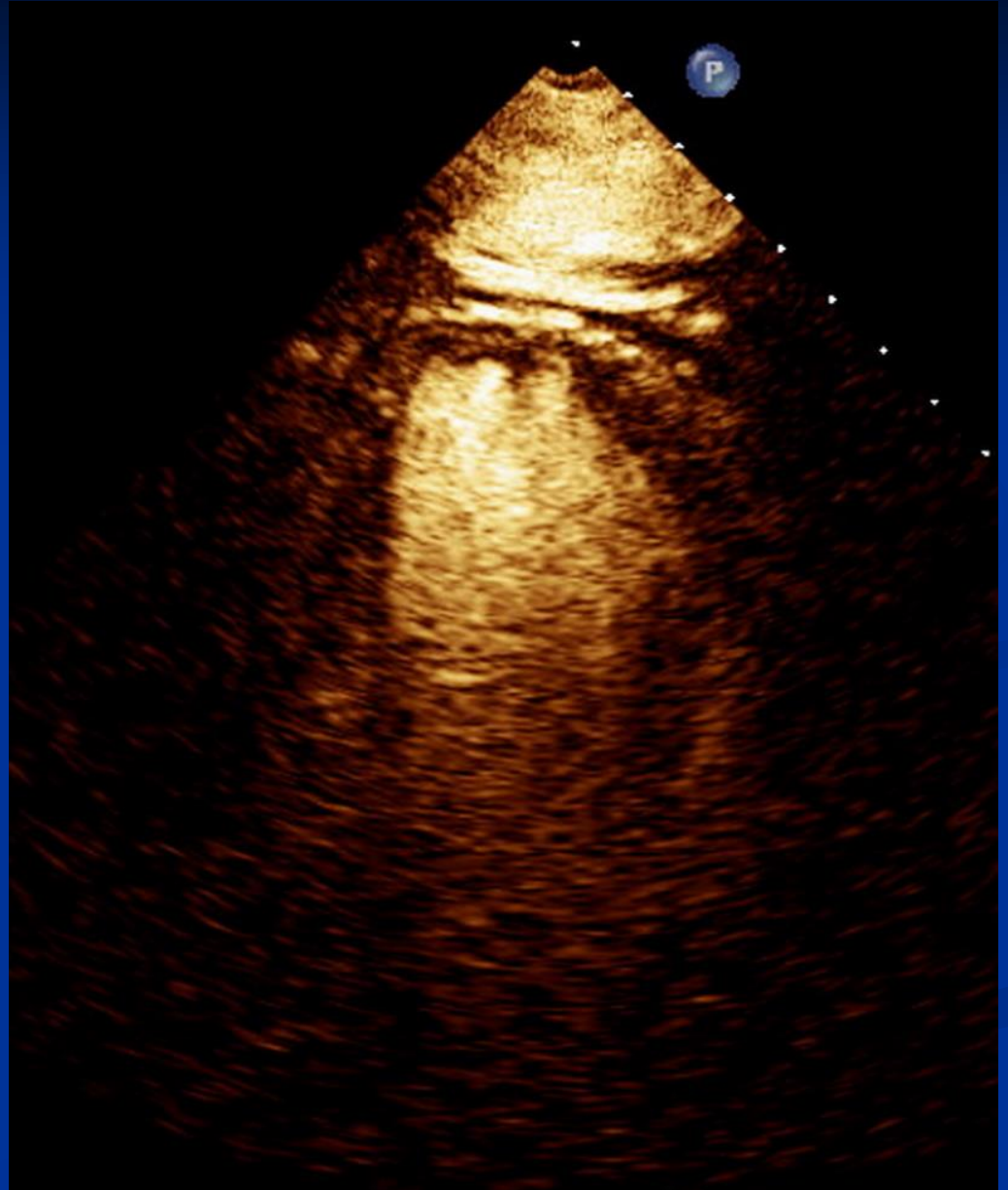


# After Impella and re-opening



# Persistent shock

Upgrade to Impella 5L  
Move to transplant center  
Spent 10 days on Impella

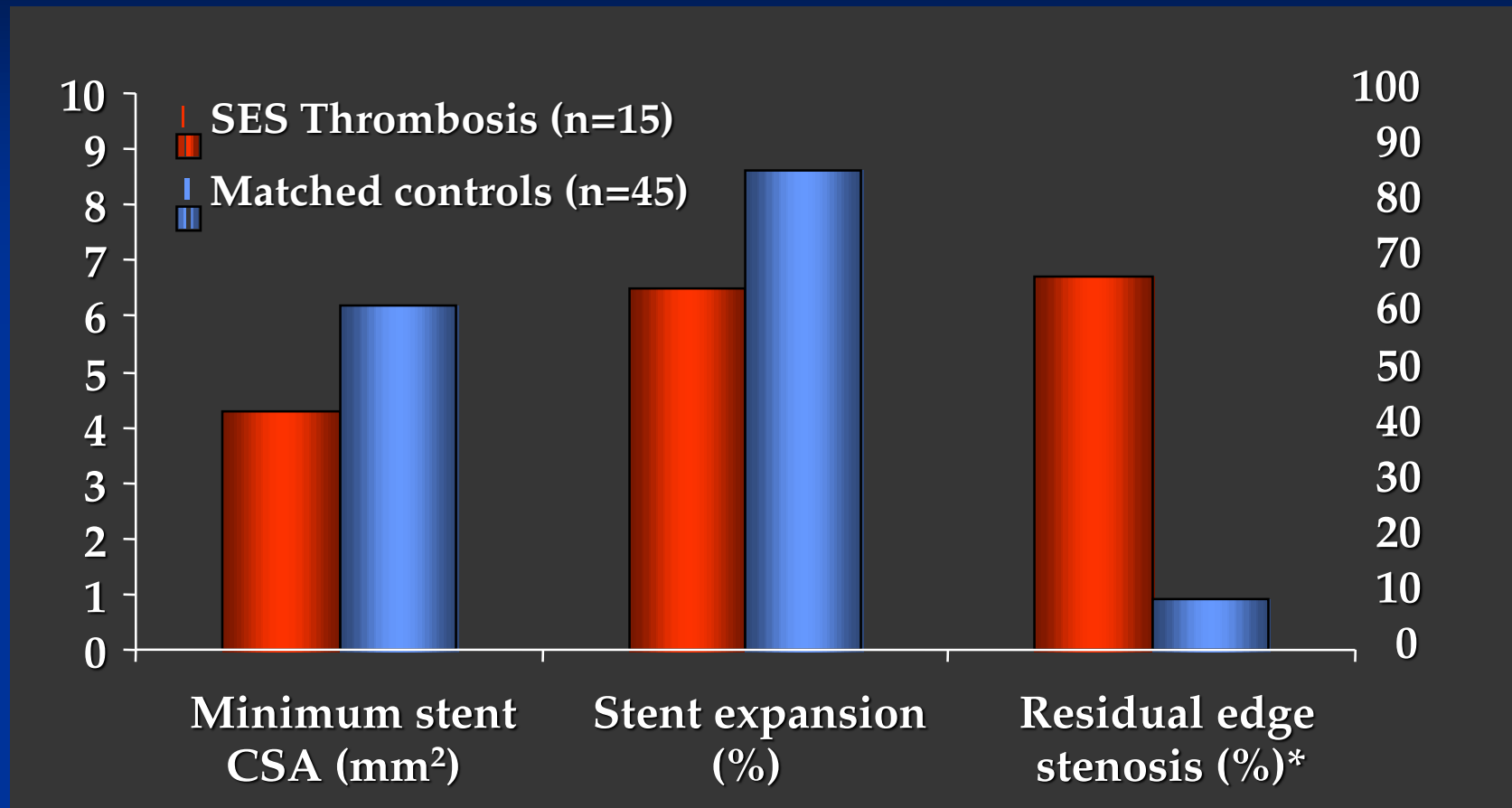


# What if my patient has stent thrombosis?

- Consider timing
- Acute: inadequate P2Y<sub>12</sub> level; mechanical stent issue
  - Solution: use “crush and chew” strategy; use IVUS guidance; use coverage with IIbIIIa inhibitor
- Subacute: ineffective P2Y<sub>12</sub> ; mechanical stent issue
  - Solution: upgrade to ticagrelor or prasugrel; use IVUS guidance
- Late: unclear
  - Recommendation: upgrade to ticagrelor or prasugrel; use IVUS guidance



# IVUS Predictors of DES Thrombosis (within 30 days)

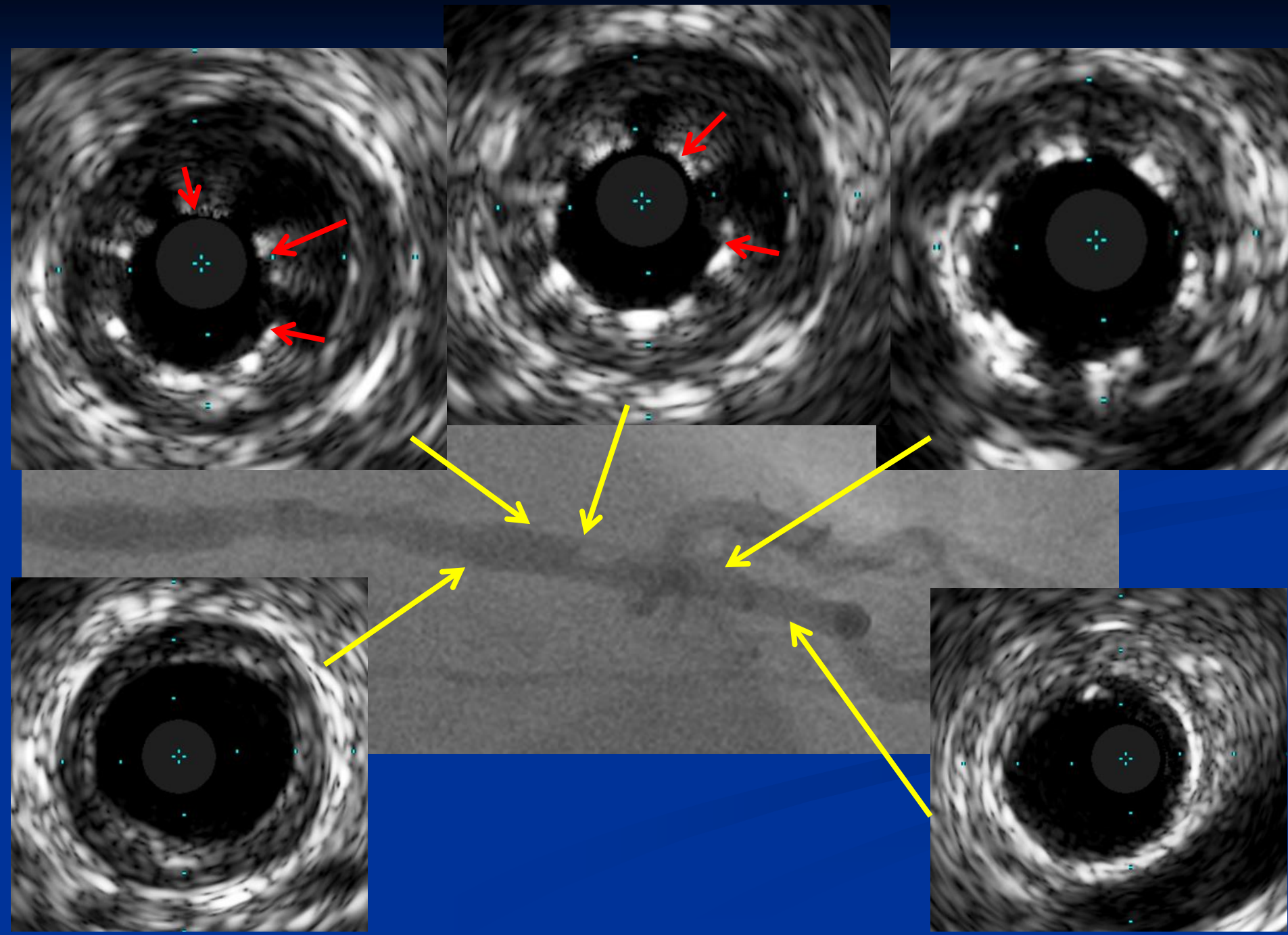


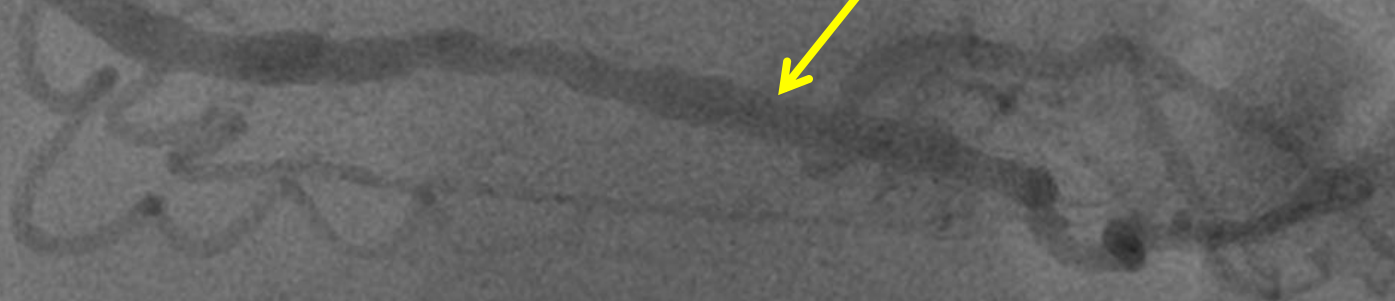
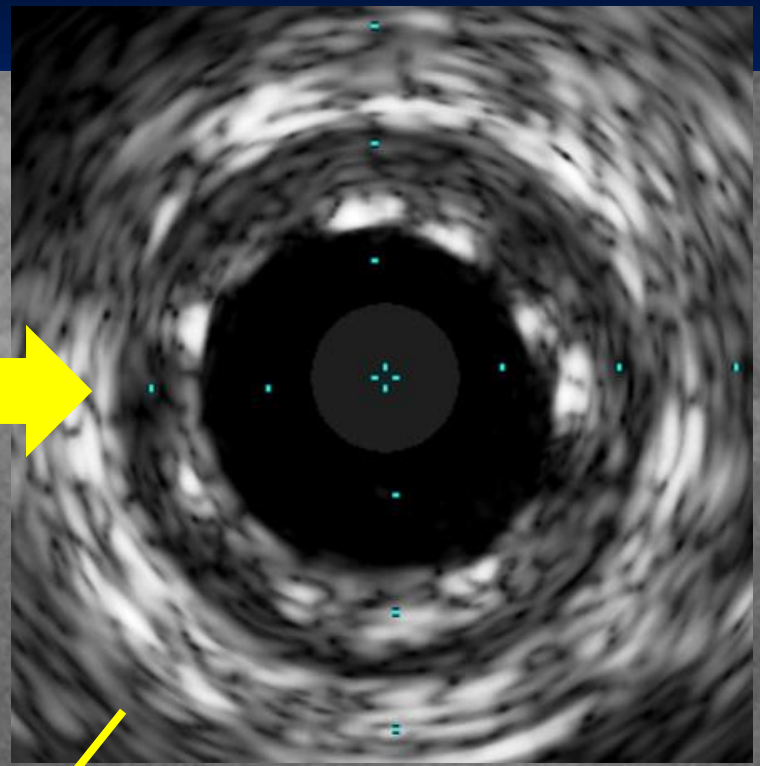
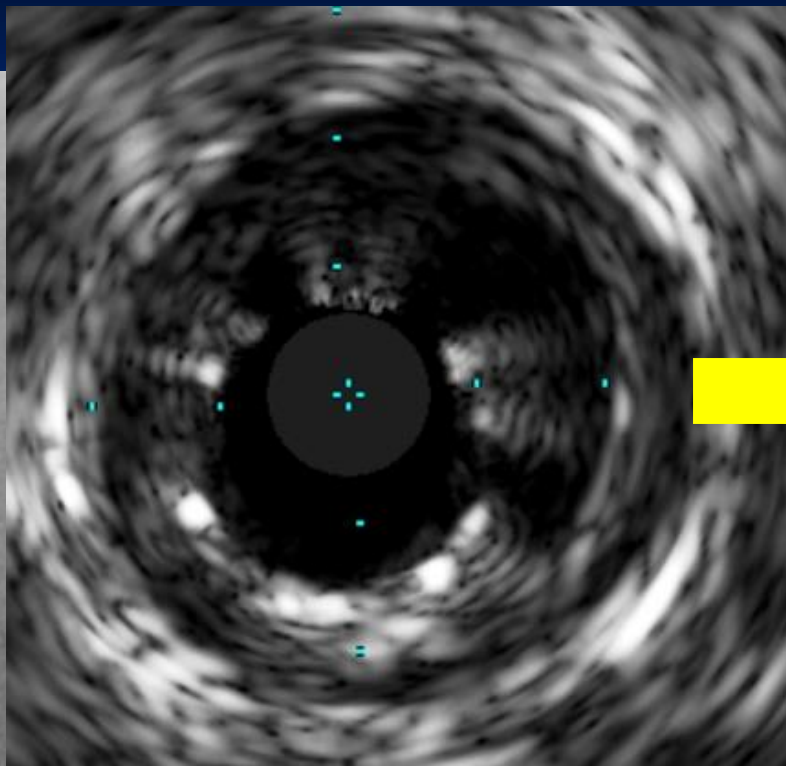
\*Residual edge stenosis = edge lumen CSA  $<4.0\text{mm}^2$  & plaque burden  $>70\%$ .

(Fujii et al. *J Am Coll Cardiol* 2005;45:995-8)

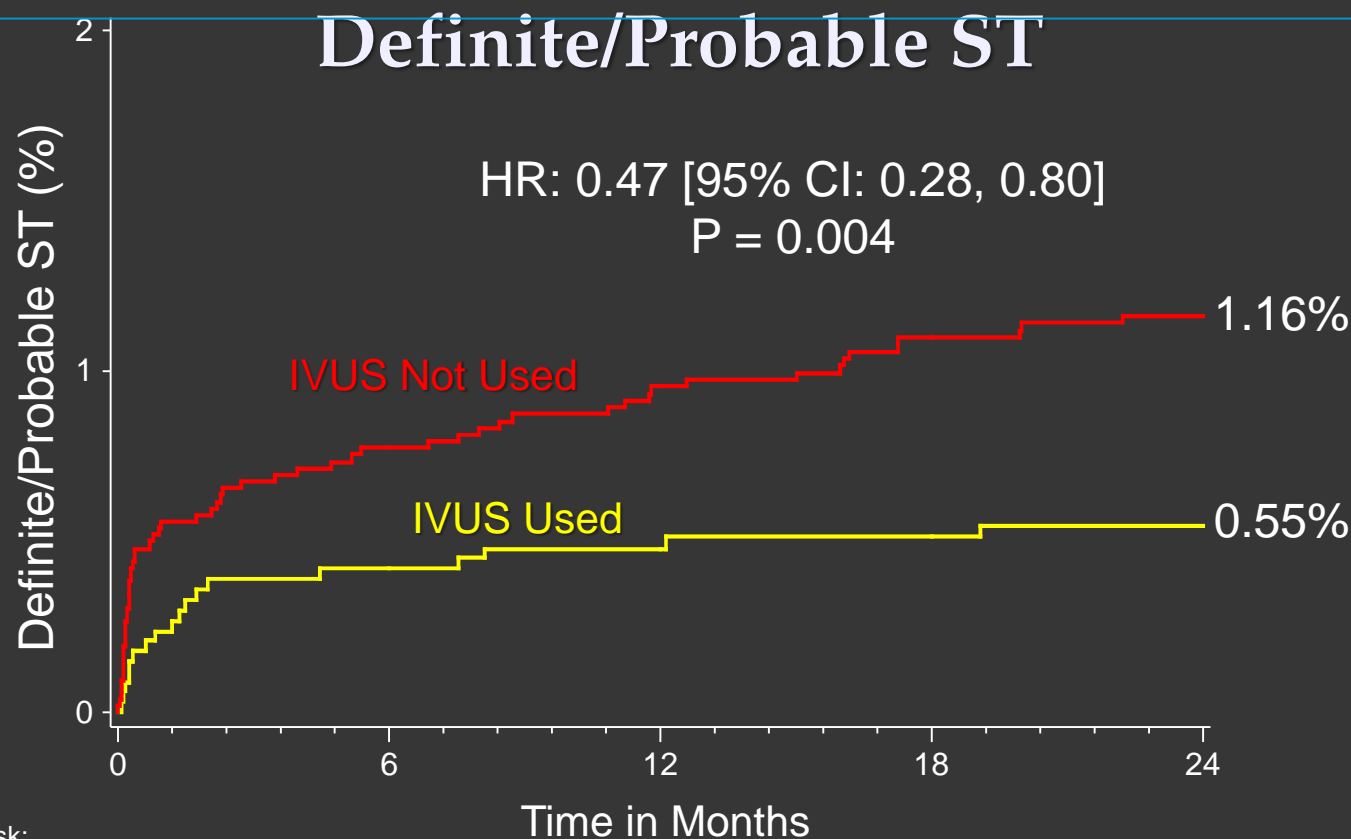
# Mal apposition resulting in SAT







# ADAPT-DES (3361 pts treated with IVUS-guidance vs 5221 pts treated with angiographic guidance)



Number at risk:

IVUS Used	3361	3260	3182	3065	1791
IVUS Not Used	5221	5019	4886	4713	2279



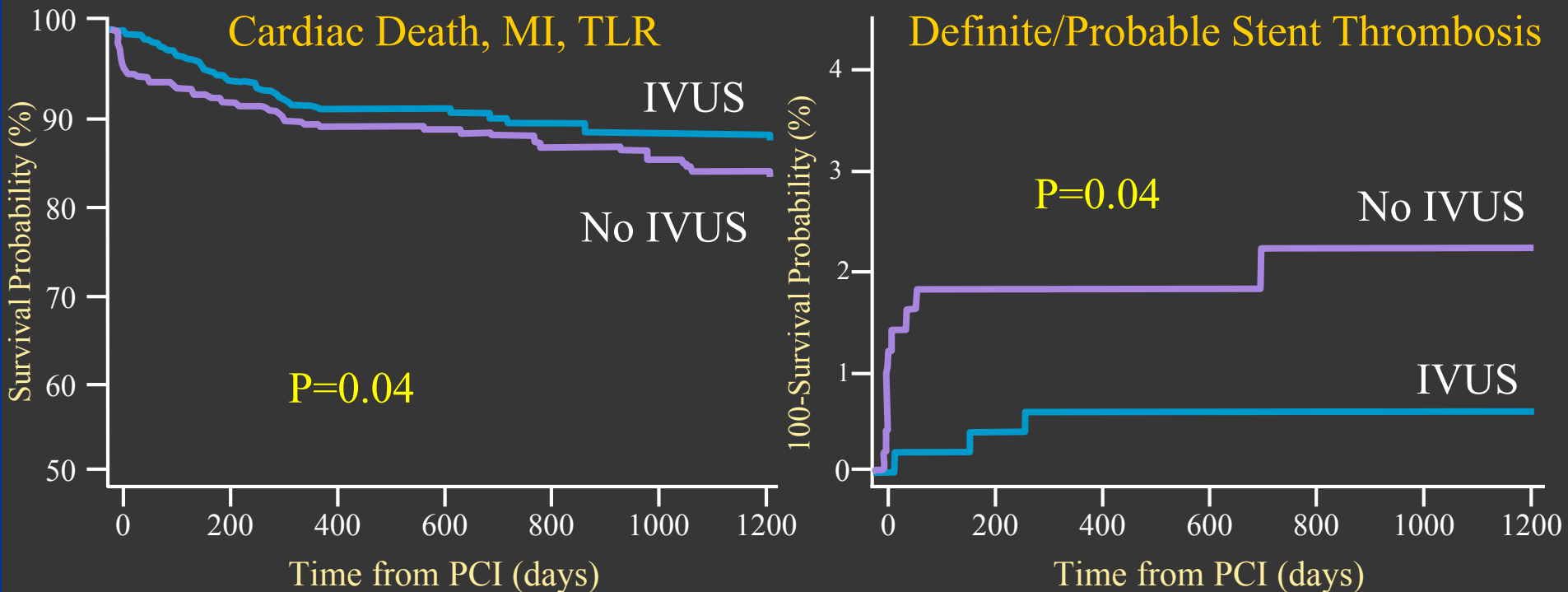
# Target Lesion Stent Thrombosis at 2 Years

	IVUS Use n = 3361	No IVUS n = 5221	P Value
Definite ST	0.46% (15)	0.85% (43)	0.036
Definite/probable ST	0.55% (18)	1.16% (59)	0.004
- Acute <1day	0.00% (0)	0.04% (2)	0.26
- Subacute (1-30 days)	0.24% (8)	0.52% (27)	0.047
- Late (>30 days to 1 yr)	0.24% (8)	0.40% (20)	0.24
- Very late (1 yr to 2 yrs)	0.06% (2)	0.21% (10)	0.11



# Impact of IVUS Guidance of Unprotected LM Propensity Matched 1010 pts in 4 Registries

- Distal LM lesion ~60%, 2 stent technique ~13%
- IVUS guidance was an independent predictor of MACE



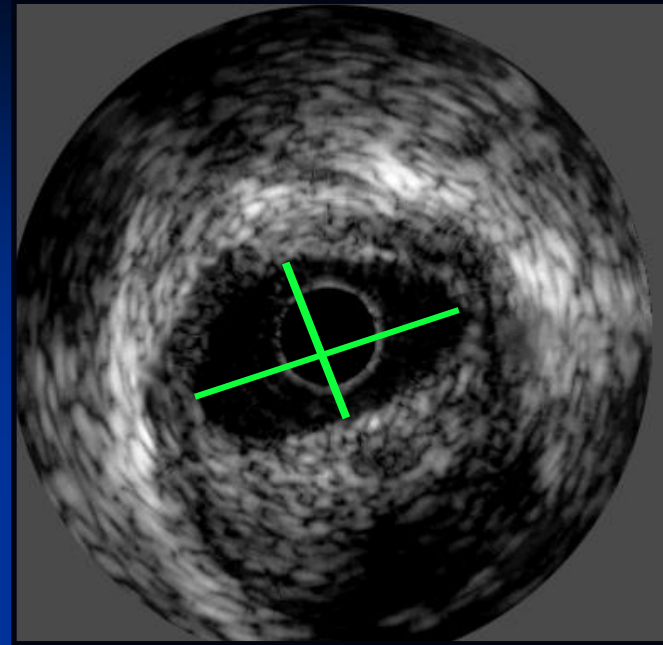
# Post stent thrombosis: ESC suggests

- The number of recurrent events is significantly decreased by treatment with ticagrelor or prasugrel as compared to clopidogrel. Hence, the use of clopidogrel after stent thrombosis cannot be regarded as an effective treatment option.
- Considering the long-term risk of recurrence after first stent thrombosis, it may be reasonable to make every effort to maintain DAPT for a very long-term period in this highly selected high-risk patient population, if tolerated.

# Routine Stenting

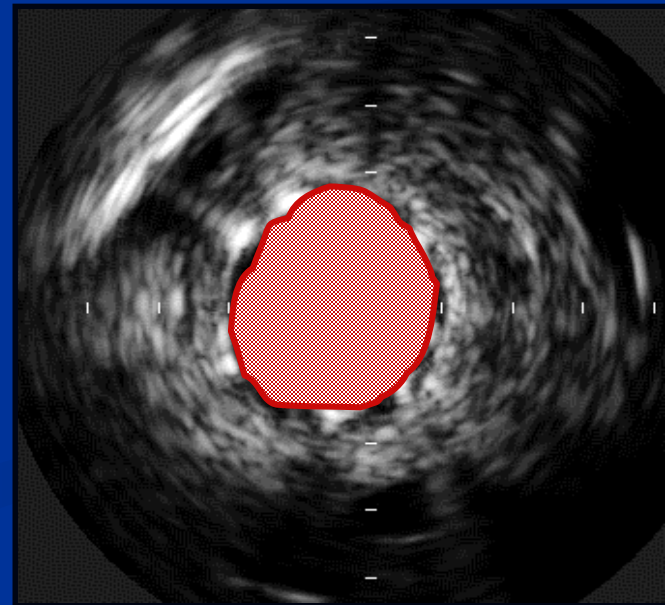
Stent size selection:

**Reference** lumen diameter  
(package size)

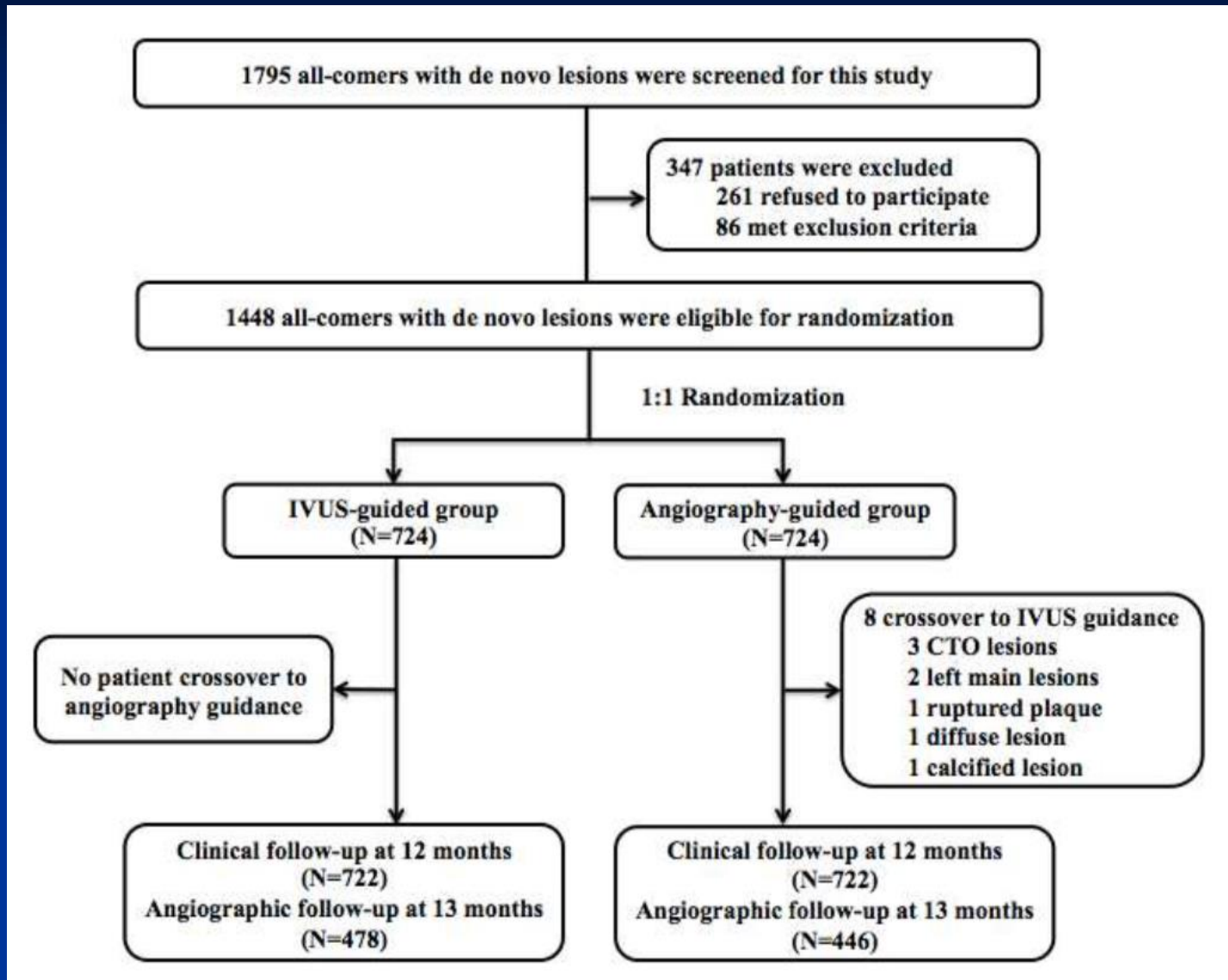


Result optimization:

**Stent** lumen  
cross sectional area  
> 80% of reference  
(Bernoulli)

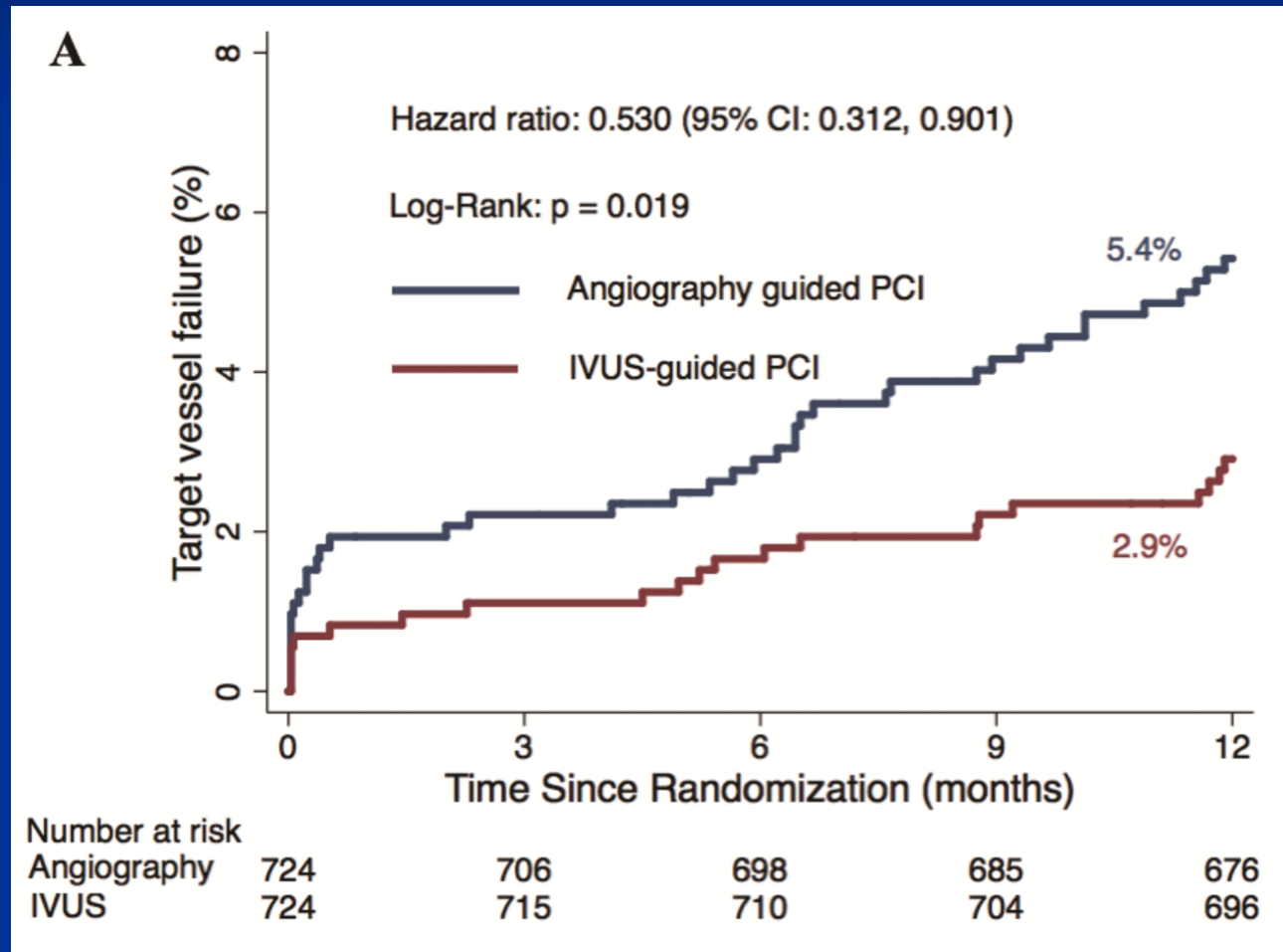


# Ultimate trial: IVUS vs Angio Guidance of DES

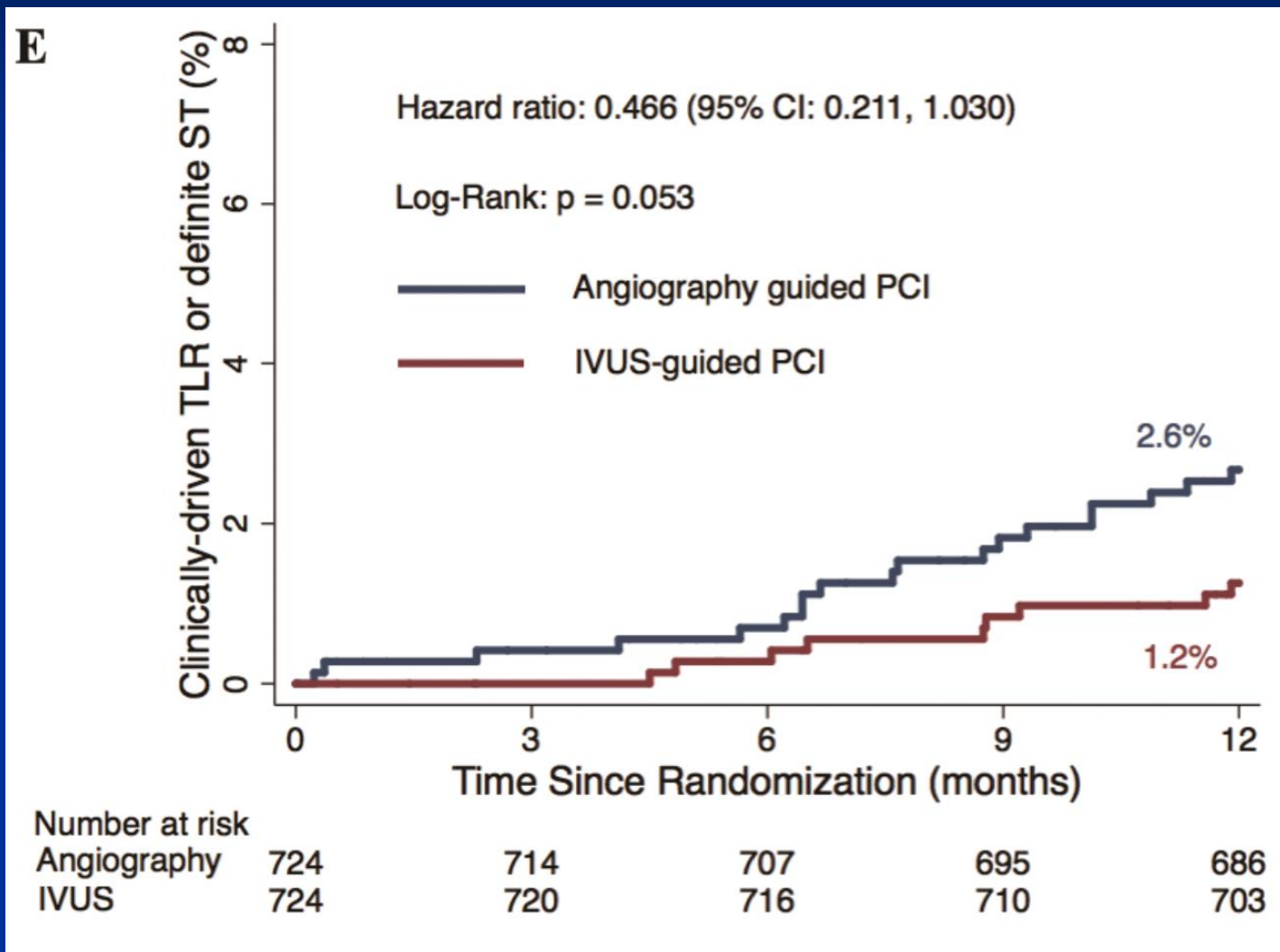


# Ultimate: all comer population

Diameter: 67% B2/C, diameter 3 mm, length 50 mm, Post dilate to 19 atm



Of the 6 stent thrombosis cases, only 1 was IVUS guided:  
Patient received 5 stents, 150mm, thrombosed @ 16 d





# PCI without IVUS:

**INSANITY**  
is doing the  
same thing  
over and over  
again expecting  
different results

# What if my patient also needs antithrombin therapy, or oral anticoagulants (OAC)

- Most common is atrial fibrillation
- Also applies to recent VTE, heart valves
- Key is to assess both bleeding and thrombosis risk and then craft a strategy that will allow discontinuing “triple therapy” at the earliest possible safe interval.
- Consider new “low dose” OAC combinations
- Risk estimating scores must be utilized.

# Triple therapy: DAPT and OAC

**Table 6** Unfavourable patient profile for a combination of oral anticoagulant and antiplatelet therapy

• Short life expectancy
• Ongoing malignancy
• Poor expected adherence
• Poor mental status
• End stage renal failure
• Advanced age
• Prior major bleeding/prior haemorrhagic stroke
• Chronic alcohol abuse
• Anaemia
• Clinically significant bleeding on dual antithrombotic therapy

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**Table 4** Strategies to avoid bleeding complications in patients treated with oral anticoagulant

- |                                                                                                                                                                             |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| • Assess ischaemic and bleeding risks using validated risk predictors (e.g. CHA <sub>2</sub> DS <sub>2</sub> -VASc, ABC, HAS-BLED) with a focus on modifiable risk factors. |
| • Keep triple therapy duration as short as possible; dual therapy after PCI (oral anticoagulant and clopidogrel) to be considered instead of triple therapy.                |
| • Consider the use of NOACs instead of VKA.                                                                                                                                 |
| • Consider a target INR in the lower part of the recommended target range and maximize time in therapeutic range (i.e. > 65–70%) when VKA is used.                          |
| • Consider the lower NOAC regimen tested in approval studies and apply other NOAC regimens based on drug-specific criteria for drug accumulation. <sup>a</sup>              |
| • Clopidogrel is the P2Y <sub>12</sub> inhibitor of choice.                                                                                                                 |
| • Use low-dose (≤ 100 mg daily) aspirin.                                                                                                                                    |
| • Routine use of PPIs.                                                                                                                                                      |

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**Table 4. Dual pathway and triple therapy regimens evaluated in clinical trials**

---

Dual pathway

1. Rivaroxaban 15 mg OD with clopidogrel 75 mg OD<sup>99</sup>
2. Dabigatran 110\* or 150 mg BID with clopidogrel 75 mg OD<sup>101</sup>
3. Warfarin with clopidogrel 75 mg OD<sup>97</sup>

Triple therapy

1. Rivaroxaban 2.5 mg BID with ASA 81 mg OD and clopidogrel 75 mg OD<sup>99</sup>
2. Warfarin (INR, 2.0-2.5) with ASA 81 mg OD and clopidogrel 75 mg OD<sup>98</sup>

---

ASA, acetylsalicylic acid; BID, twice daily; INR, international normalized ratio; OD, every day.

## AF and elective PCI without high-risk features<sup>1</sup>

Age < 65 and CHADS<sub>2</sub> = 0

**ASA + Clopidogrel**  
Duration: at least 1 month for BMS  
and at least 3 months for DES  
(and up to 12 months)

ASA +/- P<sub>2</sub>Y<sub>12</sub> inhibitor<sup>3</sup>

Age ≥ 65 or CHADS<sub>2</sub> ≥ 1

**OAC<sup>2</sup> + Clopidogrel**  
Duration: at least 1 month for BMS  
and at least 3 months for DES  
(and up to 12 months)

OAC<sup>4</sup> +/- SAPT



## AF and PCI for ACS or high-risk<sup>1</sup> elective PCI

Age < 65 **and** CHADS<sub>2</sub> = 0

**ASA + P<sub>2</sub>Y<sub>12</sub> inhibitor<sup>2</sup>**  
(ticagrelor, prasugrel preferred over  
clopidogrel for ACS)  
Duration after PCI: Up to 12 months

ASA + /- P<sub>2</sub>Y<sub>12</sub> inhibitor<sup>5</sup>

Age ≥ 65 **or** CHADS<sub>2</sub> ≥ 1\*

**Reduced OAC<sup>3</sup> + ASA + clopidogrel**  
ASA: stop 1 day post PCI or any time  
up to 6 months<sup>4</sup>  
Followed by: **clopidogrel + OAC**  
Duration after PCI: Up to 12 months

OAC<sup>6</sup> + /- SAPT

\*If CHADS<sub>2</sub> = 1 and Age < 65 another option for initial treatment (especially if high-risk for ischemic events) is DAPT alone using ASA+ticagrelor or ASA+prasugrel, similar to the recommendation for the CHADS<sub>2</sub>=0 patient

# Patients with an indication for oral anticoagulation undergoing PCI<sup>1</sup>

Concerns about ischaemic risk<sup>2</sup> prevailing

Concerns about bleeding risk<sup>3</sup> prevailing

Time from treatment initiation

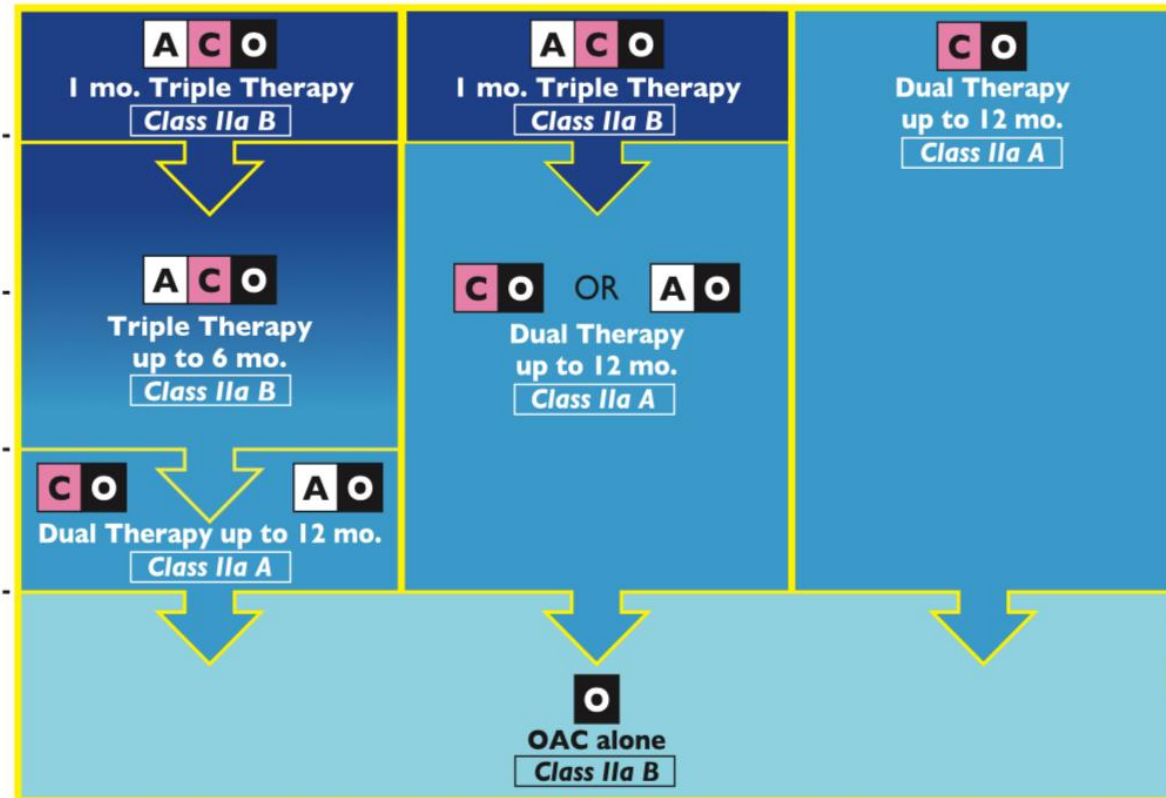
1 mo.

3 mo.

6 mo.

12 mo.

Beyond 12 mo.



**A** = Aspirin    **C** = Clopidogrel    **O** = Oral anticoagulation

# Triple therapy: key takeaways

- Always calculate risk scores
- P2Y12 is always Clopidogrel
- ASA is always 81mg
- PPI should be used
- If ischemia risk > bleeding risk use triple therapy for 3-6 months
- If bleeding risk > ischemia risk use one month triple therapy
- De-escalate by removing ASA

# What if my patient bleeds?

- Specific details matter:
  - Clinical indication for stent: stable or ACS
  - Type of stent: DES or BMS
  - How severe is bleeding
  - What are the risk scores
- Let's process two examples

## Bleeding during treatment with dual antiplatelet therapy $\pm$ OAC

### TRIVIAL BLEEDING

Any bleeding not requiring medical intervention or further evaluation

e.g. skin bruising or ecchymosis, self-resolving epistaxis, minimal conjunctival bleeding

- Continue DAPT

### MILD BLEEDING

Any bleeding that requires medical attention without requiring hospitalization

e.g. not self resolving epistaxis, moderate conjunctival bleeding, genitourinary or upper/lower gastrointestinal bleeding without significant blood loss, mild haemoptysis

- Continue DAPT
- Consider shortening DAPT duration or switching to less potent P2Y<sub>12</sub> inhibitor (i.e. from ticagrelor/prasugrel to clopidogrel), especially if recurrent bleeding occurs

### MODERATE BLEEDING

Any bleeding associated with a significant blood loss ( $>3$  g/dL HB) and/or requiring hospitalization, which is haemodynamically stable and not rapidly evolving

e.g. genitourinary, respiratory or upper/lower gastrointestinal bleeding with significant blood loss or requiring transfusion

- Consider stopping DAPT and continue with SAPT, preferably with the P2Y<sub>12</sub> inhibitor especially in case of upper GI bleeding
- Reinitiate DAPT as soon as deemed safe
- Consider shortening DAPT duration or switching to less potent P2Y<sub>12</sub> inhibitor (i.e. from ticagrelor/prasugrel to clopidogrel), especially if recurrent bleeding occurs



## Bleeding during treatment with dual antiplatelet therapy $\pm$ OAC

### SEVERE BLEEDING

Any bleeding requiring hospitalisation, associated with a severe blood loss ( $>5$  g/dL HB) which is haemodynamically stable and not rapidly evolving

e.g. severe genitourinary, respiratory or upper/lower gastrointestinal bleeding

- Consider stopping DAPT and continue with SAPT, preferably with the P2Y<sub>12</sub> inhibitor especially in case of upper GI bleeding
- If bleeding persists despite treatment or treatment is not possible, consider stopping all antithrombotic medications
- Once bleeding has ceased, re-evaluate the need for DAPT or SAPT, preferably with the P2Y<sub>12</sub> inhibitor especially in case of upper GI bleeding
- If DAPT is re-started, consider shortening DAPT duration or switching to less potent P2Y<sub>12</sub> inhibitor (i.e. from ticagrelor/prasugrel to clopidogrel), especially if recurrent bleeding occurs

### LIFE-THREATENING BLEEDING

Any severe active bleeding putting patient's life immediately at risk

e.g. massive overt genitourinary, respiratory or upper/lower gastrointestinal bleeding, active intracranial, spinal or intraocular haemorrhage, or any bleeding causing haemodynamic instability

- Immediately discontinue all antithrombotic medications
- Once bleeding has ceased, re-evaluate the need for DAPT or SAPT, preferably with the P2Y<sub>12</sub> inhibitor especially in case of upper GI bleeding



# Case Example 1

- 50 yo man presents with anterior STEMI
- Acute PCI performed with DES to proximal LAD with TIMI II-III flow post; no IVUS
- EF 30% acutely
- Smoker, DM, HBg 13.5, WBC 8.5, Creat 0.8 (GFR =90)
- NSR, no prior bleed or TIA/CVA
- Discharged on Ticagerlor and ASA
- No PPI prescribed

**TABLE 4****Clinical and Procedural Factors Associated With Increased Ischemic Risk (Including Stent Thrombosis) or Increased Bleeding Risk (62-70)**

<b>Increased Ischemic Risk/Risk of Stent Thrombosis (may favor longer-duration DAPT)</b>	<b>Increased Bleeding Risk (may favor shorter-duration DAPT)</b>
<b>Increased ischemic risk</b>	History of prior bleeding
Advanced age	Oral anticoagulant therapy
ACS presentation	Female sex
Multiple prior MIs	Advanced age
Extensive CAD	Low body weight
Diabetes mellitus	CKD
CKD	Diabetes mellitus
<b>Increased risk of stent thrombosis</b>	Anemia
ACS presentation	Chronic steroid or NSAID therapy
Diabetes mellitus	
Left ventricular ejection fraction <40%	
First-generation drug-eluting stent	
Stent undersizing	
Stent underdeployment	
Small stent diameter	
Greater stent length	
Bifurcation stents	
In-stent restenosis	

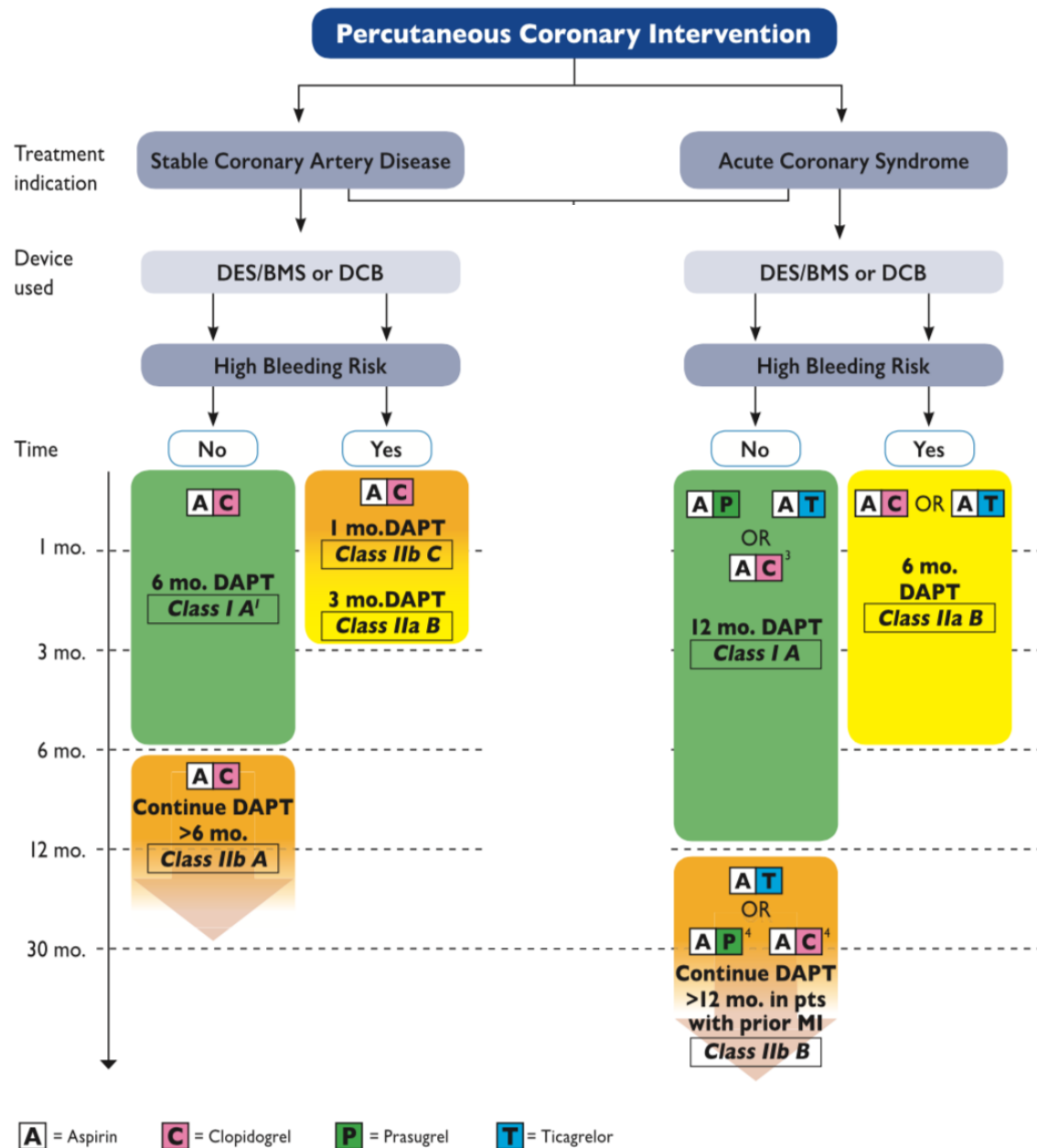
ACS indicates acute coronary syndrome; CAD, coronary artery disease; CKD, chronic kidney disease; DAPT, dual antiplatelet therapy; MI, myocardial infarction; and NSAID, nonsteroidal anti-inflammatory drug.

# Case example 1

- Calculate Risk scores:
- Precise DAPT: 6. “low risk” 1 yr bleed: 0.45%
- Stent thrombosis risk factors: prox LAD, smoker, DM, low EF, no IVUS guidance

# Case example 1

- Presents 90 days post PCI with LGI bleed and hemoglobin down to 6.5. Transfused 3 u PRBC. Hemodynamically stable
- Presents 30 days post PCI with same bleeding as above
- Presents 11 months post PCI with same bleeding as above.



## Bleeding during treatment with dual antiplatelet therapy $\pm$ OAC

### SEVERE BLEEDING

Any bleeding requiring hospitalisation, associated with a severe blood loss ( $>5$  g/dL HB) which is haemodynamically stable and not rapidly evolving

e.g. severe genitourinary, respiratory or upper/lower gastrointestinal bleeding

- Consider stopping DAPT and continue with SAPT, preferably with the P2Y<sub>12</sub> inhibitor especially in case of upper GI bleeding
- If bleeding persists despite treatment or treatment is not possible, consider stopping all antithrombotic medications
- Once bleeding has ceased, re-evaluate the need for DAPT or SAPT, preferably with the P2Y<sub>12</sub> inhibitor especially in case of upper GI bleeding
- If DAPT is re-started, consider shortening DAPT duration or switching to less potent P2Y<sub>12</sub> inhibitor (i.e. from ticagrelor/prasugrel to clopidogrel), especially if recurrent bleeding occurs

### LIFE-THREATENING BLEEDING

Any severe active bleeding putting patient's life immediately at risk

e.g. massive overt genitourinary, respiratory or upper/lower gastrointestinal bleeding, active intracranial, spinal or intraocular haemorrhage, or any bleeding causing haemodynamic instability

- Immediately discontinue all antithrombotic medications
- Once bleeding has ceased, re-evaluate the need for DAPT or SAPT, preferably with the P2Y<sub>12</sub> inhibitor especially in case of upper GI bleeding



# Case example 1

- Presents 90 days post PCI with LGI bleed and hemoglobin down to 6.5. Transfused 3 u PRBC. Hemodynamically stable
  - Stop ASA, de-escalate to clopidogrel; try to make it 6 months. If IVUS guided: 3 months
- Presents 30 days post PCI with same bleeding as above
  - Stop ASA, continue ticagrelor, unless more bleeding, then de-escalate to clopidogrel; try to make it 6 months.
- Presents 11 months post PCI with same bleeding as above.
  - Stop both, if stabilizes, consider restart clopidogrel

## Case example 2

- 85 yo woman with chronic stable angina
- Elective PCI with DES to OM2.
- Discharged on ASA and Clopidogrel
- Prior Hx of TIA, remote history of black stools and anemia, easy bruising in the past
- Non smoker, no DM, Hbg 10.2, WBC 5.3, GFR 45

## Case example 2

- Calculate Risk scores:
- Precise DAPT: 70. “high risk” 1 yr bleed:  $> 4\%$
- Stent thrombosis risk factors: CKD

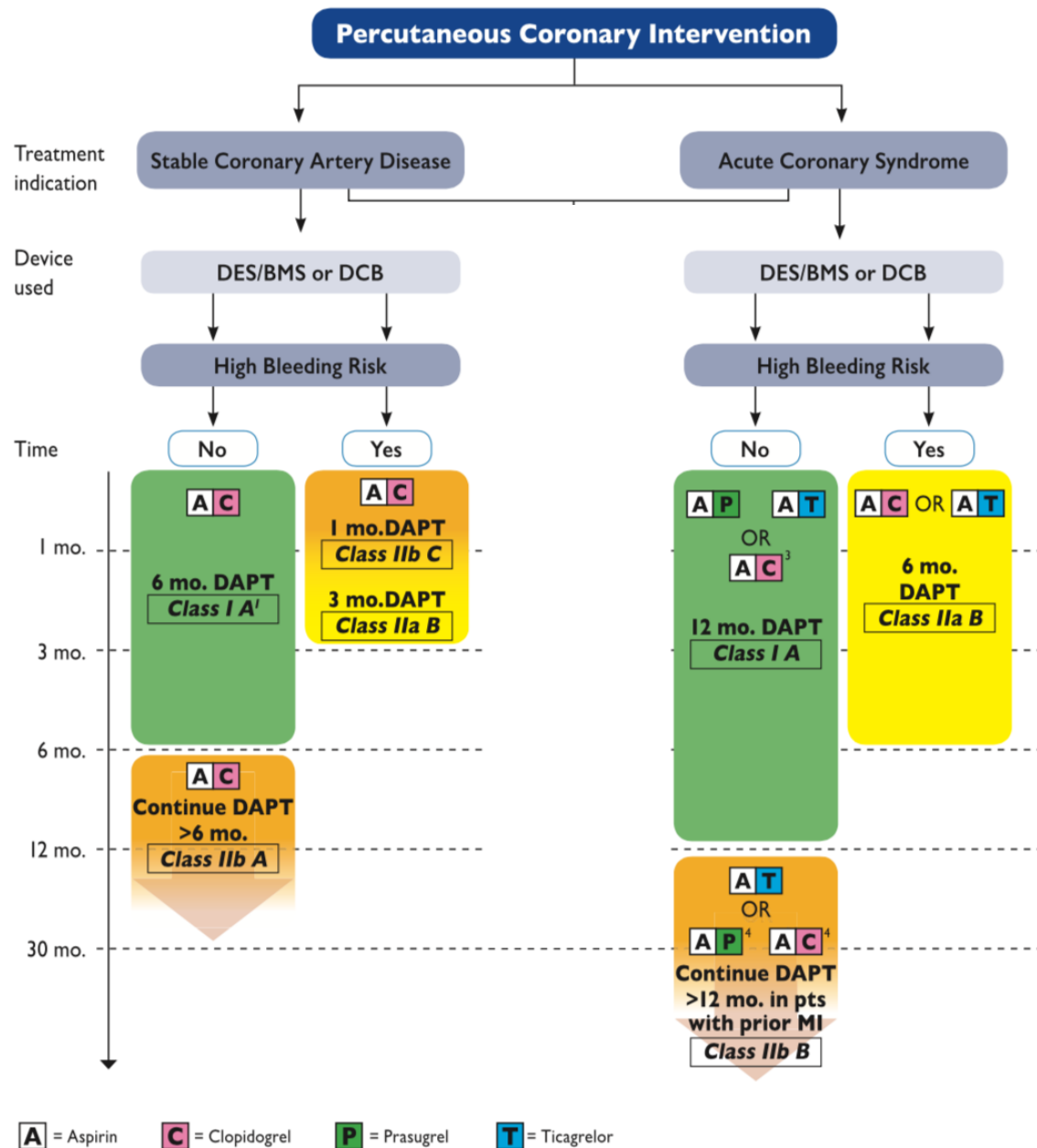
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<b>Increased ischemic risk</b>	History of prior bleeding
Advanced age	Oral anticoagulant therapy
ACS presentation	Female sex
Multiple prior MIs	Advanced age
Extensive CAD	Low body weight
Diabetes mellitus	CKD
CKD	Diabetes mellitus
<b>Increased risk of stent thrombosis</b>	Anemia
ACS presentation	Chronic steroid or NSAID therapy
Diabetes mellitus	
Left ventricular ejection fraction <40%	
First-generation drug-eluting stent	
Stent undersizing	
Stent underdeployment	
Small stent diameter	
Greater stent length	
Bifurcation stents	
In-stent restenosis	

ACS indicates acute coronary syndrome; CAD, coronary artery disease; CKD, chronic kidney disease; DAPT, dual antiplatelet therapy; MI, myocardial infarction; and NSAID, nonsteroidal anti-inflammatory drug.

## Case example 2

- Presents 90 days post PCI with LGI bleed and hemoglobin down to 6.5. Transfused 3 u PRBC. Hemodynamically stable
- Presents 30 days post PCI with same bleeding as above
- Presents 11 months post PCI with same bleeding as above.





## Bleeding during treatment with dual antiplatelet therapy $\pm$ OAC

### SEVERE BLEEDING

Any bleeding requiring hospitalisation, associated with a severe blood loss ( $>5$  g/dL HB) which is haemodynamically stable and not rapidly evolving

e.g. severe genitourinary, respiratory or upper/lower gastrointestinal bleeding

- Consider stopping DAPT and continue with SAPT, preferably with the P2Y<sub>12</sub> inhibitor especially in case of upper GI bleeding
- If bleeding persists despite treatment or treatment is not possible, consider stopping all antithrombotic medications
- Once bleeding has ceased, re-evaluate the need for DAPT or SAPT, preferably with the P2Y<sub>12</sub> inhibitor especially in case of upper GI bleeding
- If DAPT is re-started, consider shortening DAPT duration or switching to less potent P2Y<sub>12</sub> inhibitor (i.e. from ticagrelor/prasugrel to clopidogrel), especially if recurrent bleeding occurs

### LIFE-THREATENING BLEEDING

Any severe active bleeding putting patient's life immediately at risk

e.g. massive overt genitourinary, respiratory or upper/lower gastrointestinal bleeding, active intracranial, spinal or intraocular haemorrhage, or any bleeding causing haemodynamic instability

- Immediately discontinue all antithrombotic medications
- Once bleeding has ceased, re-evaluate the need for DAPT or SAPT, preferably with the P2Y<sub>12</sub> inhibitor especially in case of upper GI bleeding

## Case example 2

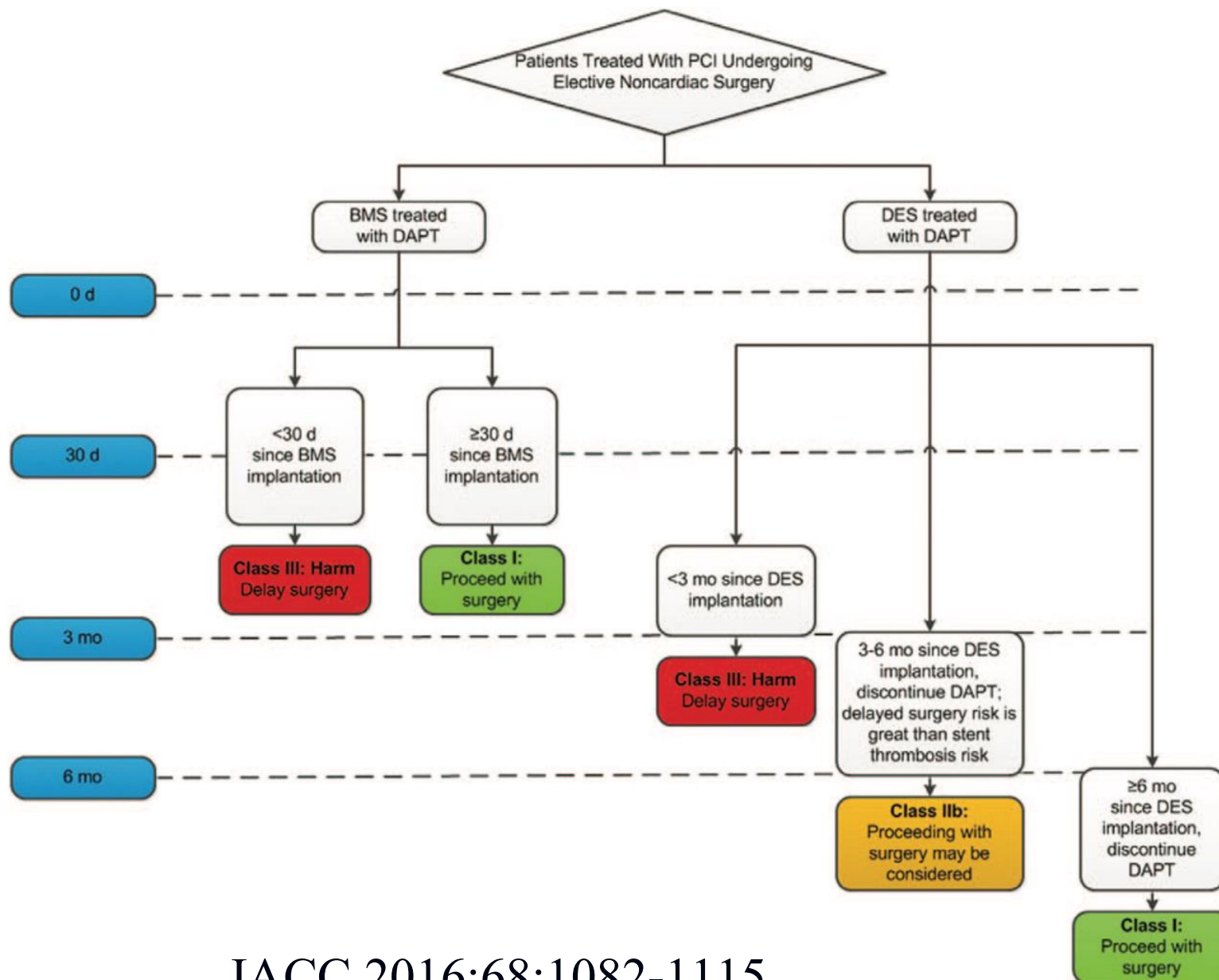
- Presents 90 days post PCI with LGI bleed and hemoglobin down to 6.5. Transfused 3 u PRBC. Hemodynamically stable
  - Stop ASA, stop clopidogrel;
- Presents 30 days post PCI with same bleeding as above
  - Stop ASA, stop clopidogrel; alternative try for 3 mo
- Presents 11 months post PCI with same bleeding as above.
  - Stop both. Should have had clopidogrel stopped prior

# What if my patient needs surgery?

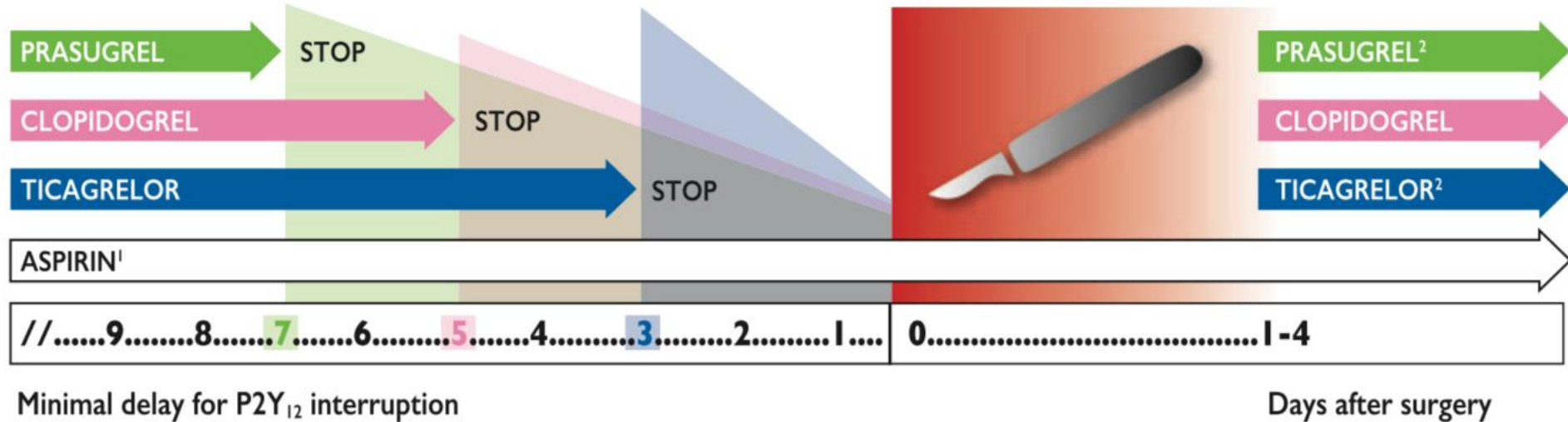
## ■ Individualize

- Type of surgery. Surgeons will ALWAYS want EVERYBODY off ALL anticoagulant/platelet drugs
- Urgency, ability to wait
- Type of DAPT used

**FIGURE 6** Treatment Algorithm for the Timing of Elective Noncardiac Surgery in Patients With Coronary Stents



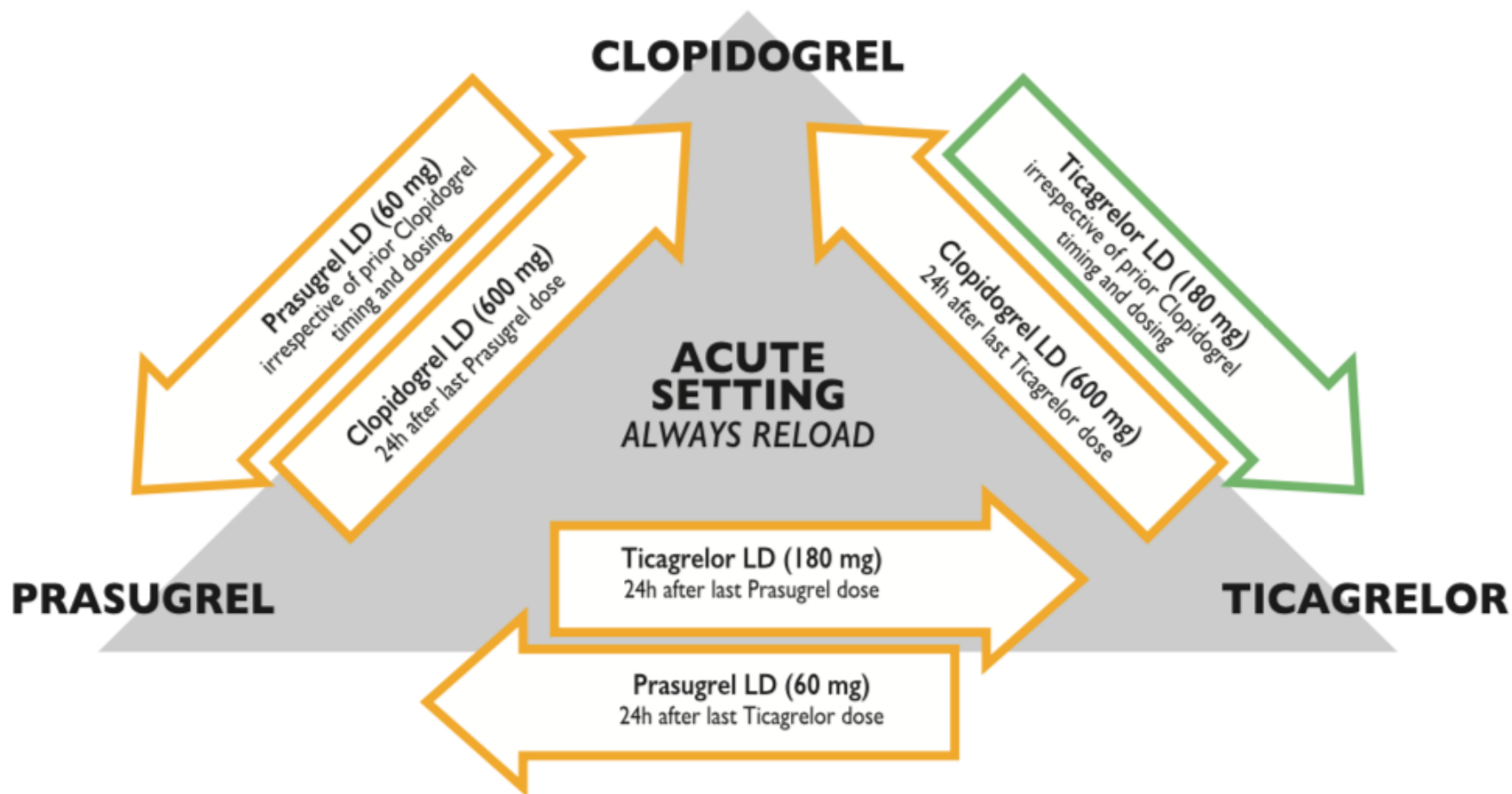
# Interruption schedules for surgery



# What if my patient needs to switch drugs

- Common reasons:
  - Cost of ticagrelor
  - Breathlessness with ticagrelor
  - Rash with clopidogrel
  - Change in insurance/finances





**CLOPIDOGREL**

Prasugrel MD (10 mg q.d.)  
24h after last Clopidogrel dose

Clopidogrel MD (75 mg q.d.)  
24h after last Prasugrel dose

**CHRONIC  
SETTING**

Ticagrelor MD (90 mg b.i.d.)  
24h after last Clopidogrel dose

Clopidogrel LD (600 mg)  
24h after last Ticagrelor dose

**PRASUGREL**

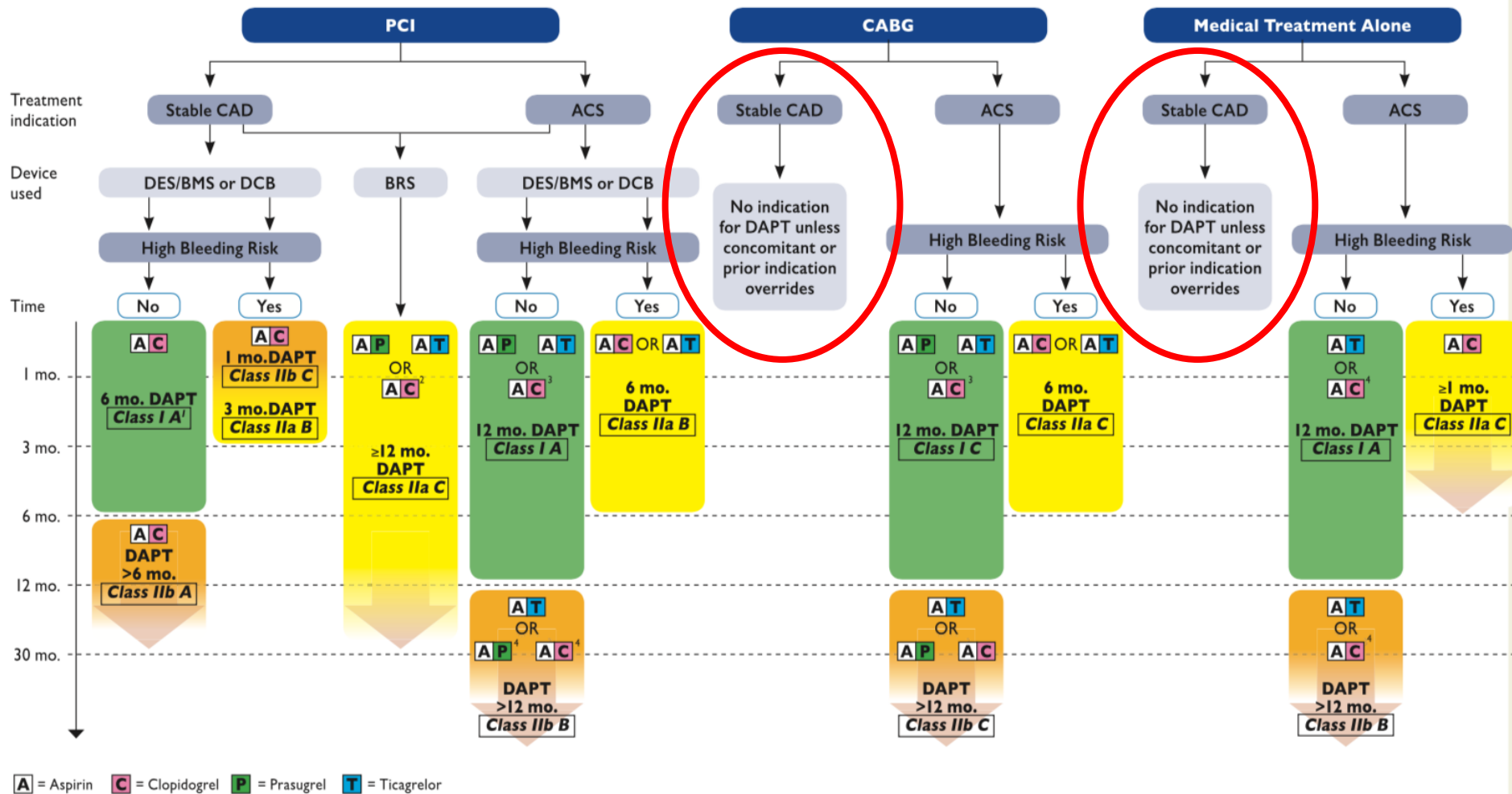
Ticagrelor MD (90 mg b.i.d.)  
24h after last Prasugrel dose

**TICAGRELOR**

Prasugrel LD (60 mg)  
24h after last Ticagrelor dose

# General considerations

- Balancing thrombotic events with bleeding events
- Liberal use of risk estimating scores
- All aspirin doses are 81mg
- Choice of P2Y<sub>12</sub> depends on the balance
  - Clopidogrel less effect on platelets
  - Ticagrelor more effect on platelets
  - Prasugrel more effect, but risk in prior CVA
- Clinical syndrome class effect: Stable (SIHD) or acute coronary syndrome (STEMI, NSTEMI)



## Change in recommendations

Before → 2017

Pretreatment with P2Y<sub>12</sub> inhibitors when PCI is planned

Liberal use of PPI to mitigate GI bleeding risk

Elective surgery requiring discontinuation of the P2Y<sub>12</sub> inhibitor after 1 month

Ticagrelor interruption of 3 days prior elective surgery

Dual therapy as an alternative to triple therapy when bleeding risk outweighs the ischaemic risk

Discontinuation of antiplatelet treatment in patients treated with OAC should be considered at 12 months.

Routine platelet function testing to adjust therapy

## New recommendations 2017

The occurrence of actionable bleeding while on DAPT should prompt reconsideration of type and duration of DAPT regimen.

The decision for DAPT duration should be dynamic and reassessed during the course of the initially selected DAPT regimen.

Discontinuation of P2Y<sub>12</sub> inhibitor therapy after 6 months when stenting ACS patients with PRECISE-DAPT ≥ 25

6-month DAPT regimen in patients with SCAD treated with drug-coated balloon

Early administration of ticagrelor/ clopidogrel in NSTEMI-ACS with invasive approach

Ticagrelor 60 mg b.i.d preferred over other oral P2Y<sub>12</sub> inhibitors for DAPT continuation >12 months in post-MI

I    IIA    IIB    III