Tricky ones Cardiology cases

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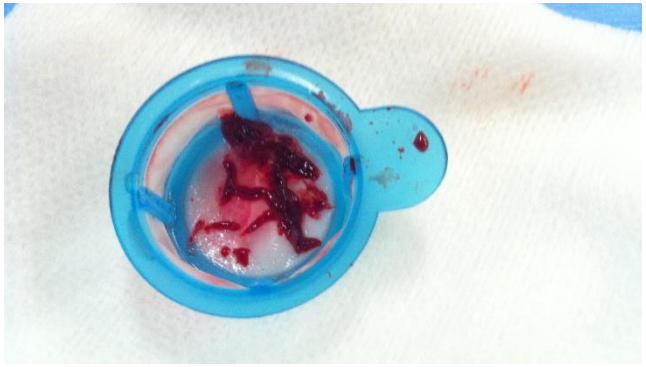
Why do Cardiologists care about bleeding?

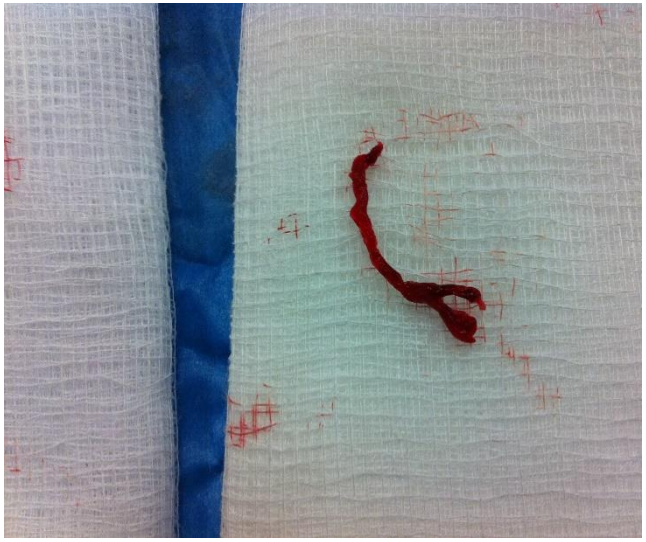


Blood clots are bad

- Clot in coronaries – heart attacks
- Clot in left atrial appendage (AF) - stroke

Metal is thrombogenic

- Stents – coronaries
- Heart valves (metal, bioprosthetic, TAVI)
- Closure devices (VSD, ASD, PFO etc.)



We use a lot of anti-clotting drugs

Anti-clotting drugs lead to increased bleeding

<u>Bleeding kills</u>

Anti-thrombotics….

Oral antiplatelets (often 2)
Aspirin
Clopidogrel
Prasugrel
Ticagrelor

Intravenous anticoagulants
Heparin
Bivalirudin

Intravenous antiplatelets
Abciximab (ReoPro)
Tirofiban (Aggrastat)
Eptifibatide (Integrelin)
Cangrelor

Subcutaneous anticoagulants
LMWH (enoxaparin, dalteparin)
Fondaparinux

Oral anticoagulants
Warfarin
NOACs (rivaroxban, edoxaban, apixaban, dabigatran)

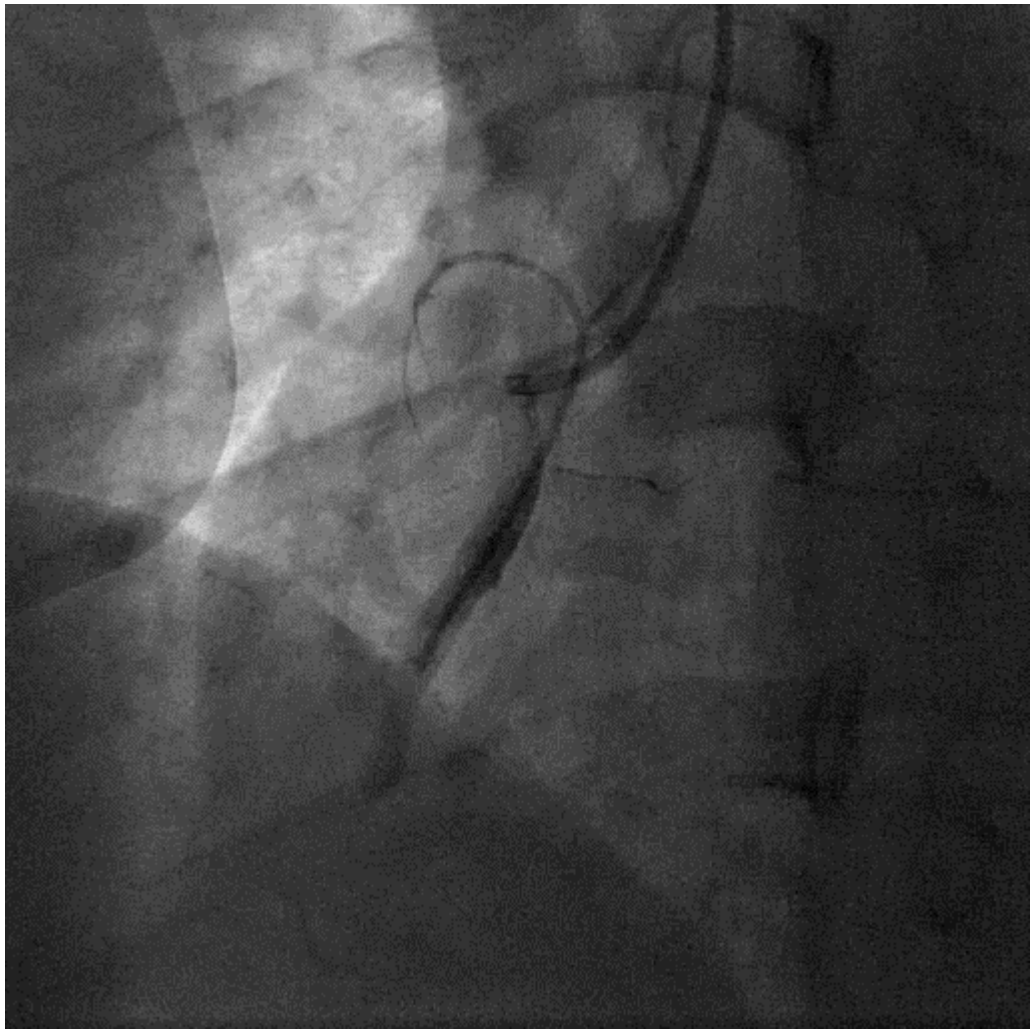
Thrombolytics
Streptokinase
Tenecteplase
tPA

38yo man
No cardiac hx
Inferior STEMI
Failed thrombolysis

Aspirin 300mg
Clopidogrel 600mg
Tenecteplase

On arrival
Prasugrel 60mg

In lab
Heparin 8000 U



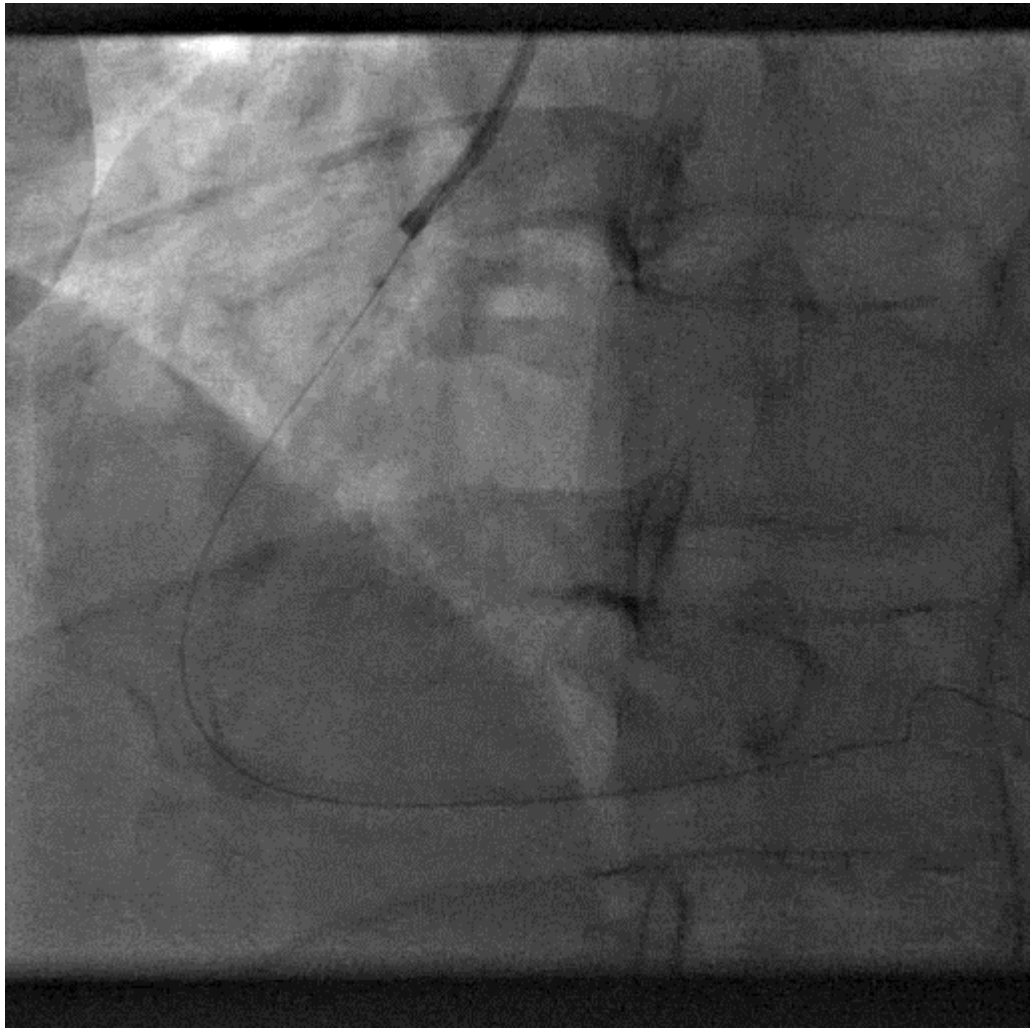
Thrombectomy
Balloon inflation

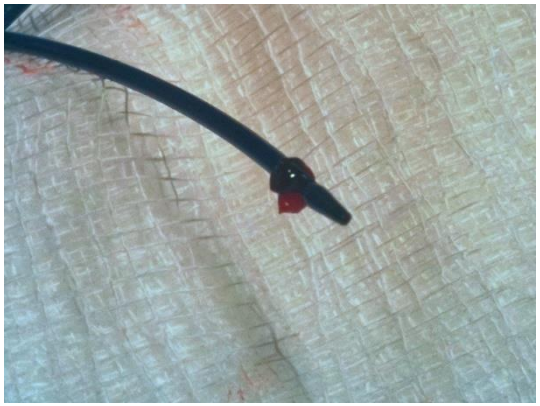
Intracoronary abciximab

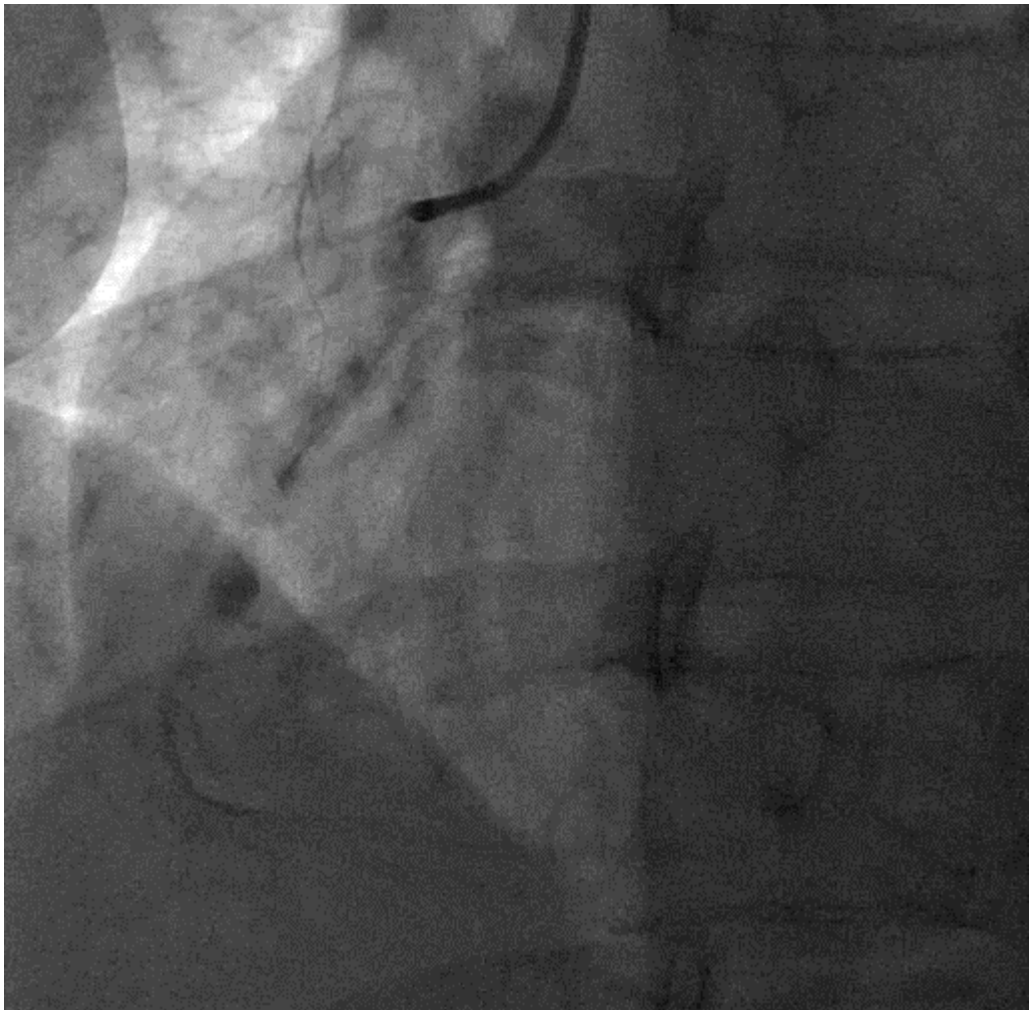
Stented

Still huge thrombus

Intracoronary tPA







Aspirin
Clopidogrel
Prasugrel
Heparin
Abciximab
Tenecteplase
tPA

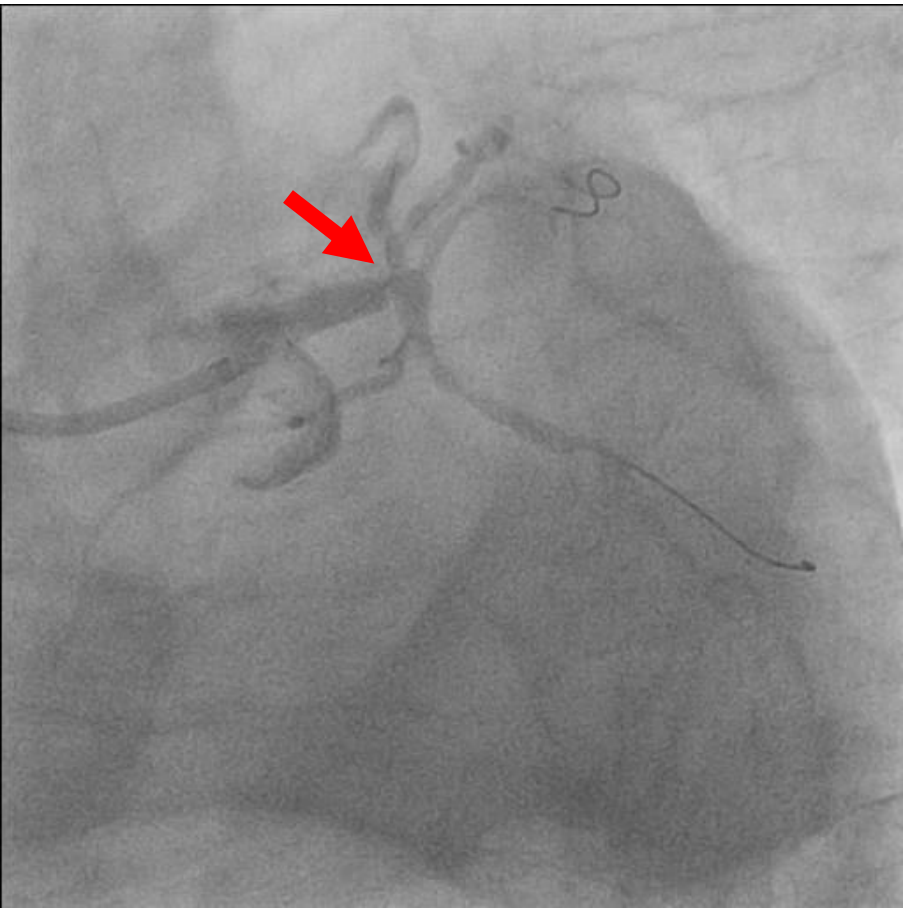
No bleeding (phew!)

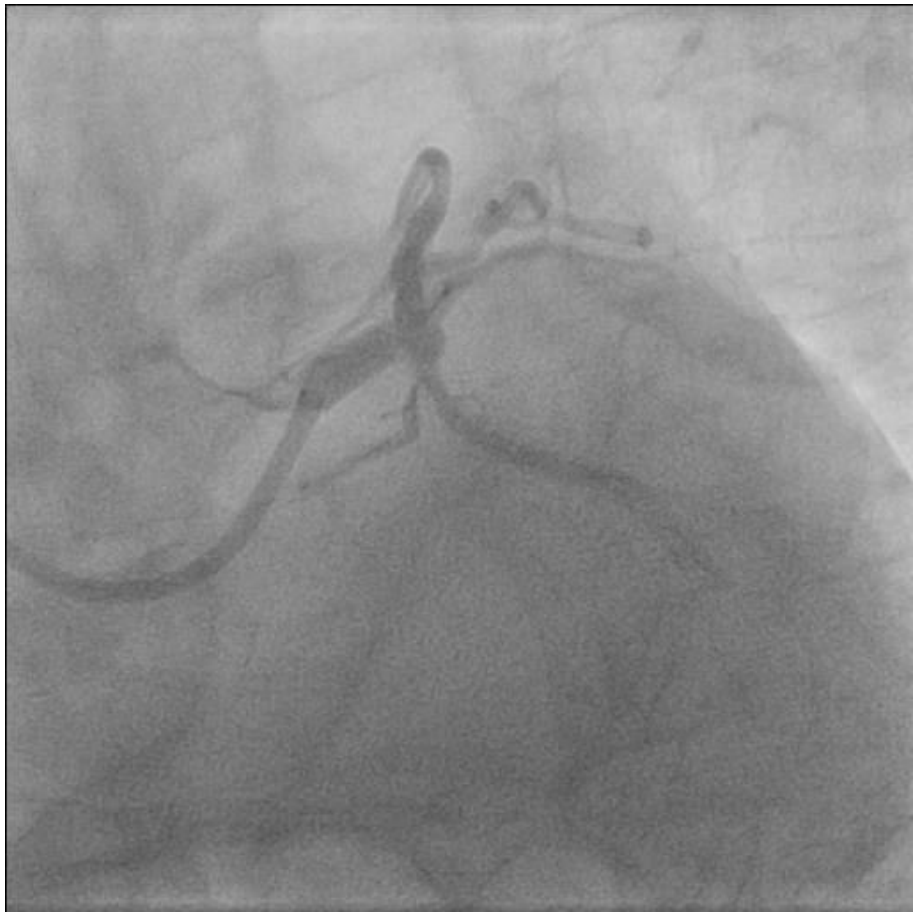
Went home at 48 hours on aspirin & prausgrel

A more complex patient

- 72yo man
- CABG 1990s (single graft to RCA)
- Presented N Tees with renal colic and AKI (Cr 250). Right ureteric stone with hydronephrosis
- GA and ureteric stent
- Pulseless VT, ischaemic ECG, TN 1300
- Pulmonary oedema
- Echo –severe LVSD. Aspirin & clopidogrel
- Emergency angiography

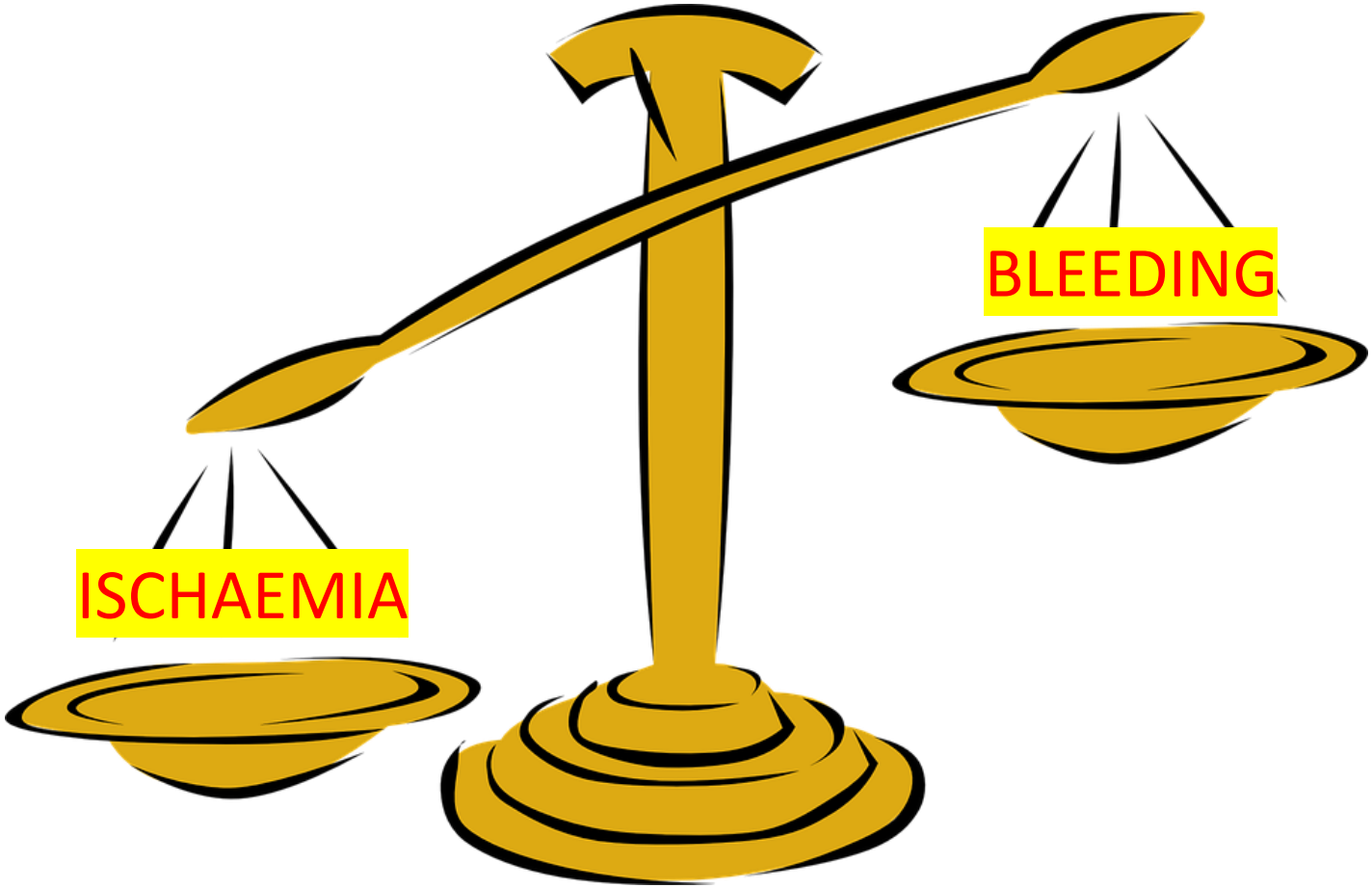
Complex PCI LMS (3.5hrs)



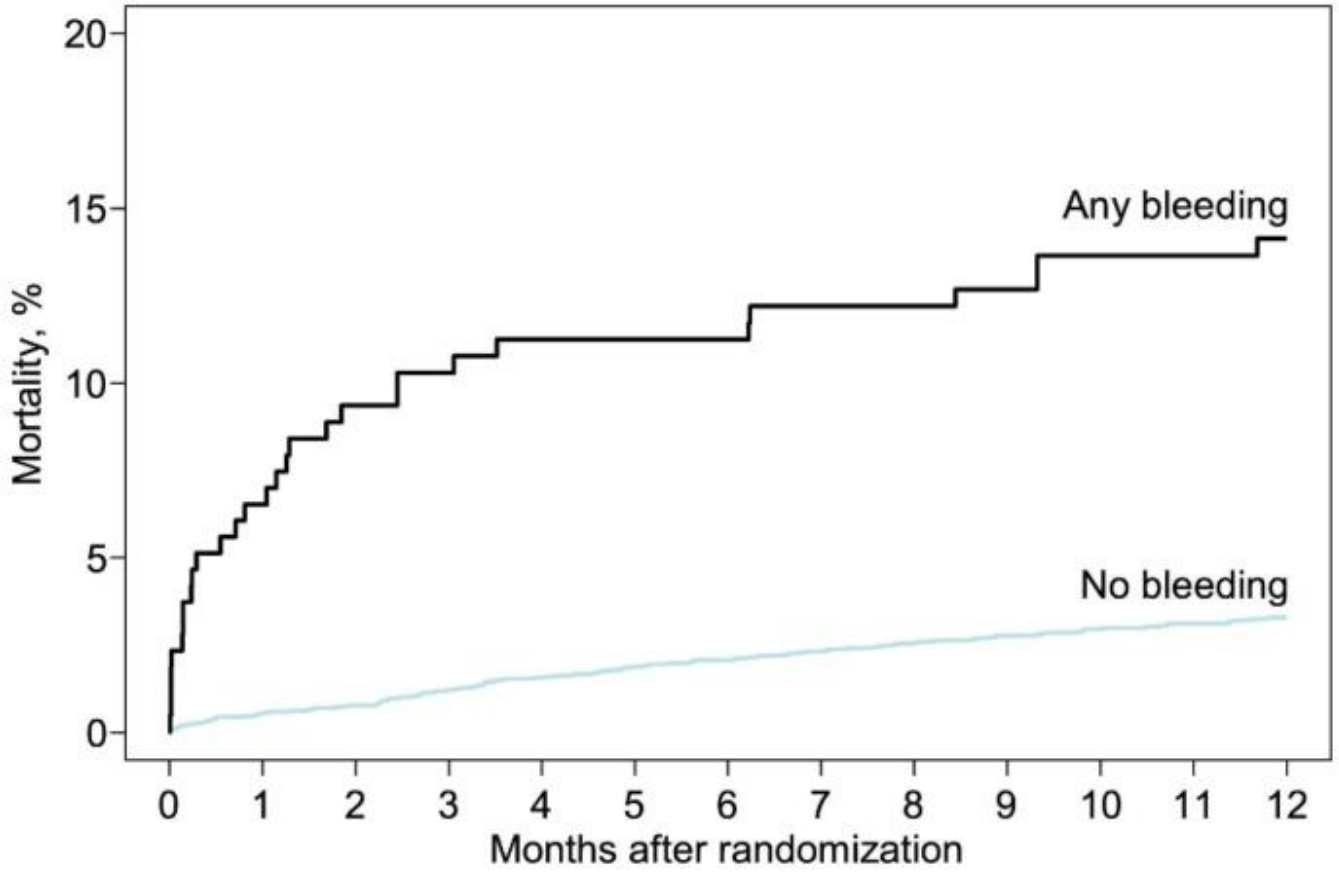


- Heparin during procedure. Ticagrelor loaded at end.

- Stroke post-PCI with left hemiplegia
- Thrombolysed (on top of aspirin, clopidogrel, ticagrelor, heparin) – neurology improved ++
- Massive GI bleed
- Gastroscopy – bleeding gastric ulcer - injected
- Discharged home on DAPT.
- Repeat gastroscopy- GU healed. Oesophageal bx – cancer
- Oesophagectomy planned but on DAPT
- Stopped clopidogrel after 6 months to facilitate oesophagectomy
- Doing well at 18 months. Mild left weakness. Cycling 5 miles/day
- Moderate LV dysfunction. Normal kidney function.


BLEEDING
ISCHAEMIA

Bleeding kills



Ndrepepa G et al. Journal of the American College of Cardiology, 2008, 690 - 697

Meta-analysis of 5834 patients undergoing PCI

50% bleeds are access site related[1]

Increases mortality by 1.7x

Radial access almost eliminates this risk

Non-access site related bleeds increase mortality by 4x

1. Kwok Circ Int 2015

Risk scores for post-PCI bleeding

HAS-BLED
CRUSADE
ACUITY

- Age
- Female gender
- Anaemia
- Bleeding history
- Previous stroke
- Renal impairment
- Cancer
- Need for oral anticoagulation

Dual antiplatelet therapy (DAPT)

Mainstay of treatment post-PCI to prevent stent thrombosis

Aspirin + 2nd agent

Clopidogrel

Prasugrel

Ticagrelor

Stent *thrombosis* : A time based classification

Acute stent thrombosis	0 to 24 hours after stent implantation
Subacute stent thrombosis	>24 hours to 30 days after stent implantation
Late stent thrombosis	>30 days to 1 year after stent implantation
Very late stent thrombosis	>1 year after stent implantation

Adopted from academic research consortium .www.drsvenkatesan.co.in

Duration of DAPT

- Depends on the stent-type and indication
- 1st generation DES - 1 year DAPT (expert guidelines)
- Modern DES are far safer
  - Thinner struts
  - Better polymers
- Good registry data that DAPT of 3/12 probably sufficient with modern DES
- However if had an MI, then DAPT for 1 year is recommended anyway
- If not sure, ask an interventionist

ESC guidelines 2014

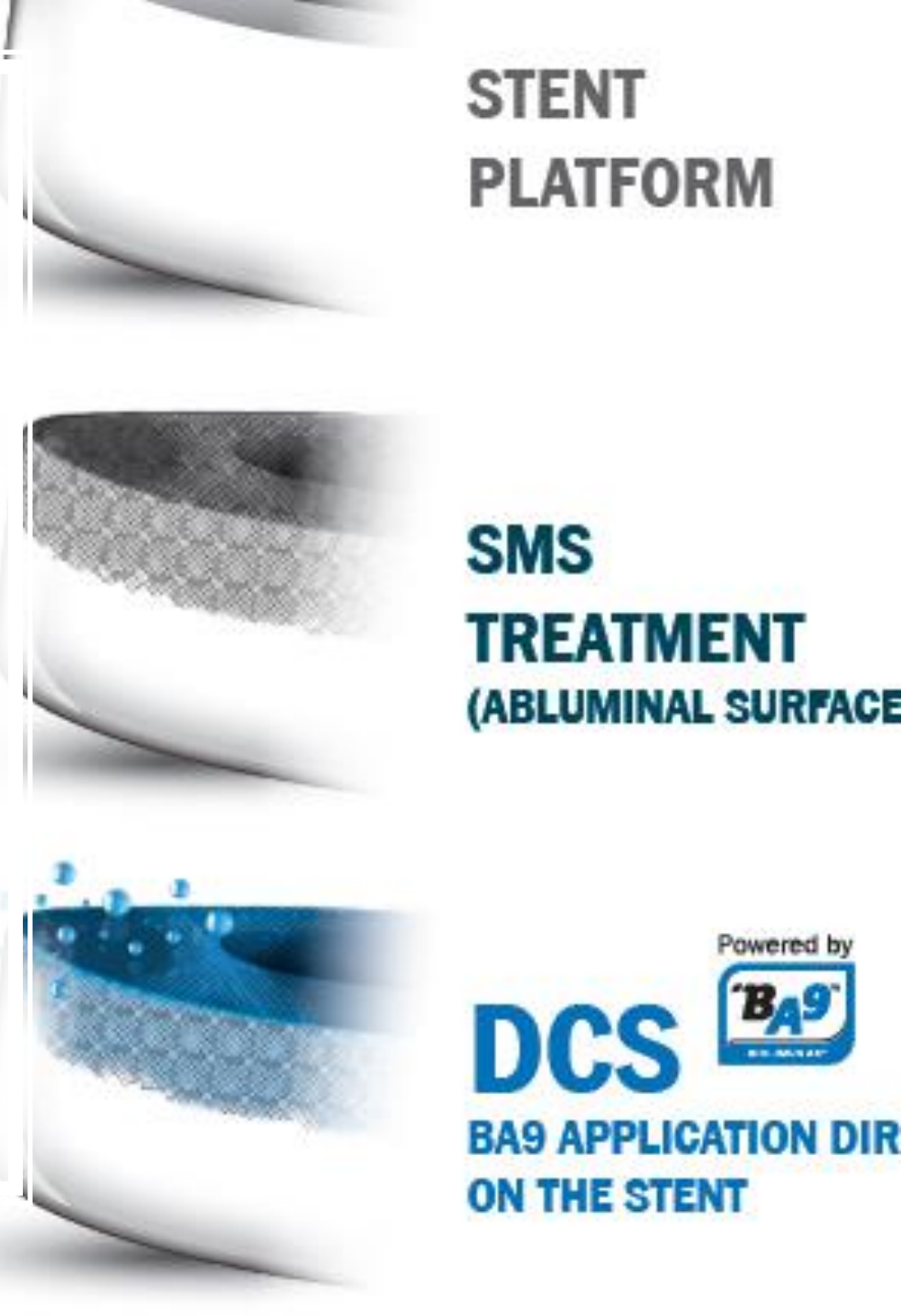
MI – 1 year

Elective PCI:

Antiplatelet therapy after stenting		
DAPT is indicated for at least 1 month after BMS implantation.	I	A
DAPT is indicated for 6 months after DES implantation.	I	B
Shorter DAPT duration (<6 months) may be considered after DES implantation in patients at high bleeding risk.	IIb	A
Life-long single antiplatelet therapy, usually ASA, is recommended.	I	A
Instruction of patients about the importance of complying with antiplatelet therapy is recommended.	I	C
DAPT may be used for more than 6 months in patients at high ischaemic risk and low bleeding risk.	IIb	C

BIOFREEDOM DES

- Drug coated stent (no polymer)
- LEADERS FREE (NEJM 2015)
- 2466 patients at high bleeding risk
- Randomized BMS vs BIOFREEDOM
- DAPT for only 1 month

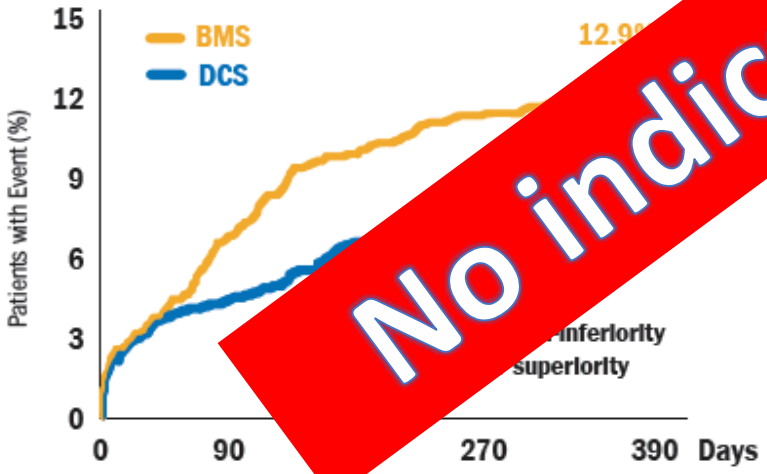


1 month DAPT for DES PCI

Significantly Safer than BMS[11]

29% Reduction in the Rate of the Composite of Cardiac Death, MI, ST

Primary Safety Endpoint (Composite of Cardiac Death, MI



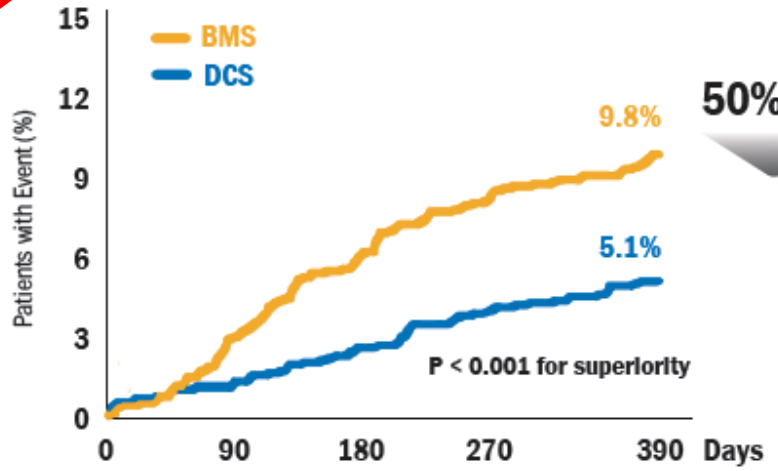
Number at Risk

DCS	1221	1146	1105	1081	1045
BMS	1211	1115	1066	1037	1000

Significa... Effe... BMS[11]

...n the Rate of Restenosis

...ry Efficacy Endpoint (Clinically-Driven TLR)



Number at Risk

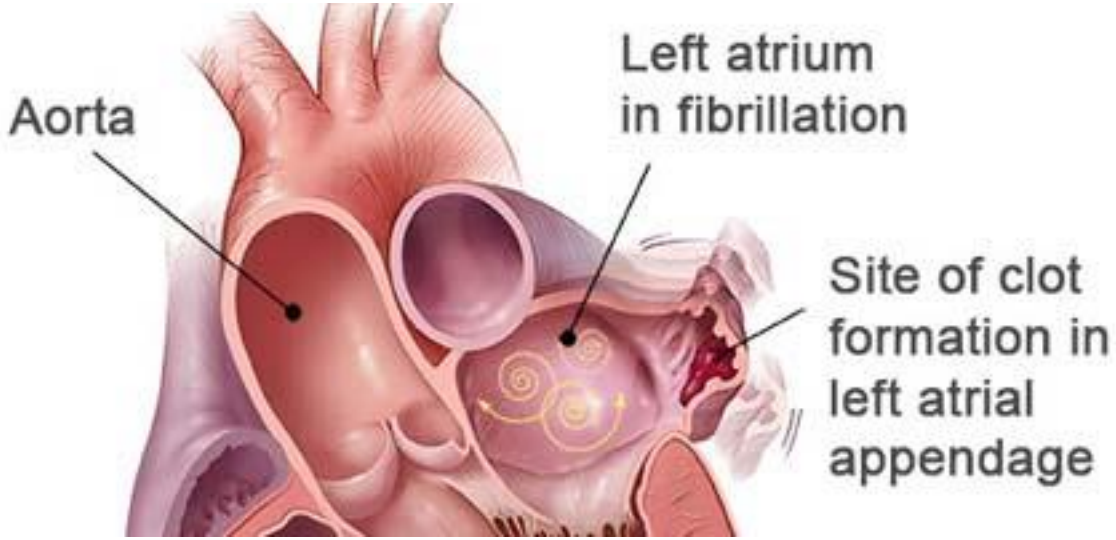
DCS	1221	1167	1130	1098	1053
BMS	1211	1131	1072	1034	984

No indication for BMS

Atrial fibrillation

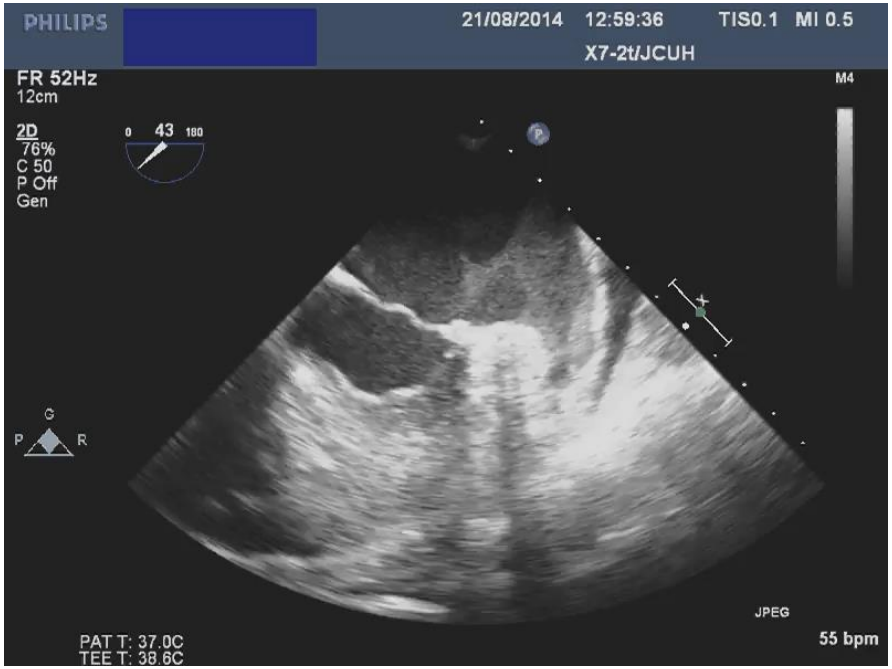
Major cause of preventable stroke

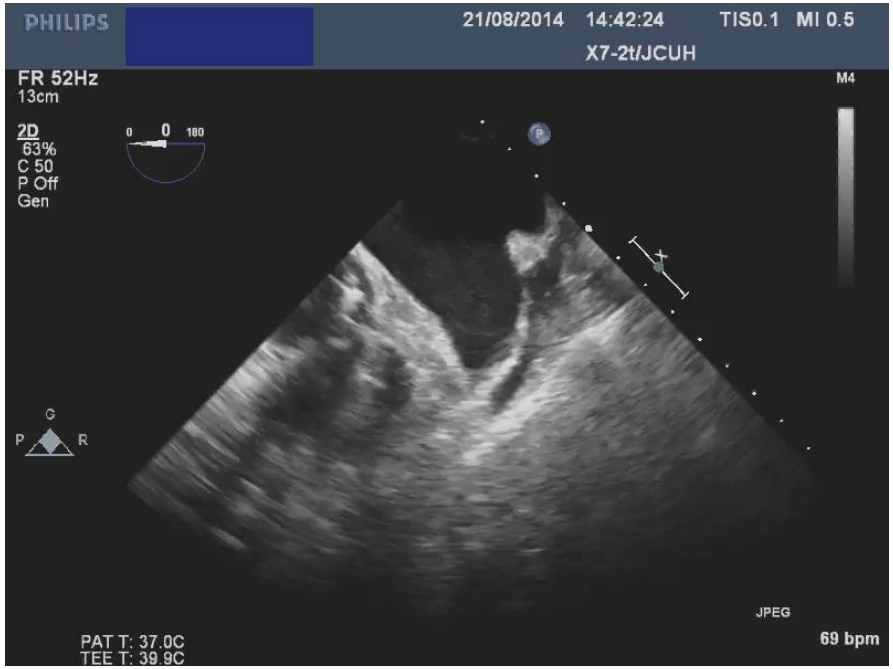
Stasis in the left atrial appendage which results in spontaneous thrombus formation

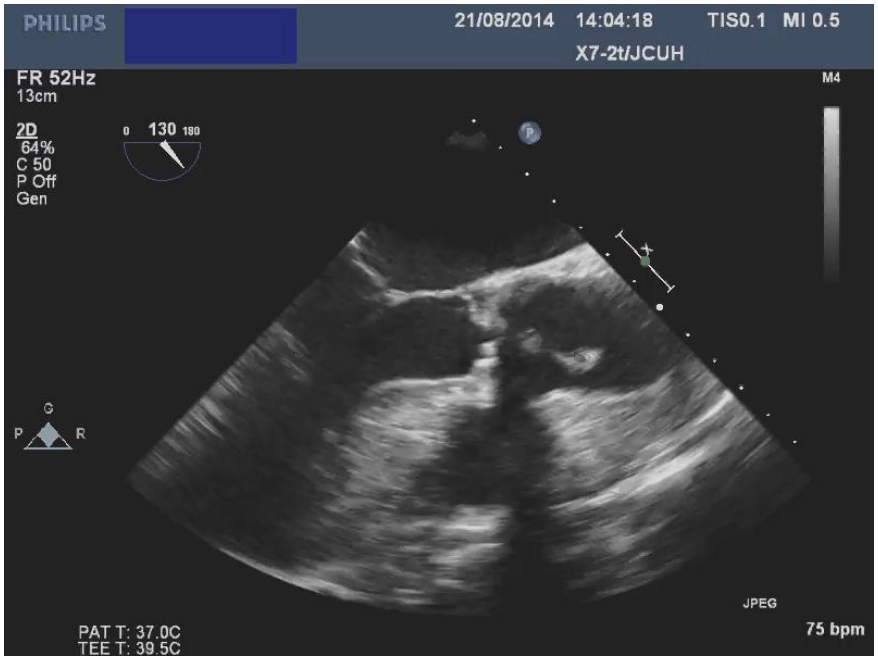


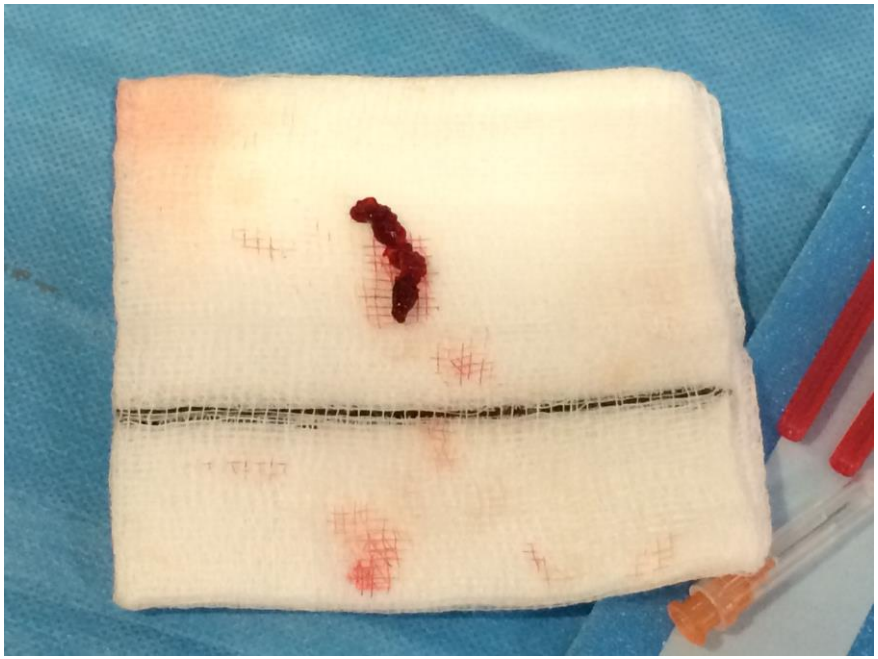
Anticoagulation indicated to reduce risk of stroke

85 year old man undergoing elective TAVI
Permanent AF
On warfarin – stopped 5 days pre-procedure









Left atrial appendage thrombus straddling aortic valve

What about PCI patients who need anticoagulation?

AF very common in the PCI population

Anticoagulation protects against strokes but not against stent thrombosis

DAPT protects against stent thrombosis but doesn't protect against strokes

Warfarin (or NOAC) + aspirin + 2nd antiplatelet **Triple therapy**

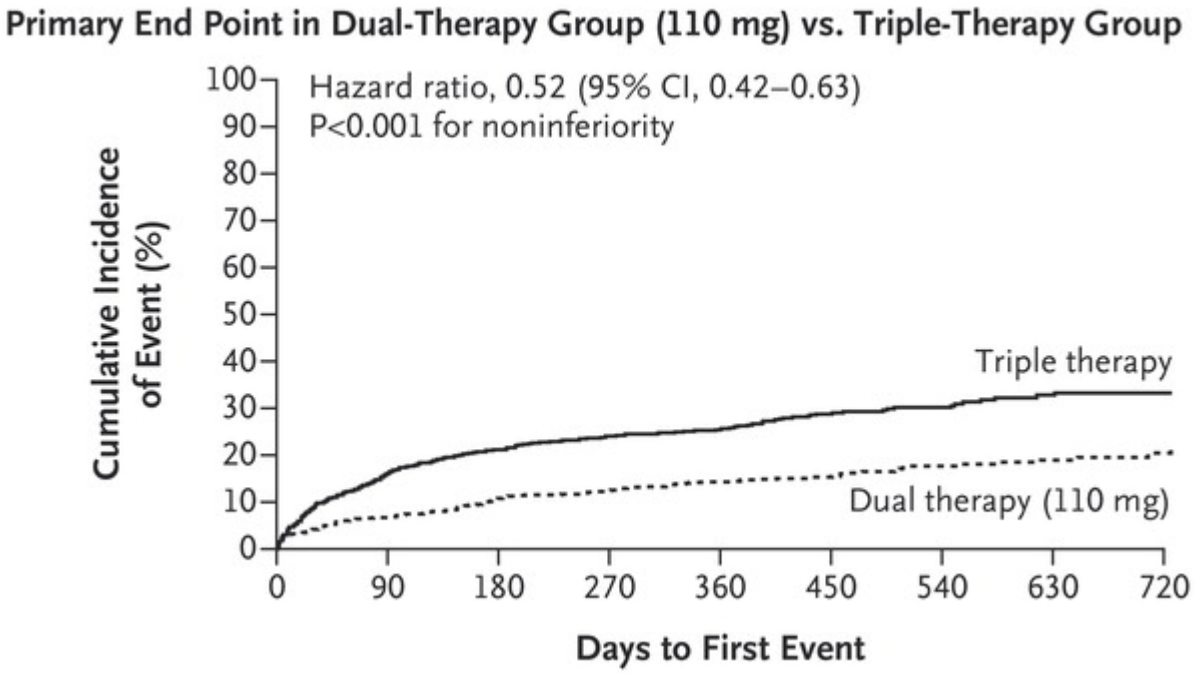
Warfarin (or NOAC) + single antiplatelet **Double therapy**

Triple vs dual therapy for AF

WOEST (warfarin)

PIONEER-AF (rivaroxaban). NEJM November 2016

RE-DUAL PCI (dabigatran) . NEJM August 2017



Bleeding events in RE-DUAL

27% triple therapy
15% double therapy

- Long-term triple therapy kills (fatal bleeds)
- Use warfarin or NOAC and <u>single</u> antiplatelet
- Can probably stop antiplatelet at 1 year

Conclusions

- Bleeding is a major issue in cardiology patients due to need for longterm antithrombotic therapy
- Crucial to consider both ischaemic and bleeding risk for all patients
- Move to shorter durations of DAPT following PCI
- Some DES can be treated with very short durations of DAPT (BioFreedom 1 month)
- AF patients undergoing PCI - anticoagulant and single antiplatelet for 1 year, then anticoagulant longterm
- If not sure, ask an interventionist

THANK YOU