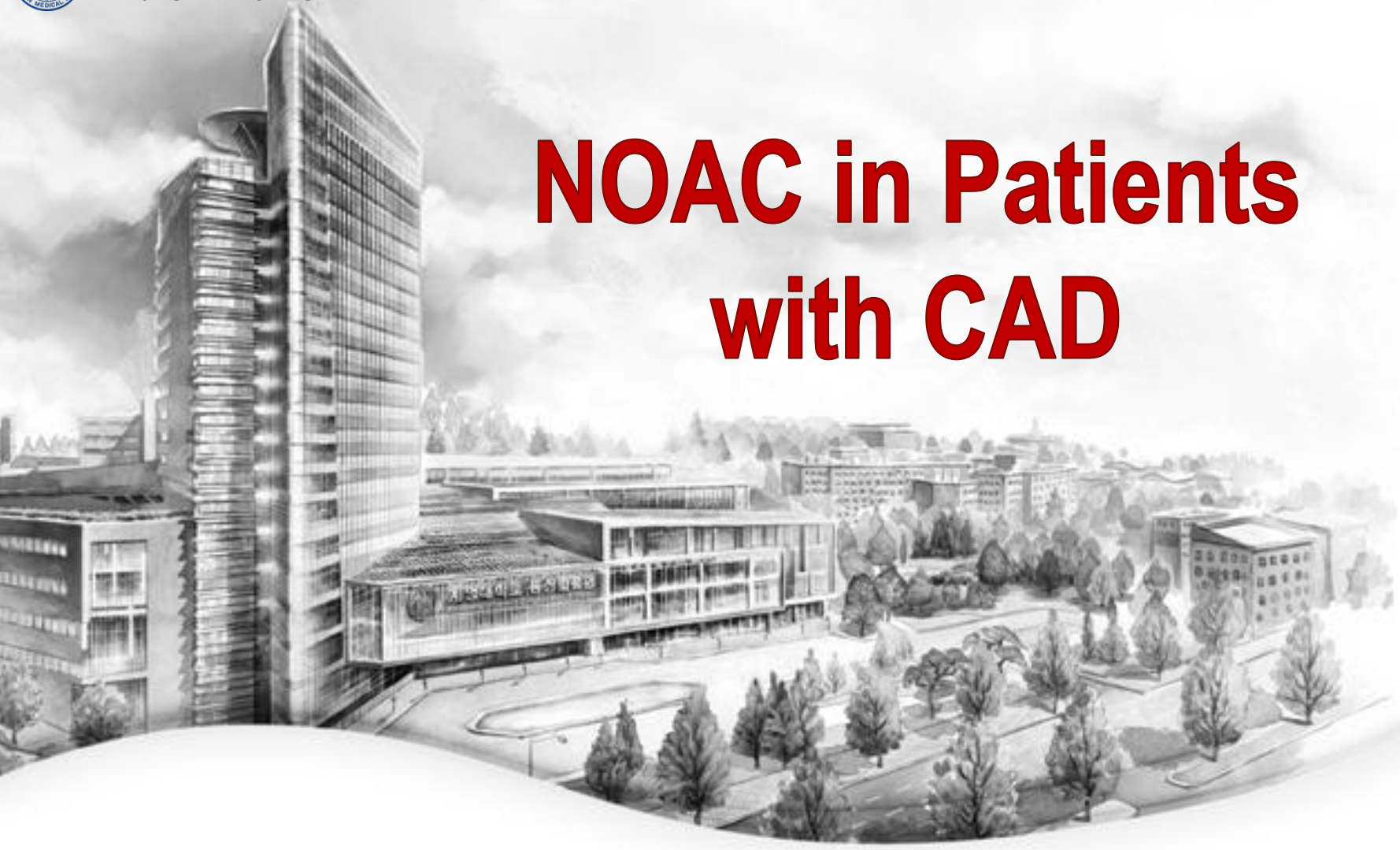
계명대학교 동산의료원
Keimyung University Dongsan Medical Center



NOAC in Patients with CAD

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Arrhythmia Service, Cardiology, Dongsan Medical Center

Atrial fibrillation management: a prospective survey in ESC Member Countries

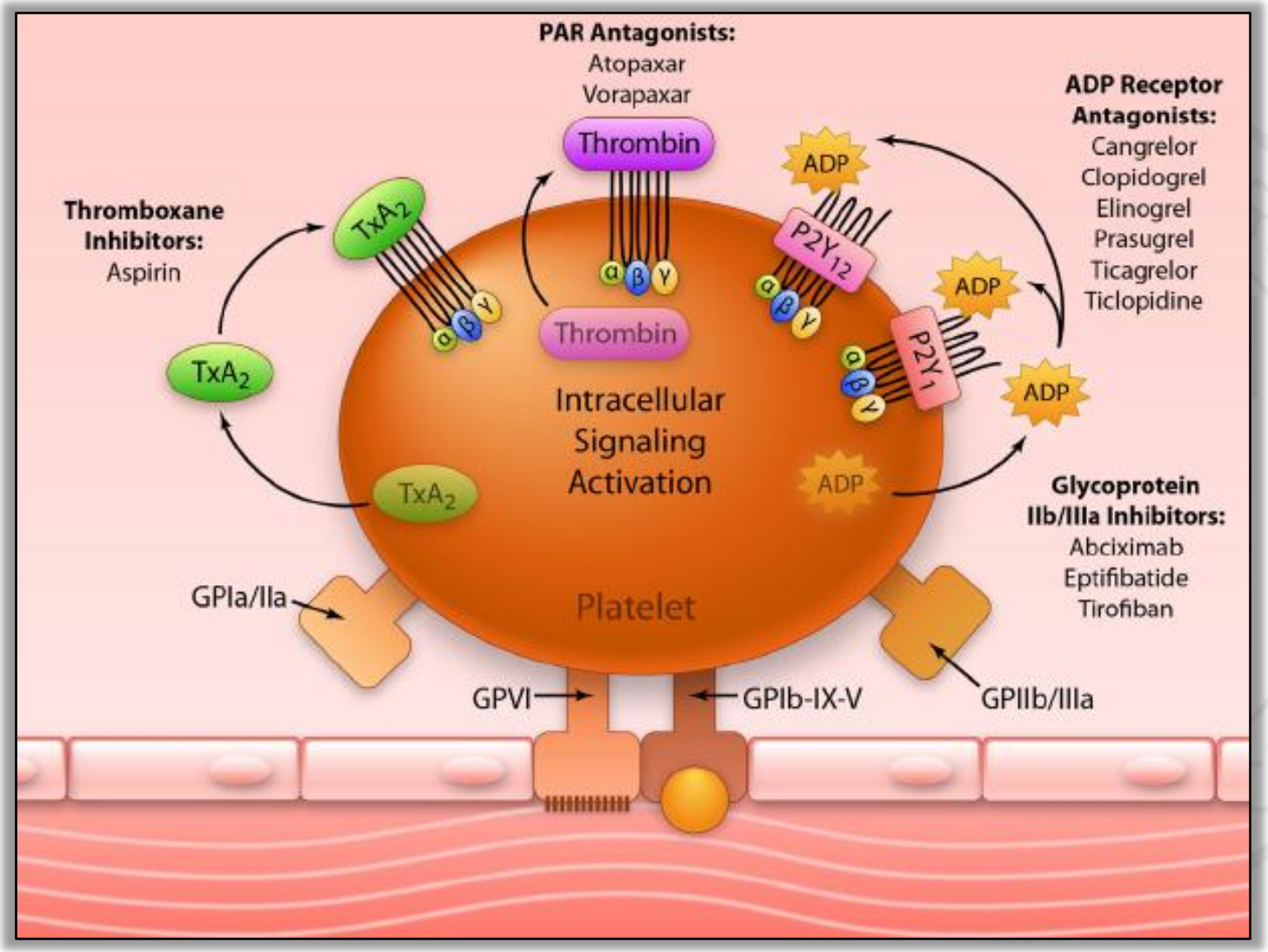
The Euro Heart Survey on Atrial Fibrillation

- 182 hospitals in 35 countries: **5333 AF patients** in 2003~2004
- ***Coronary artery disease*** was present in ***1/3 patients***

	First detected (n=978)	Paroxysmal (n=1517)	Persistent (n=1167)	Permanent (n=1541)
Coronary artery disease	**309 (32%)**	**514 (34%)**	**338 (29%)**	**543 (36%)**
✓ Acute infarction	65 (7%)	32 (2%)	24 (2%)	41 (3%)
✓ Old infarction	124 (13%)	228 (15%)	142 (12%)	259 (17%)
✓ Pervious PCI/CABG	102 (11%)	187 (12%)	136 (12%)	166 (11%)
✓ angina	179 (19%)	350 (23%)	172 (15%)	304 (20%)

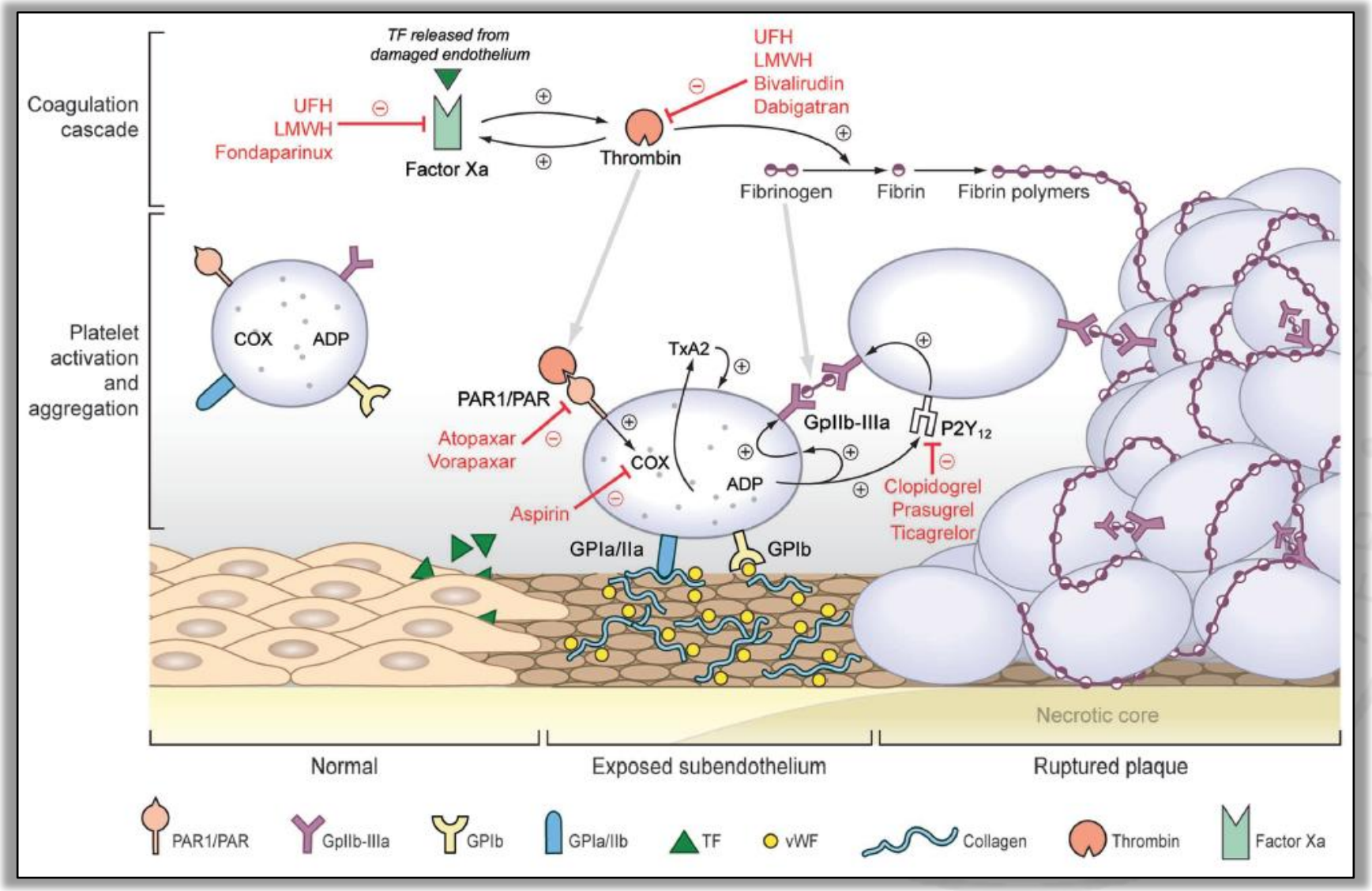
Nieuwlaat R, et al. Eur Heart J 2005;26:2422

Platelet activation & aggregation



Bhatt DL, et al. Circ Res. 2014;114:1929

Site of action of various oral antithrombotics



Lilly SM, et al. doi: 10.3389/fphar.2011.00061

Antiplatelet and Anticoagulation Therapy for Acute Coronary Syndromes

- ***Both antiplatelets and anticoagulants seem to be necessary*** in the management of ACS
- The more ***potent antithrombotic effect is associated with a decreased risk of ischemic events***
- However, there is a ***tipping point*** beyond which more potent antithrombotic effect leads to major bleeding complications that diminish or exceed the benefit on ischemic end points
- *Finding the so-called* ***sweet spot*** *of antithrombotic therapy* ***remains a major challenge***

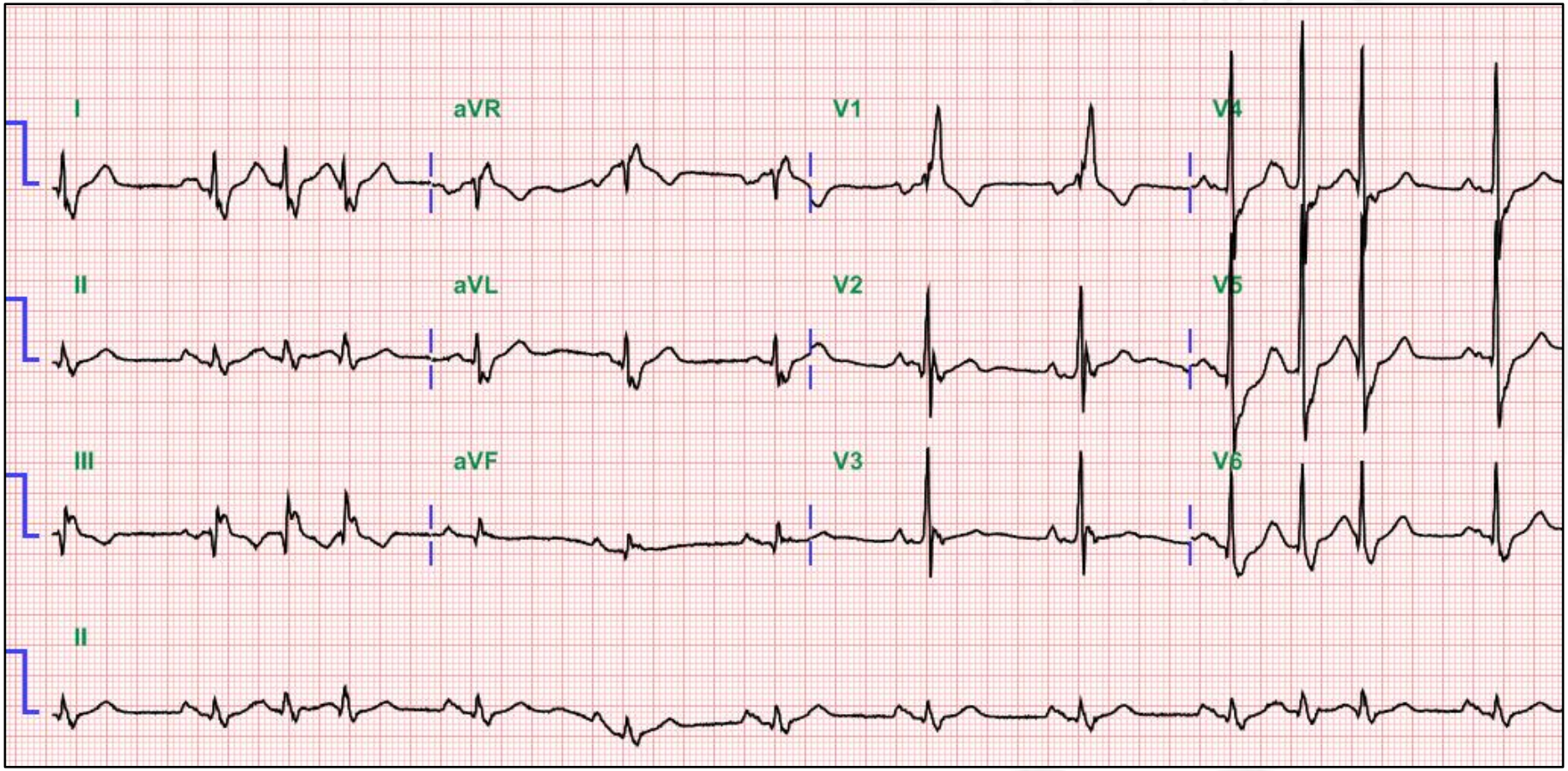
Bhatt DL, et al. Circ Res. 2014;114:1929

~ Our Story ~

- M/51: KDJ
- Chief complaints: uncontrolled AF
- Mr. Kim presents for the management of uncontrolled AF. He had an episode of dysarthria with left side numbness 8 months ago. He was diagnosed with embolic cerebral infarction associated with AF. He had been taking antiarrhythmics (propafenone 150mg bid with warfarin) for controlling the AF but in vain. He was planned to undergo catheter ablation but cancelled due to possible thrombi in LA appendage
- ***CHA_2DS_2VASc score***: HBP (+), DM, (+), stroke (+): **4**

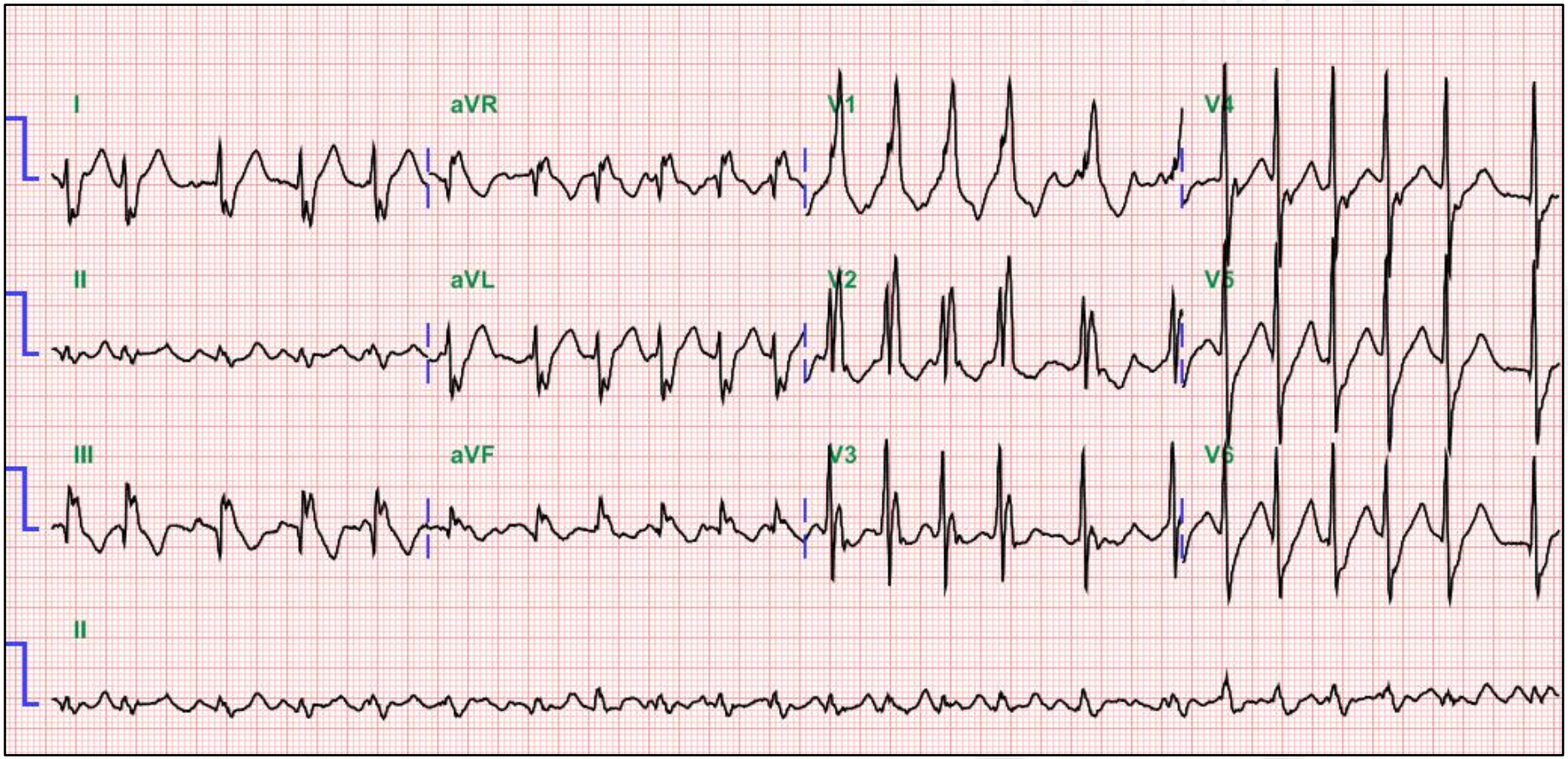
~ Our Story ~

- ***The first encounter***
- On: propafenone 150mg bid, ***warfarin 5mg (INR 4.01)***



~ Our Story ~

- ***1 week later***
- On: amiodarone 600mg, Dilatrend SR 16mg, ***warfarin 2.5mg (INR 1.24)***



~ Our Story ~

- ***4 weeks later***
- On: amiodarone 200mg, Dilatrend SR 16mg, ***Eliquis 5mg bid***

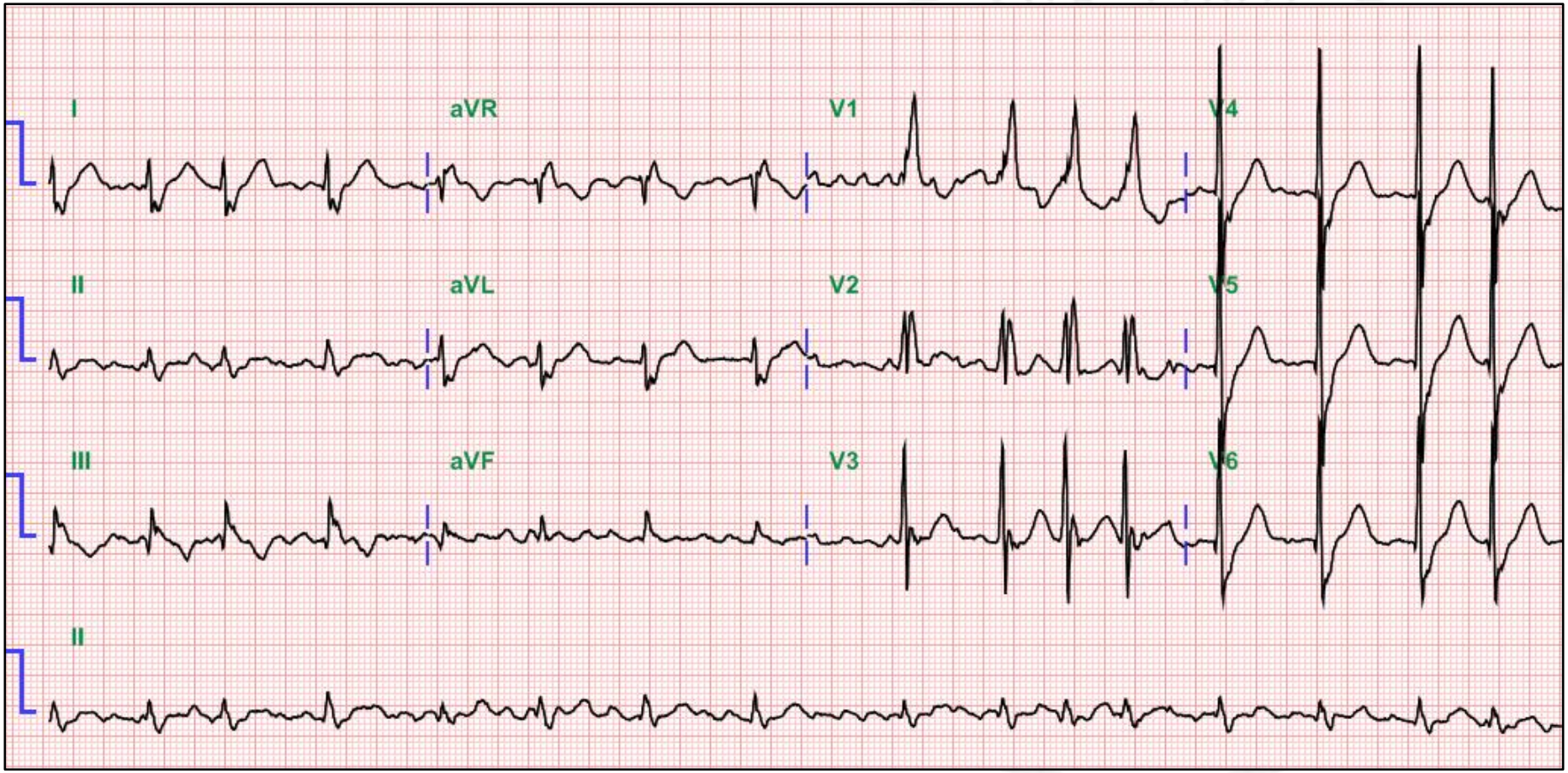
- TEE: Dilated LA, SEC (+: grade 3), No visible thrombi in LAA

- Echo: EF 38%, LA volume: 128.89, LAV index: 63.49 on HR 75~122 BPM
  No regional wall motion abnormality

- SPECT: No regional perfusion defect.
  - ✓ EF: rest 42%, stress 37% ➔ highly suggestive multivessel disease

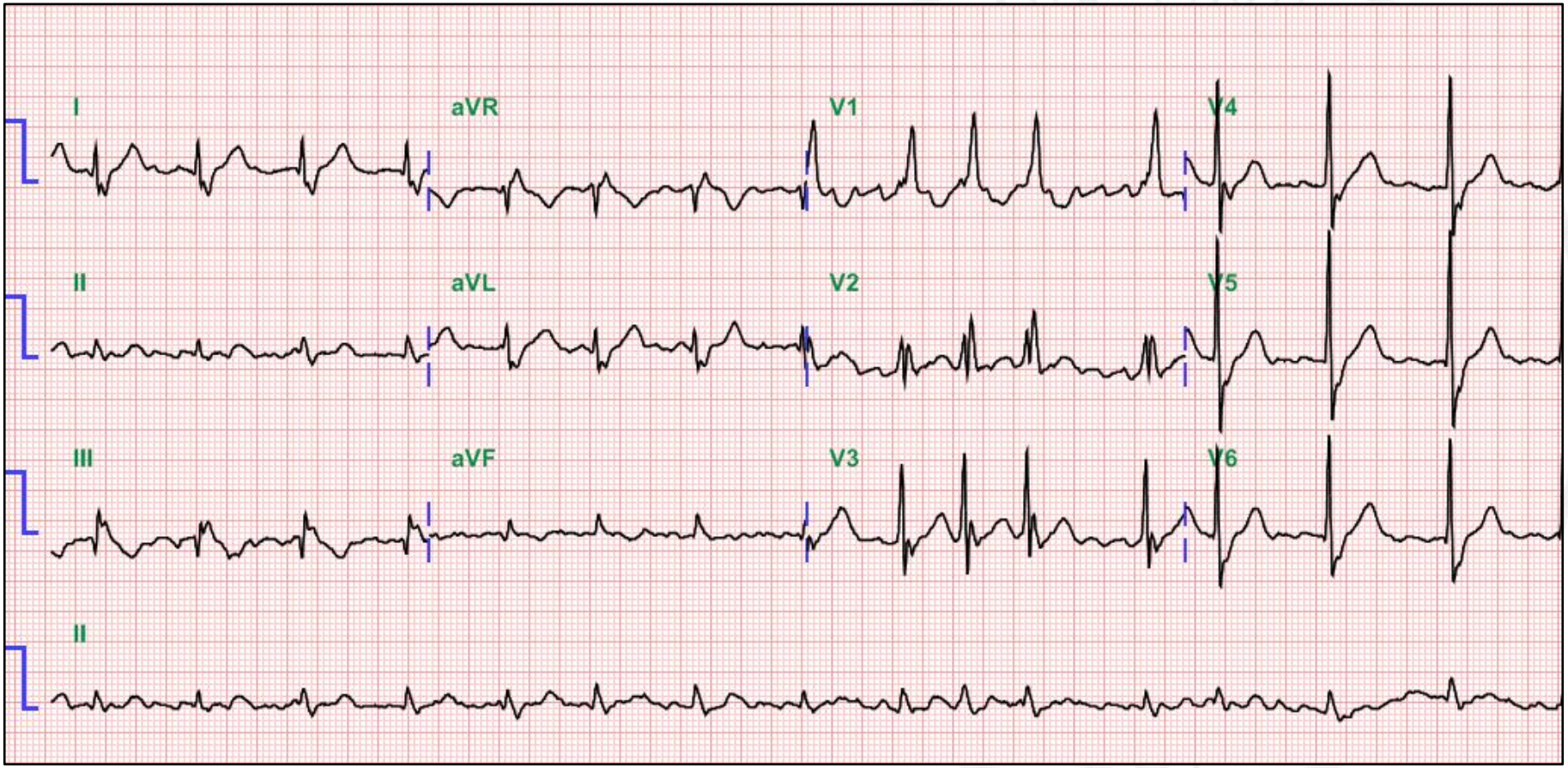
~ Our Story ~

- ***4 weeks later***
- On: amiodarone 200mg, Dilatrend SR 16mg, ***Eliquis 5mg bid***



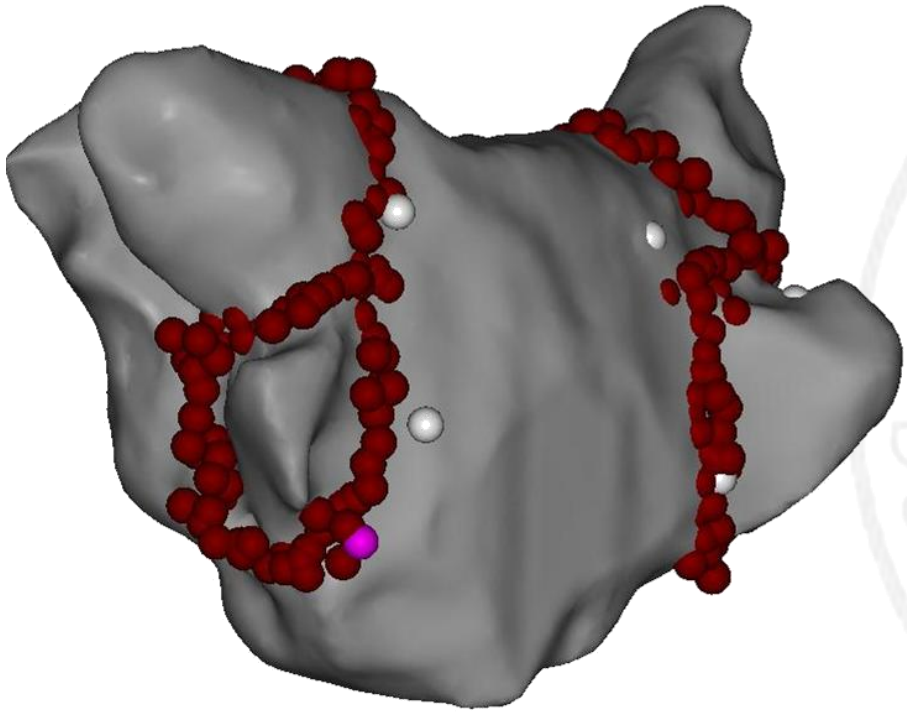
~ Our Story ~

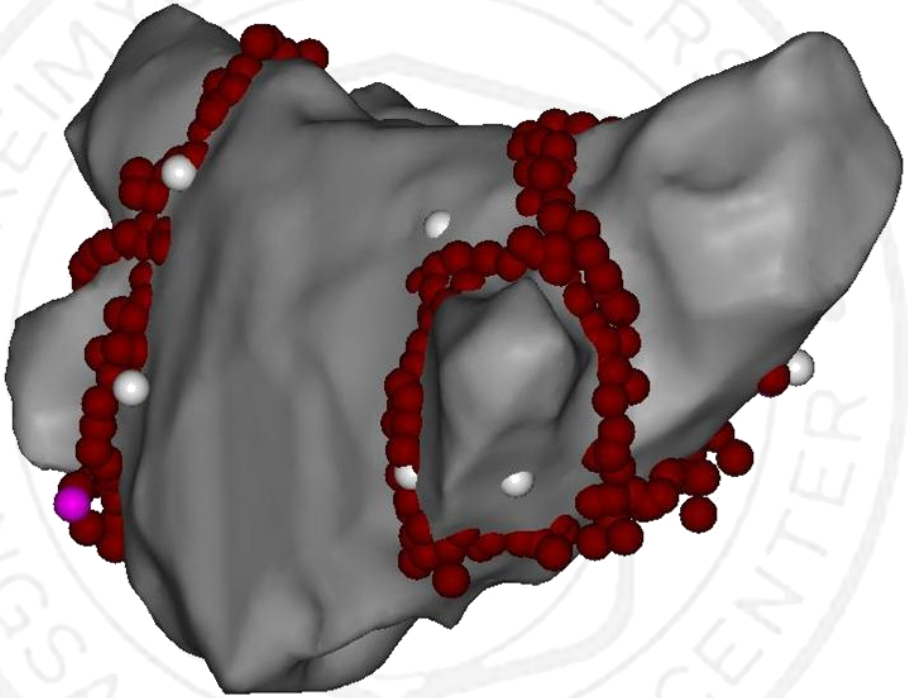
- ***8 weeks later***
- On: amiodarone 200mg, Dilatrend SR 16mg, ***Eliquis 5mg bid***



~ Our Story ~

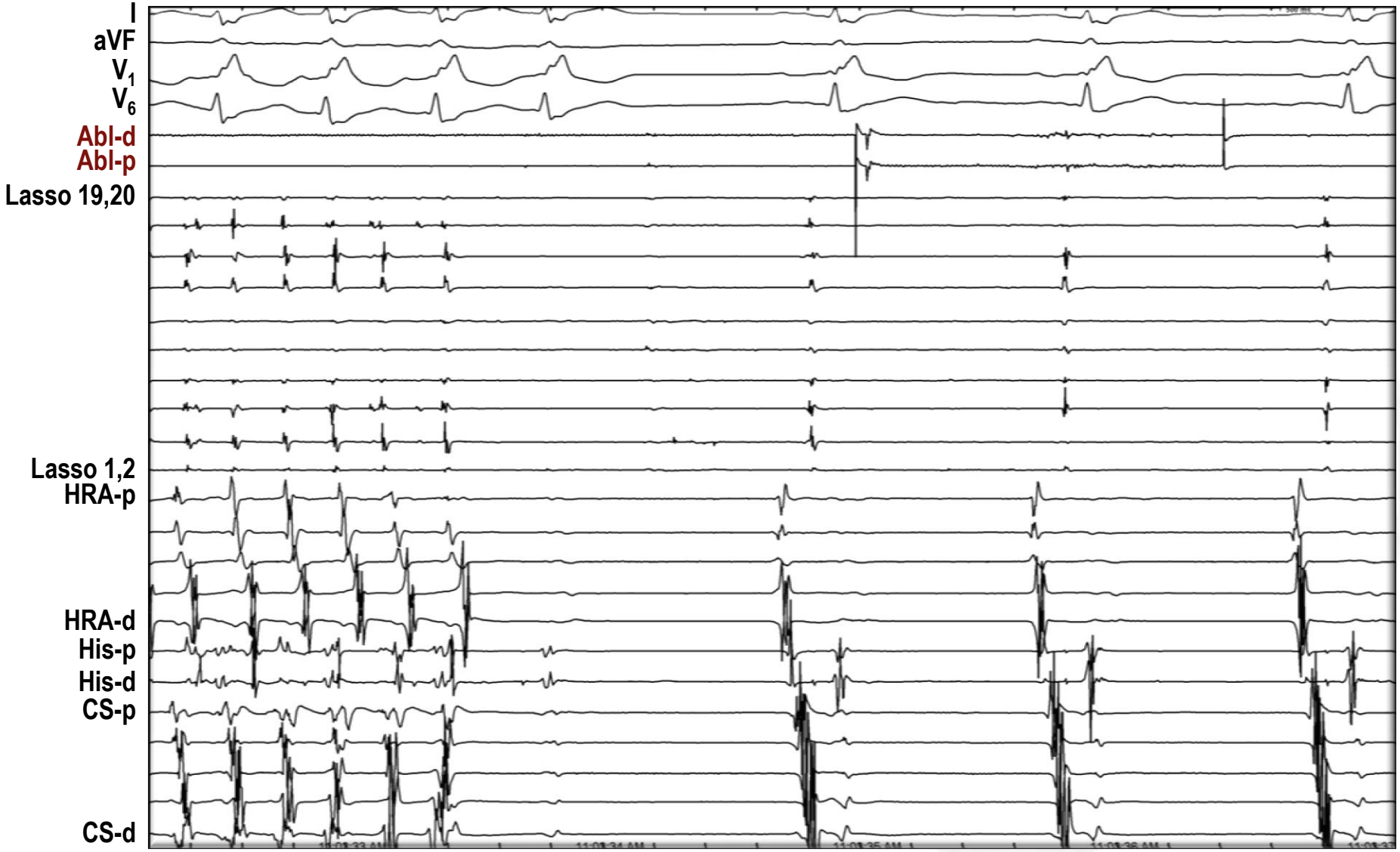
RF catheter ablation: Biantral ablation





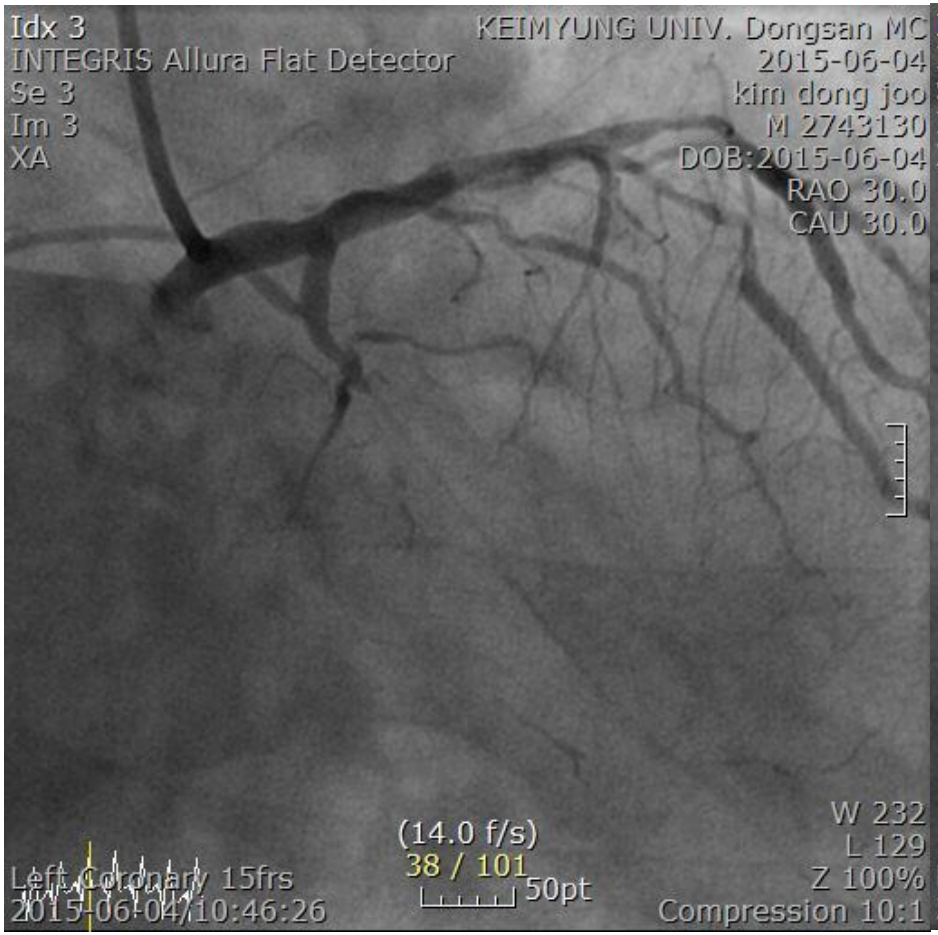
KUDMC

Termination of AF during antral ablation

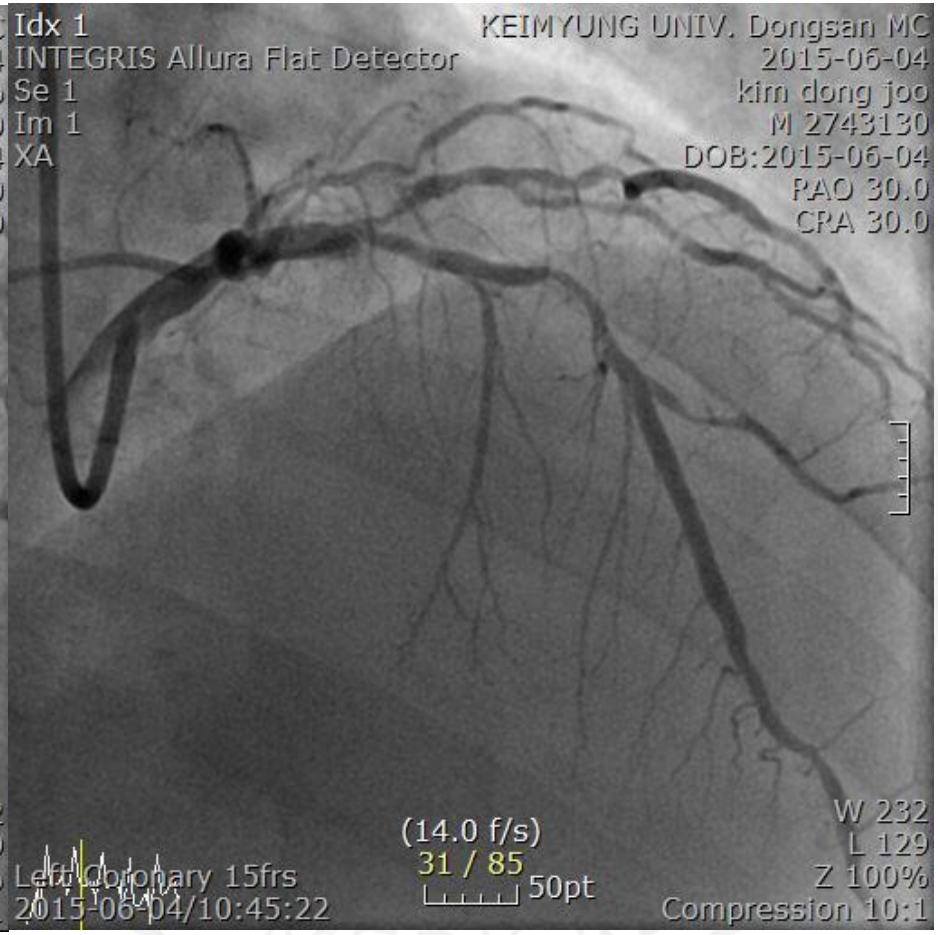


~ Our Story ~

Coronary Angiography



RAO caudal view

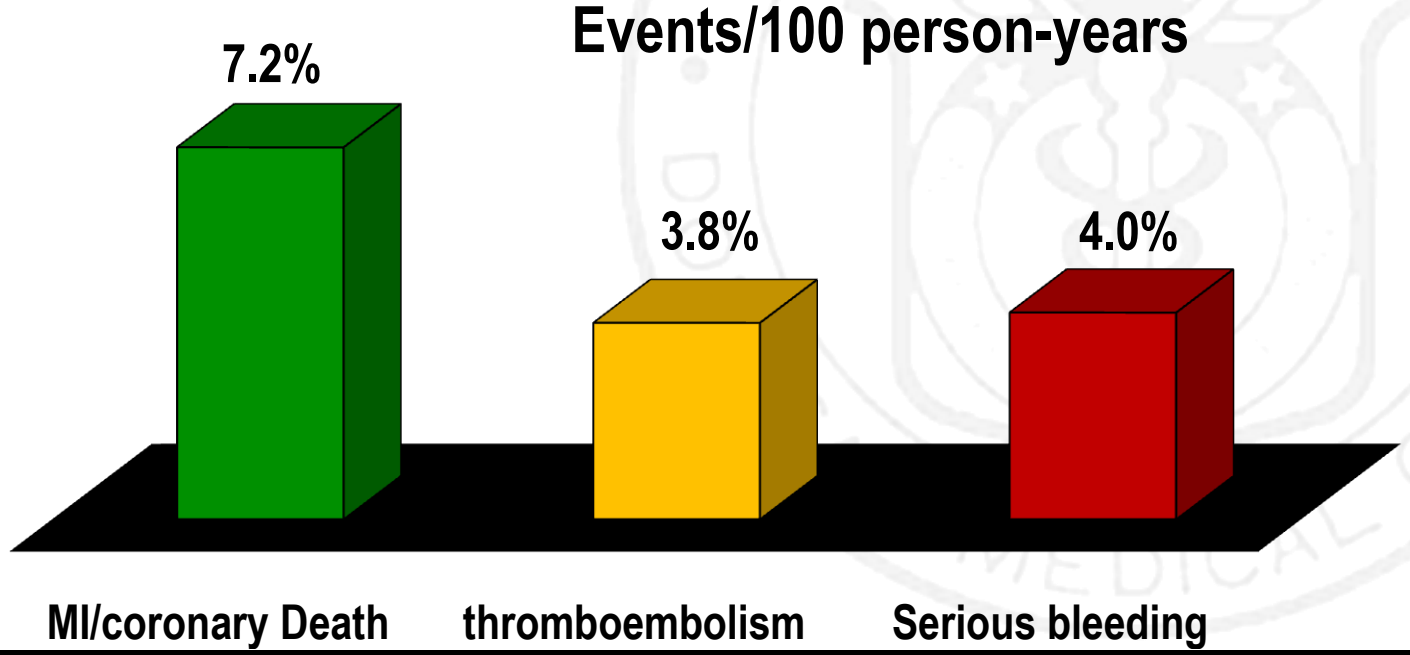


RAO cranial view

Antiplatelet Therapy for Stable Coronary Artery Disease in Atrial Fibrillation Patients Taking an Oral Anticoagulant

A Nationwide Cohort Study

- 8700 patients from Danish Registry (2002~2011)
- ***AF & Stable CAD*** (> 12 months after ACS) with 3.3 Yr FU
- ***VKA only*** vs ***VKA + Aspirin*** vs ***VKA + Clopidogrel***

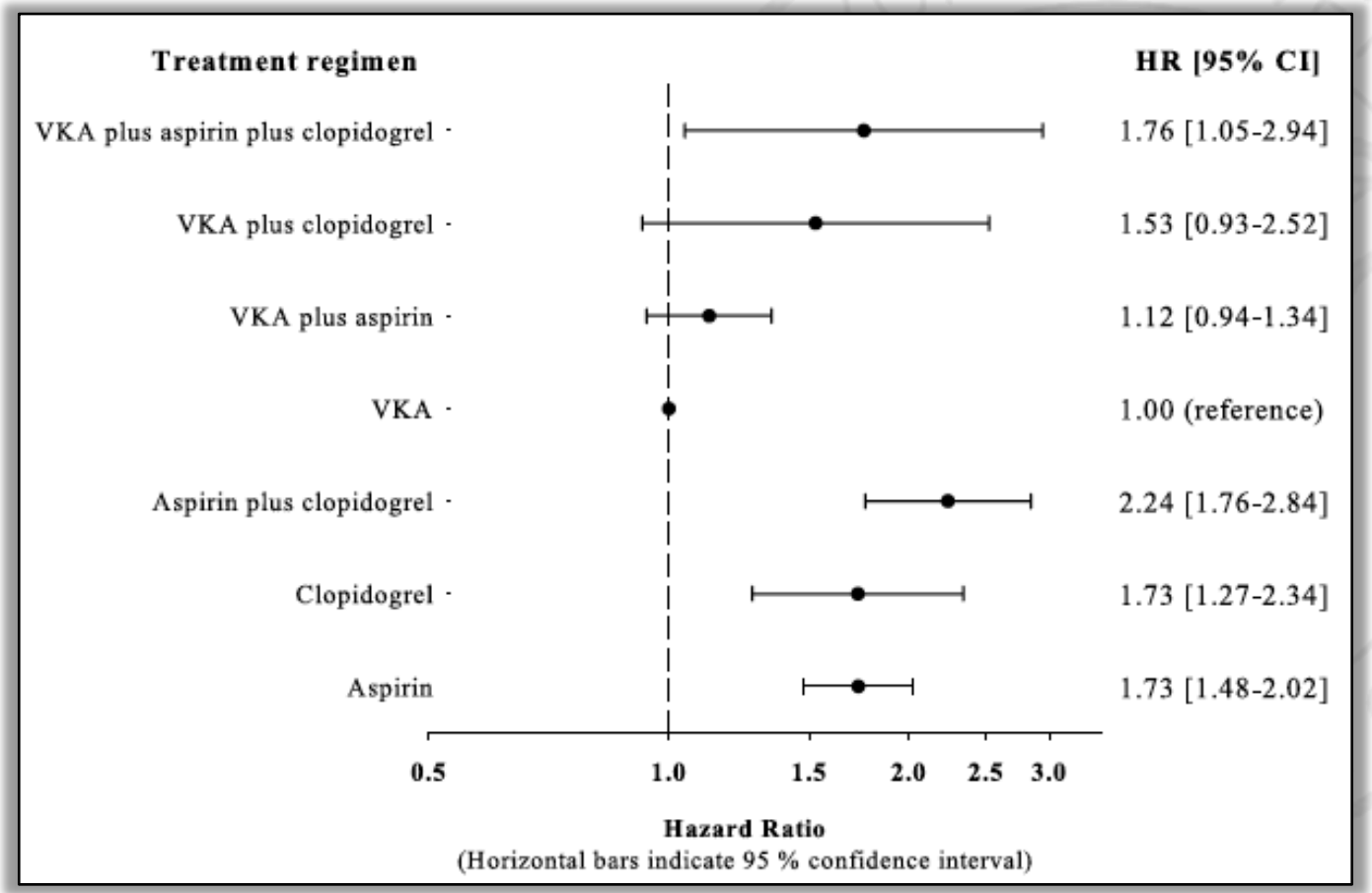


Lambert M, et al. Circulation 2014; 2005;143:241

Antiplatelet Therapy for Stable Coronary Artery Disease in Atrial Fibrillation Patients Taking an Oral Anticoagulant

A Nationwide Cohort Study

Risk of myocardial infarction/coronary death

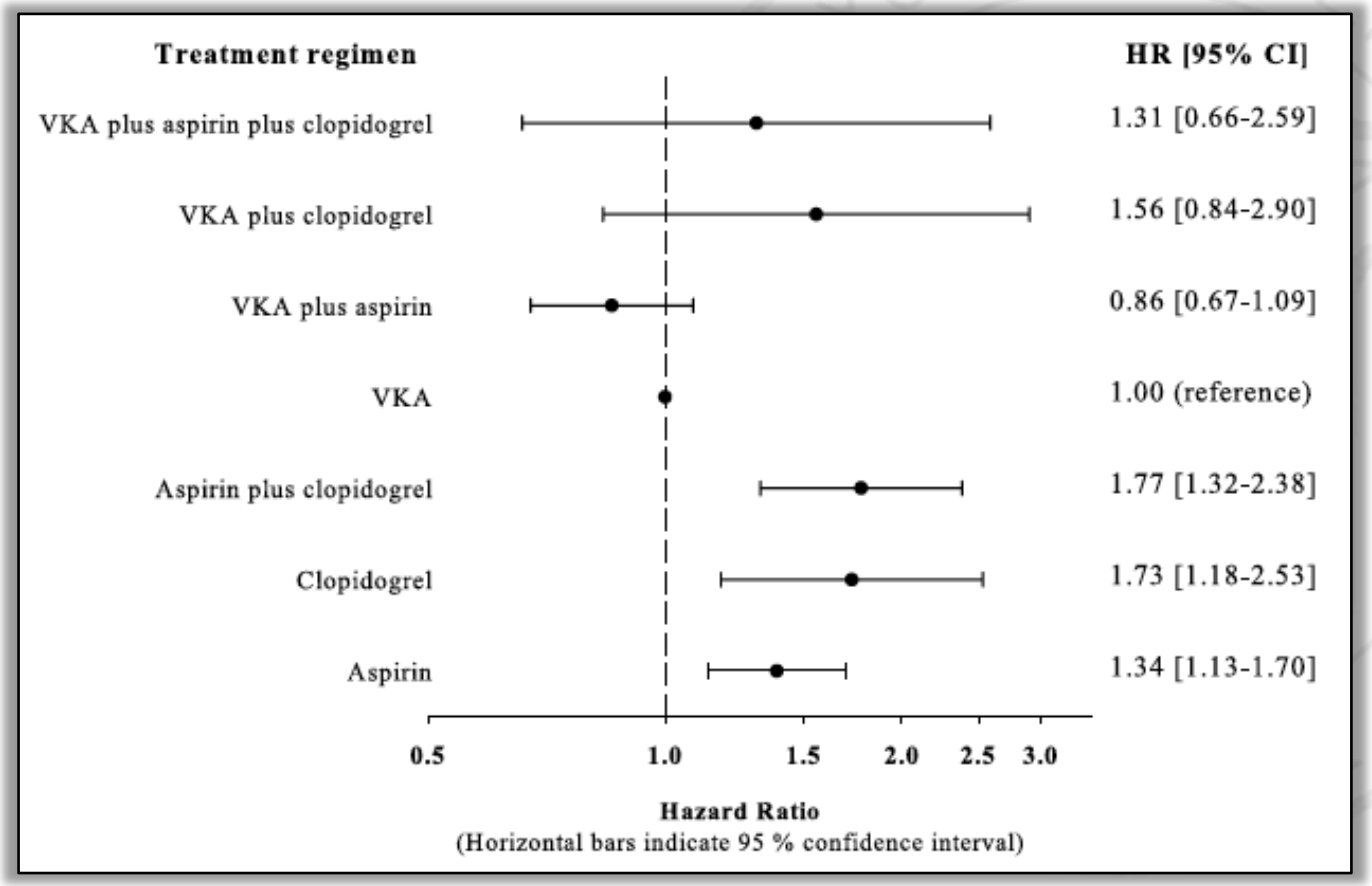


Lambert M, et al. Circulation 2014; 2005;143:241

Antiplatelet Therapy for Stable Coronary Artery Disease in Atrial Fibrillation Patients Taking an Oral Anticoagulant

A Nationwide Cohort Study

Risk of thromboembolism

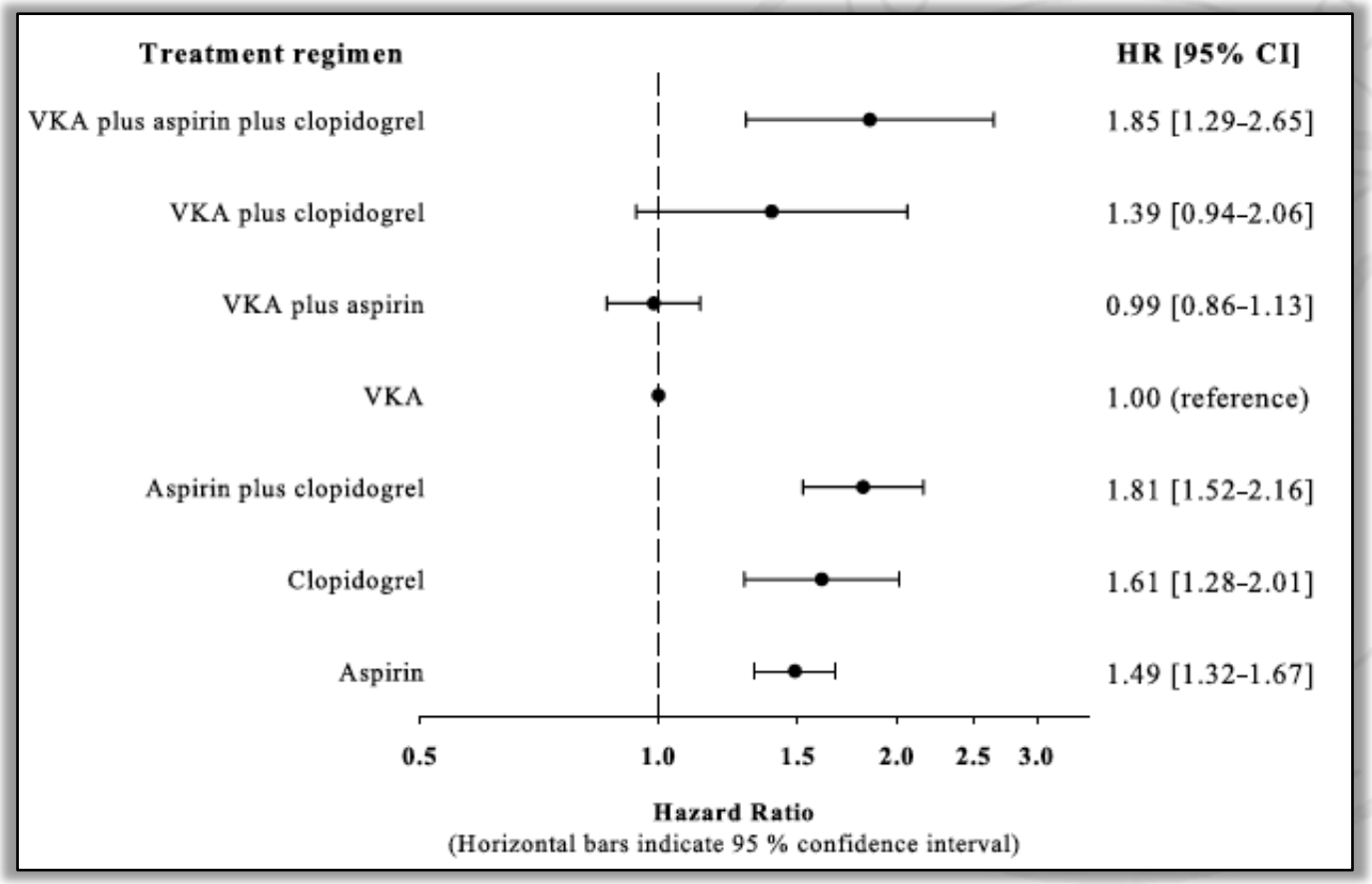


Lambert M, et al. Circulation 2014; 2005;143:241

Antiplatelet Therapy for Stable Coronary Artery Disease in Atrial Fibrillation Patients Taking an Oral Anticoagulant

A Nationwide Cohort Study

Risk of All cause of death

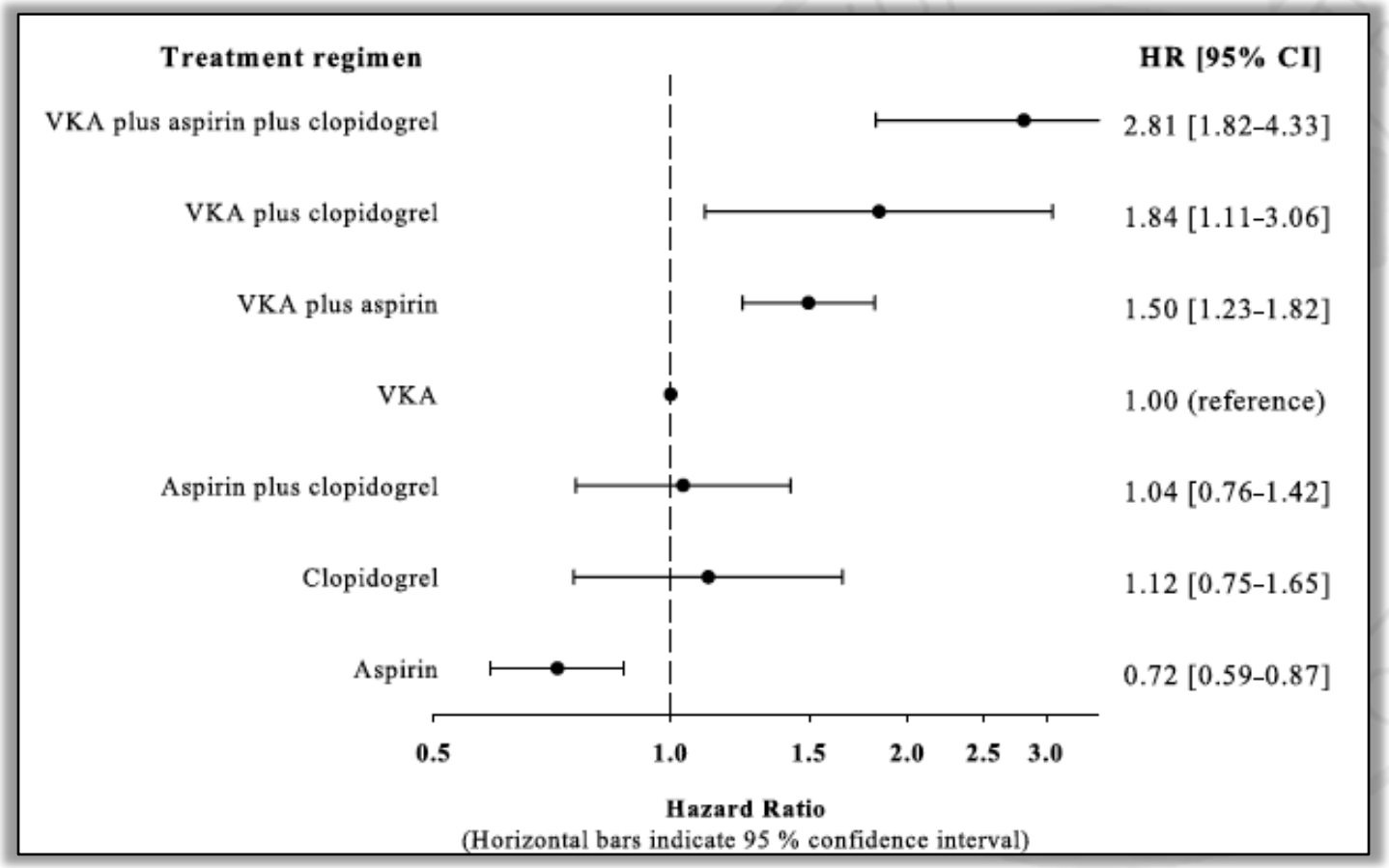


Lambert M, et al. Circulation 2014; 2005;143:241

Antiplatelet Therapy for Stable Coronary Artery Disease in Atrial Fibrillation Patients Taking an Oral Anticoagulant

A Nationwide Cohort Study

Risk of Bleeding



Lambert M, et al. Circulation 2014; 2005;143:241

Antiplatelet Therapy for Stable Coronary Artery Disease in Atrial Fibrillation Patients Taking an Oral Anticoagulant

A Nationwide Cohort Study

Table 3. Risk of the Combined Outcome of Myocardial Infarction, Thromboembolism, Bleeding, and All-Cause Mortality

Treatment	Number of Events	Crude Rate	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
VKA plus aspirin plus clopidogrel	39	20.8	1.33 (0.96–1.84)	1.70 (1.22–2.36)
VKA plus clopidogrel	39	19.0	1.28 (0.92–1.77)	1.42 (1.02–1.97)
VKA plus aspirin	298	13.8	1.00 (0.90–1.12)	1.15 (1.03–1.29)
VKA	490	13.8	Reference	Reference
Aspirin plus clopidogrel	243	26.3	1.71 (1.46–2.00)	1.63 (1.39–1.91)
Clopidogrel	111	20.4	1.43 (1.16–1.75)	1.29 (1.04–1.59)
Aspirin	2222	19.4	1.39 (1.26–1.53)	1.35 (1.22–1.49)

Conclusions—In **atrial fibrillation patients with stable coronary artery disease**, the ***addition of antiplatelet therapy to VKA therapy is not associated with a reduction in risk*** of ***recurrent coronary events or thromboembolism***, whereas ***risk of bleeding is increased significantly***

Lambert M, et al. Circulation 2014; 2005;143:241

Concomitant Use of Antiplatelet Therapy with Dabigatran or Warfarin in the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) Trial

Of 18,113 patients, 6952 (***38.4%***) received concomitant aspirin or clopidogrel at some time during the study

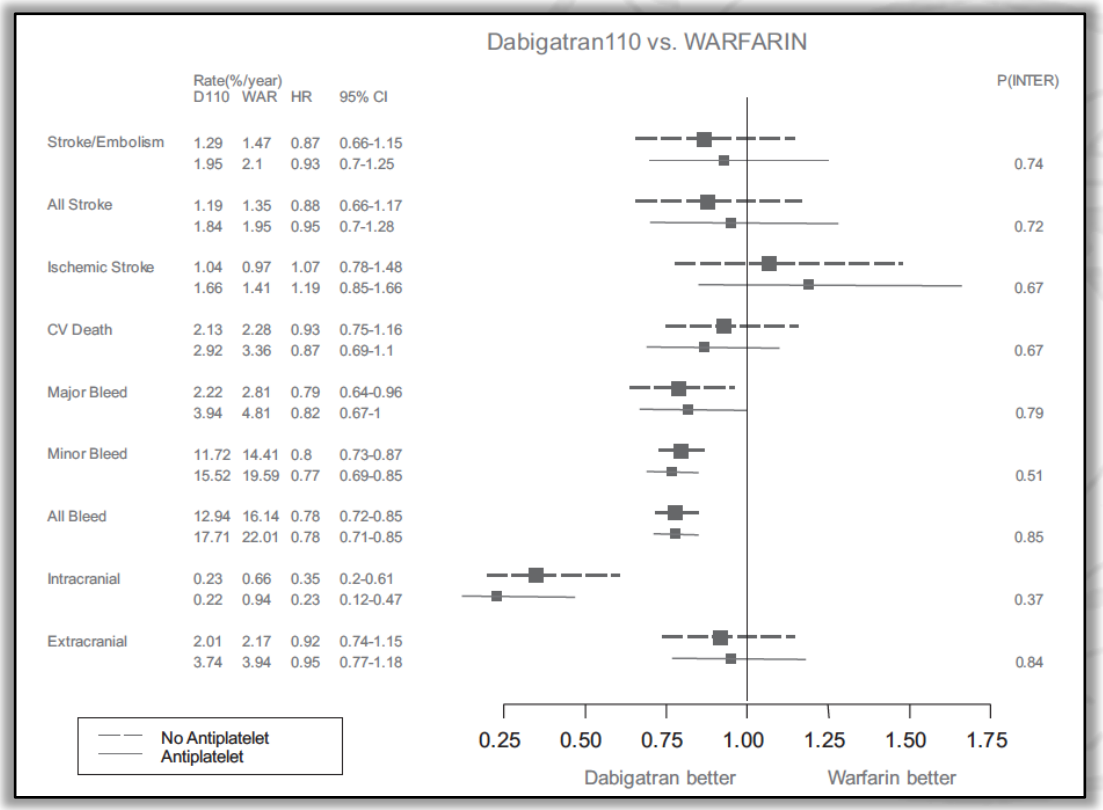
Table 2. Concomitant Use of ASA in Different Regions of the World

Region	Concomitant ASA Used	%
North America/western Europe	4120	39.3
Central/South America	410	42.9
Eastern/southern Europe	885	31.3
Southeast/East Asia	1232	44.3
Others	548	51.12

Dans AL, et al. Circulation 2013;127:634

Concomitant Use of Antiplatelet Therapy with Dabigatran or Warfarin in the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) Trial

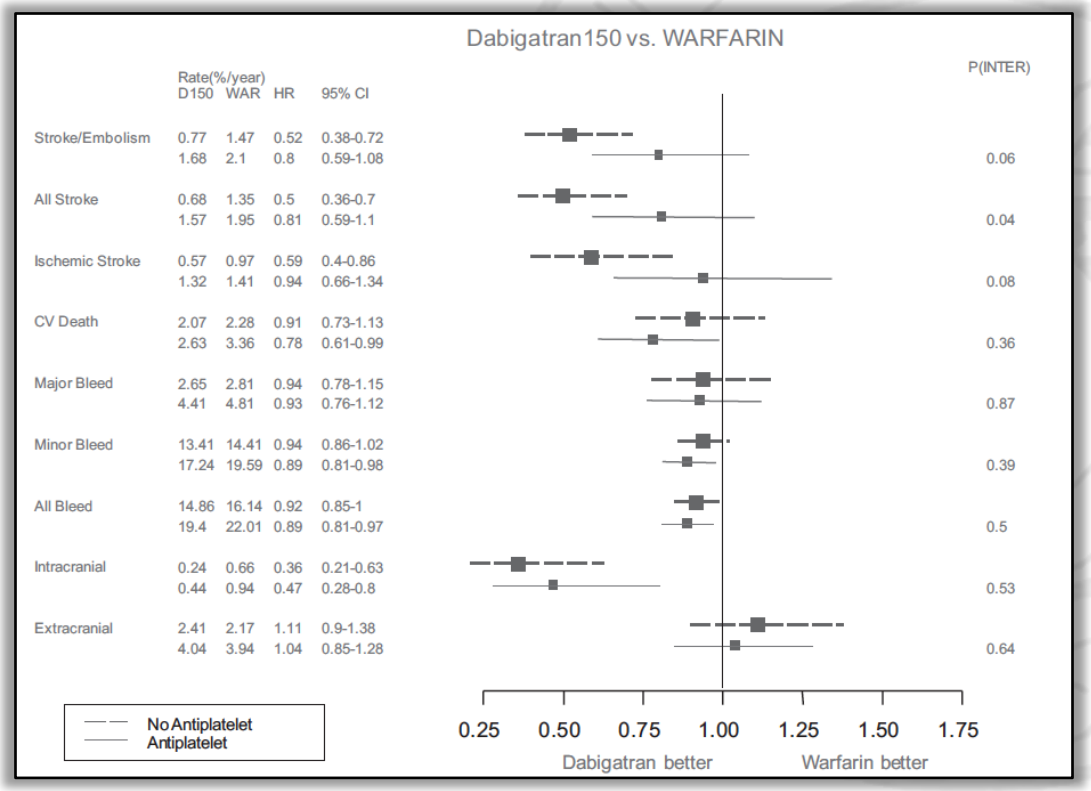
Dabigatran 110 mg BID was noninferior to warfarin in reducing stroke/SE regardless of antiplatelets



Dans AL, et al. Circulation 2013;127:634

Concomitant Use of Antiplatelet Therapy with Dabigatran or Warfarin in the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) Trial

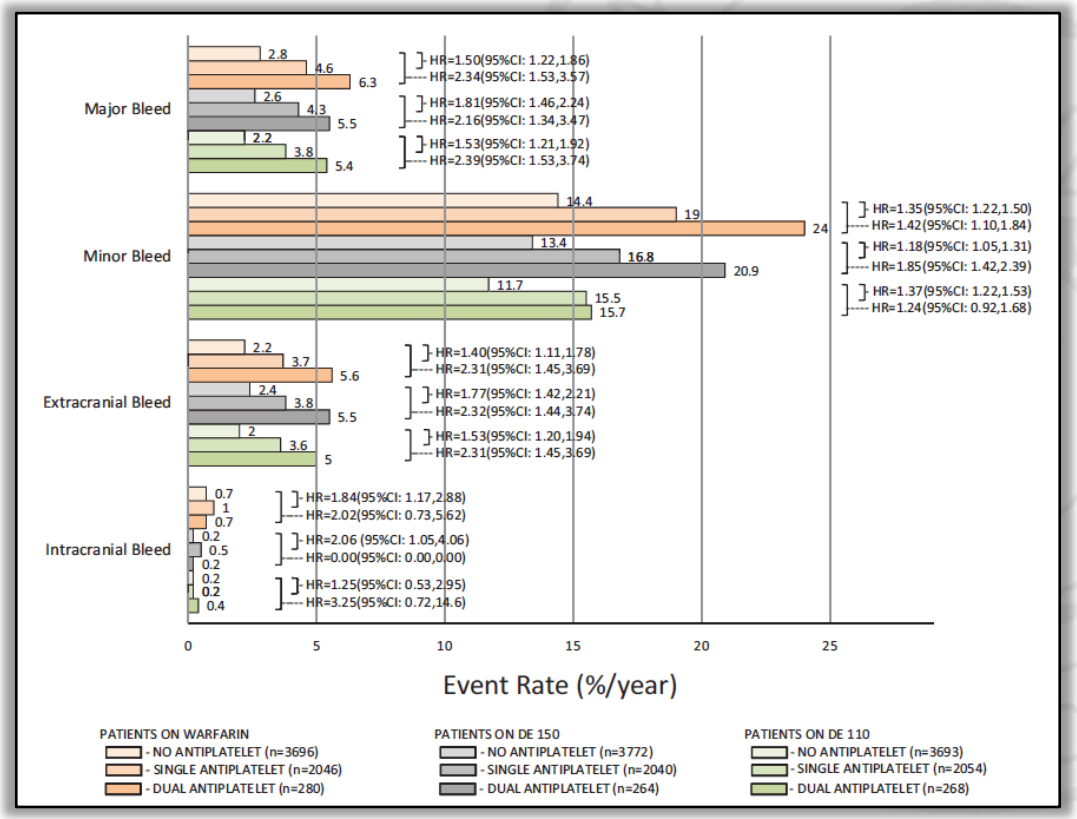
Dabigatran 150 mg BID reduced the stroke/SE in comparison with warfarin. This effect seemed attenuated by antiplatelets



Dans AL, et al. Circulation 2013;127:634

Concomitant Use of Antiplatelet Therapy with Dabigatran or Warfarin in the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) Trial

SAPT increased the ***risk of major bleeding*** (**HR, 1.60**; 95% CI, 1.42–1.82). **DAPT** increased this ***even more*** (**HR, 2.31**; 95% CI, 1.79–2.98)



Dans AL, et al. Circulation 2013;127:634

Concomitant Use of Antiplatelet Therapy with Dabigatran or Warfarin in the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) Trial

Conclusions — ***Concomitant antiplatelet*** *drugs appeared to* ***increase the risk for major bleeding*** *in RE-LY* ***without affecting the advantages of dabigatran over warfarin***. Choosing between dabigatran etexilate 110 mg BID and dabigatran etexilate 150 mg BID requires a careful assessment of characteristics that influence the balance between benefit and harm.

Dans AL, et al. Circulation 2013;127:634

Choosing a particular oral anticoagulant and dose for stroke prevention in individual patients with non-valvular atrial fibrillation: part 1

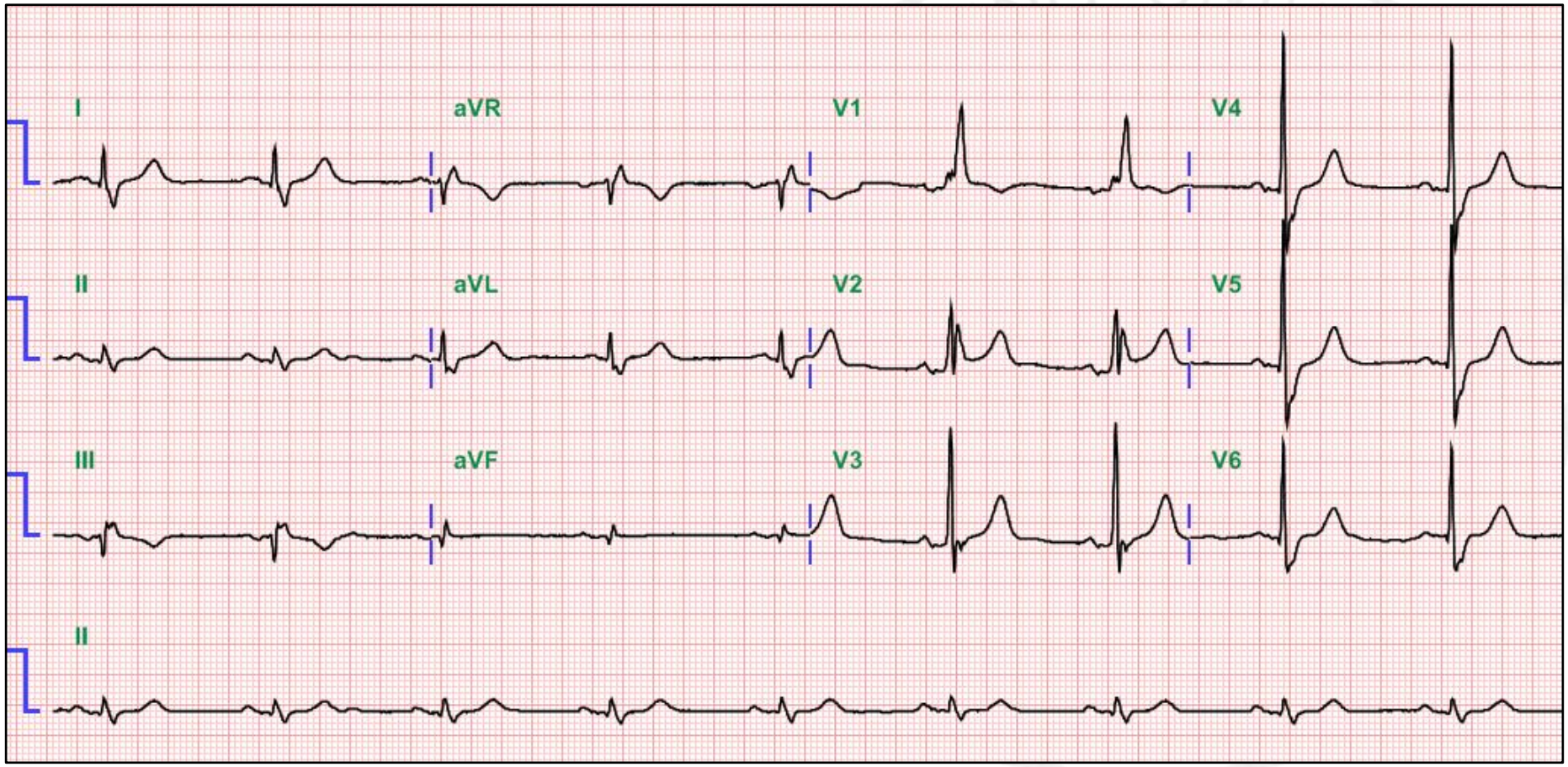
Patients with stable coronary artery disease

First choice	***Monotherapy with an NOAC*** is preferable for patients with AF and stable CAD. This suggestion is applicable to all NOACs
Second choice	In selected patients, addition of aspirin is still indicated in the long-term, based on individual risk assessment and coronary anatomy
Comments	In the absence of direct comparative studies, no particular NOAC can be favoured over another

Diener H-C, et al. Eur Heart J Doi:10.1093/eurheartj/ehv643

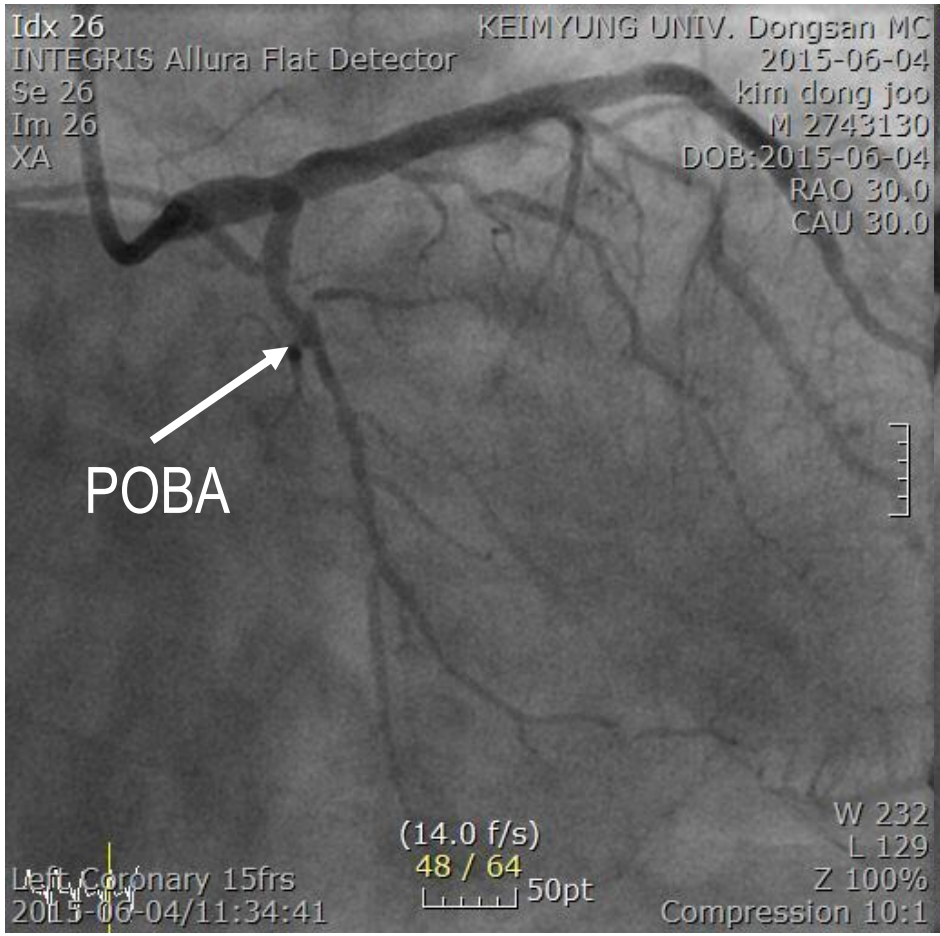
~ Our Story ~

- ***5 months after RFCA***
- On: Dilatrend SR 16mg, Kanarb 60mg, lipitor 10mg, ***Eliquis 5mg bid***, nitrate 40mg

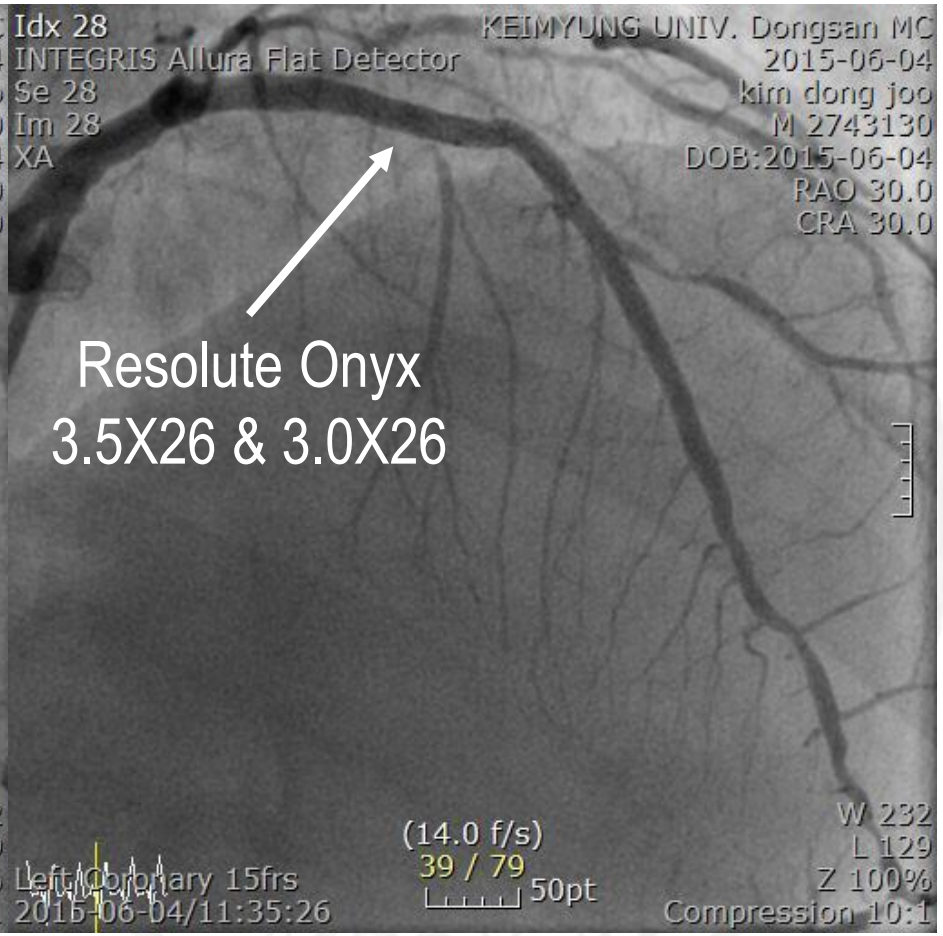


~ Our Story ~

- ***5 months after RFCA:*** Stop the NOAC 1 day before the admission



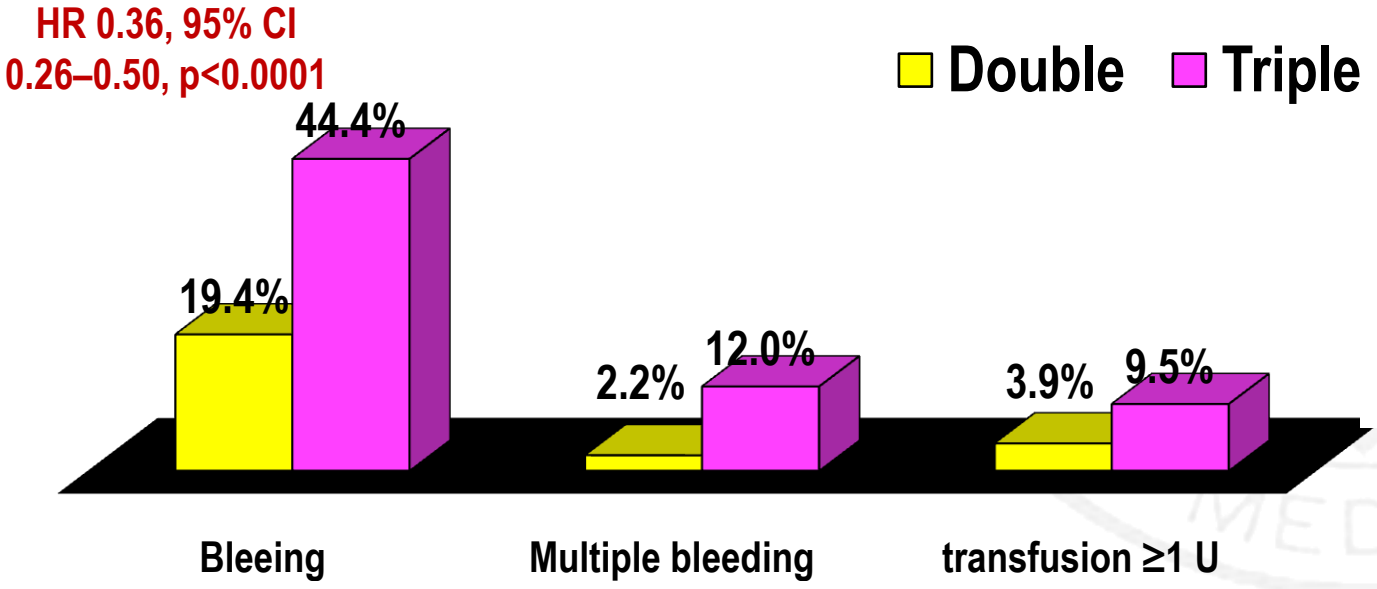
RAO caudal view



RAO cranial view

Use of clopidogrel with or without aspirin in patients taking oral anticoagulant therapy and undergoing percutaneous coronary intervention: an open-label, randomised, controlled trial (**WOEST**)

- Open labelled, multicenter, randomized controlled study
- 573 Patients with ***OAC undergoing PCI*** (Nov 2008 ~ Nov 2011)
- ***Double Tx*** (+clopidogrel) vs ***Triple Tx*** (+clopidogrel+ASA)
- Primary endpoint: any bleeding within 1 year of PCI



***Proportionof ACS**
Double: 25%, Triple: 30%
***Proportion of AF**
Double: 69%, Triple: 69%

Dewilde WJ, et al. Lancet 2013;381:1107

Use of clopidogrel with or without aspirin in patients taking oral anticoagulant therapy and undergoing percutaneous coronary intervention: an open-label, randomised, controlled trial (**WOEST**)

	Double therapy (n=297)	Triple therapy (n=284)	Hazard ratio (95% CI)	p value
Combined secondary endpoint	31 (11·1%)	50 (17·6%)	0·60 (0·38–0·94)	0·025
Death				
All-cause	7 (2·5%)	18 (6·3%)	0·39 (0·16–0·93)	0·027
Cardiac	3 (1·1%)	7 (2·5%)	0·43 (0·11–1·66)	0·207
Non-cardiac	4 (1·4%)	11 (3·9%)	0·36 (0·11–1·13)	0·069
Myocardial infarction				
Any	9 (3·2%)	13 (4·6%)	0·69 (0·29–1·60)	0·382
STEMI	1 (0·4%)	3 (1·1%)	0·34 (0·04–3·25)	0·325
Non-STEMI	8 (2·9%)	10 (3·5%)	0·79 (0·31–2·01)	0·625
Target-vessel revascularisation				
PCI or CABG	20 (7·2%)	19 (6·7%)	1·05 (0·56–1·97)	0·876
PCI	17 (6·1%)	16 (5·6%)	1·06 (0·54–2·10)	0·869
CABG	3 (1·1%)	3 (1·1%)	1·00 (0·20–4·90)	0·998
Stroke				
Any	3 (1·1%)	8 (2·8%)	0·37 (0·10–1·40)	0·128
Ischaemic	2 (0·7%)	8 (2·8%)	0·25 (0·05–1·17)	0·056
Haemorrhagic	1 (0·4%)	0	NA	0·321
Disabling	2 (0·7%)	2 (0·7%)	0·99 (0·14–6·99)	0·988
Non-disabling	1 (0·4%)	7 (2·5%)	0·14 (0·02–1·16)	0·034
Stent thrombosis				
Any	4 (1·4%)	9 (3·2%)	0·44 (0·14–1·44)	0·165
Definite	1 (0·4%)	3 (1·1%)	0·33 (0·03–3·22)	0·319
Probable	0	2 (0·7%)	NA	0·161
Possible	3 (1·1%)	4 (1·4%)	0·75 (0·17–3·30)	0·708

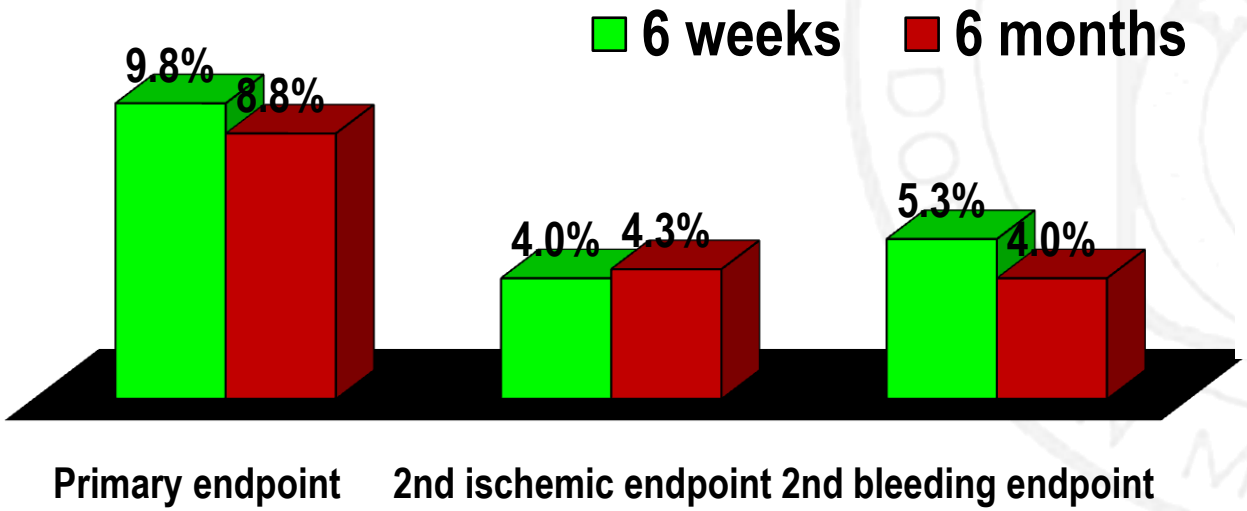
Interpretation:

Use of clopidogrel without aspirin was associated with a ***significant reduction in bleeding complications*** and ***no increase in the rate of thrombotic events***

Dewilde WJ, et al. Lancet 2013;381:1107

Duration of Triple Therapy in Patients Requiring Oral Anticoagulation After Drug-Eluting Stent Implantation: **The ISAR-TRIPLE trial**

- Randomized, open label trial : Sep 2008 – Dec 2013
- 614 patients with ***OAC & aspirin undergoing DES*** implantation
- **+ clopidogrel *for 6 weeks vs 6 months***
- **Primary endpoint**: death, MI, definite stent thrombosis, stroke, or TIMI major bleeding at 9 months

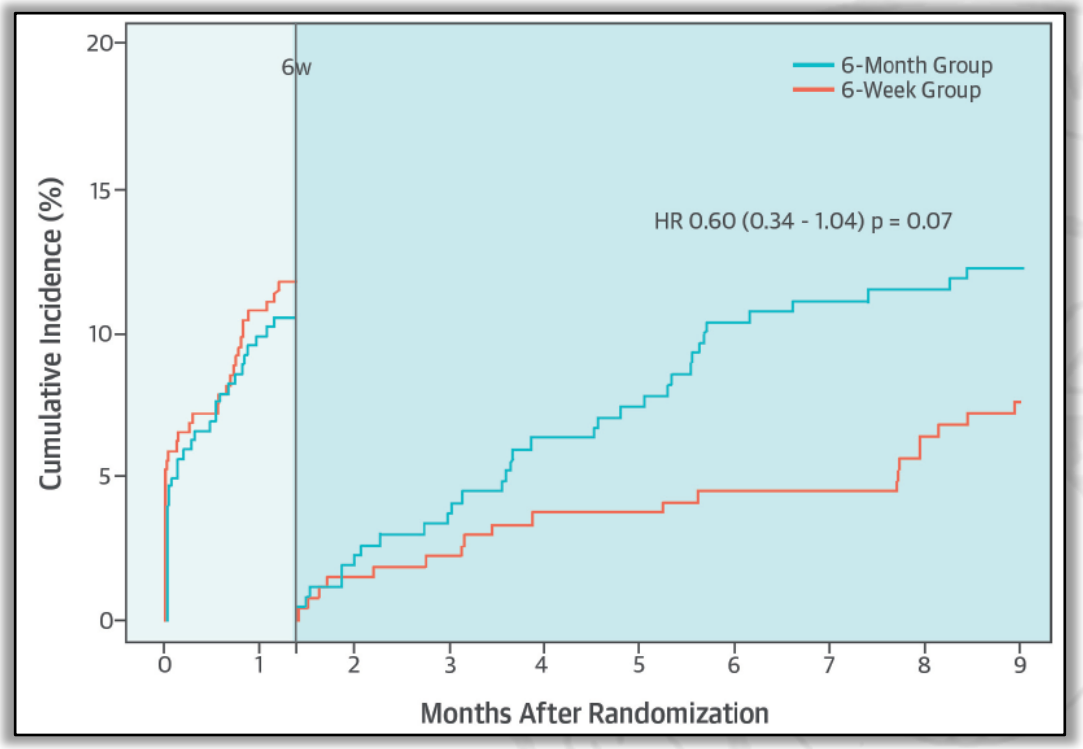


*Proportionof ACS: 1/3
*Proportion of AF
6 week: 82.7%, 6 months: 85%

Fiedler KA, et al. JACC 2015;65:1619

Duration of Triple Therapy in Patients Requiring Oral Anticoagulation After Drug-Eluting Stent Implantation: **The ISAR-TRIPLE trial**

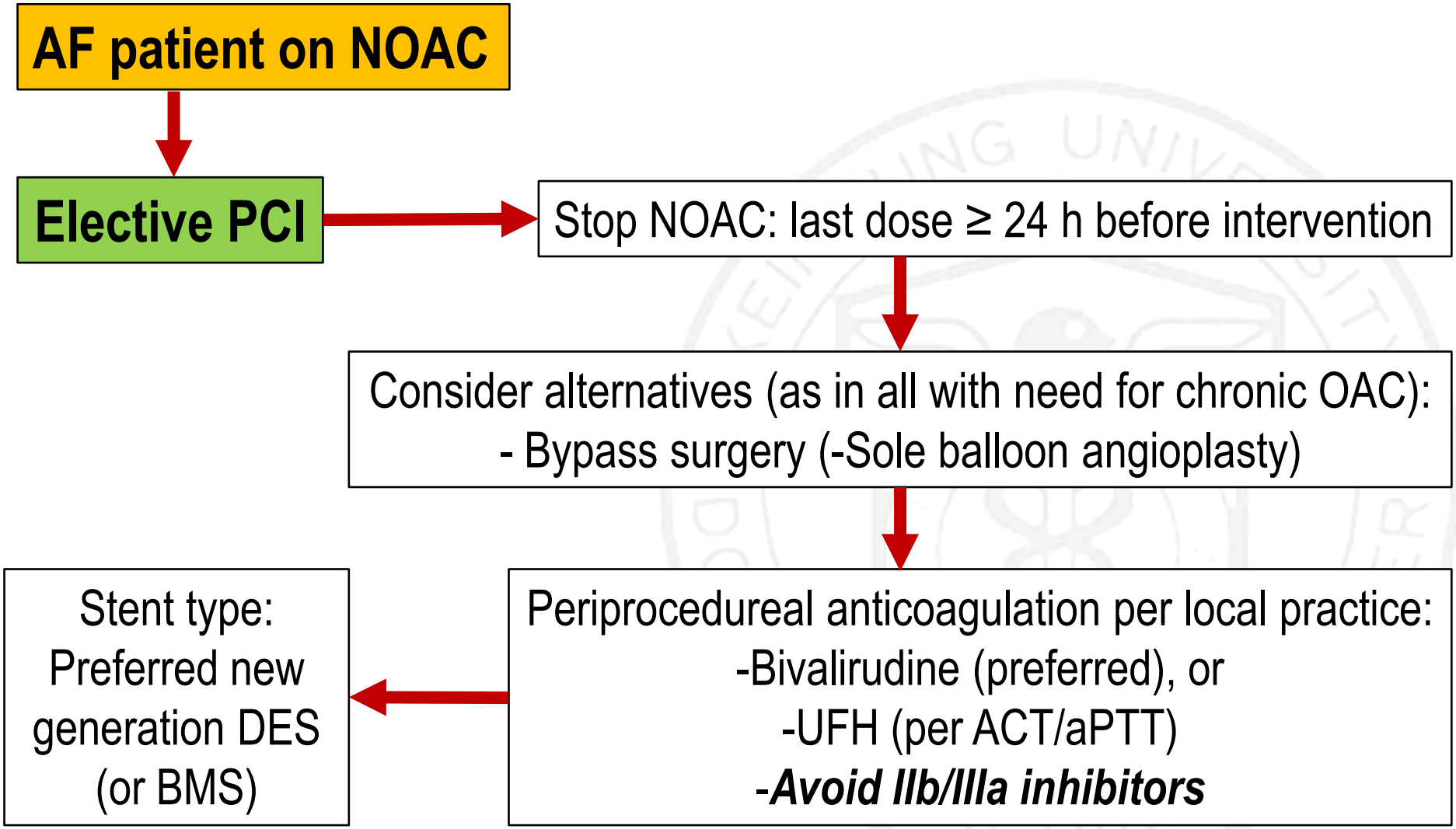
Cumulative Incidence of BARC Type ≥2 Bleeding Before and After 6 Weeks



CONCLUSIONS **Six weeks** of triple therapy **was not superior to 6 months** with respect to net clinical outcomes. These results suggest that physicians should ***weigh the trade-off between ischemic & bleeding risk when choosing the shorter or longer duration of triple therapy***

Fiedler KA, et al. JACC 2015;65:1619

2015 Updated EHRA Practical Guide on NOAC



Heidbuchel H, et al. DOI:10.1093/europace/euv309

2015 Updated EHRA Practical Guide on NOAC

After discontinuation of parenteral anticoagulation: restart same NOAC, in combination with SAPT or DAPT

- Consider dabigatran 110 mg BID for patients on 150 mg BID
- When considering apixaban 2.5 mg BID, rivaroxaban 15 mg OD or Edoxaban 30 mg OD: no data on stroke prevention if no normal dose reduction criterion (mainly CrCl)

PPI should be considered

Discharge with prespecified step-down plan

Heidbuchel H, et al. DOI:10.1093/europace/euv309

Choosing a particular oral anticoagulant and dose for stroke prevention in individual patients with non-valvular atrial fibrillation: part 1

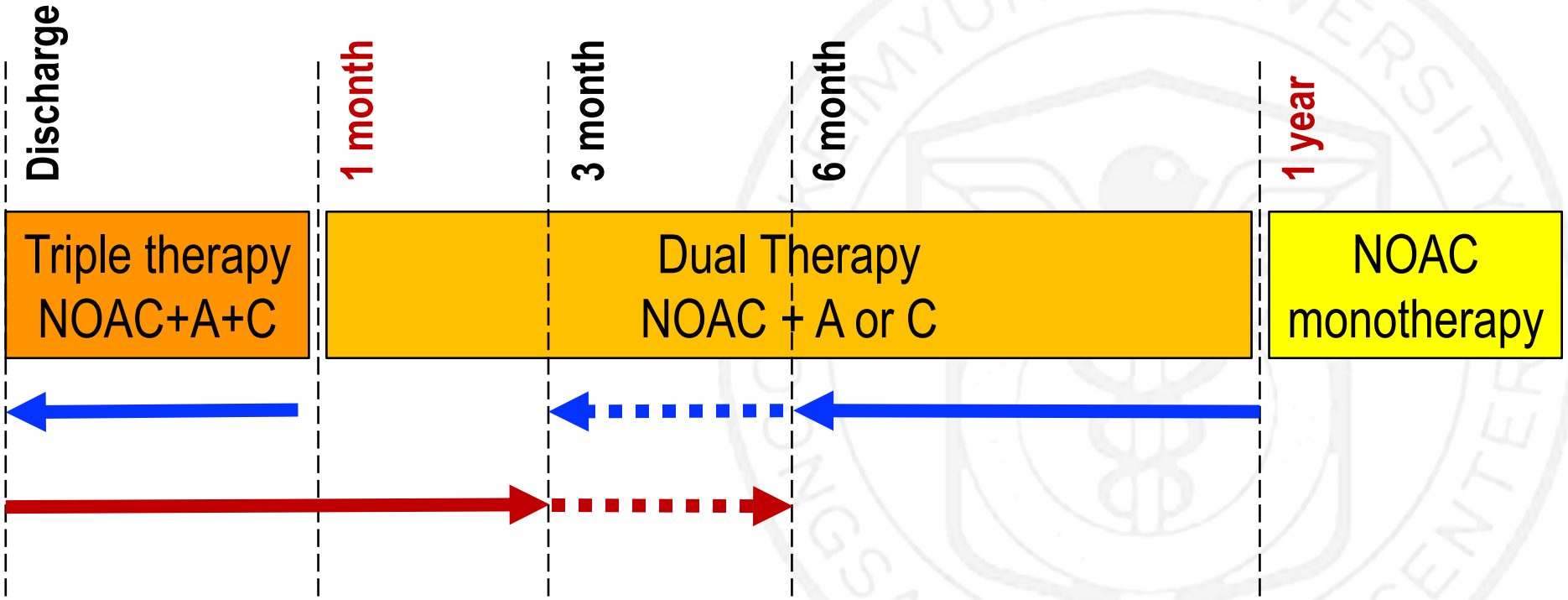
Patients undergoing PCI & stenting

First choice	• In patients with PCI after stenting receiving triple therapy, ***well-controlled VKA*** (TTR >70%, preferred INR range 2.0–2.5) or an ***NOAC may be*** chosen • When an ***NOAC*** is used in combination with dual antiplatelet therapy, the ***lower tested and licensed dose*** for stroke prevention in AF is preferred: dabigatran 110 mg twice daily, rivaroxaban 15 mg once daily, apixaban 2.5 mg twice daily, or edoxaban 30 mg once daily
Comments	• There is no preference for one NOAC over another. • Published evidence on the combination of dual antiplatelet therapy and an NOAC is currently available only for dabigatran from the RE-LY trial

Diener H-C, et al. Eur Heart J Doi:10.1093/eurheartj/ehv643

2015 Updated EHRA Practical Guide on NOAC

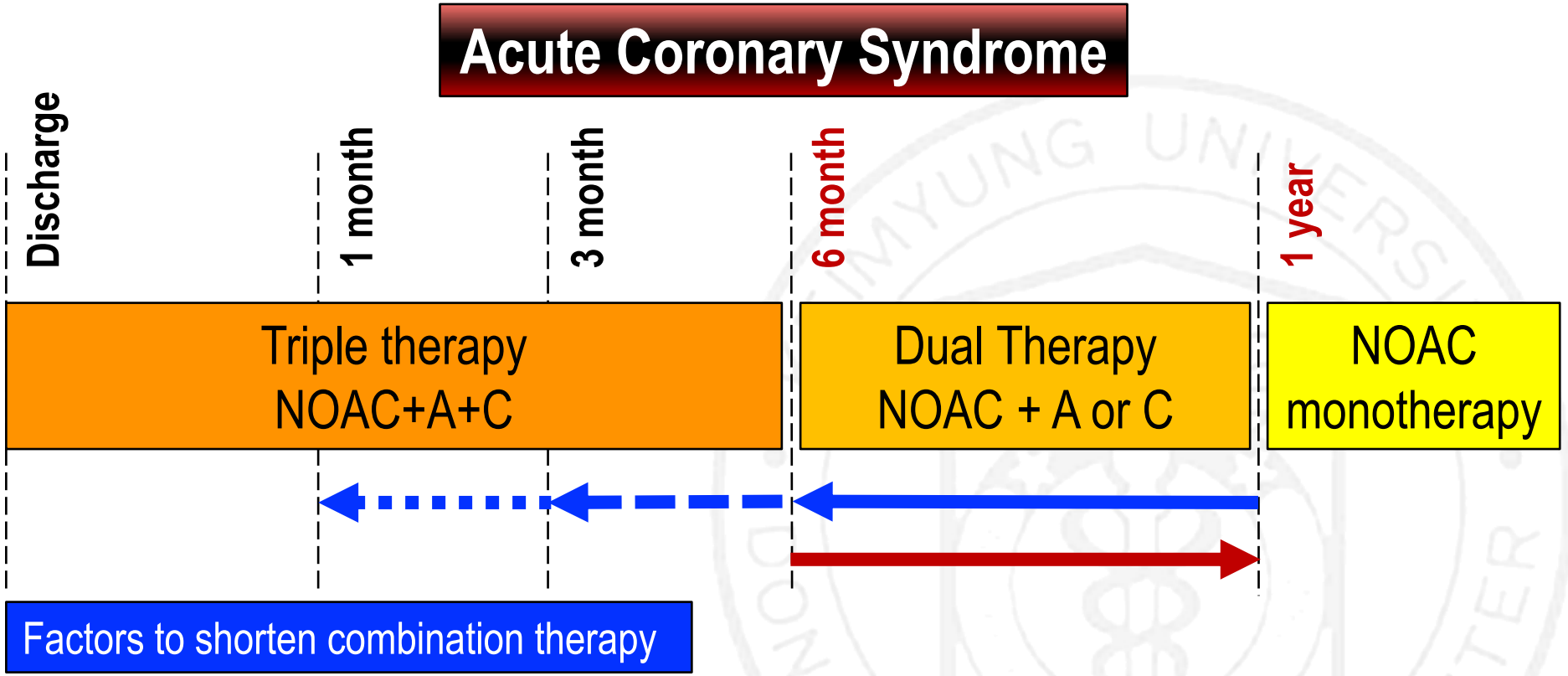
Elective PCI with new generation DES or BMS



Alternative: DAPT only, if CHADSVASc = 1 (men) or 2 (women) (only CAD) & elevated bleeding risk

Heidbuchel H, et al. DOI:10.1093/europace/euv309

2015 Updated EHRA Practical Guide on NOAC



Factors to shorten combination therapy

(uncorrectable) high bleeding risk

Low atherothrombotic risk (by REACH or SYNTAX score if elective?;GRACE ≥ 118 if ACS?)

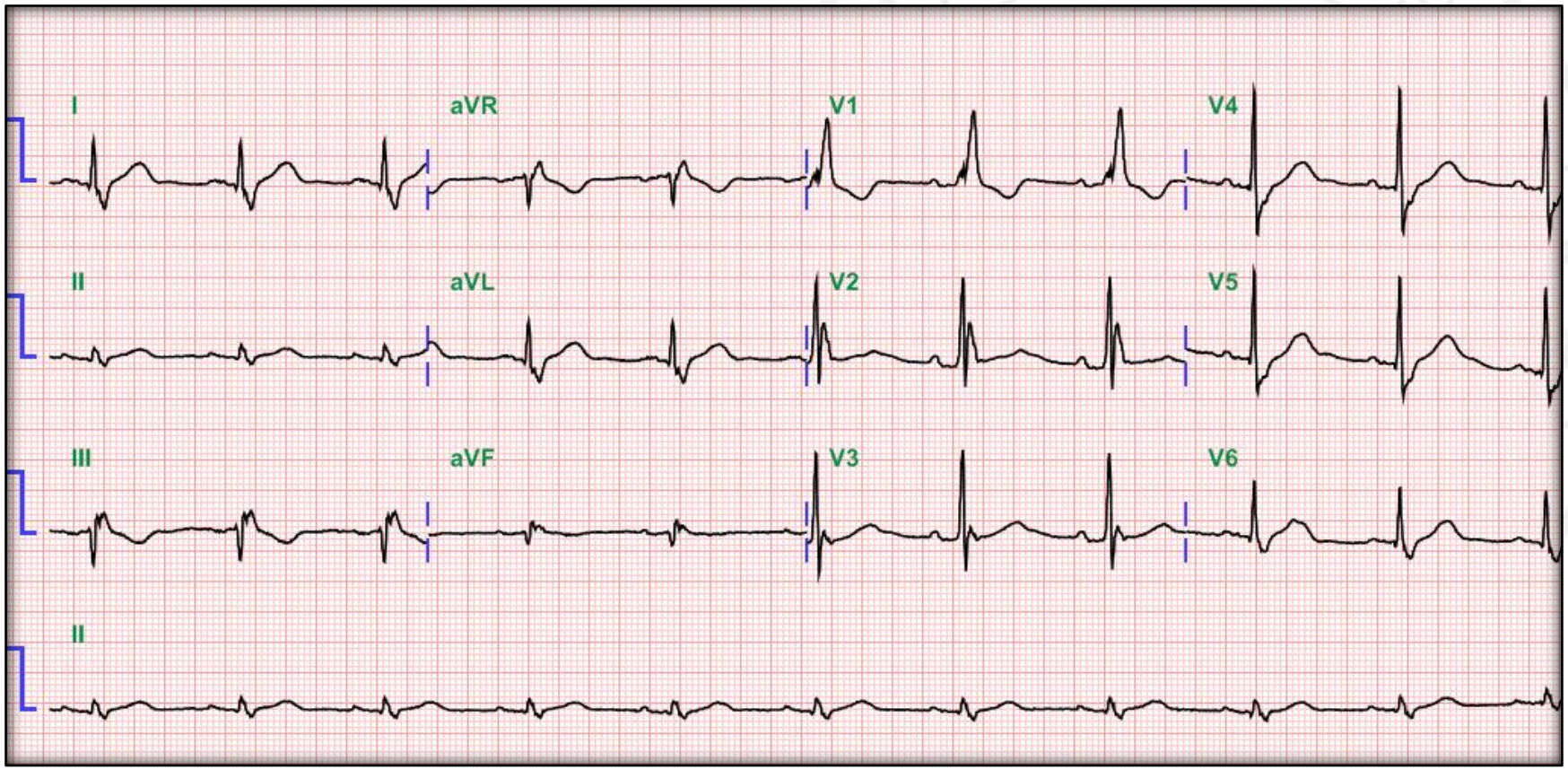
Factors to lengthen combination therapy

First generation DES: high atherothrombotic risks (score as above; stenting of left main, proximal LAD, proximal bifurcation; recurrent MIs; etc) and low bleeding risk

Heidbuchel H, et al. DOI:10.1093/europace/euv309

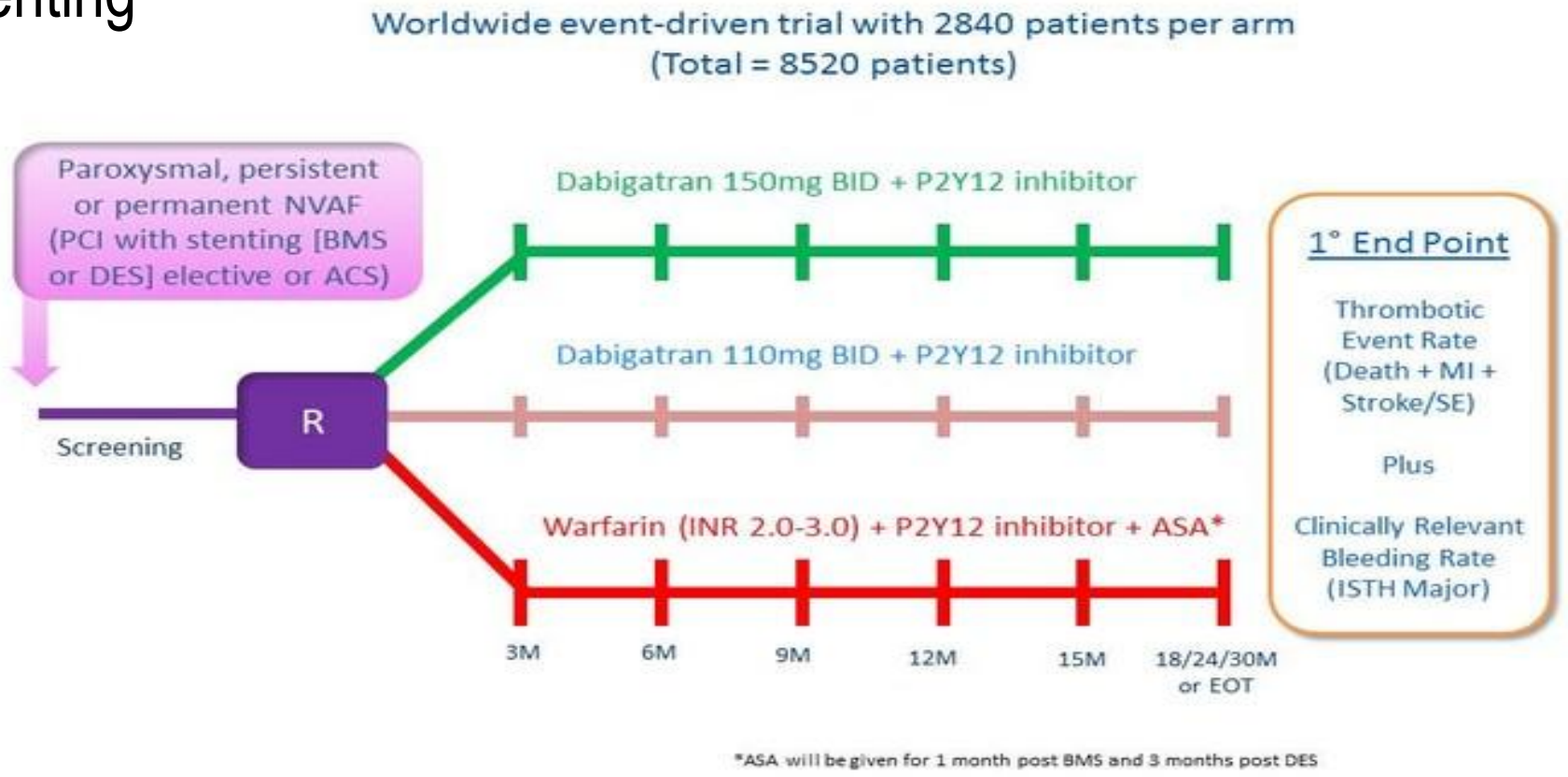
~ Our Story ~

- ***9 months after PCI***
- On: Dilatrend SR 16mg, Kanarb 120mg, lipitor 40mg, nitrate 120mg, norvasc 5mg, dichlozid 12.5mg***, aspirin 100mg, plavix 75mg, warfarin 5mg (INR 2.18)***
- ***HAS BLED score: 1***

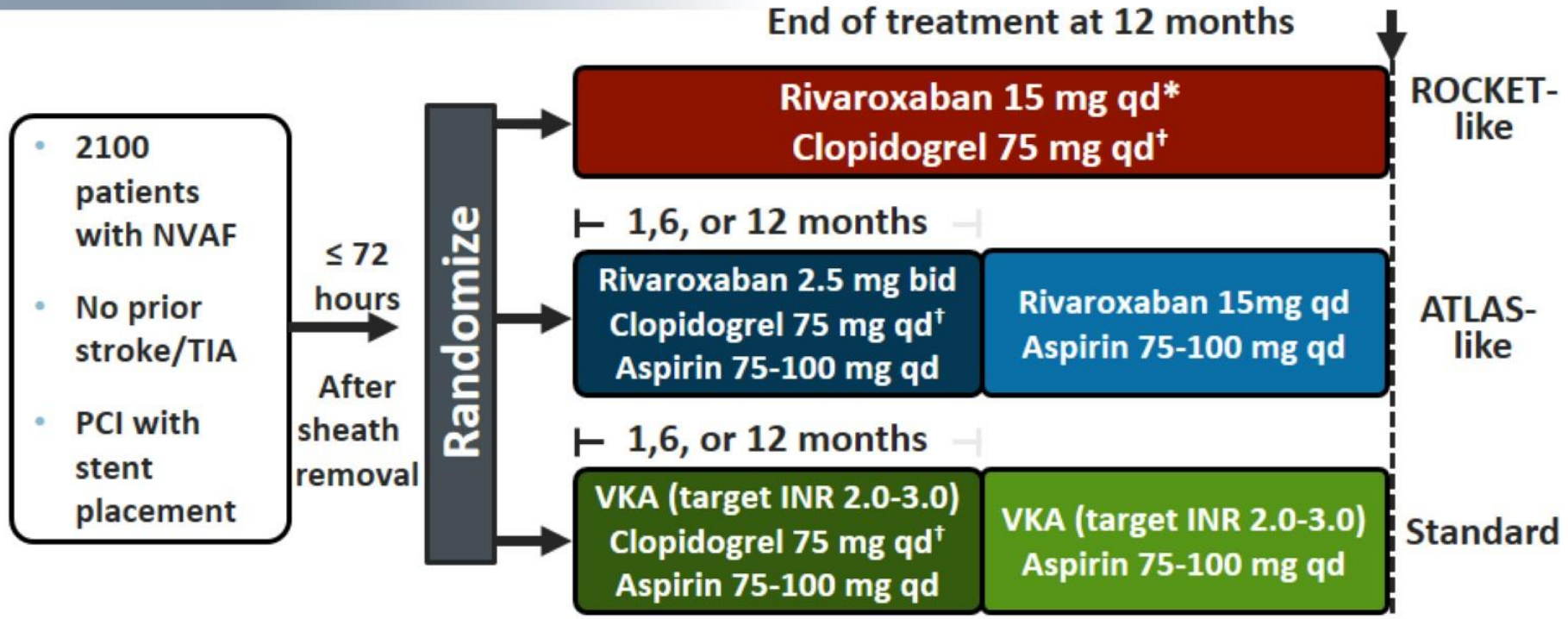


RE-DUAL PCI

Evaluation of ***Dual Therapy With Dabigatran*** vs. ***Triple Therapy With Warfarin*** in Patients With AF That Undergo a PCI With Stenting



Rivaroxaban Use in Patients With AF Undergoing PCI: *PIONEER AF-PCI*



Primary end point: TIMI major, minor, and bleeding requiring medical attention
Secondary end point: CV death, MI, stroke, and stent thrombosis

*10 mg/d in patients with CrCl of 30 to < 50 mL/min.

†Alternatively: 10 mg/d prasugrel or 90 mg ticagrelor twice daily.

Gibson CM, et al. *Am Heart J*. 2015;169:472-478.

theheart.org | Medscape CARDIOLOGY

Augustus study

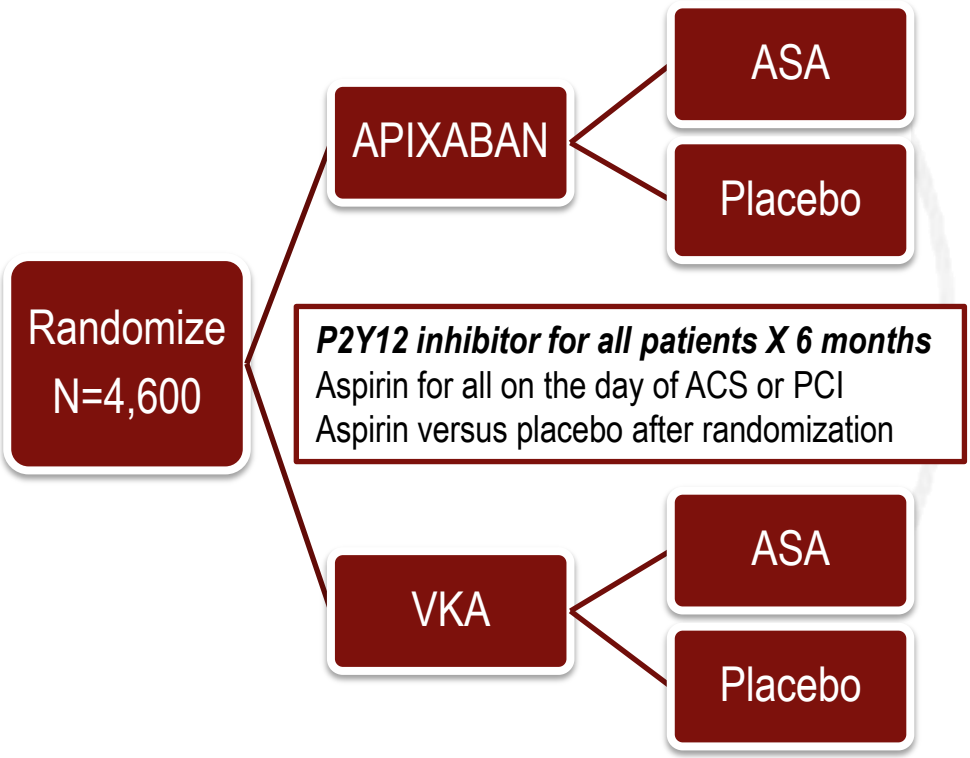
Study ***Apixaban to Vitamin K Antagonist*** for the Prevention of Stroke or Systemic Embolism and Bleeding in Patients With ***NVAF*** and ***ACS/PCI***

❖ **Inclusion**

- ✓ **AF patients need anticoagulation**
- ✓ **ACS or PCI planned P2Y12 inhibitor for 6 months within 2 weeks after PCI or ACS**

❖ **Exclusion**

- ✓ **Contraindication to DAPT**
- ✓ **Other reason for VKA (e.g. prosthetic valve, mid/severe mitral stenosis)**
- ✓ **CABG**



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Thank You for Your Attention !

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