



## **Anticoagulant and Antiplatelet Therapy**

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# Case 1

NOAC in  
AF + CAD

## Medical History



74 years old man



Hypertensive  
Cigarette smoker  
Paroxysmal AF



Admitted to CCU with NSTEMI  
Underwent successful PCI of a bifurcation lesion in LAD with  
stenting of both LAD & diagonal



# Case

**NOAC in  
AF + CAD**



## Medical History



**EF 40%, HK in anterior circulation  
Moderate MR, Mild TR**



**CBC NL  
Cr 1.7 (CrCl 46 ml/min)  
LFT NL**

## Medical History

# Case

**NOAC in  
AF + CAD**



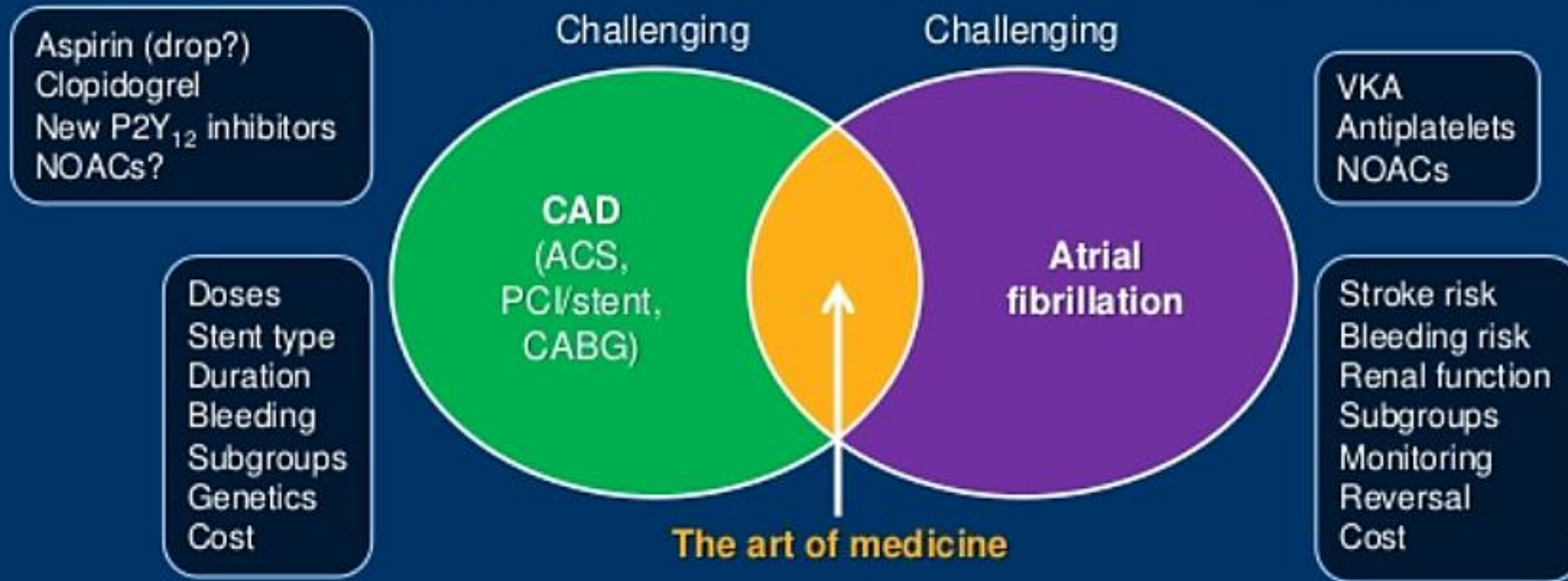
**How long you will continue triple therapy in this patient with Ticagrelor or Clopidogrel?**

- **1 month for both drugs**
- **1 week for both drugs**
- **1 week with ticagrelor and 1 month with clopidogrel**
- **Ticagrelor is contraindicated in this setting and the only choice is clopidogrel for 1 week to 1 month**

# AF and CAD

## Overlapping patient populations

### Overlapping indications for antithrombotic therapy<sup>1,2</sup>



Practice guidelines largely based on clinical trials that exclude patients with other diseases/indications

1. Euro Heart J. 2016; 37:2893-2962.  
2. Euro Heart J. 2013;34:2949-3003.



# Anticoagulant and Antiplatelet Therapy

CAD is a common comorbidity in patients with AF, occurring in roughly **25% to 35%** of this population.

Approximately **10%** of patients with recent PCI have concomitant AF. Others may have concomitant VTE. Choosing the optimal antithrombotic regimen can be a challenge.

The addition of single APT to an OAC increases the risk of bleeding  $\geq$  **20% to 60%** and the addition of DAPT to an OAC further increases the risk 2- to 3-fold.

The risk of major bleeding with triple antithrombotic therapy can be as high as 2.2% at 1 month and 4% to 12% at 1 year. Major bleeding is associated with an up to **5-fold increased risk of death** following an ACS.





## What evidence is there for NOACs in AF + ACS?

Clip slide

**PIONEER  
AF-PCI<sup>1</sup>**  
Rivaroxaban

N=2,124

**RE-DUAL  
PCI<sup>2</sup>**  
Dabigatran

N=2,725

**AUGUSTUS  
ACS/PCI<sup>3</sup>**  
Apixaban

N=4,614

**ENTRUST  
AF-PCI<sup>4,5</sup>**  
Edoxaban

N=1,508



1. N Engl J Med. 2016; 375:2423-2434.
2. N Engl J Med. 2017;377: 1513-1524
3. N Engl J Med. 2019; 380: 1509-1524.
4. Am Heart J. 2018; 196:105-112.
5. Available at: [clinicaltrials.gov/ct2/show/NCT02866175](https://clinicaltrials.gov/ct2/show/NCT02866175).

# What's his CHA<sub>2</sub>DS<sub>2</sub>-VASc Score?

- 0
- 1
- 2
- 3
- 4

Risk Index	Score
Congestive heart failure	1
Hypertension	1
Age >75	2
Diabetes mellitus	1
prior Stroke or TIA	2
Vascular disease	1
Age 65-74	1
Sex category (female)	1



# What's his bleeding risk?

## HAS-BLED score

- 0

- 1

- 2

- **3**

- 4

Letter	Clinical characteristic*	Points awarded
H	Hypertension	<b>1</b>
A	Abnormal renal and liver function (1 point each)	<b>1 or 2</b>
S	Stroke	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly (e.g. age > 65 years)	<b>1</b>
D	Drugs or alcohol (1 point each)	1 or 2
		Maximum 9 points

\*Hypertension is defined as systolic blood pressure > 160 mmHg.



# Thrombotic vs. Bleeding Risk Factors

## THROMBOTIC RISK FACTORS

- Diabetes mellitus requiring therapy
- Prior ACS/recurrent myocardial infarction
- Multivessel CAD
- Concomitant PAD
- Premature CAD (occurring at age of <45 y) or accelerated CAD (new lesion within 2 years)
- CKD (eGFR <60 mL/min)
- Clinical presentation (ACS)
- Multivessel stenting
- Complex revascularisation (left main stenting, bifurcation lesion stenting, chronic total occlusion intervention, last patent vessel stenting)
- Prior stent thrombosis on antiplatelet treatment
- Procedural factors (stent expansion, residual dissection, stent length, etc.)

## BLEEDING RISK FACTORS

- Hypertension
- Abnormal renal or liver function
- Stroke or ICH history
- Bleeding history or bleeding diathesis (e.g., anaemia with haemoglobin <110 g/L)
- Labile INR (if on VKA)
- Elderly (>65 years)
- Drugs (concomitant OAC and antiplatelet therapy, NSAIDs), excessive alcohol consumption

## STRATEGIES TO REDUCE BLEEDING ASSOCIATED WITH PCI

- Radial artery access
- PPIs in patients taking DAPT who are at increased risk of bleeding (e.g., the elderly, dyspepsia, gastro-oesophageal reflux disease, Helicobacter pylori infection, chronic alcohol use)
- Non-administration of unfractionated heparin in patients on VKA with INR >2.5
- Pre-treatment with aspirin only, add a P2Y<sub>12</sub> inhibitor when coronary anatomy is known or if STEMI
- GP IIb/IIIa inhibitors only for bailout or periprocedural complications
- Shorter duration of combined antithrombotic therapy

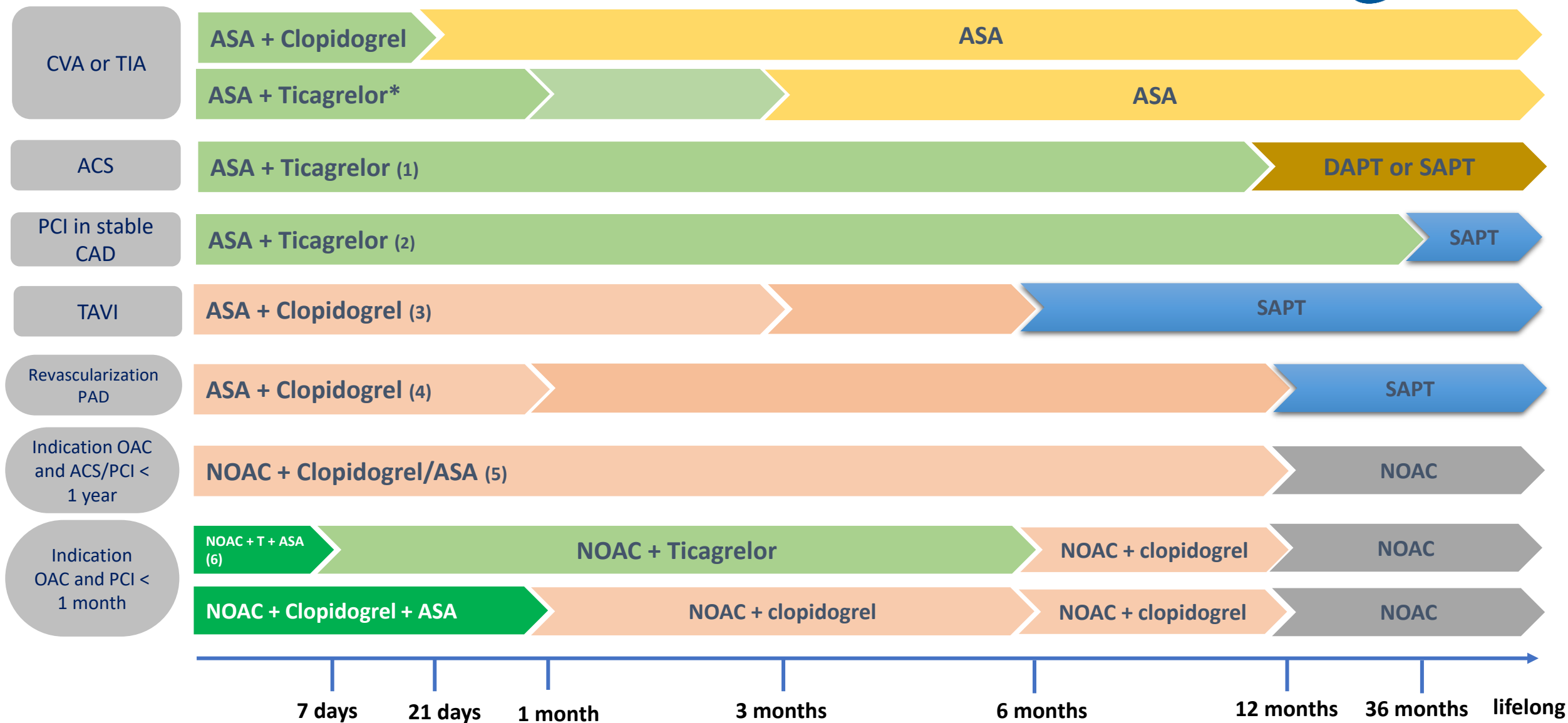


# Anticoagulant and Antiplatelet Therapy

In general, the use of “**Triple Therapy**” (dual antiplatelet therapy plus anticoagulation) is not recommended for most patients due to an increased risk of bleeding.

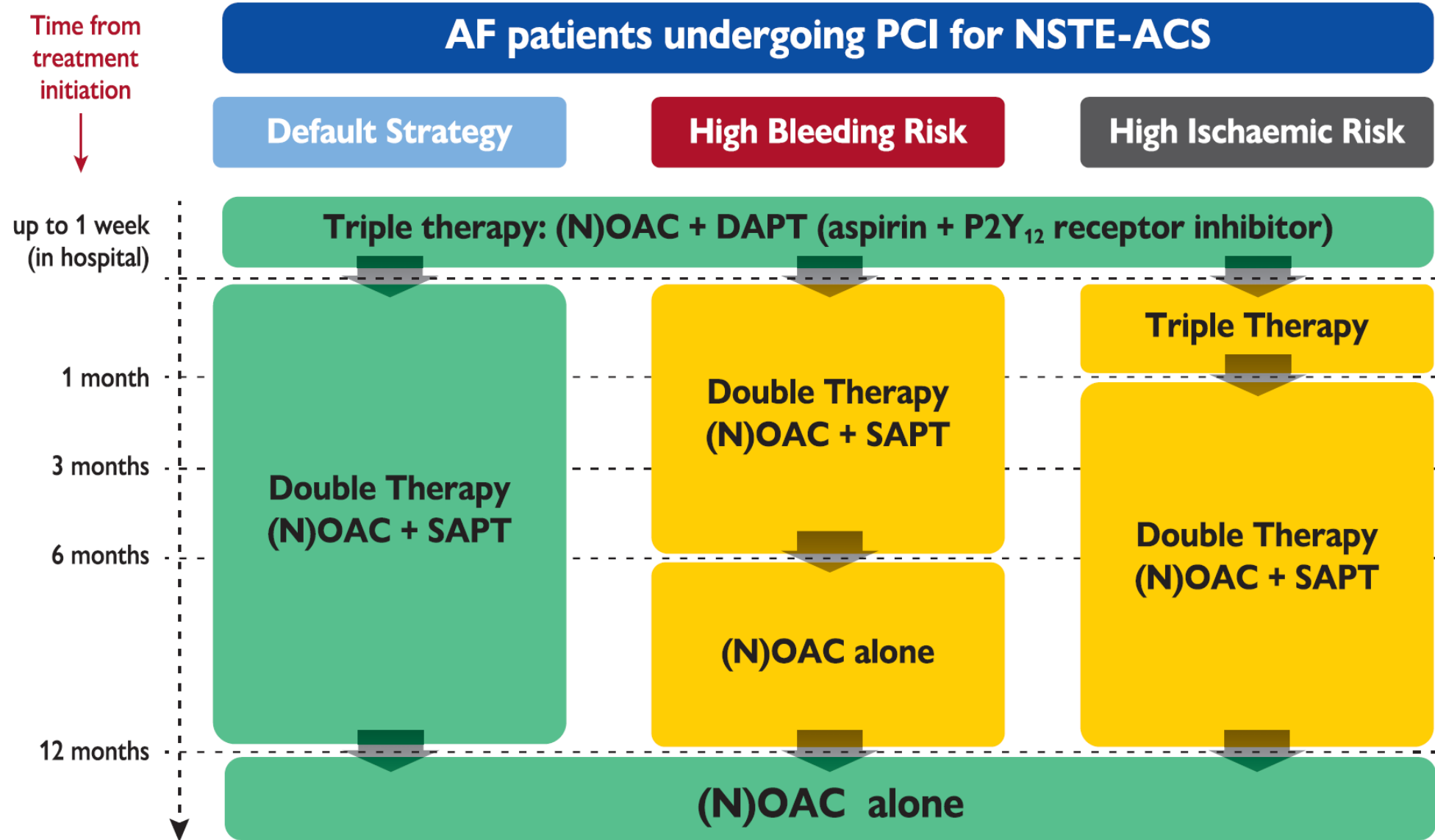
If triple therapy is needed, a short duration (e.g., **no more than 30 days**) is recommended. et agent for most patients.

In patients with ACS undergoing PCI, it is reasonable to use **Ticagrelor** or **Prasugrel** in preference to Clopidogrel to reduce ischemic events.  
However, when combined with an anticoagulant, **Clopidogrel** is the recommended antiplatelet agent for most patients.





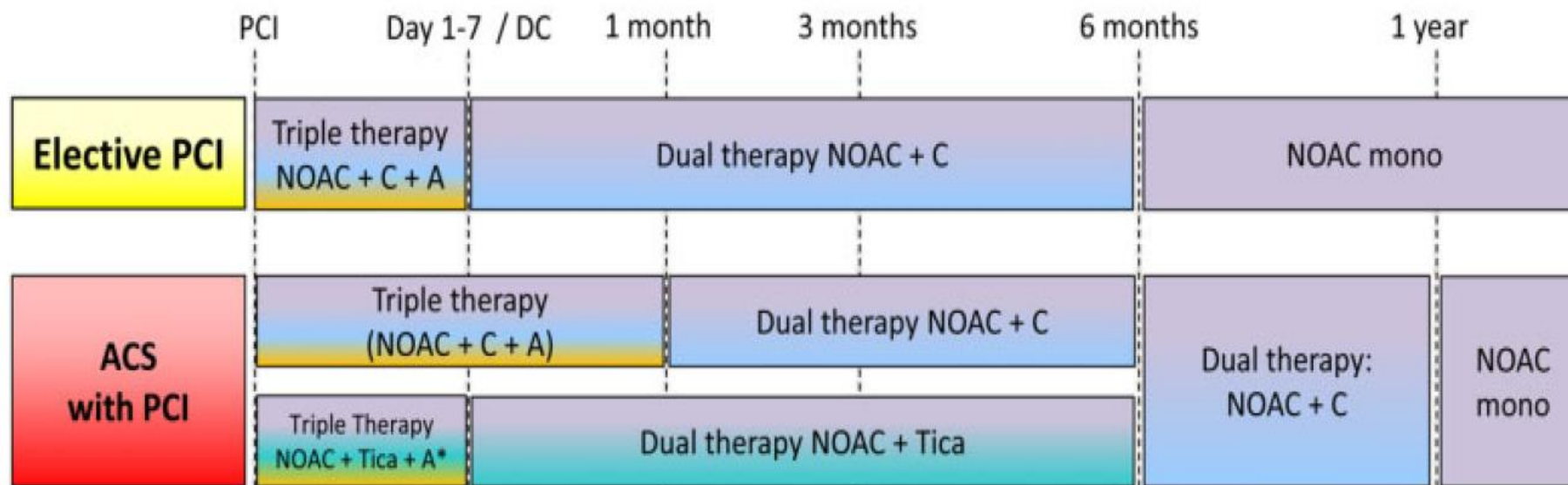
2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS)







2021 European Heart Rhythm Association  
Practical Guide on the Use of Non-Vitamin K  
Antagonist Oral Anticoagulants in Patients with  
Atrial Fibrillation



Factors to shorten / de-intensify combination therapy

- (Uncorrectable) high bleeding risk
- Low atherothrombotic risk (by REACH or SYNTAX score if elective; GRACE < 140 if ACS)

Factors to lengthen / intensify combination therapy

- High atherothrombotic risk (scores as above; stenting of left main, proximal LAD, proximal bifurcation; recurrent MIs; stent thrombosis etc.) and low bleeding risk



## Medical History

# Case

**NOAC in  
AF + CAD**



**What is your preferred regimen in this patient after 1 week of triple therapy with Ticagrelor?**

- **Apixaban 5mg BID + Ticagrelor 90mg BID + Pantoprazole 40mg QD**
- **Apixaban 5mg BID + Clopidogrel 75mg QD + Pantoprazole 40mg QD**
- **Rivaroxaban 20mg QD + Clopidogrel 75mg QD**
- **Rivaroxaban 15mg QD + Ticagrelor 90mg BID**
- **Rivaroxaban 10mg QD + Clopidogrel 75mg QD + Pantoprazole 40mg QD**



# Case

NOAC in  
AF + CAD

## NOAC dosing in AF patients post-ACS/PCI

	Standard dose	Comments/dose reduction
<b>Apixaban</b>	5 mg BID	Dose reduction as for SPAF
<b>Rivaroxaban</b>	15 mg QD	Dose reduction to 10 mg QD if CrCl 30–49 mL/min
<b>Dabigatran</b>	150 mg BID or 110 mg BID	110mg as for SPAF
<b>Edoxaban</b>	60 mg QD	Dose reduction as for SPAF





# How to reduce GI bleeding risk?

Starting or continuing a **Proton Pump Inhibitor**

and

**Avoiding other anti-inflammatory** medications

**Should be employed** For patients taking **≥2 antithrombotic agents** to reduce gastrointestinal bleeding risk.



## **Grey Zones in NOAC prescription**



## Case 2

**NOAC eligibility:  
RHD**



### Medical History



**42 years old lady**



**Known case of rheumatic heart disease**



**Admitted to CCU with complaint of sudden onset palpitation since 5 hours ago.**



## Case 2

**NOAC eligibility:  
RHD**



### Medical History



**LD & Fefol QD**



**AF rhythm with RVR in ECG**

**Weight 65 Kg**

**BP 120/80 mmHg**

**EF 55%**



**Thick & dome-shape MV (rheumatic changes) with moderate to severe stenosis (MVA 1.5 cm<sup>2</sup>)**

**No visible clot**





## Case 2

**NOAC eligibility:  
RHD**

**The patient lives in a far away village without laboratory facilities.  
What is your recommendation regarding the stroke prevention strategy in this patient?**

- **No OAC is indicated due to low CHA<sub>2</sub>DS<sub>2</sub>-VASc Score (1)**
- **ASA + clopidogrel**
- **Warfarin with TTR > 70%**
- **Apixaban 5mg BID**



# Rheumatic Mitral Stenosis

2018

Condition	Eligibility for NOAC therapy
Mechanical prosthetic valve	Contraindicated
Moderate to severe mitral stenosis (usually of rheumatic origin)	Contraindicated
Mild to moderate other native valvular disease (e.g., mild-moderate aortic stenosis or regurgitation, degenerative mitral regurgitation etc.)	Included in NOAC trials
Severe aortic stenosis	Limited data (excluded in RE-LY) Most will undergo intervention
Bioprosthetic valve (after > 3 months post operatively)	Not advised if for rheumatic mitral stenosis Acceptable if for degenerative mitral regurgitation or in the aortic position
Mitral valve repair (after > 3 months post operatively)	Some patients included in some NOAC trials
PTAV and TAVI	No prospective data yet May require combination with single or dual antiplatelet therapy
Hypertrophic cardiomyopathy	Few data, but patients may be eligible for NOACs



# Rheumatic Mitral Stenosis

2021

Condition	Eligibility for NOAC	Comment
Mechanical prosthetic valve	Contraindicated	Excluded from pivotal RCTs Data indicating worse outcome <sup>15,16</sup>
Moderate to severe mitral stenosis (usually rheumatic)	Contraindicated	Excluded from pivotal RCTs Little rationale for less efficacy and safety vs. VKA
Other mild to moderate valvular disease (e.g. degenerative aortic stenosis, mitral regurgitation etc.) Bioprosthetic valve/valve repair (after >3 months postoperative)	Included in NOAC trials  Acceptable	Data regarding efficacy and safety overall consistent with patients without valvular heart disease <sup>12,17–22</sup> Some data from NOAC RCTs Single RCT indicating non-inferiority to VKA <sup>24</sup> Patients without AF usually on ASA after 3–6 months post-surgery, hence NOAC therapy acceptable for stroke prevention if diagnosed with AF
Severe aortic stenosis	Limited data (excluded in RE-LY)	No pathophysiological rationale for less efficacy and safety Most will undergo intervention
Transcatheter aortic valve implantation	Acceptable	Single RCT + observational data May require combination with APT <sup>25,26</sup>
Percutaneous transluminal aortic valvuloplasty	With caution	No prospective data May require combination with APT
Hypertrophic cardiomyopathy	Acceptable	No rationale for less efficacy and safety vs. VKA Observational data positive for NOACs <sup>33–36</sup>



## Case 2

**NOAC eligibility:  
RHD**

**The patient lives in a far away village without laboratory facilities.  
What is your recommendation regarding the stroke prevention strategy in this patient?**

- **No OAC is indicated due to low CHA<sub>2</sub>DS<sub>2</sub>-VASc Score (1)**
- **ASA + clopidogrel**
- **Warfarin with TTR > 70%**
- **Apixaban 5mg BID**



# Case 3

NOAC  
eligibility:

LV Clot

## Medical History



63 years old man



Cigarette smoker

Opium abuser

Anterior STEMI with successful primary PCI for LAD (40 days ago)



Referred due to finding of an immobile LV apical clot in TTE performed for decision regarding the need for ICD implantation



# Case 3

NOAC  
eligibility:

LV Clot

## Medical History



**ASA 80mg QD**

**Ticagrelor 90mg BID**

**Rosuvastatin 20mg QD**

**Bisoprolol 2.5 mg QD**

**Losartan 12.5mg BID**

**Pantoprazole 40mg QD**



**Normal sinus rhythm**

**EF 30%**



**Apical aneurysm formation with a fresh mid-size and immobile apical clot**





# Left Ventricular Thrombus

The incidence of LV thrombi in the pre-reperfusion era was reported to be as high as **40 percent** in patients with anterior infarction.

Data are more limited on the incidence of LV thrombus in the reperfusion era. In two series of STEMI patients treated with primary PCI, the incidence of LV thrombus was about **4 percent**.

The risk of embolization in patients with a documented LV thrombus who are not treated with anticoagulant therapy has been reported to be **10 to 15 percent**.



## Case 3

NOAC  
eligibility:

LV Clot

**What is your recommendation for overall antiplatelet/antithrombotic management in this patient?**

- **ASA 80mg QD + ticagrelor 90mg BID + warfarin for 3 months**
- **ASA 80mg QD + ticagrelor 90mg BID + rivaroxaban 15mg QD for 3 months**
- **Ticagrelor 90mg BID + warfarin for 3 months**
- **Ticagrelor 90mg BID + Rivaroxaban 20mg QD for 3 months**



# Left Ventricular Thrombus

One observational study suggests that NOACs were associated with a higher incidence of thromboembolic events compared to VKA in (mostly non-AF) patients with a left ventricular thrombus, while others showed a similar rate of thrombus resolution.

VKA should be viewed as standard of care for the treatment of patients with LV thrombus until more data are available.



# Case 3

NOAC  
eligibility:

LV Clot

**What is your recommendation for overall antiplatelet/antithrombotic management in this patient?**

- **ASA 80mg QD + ticagrelor 90mg BID + warfarin for 3 months**
- **ASA 80mg QD + ticagrelor 90mg BID + rivaroxaban 15mg QD for 3 months**
- **Ticagrelor 90mg BID + warfarin for 3 months**
- **Ticagrelor 90mg BID + Rivaroxaban 20mg QD for 3 months**



# Case 4

**NOAC  
eligibility:**

**Bioprosthetic  
Valve and AF**

## **Medical History**



**77 years old lady**



**Permanent AF**

**Severe rheumatic MS & severe MR**

**Underwent MVR with bioprosthetic valve**



**Cardiology consultation after surgery regarding the possibility of prescribing NOAC in the patient**



# Case 4

**NOAC  
eligibility:**

**Bioprosthetic  
Valve and AF**

## Medical History



**ASA 80mg QD**

**UFH infusion 1100 IU/h**

**Bisoprolol 2.5 mg BID**

**Furosemide 20mg BID**

**Losartan 12.5 mg QD**



**EF 45%, NL bioprosthesis findings**





## Case 5

**NOAC  
eligibility:**

**Bioprosthetic  
Valve and AF**

**What would be your recommendation?**

- **ASA 80mg QD + warfarin**
- **Warfarin for 3 months, then NOAC**
- **Just NOAC**



# Rheumatic Mitral Stenosis

2021

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# Rheumatic Mitral Stenosis

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Condition	Eligibility for NOAC therapy
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PTAV and TAVI	No prospective data yet May require combination with single or dual antiplatelet therapy
Hypertrophic cardiomyopathy	Few data, but patients may be eligible for NOACs



ORIGINAL ARTICLE

## Rivaroxaban in Patients with Atrial Fibrillation and a Bioprosthetic Mitral Valve

H.P. Guimarães, R.D. Lopes, P.G.M. de Barros e Silva, I.L. Liporace, R.O. Sampaio, F. Tarasoutchi, C.R. Hoffmann-Filho, R. de Lemos Soares Patriota, T.L.L. Leiria, D. Lamprea, D.B. Precoma, F.A. Atik, F.S. Silveira, F.R. Farias, D.O. Barreto, A.P. Almeida, A.C. Zilli, J.D. de Souza Neto, M.A. Cavalcante, F.A.M.S. Figueira, F.C.S. Kojima, L. Damiani, R.H.N. Santos, N. Valeis, V.B. Campos, J.F.K. Saraiva, F.H. Fonseca, I.M. Pinto, C.C. Magalhães, J.F.M. Ferreira, J.H. Alexander, R. Pavanello, A.B. Cavalcanti, and O. Berwanger, for the RIVER Trial Investigators\*

**In patients with atrial fibrillation and a bioprosthetic mitral valve, rivaroxaban was noninferior to warfarin with respect to the mean time until the primary outcome of death, major cardiovascular events, or major bleeding at 12 months.**



## Case 5

**NOAC  
eligibility:**

**Bioprosthetic  
Valve and AF**

**What would be your recommendation?**

- **ASA 80mg QD + warfarin**
- **Warfarin for 3 months, then NOAC**
- **Just NOAC**





## NOAC and Surgery



# Case 5

Surgery in AF  
patients

## Medical History

 65 years old gentleman

 Paroxysmal AF  
TIA 4 months ago  
Scheduled for ESWL

 Apixaban 5mg BD





# Case 5

Surgery in AF  
patients



## Medical History



EF 55%  
Mild MR, Mild TR



CBC : NL  
Cr 2.0 (CrCl 39 ml/min)  
LFT NL



# Case 5

## Surgery in AF patients

**What is your recommendation regarding the timing of holding NOAC and possible bridging therapy before surgery?**

- **Hold apixaban at least 48h before surgery w/o bridging therapy**
- **Hold apixaban at least 48h before surgery and start bridging therapy**
- **Hold apixaban at least 72h before surgery and start bridging therapy**
- **Hold apixaban at least 96h before surgery and start bridging therapy**



# Case 5

## Surgery in AF patients

# Classification of elective surgical interventions according to bleeding risk

### Minor risk interventions (i.e. infrequent bleeding and with low clinical impact)

Dental extractions (1–3 teeth), paradental surgery, implant positioning, subgingival scaling/cleaning

Cataract or glaucoma intervention

Endoscopy without biopsy or resection

Superficial surgery (e.g. abscess incision; small dermatologic excisions, skin biopsy)

Pacemaker or ICD implantation (except complex procedures)

Electrophysiological study or catheter ablation (except complex procedures)

Routine elective coronary/peripheral artery intervention (except complex procedures)

Intramuscular injection (e.g. vaccination)

### Low-risk interventions (i.e. infrequent bleeding or with non-severe clinical impact)

Complex dental procedures

Endoscopy with simple biopsy

Small orthopedic surgery (foot, hand, arthroscopy, ...)



# Case 5

## Surgery in AF patients

### Classification of elective surgical interventions according to bleeding risk

#### High-risk interventions (i.e. frequent bleeding and/or with important clinical impact)

Cardiac surgery

Peripheral arterial revascularization surgery (e.g. aortic aneurysm repair, vascular bypass)

Complex invasive cardiological interventions, including lead extraction, (epicardial) VT ablation, chronic total occlusion PCI etc.

Neurosurgery

Spinal or epidural anesthesia; lumbar diagnostic puncture

Complex endoscopy (e.g. multiple/large polypectomy, ERCP with sphincterotomy etc.)

Abdominal surgery (incl. liver biopsy)

Thoracic surgery

Major urologic surgery/biopsy (incl. kidney)

Extracorporeal shockwave lithotripsy

Major orthopedic surgery

# Timing of last NOAC intake before an elective intervention



## Case 5

### Surgery in AF patients

	Dabigatran		Apixaban - Edoxaban - Rivaroxaban	
No perioperative bridging with LMWH / UFH				
Minor risk procedures: - Perform procedure at NOAC trough level (i.e., 12 h / 24 h after last intake). - Resume same day or latest next day.				
	Low risk	High risk	Low risk	High risk
CrCl ≥80 ml/min	≥ 24 h	≥ 48 h	≥ 24 h	≥ 48 h
CrCl 50-79 ml/min	≥ 36 h	≥ 72 h		
CrCl 30-49 ml/min	≥ 48 h	≥ 96 h		
CrCl 15-29 ml/min	Not indicated	Not indicated	≥ 36 h	
CrCl <15 ml/min	No official indication for use			

#### Important:

- Timing of interruption may require adaptation based on individual patient characteristics (Fig. 13)
- In patients / situations with risk of NOAC accumulation (renal insufficiency, older age, concomitant medication, see Fig. 6) pausing the NOAC 12-24 hours earlier may be considered.<sup>207,208</sup>
- Resume full dose of NOAC 24h after low-risk- and 48 (-72) h after high-risk interventions



# Heparin Bridging

Pre-operative bridging with heparin is not recommended in NOAC-treated patients since the predictable waning of the anticoagulation effect allows for properly timed short-term cessation of NOAC therapy before surgery.

The very few very high-risk situations in which bridging may be discussed include urgent surgery with a high bleeding risk in patients with **a recent ( $\leq 3$  months) thromboembolic event** (including stroke, systemic embolism or venous thrombosis/pulmonary embolism) or who suffered an **event during previous adequate interruption of NOAC therapy**.

In these instances, in addition to ‘timed’ NOAC interruption, switching to UFH or low-dose dabigatran—both with the possibility of rapid reversal—around the operation may be evaluated.



# Case 5

## Surgery in AF patients

**What is your recommendation regarding the timing of holding NOAC and possible bridging therapy before surgery?**

- **Hold apixaban at least 48h before surgery w/o bridging therapy**
- **Hold apixaban at least 48h before surgery and start bridging therapy**
- **Hold apixaban at least 72h before surgery and start bridging therapy**
- **Hold apixaban at least 96h before surgery and start bridging therapy**





# Case 6

NOAC  
eligibility:

TAVI

## Medical History



88 years old man



HTN

Known case of severe AS & porcelain aorta  
TAVI procedure 1 months ago



In routine post-procedure visit at clinic, de novo AF rhythm was detected.



# Case 6

NOAC  
eligibility:

TAVI

## Medical History



**ASA 80mg QD**

**Plavix 75mg QD**

**Pantoprazole 40mg QD**

**Valsartan 80mg QD**



**AF rhythm in ECG**

**Weight 78 Kg**

**BP 165/115 mmHg**



**CBC NL**

**Cr 1.3 (CrCl 43 ml/min)**

**LFT NL**



# Case 6

NOAC  
eligibility:

TAVI

**What is your recommendation regarding stroke prevention strategy in this patient?**

- **Apixaban 5mg BID + clopidogrel 75mg QD**
- **Warfarin with TTR > 70%**
- **Apixaban 5mg BID**
- **Clopidogrel monotherapy due to high bleeding risk (HAS-BLED 3)**

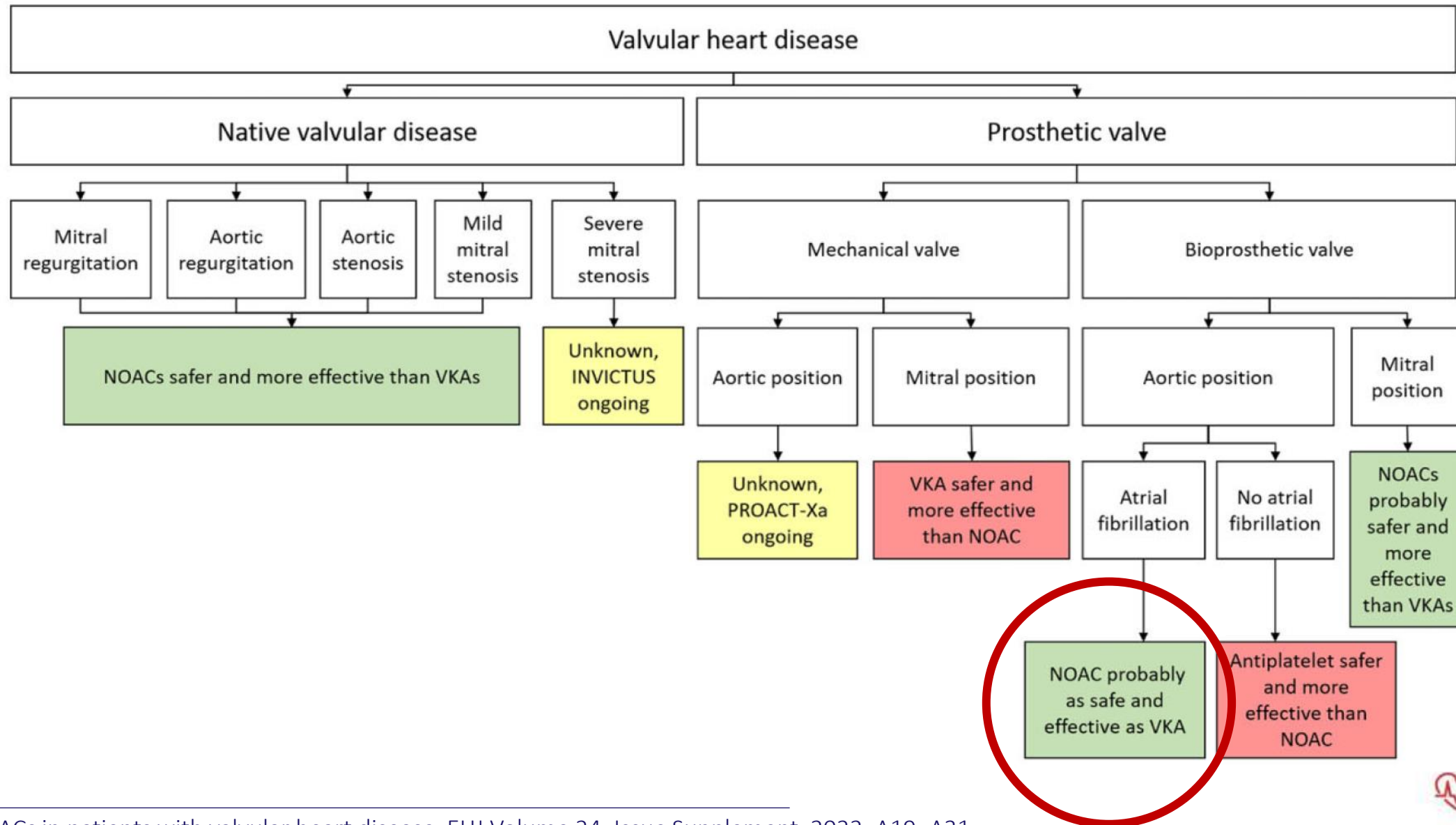


# The optimal antithrombotic strategy for patients undergoing TAVI

- **ACC/AHA guidelines** recommend against the routine use of Rivaroxaban, in particular, to prevent subclinical valve thrombosis (Class III, LOE B), and specifically recommend VKAs in patients who develop valve thrombosis (Class IIa, LOE B).
- For patients with an indication for OAC, lifelong OAC is recommended (Class I, LOE B) with no preference expressed for NOAC or VKA, consistent with the results of ENVISAGE-TAVI AF and ATLANTIS stratum.



# NOACs in Patients with VHD





## Case 6

NOAC  
eligibility:

TAVI

**What is your recommendation regarding stroke prevention strategy in this patient?**

- **Apixaban 5mg BID + clopidogrel 75mg QD**
- **Warfarin with TTR > 70%**
- **Apixaban 5mg BID**
- **Clopidogrel monotherapy due to high bleeding risk (HAS-BLED 3)**



Thank you