



# ICT 2023

28th International  
Congress on Thrombosis

## Invasive procedures in patients with high bleeding risk

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Sociedade Portuguesa de  
**CARDIOLOGIA**



**ULS**  
Matosinhos



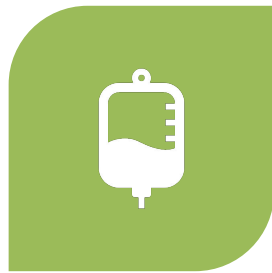
## Declaration of Conflict Of Interest

- I have no potential conflict of interest to report regarding this presentation

# INDEX



INTRODUCTION



HIGH BLEEDING  
RISK



INVASIVE  
PROCEDURES –  
WHAT TO CONSIDER



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MESSAGES



# Introduction - The challenge

Aim: To address the considerations of performing invasive procedures in patients with a heightened risk of bleeding:

- How to reduce the risk;
- What we should and should not do;



# High bleeding risk

## First things first assessing bleeding risk:

- Before performing invasive procedures or surgeries;
- To identify potential complications enabling appropriate management strategies.

## High bleeding risk definition:

- For PCI patients   $\geq 4\%$  risk of major (BARC 3 to 5) bleeding /  $\geq 1\%$  risk of intracranial hemorrhage at 1 year
  - ARC-HBR at least 1 major or 2 minor criteria; CRUSADE; ACUITY; ...
- For AF patients  HAS-BLED  $\geq 3$  = at least 3.74 bleeds per 100 patient-years; HEMORR2HAGES, ORBIT, ATRIA, ...
- For VTE prophylaxis  IMPROVE bleeding risk score  $\geq 7$  = 4.1% major bleeding rate

Defining high bleeding risk for different procedures can be quite challenging



Age  
( $\geq 75$  years)

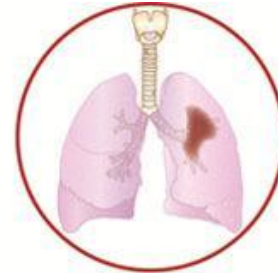
**Aging**



Renal  
disease



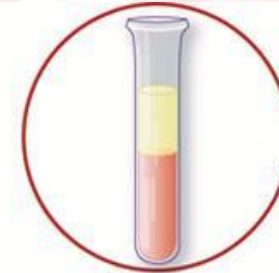
Liver  
disease



Active  
cancer



Anemia



Low platelet  
count

**Comorbidities**

**Laboratory**

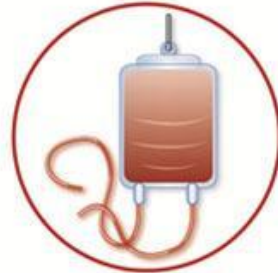


Stroke,  
ICH, bAVM

**CNS**



Bleeding  
diathesis



Prior bleeding  
or transfusion

**Bleeding history**



OAC



NSAIDs, Planned surgery on DAPT,  
steroids recent trauma or surgery

**Iatrogenic**

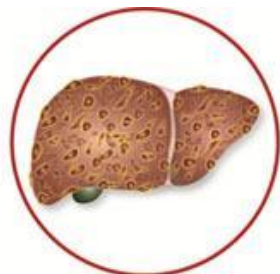


Age  
(≥75 years)

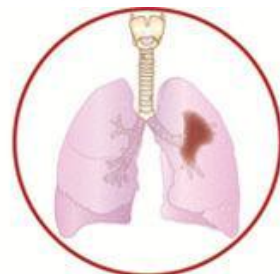
Aging



Renal  
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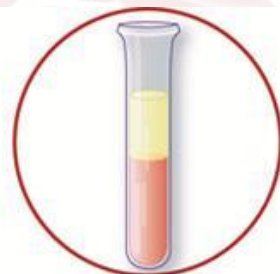
Liver  
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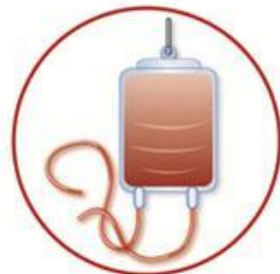


Stroke,  
ICH, bAVM

CNS



Bleeding  
diathesis



Prior bleeding  
or transfusion

Bleeding history



OAC



NSAIDs, Planned surgery on DAPT,  
steroids recent trauma or surgery



Iatrogenic



# High bleeding risk

Several factors can contribute to an increased bleeding risk in patients, including:

- Platelet disorders: e.g., idiopathic thrombocytopenic purpura or thrombotic thrombocytopenic purpura;
- Coagulation disorders: e.g., von Willebrand disease or hemophilia;
- Medications: Anticoagulants or antiplatelet drugs;
- Liver disease;
- Kidney disease;
- Advanced age;

...

**Multidisciplinary definition!**

**High bleeding risk:** Patients who are more prone to bleeding or have difficulties in blood clotting.



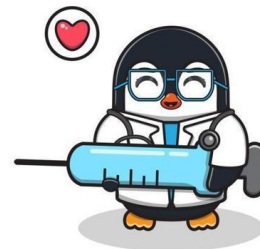
# Invasive procedures: different procedures = different risk

Surgery with minor bleeding risk	Surgery with low bleeding risk (infrequent or with low clinical impact)	Surgery with high bleeding risk (frequent or with significant clinical impact)
<ul style="list-style-type: none"><li>• <u>Cataract or glaucoma procedure</u></li><li>• <u>Dental procedures: extractions (1–3 teeth), periodontal surgery, implant positioning, endodontic (root canal) procedures, subgingival scaling/cleaning</u></li><li>• <u>Endoscopy without biopsy or resection</u></li><li>• <u>Superficial surgery</u> (e.g. abscess incision, small skin excisions/ biopsy)</li></ul>	<ul style="list-style-type: none"><li>• Abdominal surgery: cholecystectomy, hernia repair, colon resection</li><li>• Breast surgery</li><li>• Complex dental procedures (multiple tooth extractions)</li><li>• Endoscopy with simple biopsy</li><li>• Gastroscopy or colonoscopy with simple biopsy</li><li>• Large-bore needles procedures (e.g. bone marrow or lymph node biopsy)</li><li>• Non-cataract ophthalmic surgery</li><li>• Small orthopaedic surgery (foot, hand arthroscopy)</li></ul>	<ul style="list-style-type: none"><li>• Abdominal surgery with <u>liver biopsy, extracorporeal shockwave lithotripsy</u></li><li>• <u>Extensive cancer surgery</u> (e.g. pancreas, liver)</li><li>• <u>Neuraxial (spinal or epidural) anaesthesia</u></li><li>• <u>Neurosurgery (intracranial, spinal)</u></li><li>• <u>Major orthopaedic surgery</u></li><li>• Procedures with <u>vascular organ biopsy</u> (kidney or prostate)</li><li>• <u>Reconstructive plastic surgery</u></li><li>• Specific interventions (colon <u>polypectomy</u>, lumbar puncture, endovascular <u>aneurysm repair</u>)</li><li>• <u>Thoracic surgery, lung resection surgery</u></li><li>• <u>Urological surgery</u> (prostatectomy, bladder tumour resection)</li><li>• <u>Vascular surgery</u> (e.g. AAA repair, vascular bypass)</li></ul>

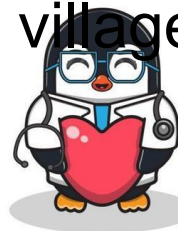


# Invasive procedures

Different patients risk needing **multidisciplinary** approach AND Procedural risk needing at least anaesthesiology + surgery approach



“It takes a village”



What can we do?



# Invasive procedures – what to consider



## Impact of Modifiable Bleeding Risk Factors on Major Bleeding in Patients With Atrial Fibrillation Anticoagulated With Rivaroxaban

Paulus Kirchhof, MD; Sylvia Haas, MD; Pierre Amarenco, MD, PhD; Susanne Hess, MD; Marc Lambelet, Dipl-Math; Martin van Eickels, MD; Alexander G. G. Turpie, MD; A. John Camm, MD; on behalf of the XANTUS Investigators\*

### What can we gain changing modifiable bleeding risk factors?

- Analyses of the XANTUS (Xarelto for Prevention of Stroke in Patients With Atrial Fibrillation) prospective registry data set (6784 rivaroxaban patients)

- 1.9%, n=128, experienced major bleeds
- 11% had no identified bleeding risk factors
- 50% had nonmodifiable bleeding risk factors only
- 39% had modifiable bleeding risk factors (with or without nonmodifiable risk factors)

Risk Factors	Partial PAR (95% CI)
Uncontrolled hypertension	0.025 (–0.019 to 0.069)
Heavy alcohol use	0.017 (–0.008 to 0.042)
Concomitant antiplatelets, NSAIDs, or paracetamol use	0.126 (0.008 to 0.242)
Uncontrolled hypertension and heavy alcohol use	0.042 (–0.020 to 0.104)
Uncontrolled hypertension and concomitant antiplatelets, NSAIDs, or paracetamol use	0.149 (0.004 to 0.289)
Heavy alcohol use and concomitant antiplatelets, NSAIDs, or paracetamol use	0.140 (0.014 to 0.262)
Uncontrolled hypertension and heavy alcohol use and concomitant antiplatelets, NSAIDs, or paracetamol use	0.163 (0.009 to 0.310)

The presence of **1 modifiable bleeding risk factor** doubled the risk of major bleeding.



# Invasive procedures – what to consider

Multidisciplinary Approach: including hematologists, anesthesiologists, surgeons, cardiologists, ...

- Joint decision-making considering the patient's bleeding risk and the procedure's urgency
- Procedures should be performed by skilled practitioners familiar with bleeding complications.

Pharmacological Strategies:

1) Medication adjustment or discontinuation: SAPT / DAPT / OAC

- For non-cardiac and cardiac procedures

2) Pharmacological interventions to enhance hemostasis during acute bleeding event

- From tranexamic acid to platelet transfusion, desmopressin, prothrombin complex concentrate...

3) Patient Blood Management



# Invasive procedures: non-cardiac procedures

2022 ESC Guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgery

## SAPT

- If AAS only– POISE 2 trial, stop all for 3 days unless previous ACS/PCI
  - Exception: high peri-operative bleeding risk (e.g., spinal surgery – stop always for 7 days)
- If clopidogrel only: 1) for CCS: short interruption of clopidogrel; 2) for post-ACS/PCI: individualized decision

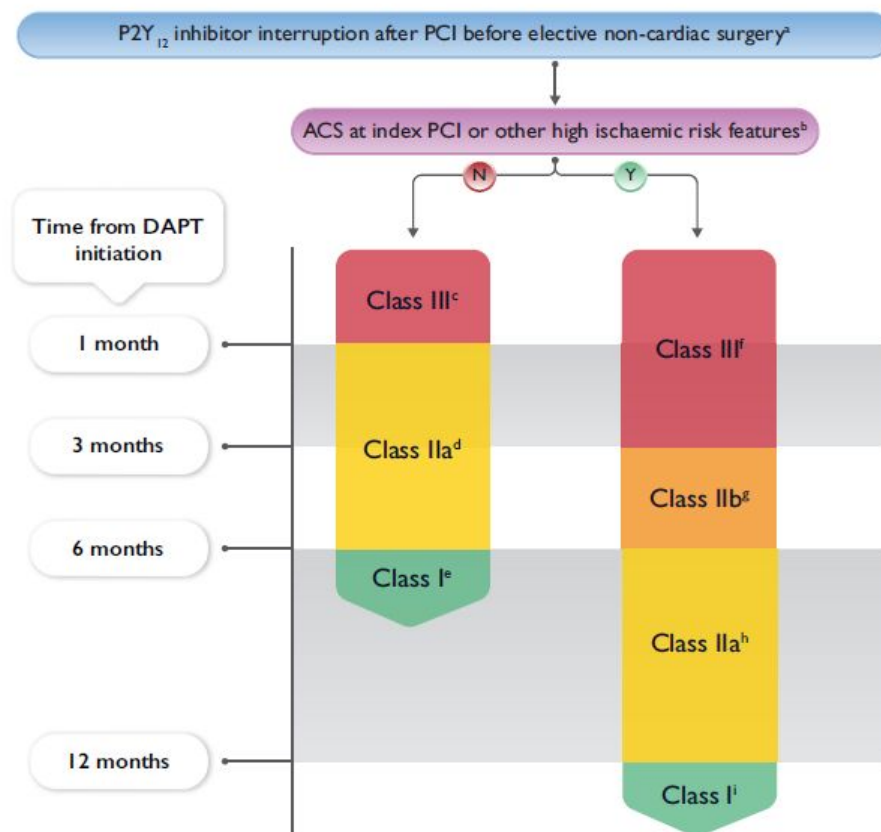
## DAPT

- **Post PCI** – best to **postpone 6 months** after PCI for and 12 months if ACS
  - If it's not possible □ at least 1-3 months
  - De-escalation is possible: tica/prasu to clopidogrel can be performed
- Stopping clopidogrel > 5 days – reduces risk of reoperation for major bleeding by 50%
- In very high bleeding risk, last measure: stop ASA + Clopidogrel, in-hospitals with cath lab only;
  - Very high bleeding risk + very high stent thrombosis risk: bridging with cangrelor / eptifibatide / tirofiban

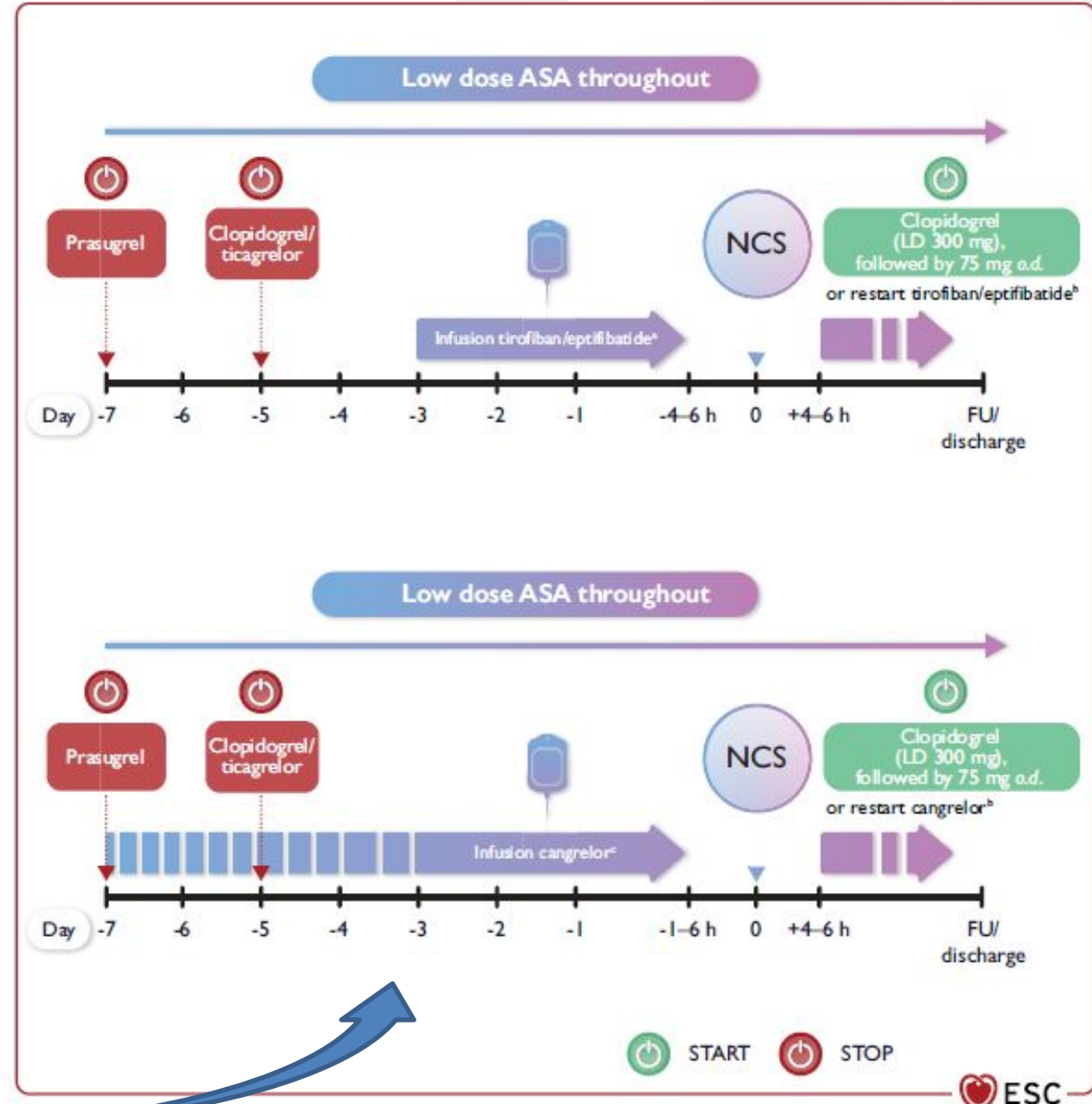
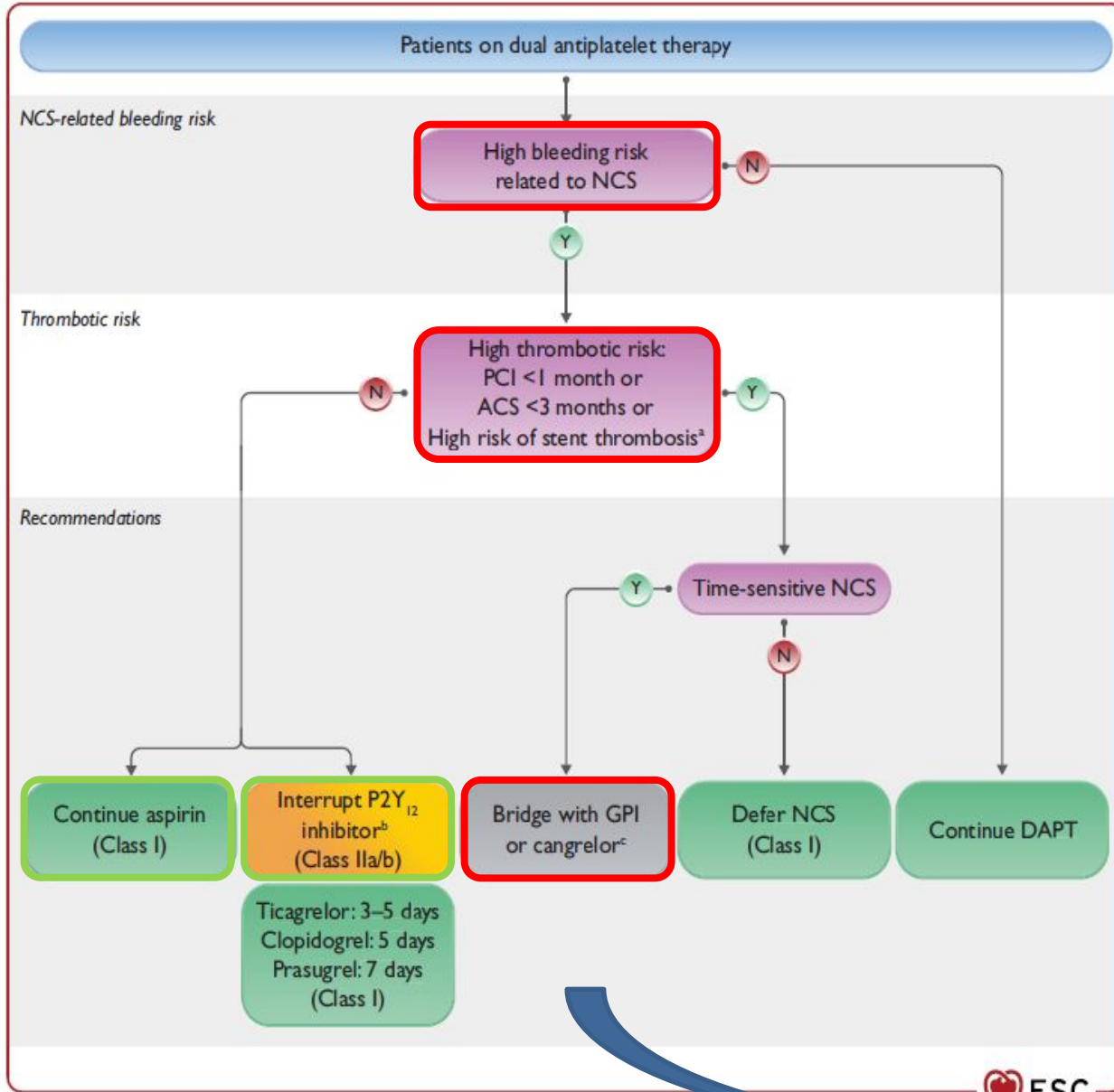


# Invasive procedures: non-cardiac procedures

## Stopping P2Y<sub>12</sub>i post PCI – The later the better



# Patients on DAPT





# High bleeding risk invasive procedures - Platelet function tests

- To identify patients on antiplatelet therapy;
- To individualize the timing of elective surgery
  - Allowing less “thrombotic risk - exposure time”
- To guide therapy in bleeding complications

Method	Sample	Method application
Bleeding time	Native WB	Screening test (obsolete)
<b>Tests based on platelet aggregation</b>		
Light transmission platelet aggregation (LTA)	Citrated PRP	Screening test for bleeding tendency Diagnostic for platelet defects Monitoring antiplatelet treatment effect
Impedance platelet aggregation	Citrated WB	Screening test for bleeding tendency Diagnostic for platelet defects Monitoring antiplatelet treatment effect
Lumiaggregometry	Citrated WB	Detection of storage/release disorders
Plateletworks	Citrated WB	Monitoring of the platelet response to antiplatelet agents
<b>Tests based on platelet adhesion under shear stress</b>		
PFA-100; Innovance PFA-200	Citrated WB	Assessment of bleeding risk and drug effects Searching severe platelet dysfunctions, revealing of VWD
Impact; Cone and Plate(let) Analyzer	Citrated WB	Screening of primary hemostasis
Global thrombosis test (GTT)	Native WB	Evaluation of platelet function and thrombolysis
<b>Platelet function methods combined with viscoelastic test</b>		
TEG/platelet mapping system	Citrated WB	Assessment of global hemostasis plus monitoring antiplatelet treatments effect
ROTEM platelet	Citrated WB	Assessment of global hemostasis plus diagnostic of platelet defects plus monitoring antiplatelet treatments effect
<b>Platelet analysis based on flow cytometry</b>		
Flow cytometry	Citrated WB, PRP, W-Pit	Cell counting, detection platelet activation by extent of expression of surface and/or cytoplasmic biomarkers
<b>Evaluation of Thromboxane metabolites</b>		
Radio- or enzyme-linked immune assays	Serum, urine, citrated Pls	Measurement of TxA2 metabolites (and Beta-TG, PF4, soluble P-selectine) <sup>a</sup>



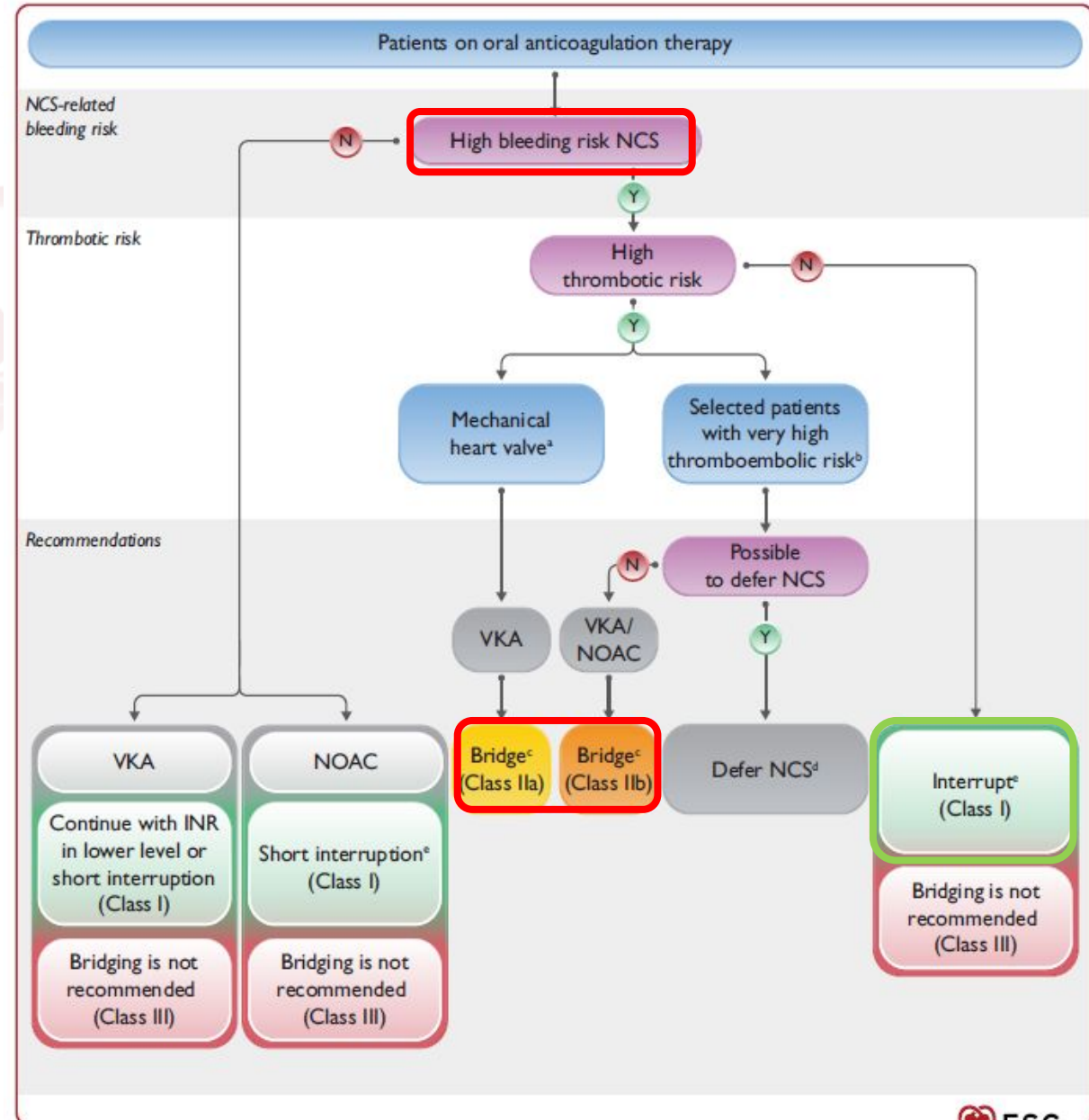
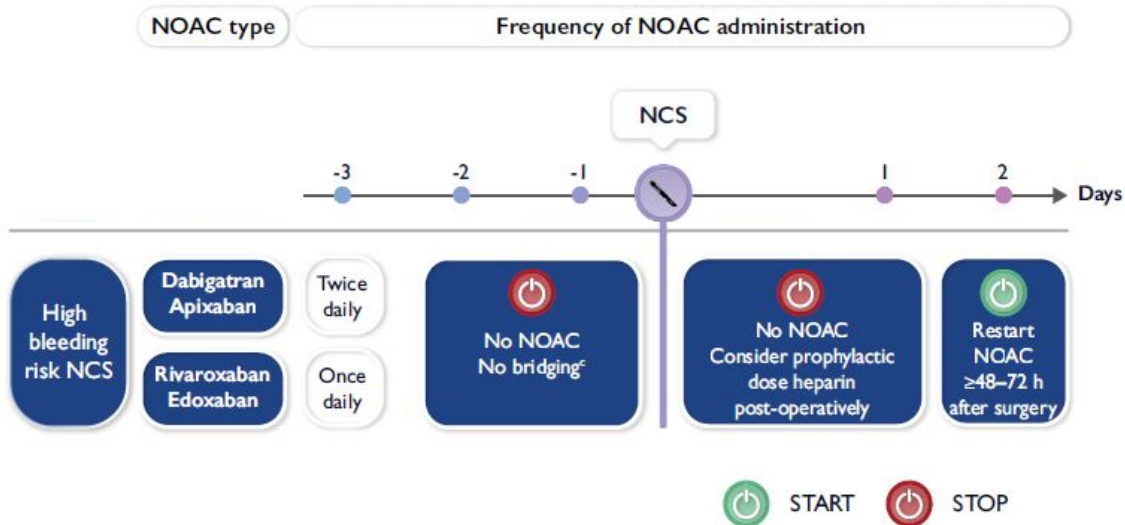
# Invasive procedures: OAC

On NOAC: High bleeding risk  Interrupt +/- 48h

On VKA: High bleeding risk

- non-high thrombotic risk = interrupt to INR<1.5
- high thrombotic risk = bridging

Stopping and re-initiation of NOAC therapy in elective NCS according to the periprocedural risk of bleeding in patients with normal renal function





# Invasive procedures: OAC

RESEARCH

## Bridging vs. Placebo

- N=1471
- Patients with either an MHV, AF, or atrial flutter who required interruption of OAC for surgery;
- No significant benefit for post-operative dalteparin bridging to prevent major thromboembolism.
- The results were consistent for the AF (n=1166) and MHVs groups (n=350).


Postoperative low molecular weight heparin bridging treatment for patients at high risk of arterial thromboembolism (PERIOP2): double blind randomised controlled trial

Michael J Kovacs,<sup>1</sup> Philip S Wells,<sup>2</sup> David R Anderson,<sup>3</sup> Alejandro Lazo-Langner,<sup>1</sup> Clive Kearon,<sup>4</sup> Shannon M Bates,<sup>4</sup> Mark Blostein,<sup>5</sup> Susan R Kahn,<sup>5</sup> Sam Schulman,<sup>4</sup> Elham Sabri,<sup>6</sup> Susan Solymoss,<sup>5</sup> Tim Ramsay,<sup>6</sup> Erik Yeo,<sup>7</sup> Marc A Rodger,<sup>5</sup> on behalf of the PERIOP2 Investigators

Mechanical Heart Valves with “low” thromboembolic risk – bridging may be avoidable  
(e.g. mechanical bileaflet aortic valve in patients with sinus rhythm)



# Invasive procedures: Timing of last NOAC

Low and high bleeding risk NCS				
	Low bleeding risk NCS	High bleeding risk NCS	Low bleeding risk NCS	High bleeding risk NCS
 Renal function (estimated GFR, mL/min)	Dabigatran		Apixaban, rivaroxaban, edoxaban	
≥80	≥24 h	≥48 h	≥24 h	≥48 h
50-79	≥36 h	≥72 h		
30-49	≥48 h	≥96 h		
15-29	Not indicated	Not indicated	≥36 h	
<15	No formal indication for use			

No peri-operative bridging with UFH/LMWH

# Invasive procedures: cardiac devices

	Dual antiplatelet therapy <sup>655,656</sup>		NOAC <sup>652</sup>	VKA <sup>650</sup>	OAC + antiplatelet <sup>657</sup>
	Thrombotic risk after PCI				
	Intermediate or low >1 month PCI >6 months acute coronary syndrome at index PCI	High <1 month PCI <6 months acute coronary syndrome at index PCI			
<b>Low procedural bleeding risk</b> First implant	Continue aspirin AND <u>Discontinue P2Y<sub>12</sub> inhibitors</u> : Ticagrelor at least 3 days before surgery Clopidogrel at least 5 days before surgery	<u>Elective surgery</u> : Consider postponement <u>Otherwise</u> : <ul style="list-style-type: none"> <li>Continue aspirin</li> <li>Continue P2Y<sub>12</sub> inhibitor</li> </ul>	Continue or interrupt as per operator preference. If interruption, then based on CrCl and specific NOAC	Continue <sup>a</sup>	Continue OAC (VKA <sup>a</sup> or NOAC). Discontinue antiplatelet per patient-specific risk/benefit analysis
<b>High procedural bleeding risk</b> Device exchange, upgrade/revision procedure	Prasugrel at least 7 days before surgery	Continue aspirin AND <u>Discontinue P2Y<sub>12</sub> inhibitors</u> : Ticagrelor at least 3 days before surgery, Clopidogrel at least 5 days before surgery, Prasugrel at least 7 days before surgery. <u>Bridging with GP IIb/IIIa inhibitors</u>		INR 2-2.5 No bridging	

CrCl = creatinine clearance; GP = glycoprotein; NOAC = non-vitamin K antagonist oral anticoagulant; OAC = oral anticoagulant; PCI = percutaneous coronary intervention; VKA = vitamin K antagonist.

<sup>a</sup>Target international normalized ratio within therapeutic range.



# Invasive procedures – what to consider

## 3) Patient Blood Management (PBM)

- Even mild anaemia increases morbidity & mortality
  - Also, long-term survival decreased 50% in anaemic patients receiving intra-operative blood transfusion
- Iron deficiency ~50% cases
  - Increased risk 90-day mortality with and without anaemia

PBM – *“patient-centred and multidisciplinary approach to manage anaemia, minimize iatrogenic blood loss and bleeding, and harness tolerance to anaemia”*

- **IV iron** reduces blood transfusion needs and improves patient outcomes
- Recombinant EPO did not improve patient outcomes in a recent Cochrane review

Parameter	Normal	Iron deficiency
Mean corpuscular haemoglobin (g/dL)	28–33	<27
Mean cellular volume (fL)	80–96	<80
Transferrin saturation (%)	16–45	<20
Ferritin (ng/mL)	18–360	<30 <sup>a</sup>
Reticulocytes haemoglobin (ng/mL)	18–360	<30

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# Take-home messages



- Individualized bleeding risk should always be defined
  - Preferably with validated scores / multidisciplinary evaluation



- Bleeding risk depends on the patient and the procedure
  - Both can be optimized with collaborative decision-making



- To mitigate bleeding-related complications in high bleeding risk patients:

## 1) Medication adjustment or discontinuation:

- No PCI/ACS: STOP SAPT/DAPT || Previous PCI/ACS: 1<sup>st</sup> delay, 2<sup>nd</sup> SAPT 3<sup>rd</sup> bridge
- NOAC  $\geq$  48h stop , VKA only bridge mechanical valves (+ mitral/tricuspid position)

## 2) Pharmacological interventions to enhance hemostasis during acute bleeding

- Platelet transfusion, desmopressin, tranexamic acid, ...

## 3) Patient Blood Management

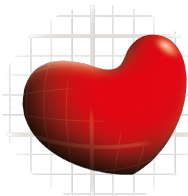


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## Thank you for your attention

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