perioperative considerations for the management of patients on NOAC & NOAC Reversal in Acute Hemorrhage

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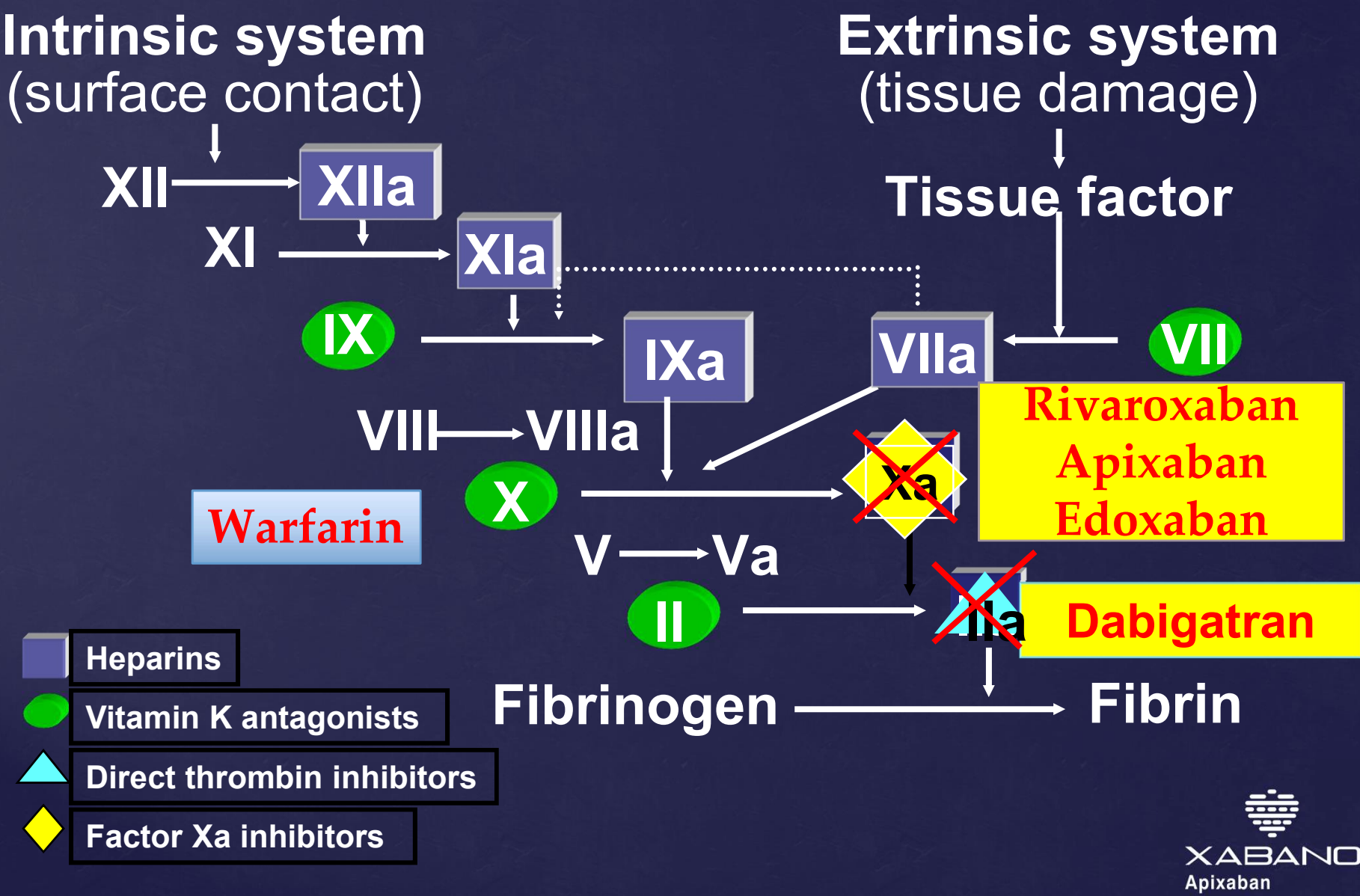
Anticoagulants: Mode of Action



XABANO
Apixaban

Case

- A 55 y/o female who presents with + LOC, a left temporal contusion, GCS 6, and rib fractures.
- She has a history of AF, CVA, HTN and DM.
- Wt. 55 kg.
- She is currently taking NOAC ?

What laboratory monitoring can be done to help determine if this patient is at risk of bleeding from NOAC ?

A. PT / INR , PTT
B. TT = thrombin time.
C. Anti-Xa activity
D. ECT = ecarin clotting time

Problems:

- anticoagulant agents currently use?

timing of last ingestion, renal function

- perioperative considerations for the management of patients on anticoagulant medications.

- Urgent reversal strategies

To detect presence

	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Therapeutic measurement	Routine not required	Routine not required	Routine not required	Routine not required
	To detect presence: aPTT, ECT (if available), TT	To detect presence: PT, aPTT, antifactor Xa activity	To detect presence: PT, aPTT, antifactor Xa activity	Prolongs PT, aPTT, antifactor Xa activity
	aPTT >2.5 times control may indicate overanticoagulation	Renal function, CBC periodically, at least annually; hepatic function	Renal function, CBC periodically, at least annually	Renal function, CBC periodically, at least annually
	Renal function, CBC periodically, at least annually			

Table 3 **Effect of NOAC in coagulation test and possible measures in case of bleedings**

Drug	Dabigatran	Factor Xa inhibitors
Effect on coagulation tests	↑: dTT, ECT, ↑ aPTT or no change: PT (not recommended)	↑: Anti-factor Xa ↑ or no change: PT, aPTT No change: dTT, ECT
Reversal in emergency bleeding	Oral charcoal Haemodialysis PCC, aPCC Desmopressin Antifibrinolytic agents	PCC, aPCC Desmopressin Antifibrinolytic agents

PT, prothrombin time; aPTT, activated partial thromboplastin time; dTT, diluted thrombin time; ECT, ecarin clotting time; PCC, prothrombin complex concentrate.

	Usefulness of lab test	Dabigatran	Rivaroxaban	Apixaban
Lab tests		• ECT • TT • aPTT • PT/INR	• Chromogenic anti-Xa • aPTT, PT	• Chromogenic anti -Xa

ECT, ecarin clotting time; TT, thrombin time; aPTT, activated partial thromboplastin time; PT, prothrombin time; INR, international normalization ratio.

In summary

- routine NOAC monitoring is unnecessary

- NOAC effect may assist clinical management in certain acute care and periprocedural settings.

- NOAC ?
- time of last drug ingestion
- CrCl (creatinine clearance)
- Risk of bleeding (standard / High)

➔ enable appropriate clinical decision making.

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Apixaban

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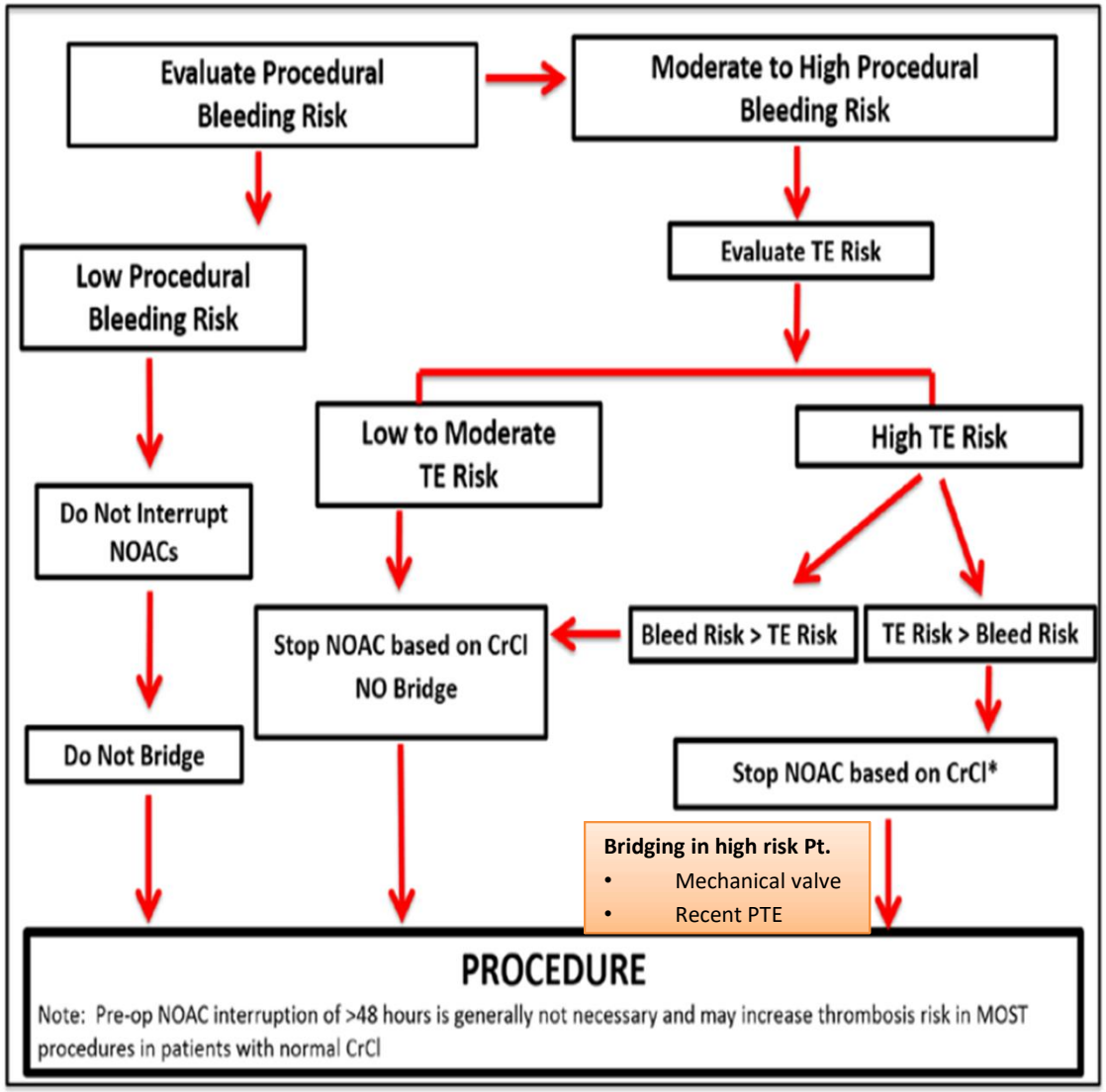
Periprocedural management of patients on NOACs

NOAC ?
time of last drug ingestion
CrCl (creatinine clearance)
Risk of bleeding (standard / High)

Periprocedural management of patients on NOACs



Peri-Procedural Bleeding Risk

Low	Moderate	High
Minor Dental	SVT ablation	Cardiovascular/Thoracic Surgery
Minor Dermatologic	ICD Implant	Intra-abdominal/Pelvic surgery
Opthalmologic	Endoscopy with Biopsy	Major Orthopedic Surgery
Endoscopy without Biopsy	Prostate Biopsy	Neurosurgery
	Cardiac catheterization via radial artery	Cardiac catheterization via femoral artery

Peri-Procedural Thromboembolic Risk

Low	Moderate to High
$CHA_2DS_2VASc \leq 1$	$CHA_2DS_2VASc \geq 2$
No Stroke/TIA, VTE within 3 months	Stroke/TIA, VTE within 3 months
Heterozygous Factor V Leiden Heterozygous PT gene mutation	Protein C or S Deficiency Antithrombin Deficiency Antiphospholipid Syndrome

Bleeding vs Thrombosis Risk

Selected Scoring Systems for Bleeding Risk Assessment in Patients with Atrial Fibrillation Receiving Oral Anticoagulant Therapy[27-29,a]

Risk Factor	Points
HEMORR$_2$HAGES[b]	
Hepatic or renal disease	1 for each
Ethanol use	1
Malignancy	1
Age >75 years	1
Reduced platelet count or function	1 for each
Re-bleeding	2
Hypertension, uncontrolled	1
Anemia	1
Genetic factors	1
Elevated fall risk ± neuropsychiatric disease	1
Stroke	1
Maximum score	14
HAS-BLED[c]	
Hypertension, systolic blood pressure >160 mm Hg	1
Abnormal renal or liver function	1 for each
Stroke	2
Bleeding history or predisposition	1
Labile INRs	2
Age >65 years	1
Antiplatelet or NSAID use	1
Alcohol use >8 servings/week	1
Maximum score	11

[a]INR = International Normalized Ratio, NSAID = nonsteroidal antiinflammatory drug.
[b]The risk for bleeding in patients with a HEMORR$_2$HAGES score of 0–1, 2–3, or 4 or more is low, moderate, or high, respectively.
[c]The risk for bleeding in patients with a HAS-BLED score of 0, 1–2, and 3 or more is low, moderate, or high, respectively.

Patient Risk Stratification for Perioperative Thromboembolism when Oral Anticoagulant Therapy Is Temporarily Interrupted[31]

High Risk (>10% annual risk for thromboembolism)

Atrial fibrillation
- Recent (within past three months) stroke or transient ischemic attack
- $CHADS_2$ score 5 or 6
- Rheumatic valvular heart disease

Mechanical heart valve
- Any caged-ball or tilting disc valve in mitral or aortic position
- Any mitral valve prosthesis
- Recent (within past six months) stroke or transient ischemic attack

Venous thromboembolism
- Recent (within past three months) venous thromboembolism
- Severe thrombophilia
  - Deficiency of protein C, protein S, or antithrombin
  - Antiphospholipid antibodies
  - Multiple thrombophilias

Moderate Risk (5–10% annual risk for thromboembolism)

Atrial fibrillation
- $CHADS_2$ score 3 or 4

Mechanical heart valve
- Bileaflet aortic valve prosthesis with major risk factors for stroke

Venous thromboembolism
- Venous thromboembolism within past 3–12 months
- Recurrent venous thromboembolism
- Non-severe thrombophilia (e.g., heterozygous factor V Leiden or prothrombin gene mutation)
- Active cancer (treated within past six months or palliative)

Low Risk (<5% annual risk for thromboembolism)

Atrial fibrillation
- $CHADS_2$ score 0–2 (without prior stroke or transient ischemic attack)

Mechanical heart valve
- Bileaflet aortic valve prosthesis without atrial fibrillation and major risk factors for stroke

Venous thromboembolism
- Venous thromboembolism more than 12 months ago with no other risk factors for thromboembolism

time of last drug ingestion + Cl-Cr

should enable appropriate clinical decision making.

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Table 11 Timing of last non-vitamin K antagonist oral anticoagulant intake before start of an elective intervention

	Dabigatran		Apixaban – Edoxaban – Rivaroxaban	
	No important bleeding risk and/or adequate local haemostasis possible: perform at trough level (i.e. 12 h or 24 h after last intake)			
	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	≥24 h	≥48 h
CrCl 30–49 mL/min	≥48 h	≥96 h	≥24 h	≥48 h
CrCl 15–29 mL/min	Not indicated	Not indicated	≥36 h	≥48 h
CrCl <15 mL/min	No official indication for use			
No bridging with LMWH/UFH				
Resume full dose of NOAC ≥24 h post-low bleeding risk interventions and 48 (–72) h post-high-bleeding risk interventions (see also *Figure 8*)				
Patients undergoing a planned intervention should receive a written note indicating the anticipated date and time of their intervention, and the date and time of the last intake of their NOAC (and any other medication)				

Low risk: with a low frequency of bleeding and/or minor impact of a bleeding; high risk: with a high frequency of bleeding and/or important clinical impact. See also *Table 12*.
CrCl, creatinine clearance; LMWH, low molecular weight heparin; UFH, unfractionated heparin.

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Black Box Warning for NOACs

- Increased risk of stroke when discontinuing use in patients without adequate continuous anticoagulation.
- Discontinuing dabigatran, rivaroxaban or apixaban places patients at an increased risk of thrombotic events
- **Bridging=?** (unless it must be discontinued for a reason other than pathological bleeding, treatment with another anticoagulant should be considered).

Tailoring peri-procedural NOAC management
to the type of invasive procedure may mitigate against bleeding.

Resumption of Therapy

- Warfarin therapy should generally be resumed:
  - 12 - 24 hours after surgery
- NOAC therapy should generally be resumed:
  - 24 - 48 hours after a minor procedure
  - 48 - 72 hours after major surgery
- If Bridging Therapy: (UFH or LMWH in high risk patients)
  - NOAC should be resumed
    - 1 hr ➔before UFH infusion is discontinued or
    - 10-12 hr ➔after the last scheduled dose of LMWH

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Apixaban

Serious Bleeding
on a NOAC protocol

Problems:

- anticoagulant agents currently use?

timing of last ingestion, renal function

- perioperative considerations for the management of patients on anticoagulant medications.

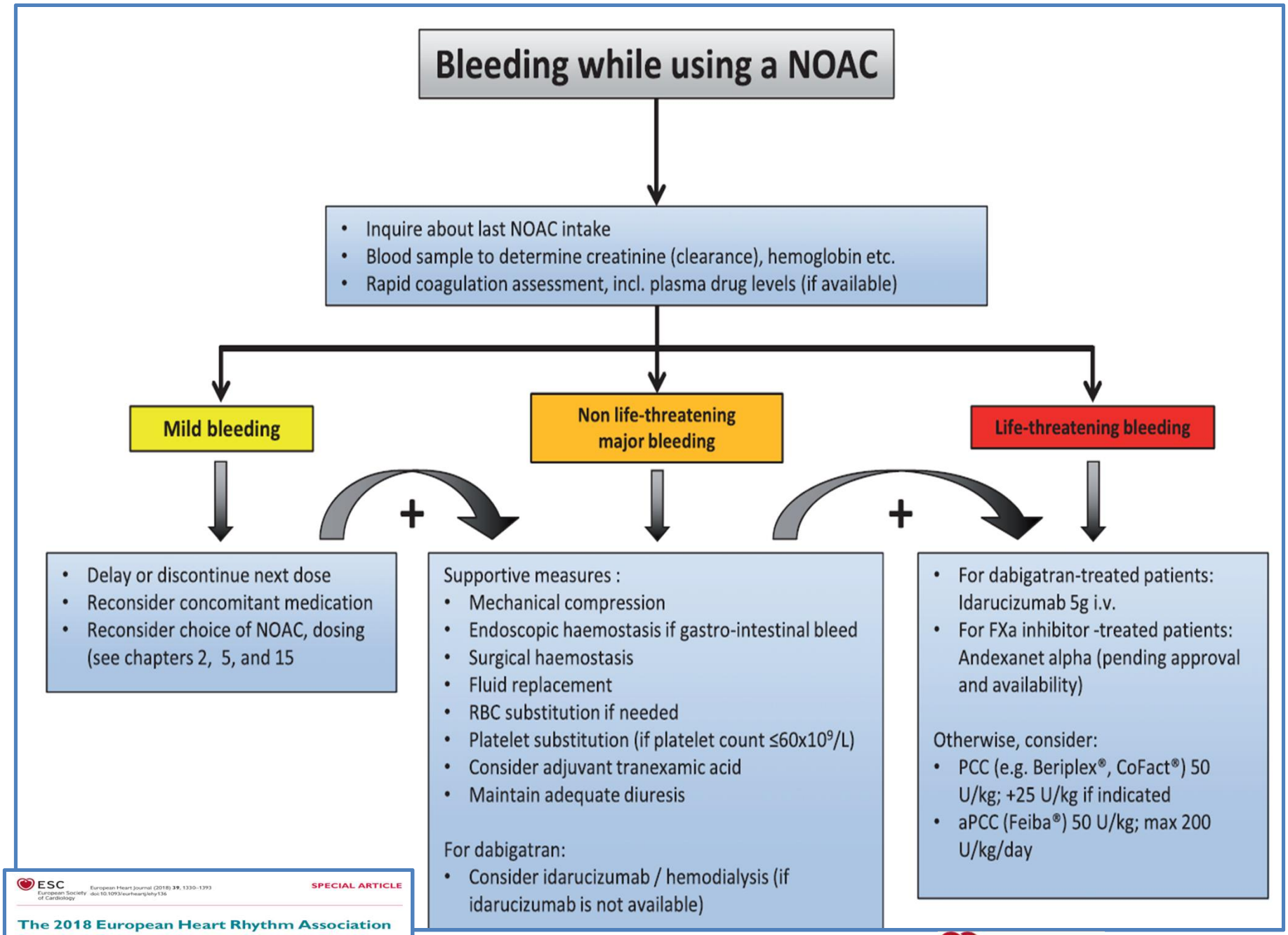
- Urgent reversal strategies

Case 2:

- 70 year old male on **rivaroxaban 20 mg daily** for VTE prevention after recurrent unprovoked pulmonary emboli.
- **Past History:** Hypertension, Epilepsy (in remission, off anti-seizure medications x 5 years)
- **Seen in the Emergency Department with:**
- Frequent melena x 48 hours. Last dose of rivaroxaban was 4 hours ago.
- Hemoglobin has dropped from 12.0 g/dL (2 months ago) to 6.0 g/dL today. Blood pressure is 95/60, heart rate is 115 beats per minute
- **Diagnosis: Upper GI bleeding exacerbated by rivaroxaban**

- **Your patient is presenting with acute, life-threatening upper GI bleeding while on an oral direct Xainhibitor.**
- **What management would you suggest for his DOAC-associated bleeding?**

- A. Cessation of Xainhibitor only
- B. 4-factor Prothrombin Complex Concentrate
- C. Coagulation factor Xa(recombinant) –andexanet
- D. Fresh Frozen Plasma
- E. Idarucizumab



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Serious Bleeding on a NOAC" protocol

EXAMPLE of a "Serious Bleeding on NOAC PROTOCOL"

General Measures

- mechanical compression if possible
- two sites of IV access
- determine timing of last NOAC dose
- CBC, BUN, Creatinine, liver enzymes
- plasma expanders/PRBC's as necessary
- consider activated charcoal if NOAC ingestion <2hours
- notify on-call hematologist
- Refer to chart below for specific measures

NOAC	Blood tests for NOAC presence or effect	Specific Antidote	Alternative Treatments Options
Dabigatran	PTT , TT	Idarucizumab 5 grams IV (2 infusions of 2.5 grams)	4 Factor PCC *(Kcentra®)* 50 IU/kg IV Factor VIIa 90µg/kg IV every 2 hours Tranexamic acid 15-30 mg/kg IV Hemodialysis
Rivaroxaban	Anti-Factor Xa	Unavailable in the U.S.	4 Factor PCC *(Kcentra®)* 50 IU/kg IV Factor VIIa 90µg/kg IV every 2 hours Tranexamic acid 15-30 mg/kg IV
Apixaban	Anti-Factor Xa	Unavailable in the U.S.	PCC *(Kcentra®)* 50 IU/kg IV Factor VIIa 90µg/kg IV every 2 hours Tranexamic acid 15-30 mg/kg IV
Edoxaban	Anti-Factor Xa	Unavailable in the U.S.	PCC *(Kcentra®)* 50 IU/kg IV Factor VIIa 90µg/kg IV every 2 hours Tranexamic acid 15-30 mg/kg IV

TT = thrombin time, PTT = partial thromboplastin time, PCC = prothrombin complex concentrate

Pharmacokinetic Comparison of Reversal Agents

Anticoagulation Reversal Pharmacokinetics			
Agent	Onset	Duration	Rebound of Anticoagulant
Vitamin K	2 – 8 h	Days for INR	Dose-dependent
FFP	1 – 4 h	6 h	4 – 6 h
PCC	10 – 15 min	12 – 24 h	~ 12 h
rFactor VIIa	10 min	4 – 6 h	6 – 12 h

Summary of Agents and Role in Reversal

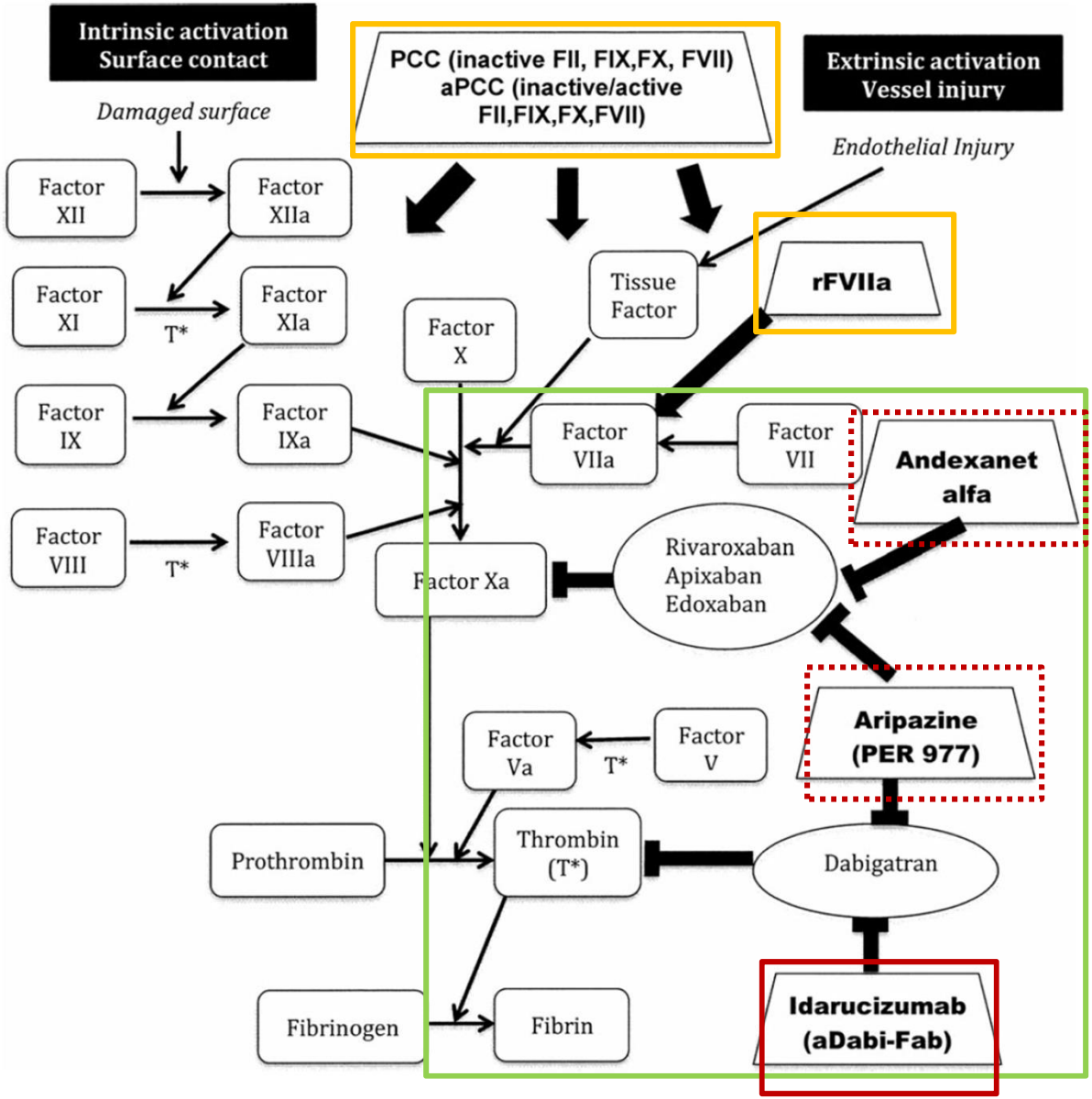
AGENT	DOSES TESTED IN STUDIES	DABIGATRAN	RIVAROXABAN/ APIXABAN
4-factor PCC	12.5 – 100 IU/kg (50 IU/kg is only doses tested in humans	Possibly beneficial	**Probably benficial**
aPCC (FEIBA)	20 – 160 IU/kg	**Probably beneficial**	**Probably beneficial**
Factor VIIa	20 – 500 mcg/kg	**Possibly beneficial**	**Possibly beneficial**
FFP	N/A	Probably ineffective	Probably ineffective
3-factor PCC	No data	No data	No data
Antifibrinolytics	No data	No data	No data
Activate Charcoal/ HD	In Vitro/volunteers	Possibly beneficial if given <2 hrs/YES	Possibly beneficial if given <2 hrs/NO

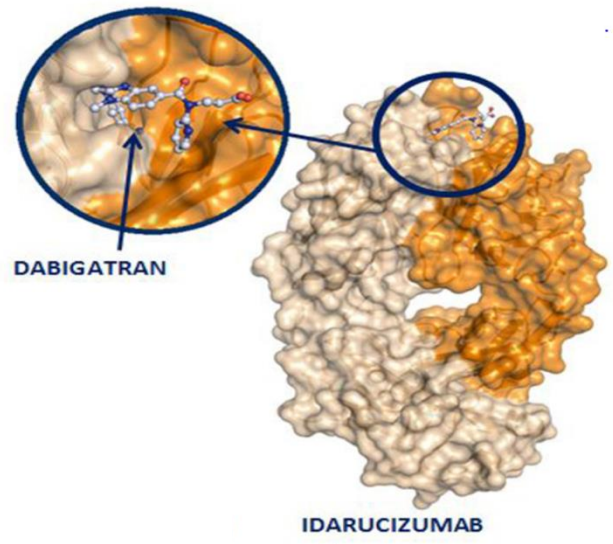
Lazo-Langner A, Lang ES, Douketis J. Clinical Review: Clinical management of new oral Anticoagulants: a structured review with emphasis on the reversal of bleeding complications. *Critical Care.* 2013; 17: 230 – 242.

Adjunctive Therapies

- **Hemodialysis and charcoal hemoperfusion**
  - Useful in accelerating plasma clearance of **dabigatran** (supported by human studies)
    - Removes about 60% of drug (non protein-bound portion)
  - Potential for rebound effects both dialysis
- **Oral activated charcoal**
  - May be given within 2 hours of ingestion of **dabigatran**, rivaroxaban and apixaban
- Desmopressin
- Aantifibrinolytic agents (i.e. tranexamic acid)

NOAC Antidotes





NEW Anticoagulant Antidotes

Agents	Target	Structure	Route	MOA	Pharmacokinetics
Idarucizumab	Dabigatran	Humanized monoclonal antibody fragment	IV	Binds to dabigatran with a high affinity (~350 times greater affinity than thrombin) No binding to thrombin substrates (no procoagulant activity)	Biphasic $t_{1/2}$, ranging from 0.4 hrs to a terminal $t_{1/2}$ of 4.3 hrs
Andexanet alfa	Direct and indirect FXa inhibitors	Modified recombinant form of FXa	IV	Binds to FXa inhibitors with affinity similar to that of native FXa	Terminal $t_{1/2}$: ~6 hrs
Aripazine	Universal (oral FXa and FIIa inhibitors, UFH, LMWH, and fondaparinux	Small synthetic molecule	IV	Binds to TSOACs and heparin and reverses the anticoagulant effects	Not available

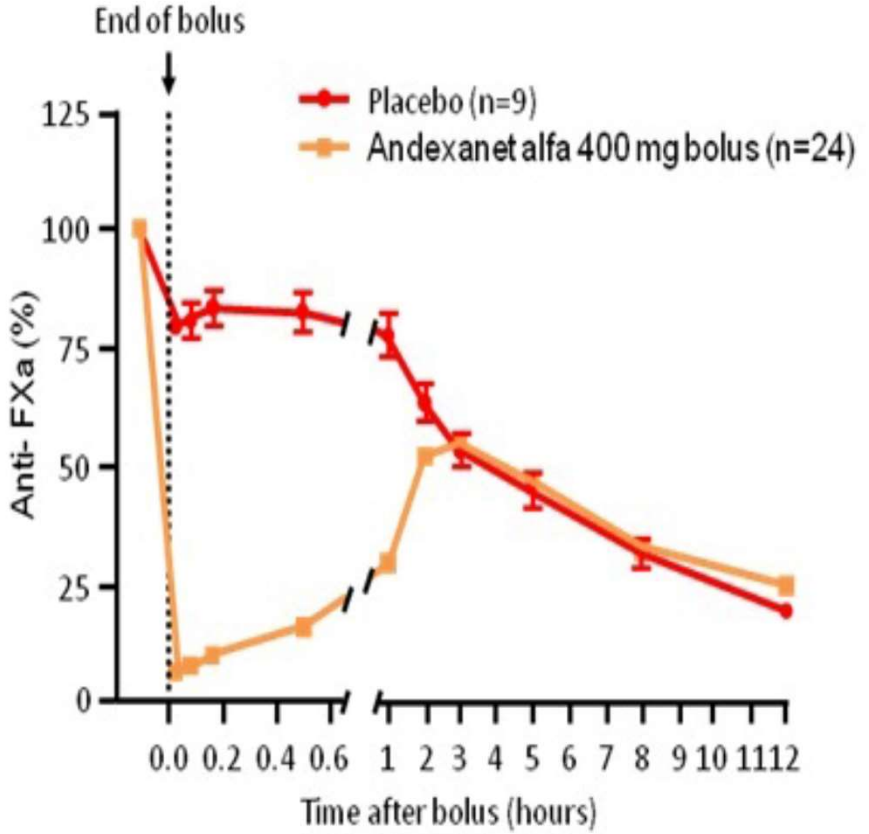
FIIa = factor IIa; FXa = factor Xa; IV = intravenous; LMWH = low-molecular-weight heparin; MOA = mechanism of action; $t_{1/2}$ = half-life; UFH = unfractionated heparin.

DTI Inhibitor Antidote

- **Idarucizumab**
  - aDabi-Fab, BI 655075; Boehringer Ingelheim Pharmaceuticals, Ingelheim,Germany
  - June 26, 2014 FDA Granted "breakthrough-therapy designation"
  - Humanized monoclonal antibody fragment (Fab) that selectively binds to and inhibits the activity of dabigatran
    - affinity to dabigatran that is ~350 times greater than its affinity for thrombin

FXa Inhibitor Antidote

- **Andexanet alfa**
  - PRT064445; Portola Pharmaceuticals, San Francisco, CA
  - An imitation factor Xa without biological properties
  - Reverses the anticoagulant action of the factor Xa inhibitors (including rivaroxaban and apixaban)
  - ANNEX-A Study
    - Apixaban reversal



Case 2= conclusion:

- **Managing bleeding on Xa - inhibitors**
  - **Two main approaches** 4-factor PCC
  - Recombinant coagulation factor Xa (andexanet)

- However, the evidence for benefit and harm for either approach is very limited, so the panel ***does not offer a recommendation for one approach over the other***

Limitations of Current Studies

- **4-factor PCC and coagulation factor Xahave not been directly compared**
- Studies of both approaches have lacked a suitable comparator group

Case-3

- A46 yo construction worker who fell off a roof (about 30 ft) at 11 AM this morning and has a TBI (IPH with midline shift). His GCS is 3. He needs emergent neurosurgery.
- Scr = 2.3 ,Clcr is 31 ml/min, PT 12, aPTT 45
- Meds: Dabigatran 150 mg BID
- What is the best recommendation for reversal of dabigatran for Pt.?

A. FFP
B. Vitamin K
C. PCC
D. Hemodialysis
E. idarucizumab

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(Re-) initiation of anticoagulation post-gastrointestinal bleeding. #Without evidence; ideally ...

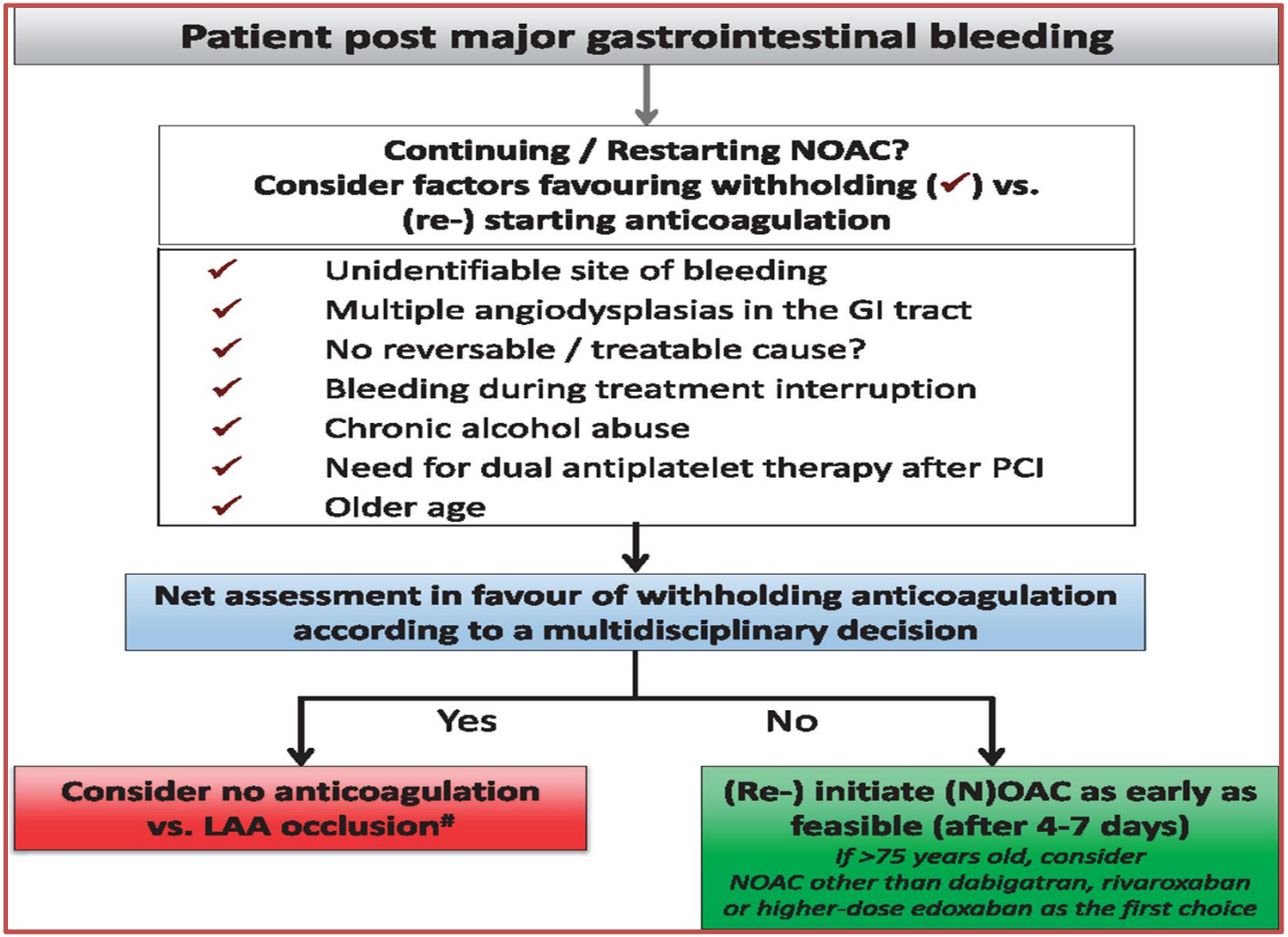

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Table 4 Pre- and postoperative management of patients taking NOACs

		Minor surgery[a]		Major surgery[b]	
NOAC	Renal function	Preoperative management	Postoperative management	Preoperative management	Postoperative management
Dabigatran	Normal or mildly impaired (CrCl >50 mL/min) Moderately impaired (CrCl 30–50 mL/min)	Stop 2 days before surgery (skip 2 doses) Stop 3 days before surgery (skip 4 doses)	Re-start 24 h after surgery	Stop 3 days before surgery (skip 4 doses) Stop 4–5 days before surgery (skip 6–8 doses)	Re-start 48 h after surgery
Rivaroxaban	Normal, mild, or moderately impaired (CrCl >30 mL/min)	Stop 2 days before surgery (skip 1 dose)	Re-start 24 h after surgery	Stop 3 days before surgery (skip 2 doses)	Re-start 48 h after surgery
Apixaban (CrCl >30 mL/min)	Normal, mild, or moderately impaired	Stop 2 days before surgery (skip 1 dose)	Re-start 24 h after surgery	Stop 3 days before surgery (skip 4 doses)	Re-start 48 h after surgery

[a]*Minor surgery:* Endoscopy with biopsy; prostate or bladder biopsy; electrophysiological study or simple radiofrequency catheter ablation tachycardia; angiography; pacemaker or ICD implantation.
[b]*Major surgery:* Complex left-sided ablation (pulmonary vein isolation and ventricular tachycardia ablation); spinal or epidural anaesthesia; lumbar diagnostic puncture; thoracic surgery; abdominal surgery; major orthopaedic surgery; liver biopsy; transurethral prostate resection; kidney biopsy.

Table 9 Plasma levels and coagulation assays in patients treated with non-vitamin K antagonist oral anticoagulants

	Dabigatran[229,230]	Apixaban[231], SmPc	Edoxaban[184,232]	Rivaroxaban[131,186]
Expected plasma levels of NOACs in patients treated for AF (based on dTT/ECA for dabigatran and anti-FXa activity for Xa inhibitors)				
Expected range of plasma levels *at peak* for standard dose (ng/mL)[a]	64–443	69–321	91–321	184–343
Expected range of plasma levels *at trough* for standard dose (ng/mL)[a]	31–225	34–230	31–230	12–137
Expected impact of NOACs on routine coagulation tests				
PT	↑	(↑)	↑(↑)	↑↑ (↑)
aPTT	↑↑(↑)	(↑)	↑	↑
ACT	↑(↑)	↑	↑	↑
TT	↑↑↑↑	—	—	—

Ranges indicate the P5/95 percentiles for dabigatran, rivaroxaban, and apixaban, and the interquartile ranges for edoxaban.
The reagents influence the sensitivity of the PT for FXa inhibitors and of the aPTT for dabigatran. When a sensitive assay is used, normal aPTT excludes above on-therapy levels in dabigatran-treated patients, and normal PT excludes above on-therapy levels in rivaroxaban and edoxaban, but not apixaban treated patients. Point-of-care INR devices developed to monitor vitamin K antagonists do not accurately reflect the anticoagulant status of NOAC treated patients.
ACT, activated clotting time; aPTT, activated partial thromboplastin time; dTT, diluted thrombin time; ECA, ecarin clotting assay; INR, international normalized ratio; PT, prothrombin time.

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Table 10 Possible measures to take in case of bleeding

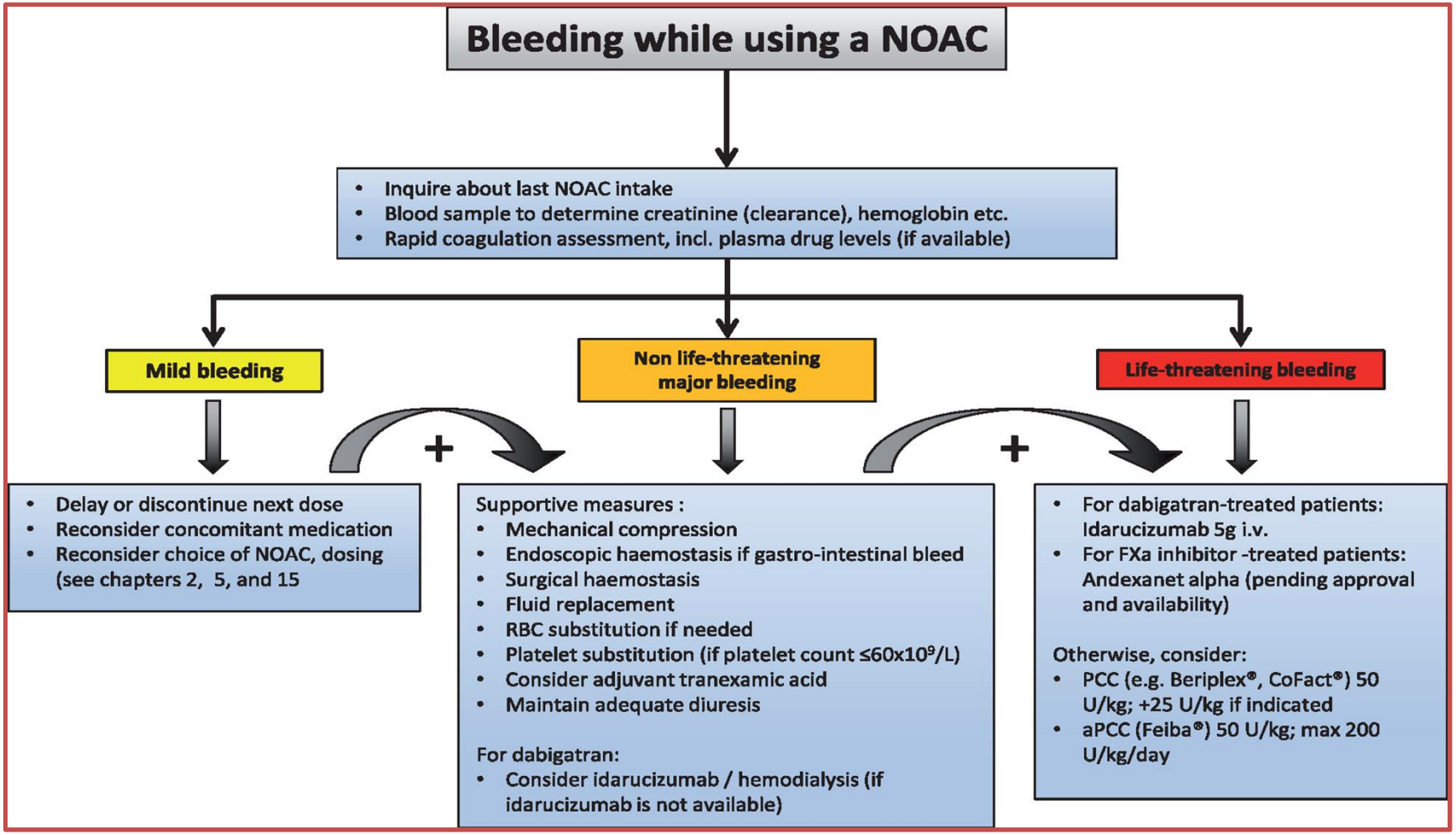
	Direct thrombin inhibitors (dabigatran)	FXa inhibitors (apixaban, edoxaban, rivaroxaban)
Non life-threatening major bleeding	• Inquire about last intake + dosing regimen • Local haemostatic measures • Fluid replacement • RBC substitution, if necessary • Platelet substitution (in case of thrombocytopenia ≤60 × 109/L or thrombopathy) • Fresh frozen plasma not as reversal agent (may be considered as plasma expander) • Tranexamic acid can be considered as adjuvant (1 g i.v., repeat every 6 h, if necessary) • Desmopressin can be considered in special cases such as coagulopathy or thrombopathy; 0.3 μg/kg i.v. infusion (max dose 20 μg)	

	• Estimate normalization of plasma levels:
	  • Normal renal function: 12–24 h
	  • CrCl 50–80 mL/min: 24–36 h
	  • CrCl 30–50 mL/min: 36–48 h
	  • CrCl <30 mL/min: ≥48 h
	• Maintain diuresis
	• Consider idarucizumab (see below)
		• Normalization of plasma levels: 12–24 h

Life-threatening bleeding	• All of the above
	• Direct reversal: Idarucizumab 5 g i.v. in two doses a 2.5 g i.v. no more than 15 min apart
		• All of the above
		• Direct reversal: Andexanet alpha (if available and approved)[a]
		  • Bolus over 15–30 min, followed by 2-h infusion
		  • Rivaroxaban (last intake >7 h before) or apixaban: 400 mg bolus, 480 mg infusion @ 4 mg/min
		  • Rivaroxaban (last intake <7 h before or unknown) or enoxaparin or edoxaban: 800 mg bolus, 960 mg infusion @ 8 mg/min

	• Prothrombin complex concentrate (PCC) 50 U/kg (with additional 25 U/kg if clinically needed) • Activated PCC 50 U/kg; max 200 U/kg/day): no strong data about additional benefit over PCC. Can be considered before PCC, if available	

Management of bleeding in patients taking non-vitamin K antagonist oral anticoagulants.



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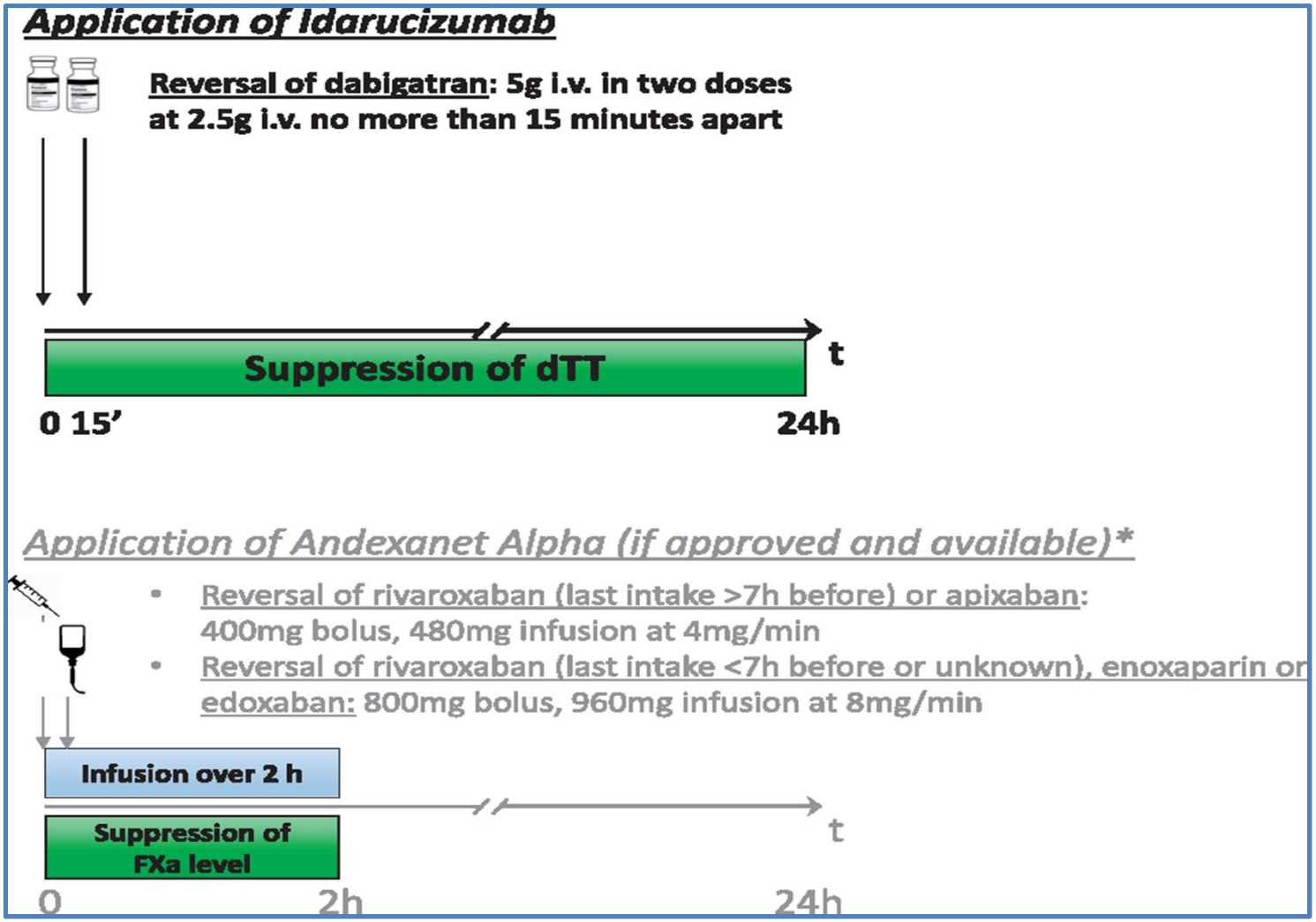
Application and effect of idarucizumab and andexanet alpha. *Per protocol of ANNEXA-4.[249]



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Classification of elective surgical interventions according to bleeding risk

Interventions with minor bleeding risk
Dental interventions
Extraction of 1–3 teeth
Paradontal surgery
Incision of abscess
Implant positioning
Cataract or glaucoma intervention
Endoscopy without biopsy or resection
Superficial surgery (e.g. abscess incision; small dermatologic excisions; . . .)

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Interventions with low bleeding risk (i.e. infrequent or with low clinical impact)
Endoscopy with biopsy
Prostate or bladder biopsy
Electrophysiological study or catheter ablation (except complex procedures, see below)
Non-coronary angiography (for coronary angiography and ACS: see Patients undergoing a planned invasive procedure, surgery or ablation section)
Pacemaker or ICD implantation (unless complex anatomical set-ting, e.g. congenital heart disease)

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Interventions with high bleeding risk (i.e. frequent and/or with high impact)
Complex endoscopy (e.g. polypectomy, ERCP with sphincterotomy etc.)
Spinal or epidural anaesthesia; lumbar diagnostic puncture
Thoracic surgery
Abdominal surgery
Major orthopaedic surgery
Liver biopsy
Transurethral prostate resection
Kidney biopsy
Extracorporeal shockwave lithotripsy (ESWL)

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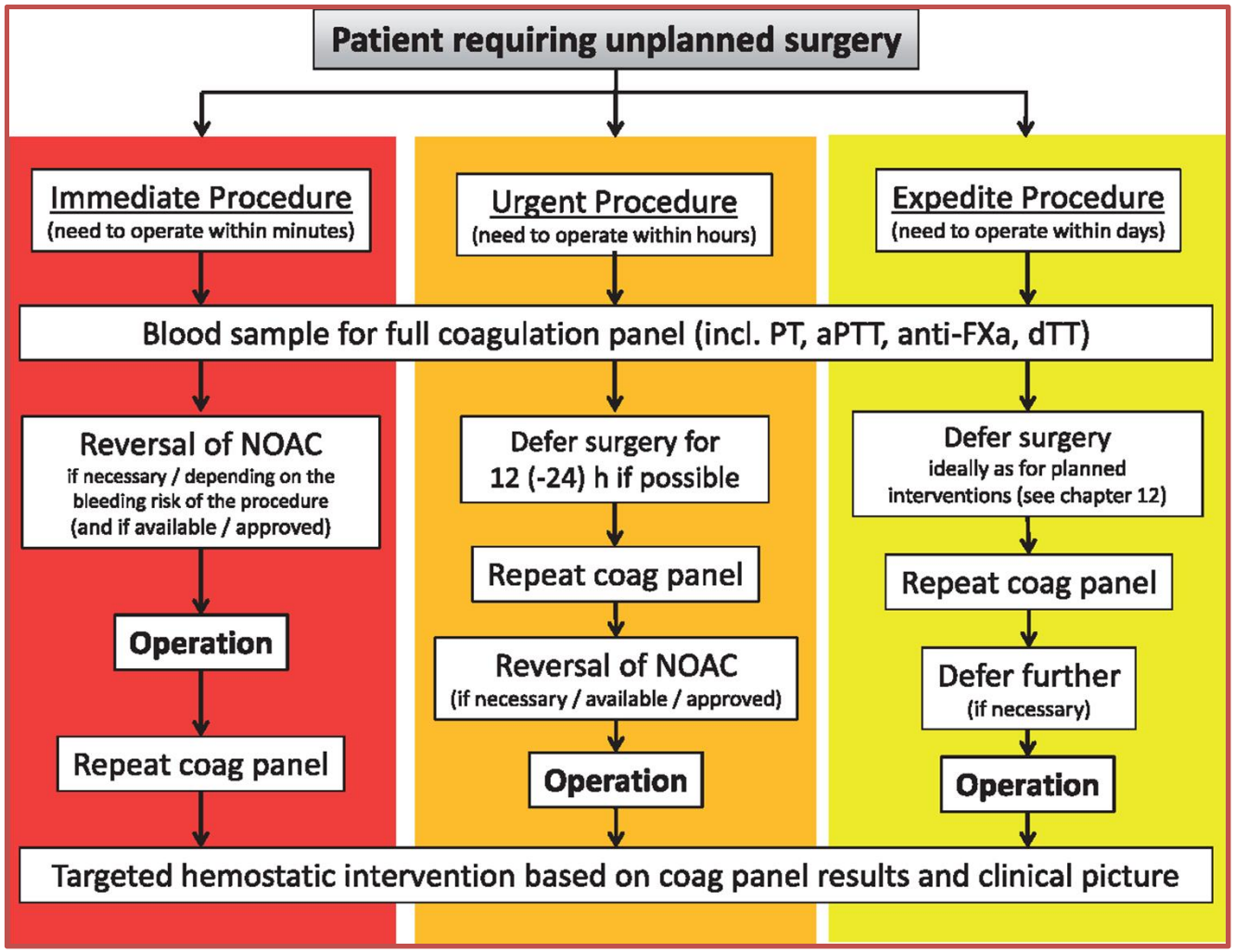
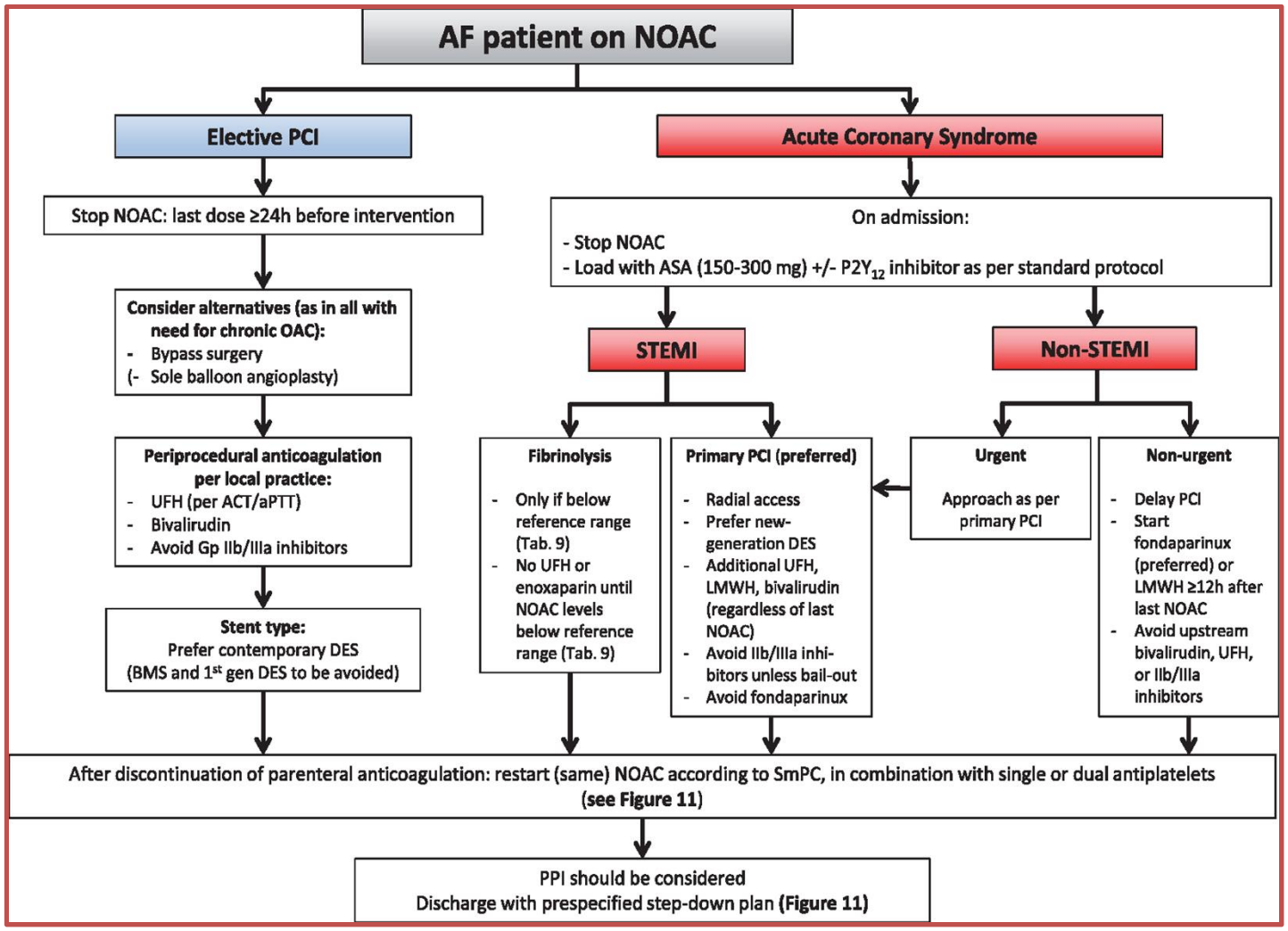
Interventions with high bleeding risk AND increased thrombo-embolic risk
Complex left-sided ablation (pulmonary vein isolation; some VT ablations)

Non-vitamin K antagonist oral anticoagulant management in the setting of unplanned surgery.



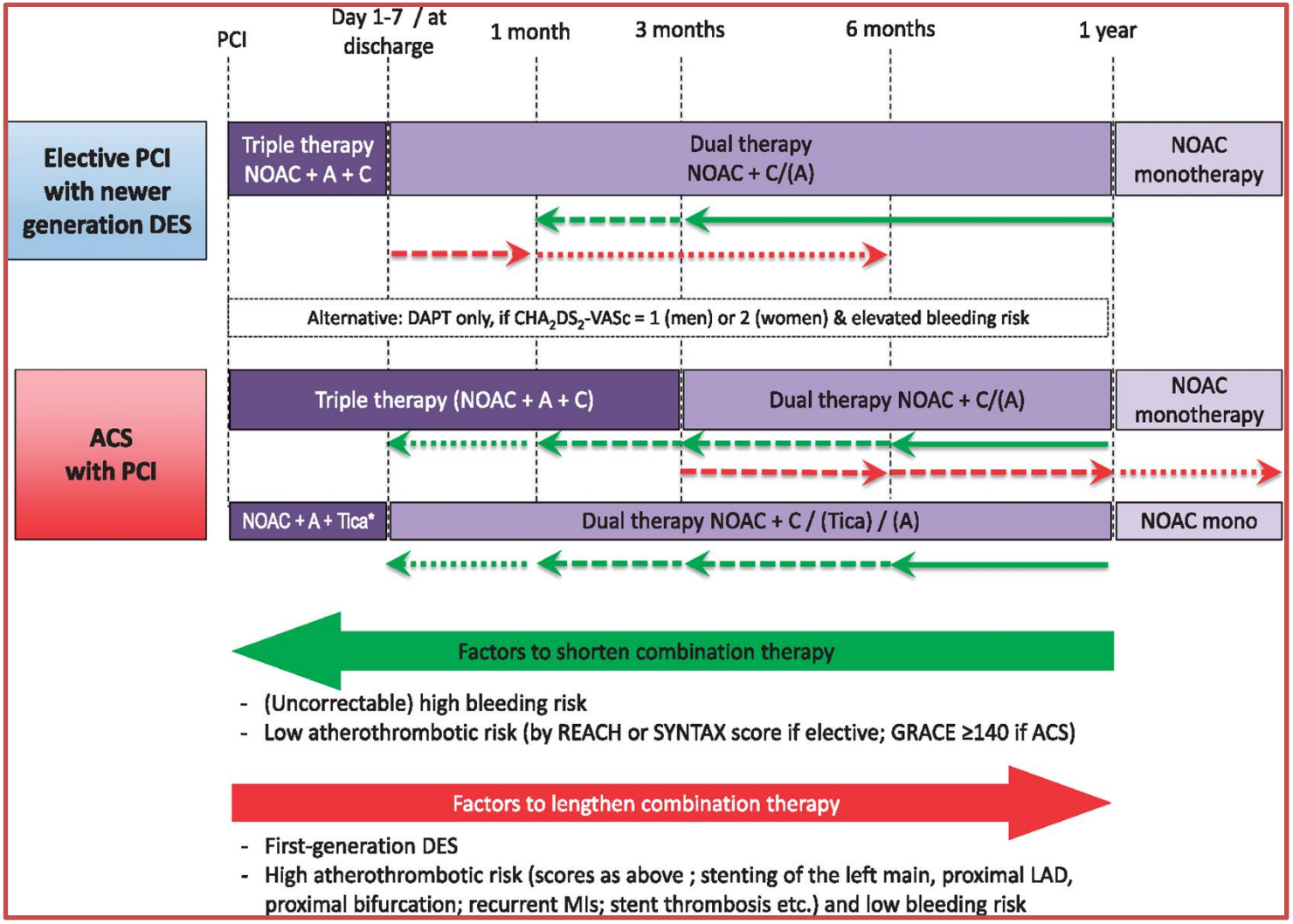
Eur Heart J, Volume 39, Issue 16, 21 April 2018, Pages 1330–1393, https://doi.org/10.1093/eurheartj/ehy136

Acute management of elective PCI or ACS in AF patients treated with non-vitamin K antagonist oral anticoagulant.



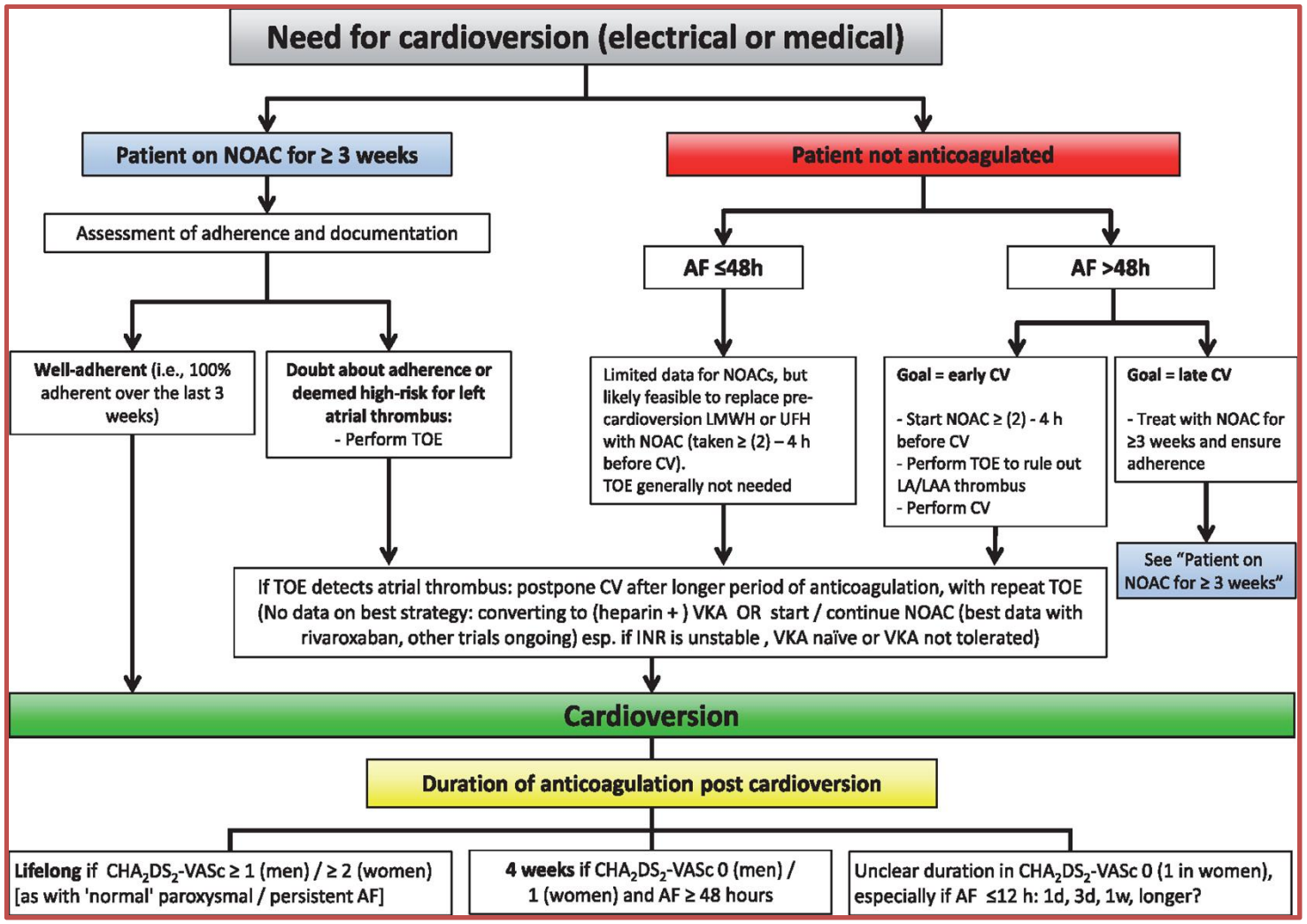
Eur Heart J, Volume 39, Issue 16, 21 April 2018, Pages 1330–1393, https://doi.org/10.1093/eurheartj/ehy136

Long-term treatment of patients on non-vitamin K antagonist oral anticoagulant therapy after elective PCI or ACS



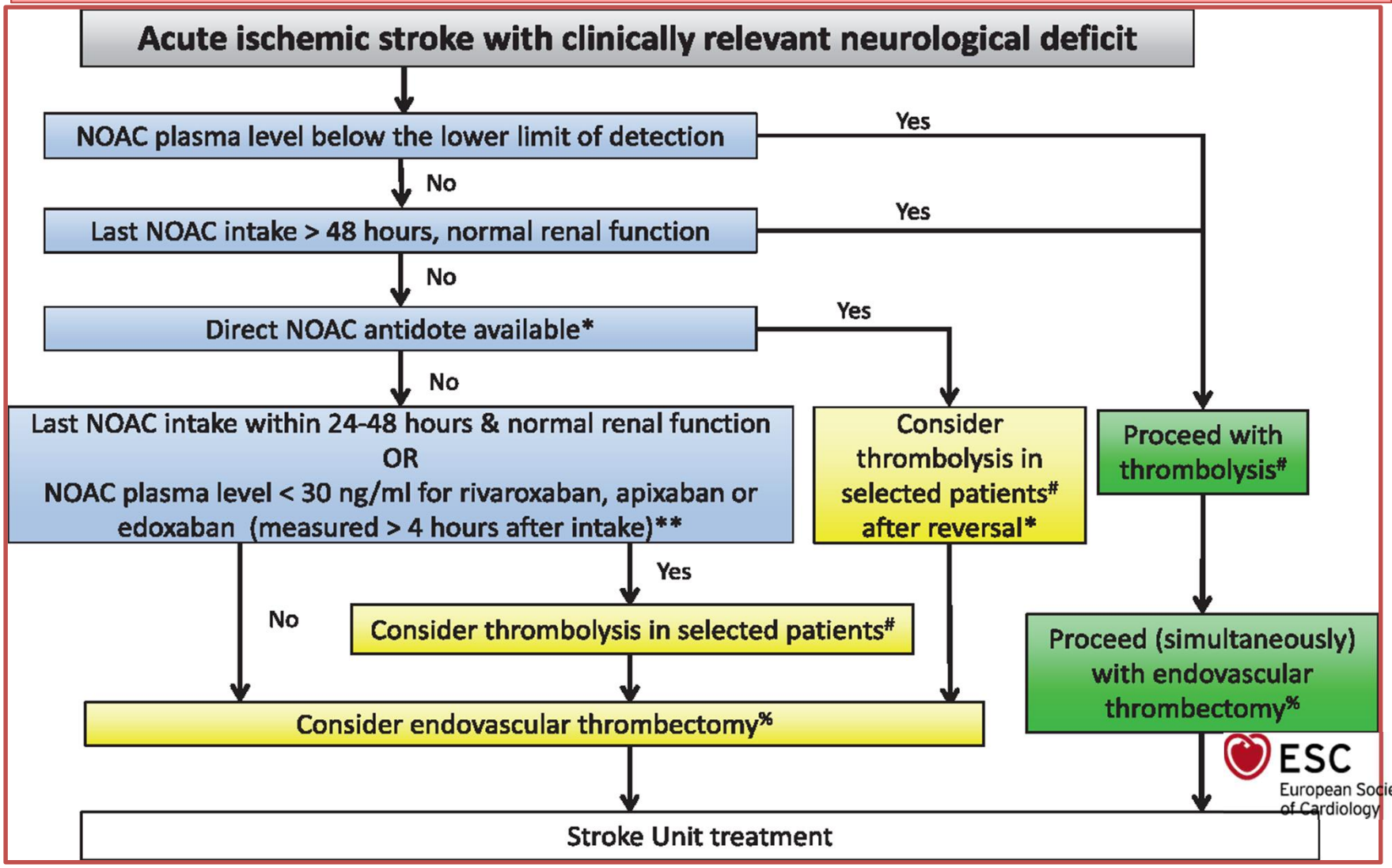
Eur Heart J, Volume 39, Issue 16, 21 April 2018, Pages 1330–1393, https://doi.org/10.1093/eurheartj/ehy136

Cardioversion work-flow in atrial fibrillation patients treated with NOACs, depending on the duration of the **arrhythmia and prior anticoagulation**



Eur Heart J, Volume 39, Issue 16, 21 April 2018, Pages 1330–1393, https://doi.org/10.1093/eurheartj/ehy136

Acute management of acute ischemic stroke in a patient on non-vitamin K antagonist oral anticoagulant.



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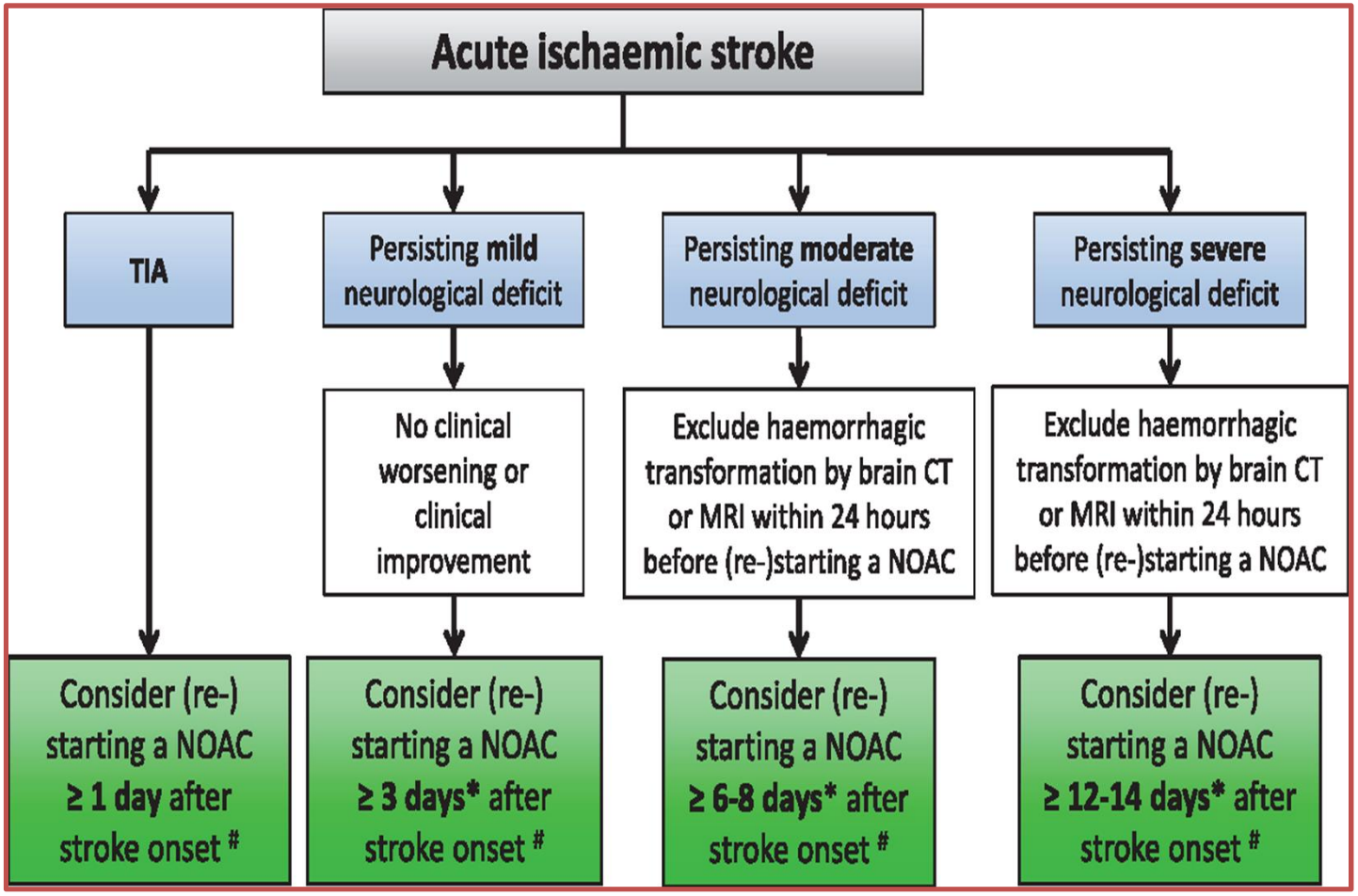
(Re-) initiation of anticoagulation after transient ischaemic attack/stroke.

(Re-) start only in the absence of contraindications and if stroke size is not expected to substantially increase the risk of secondary haemorrhagic transformation**.**



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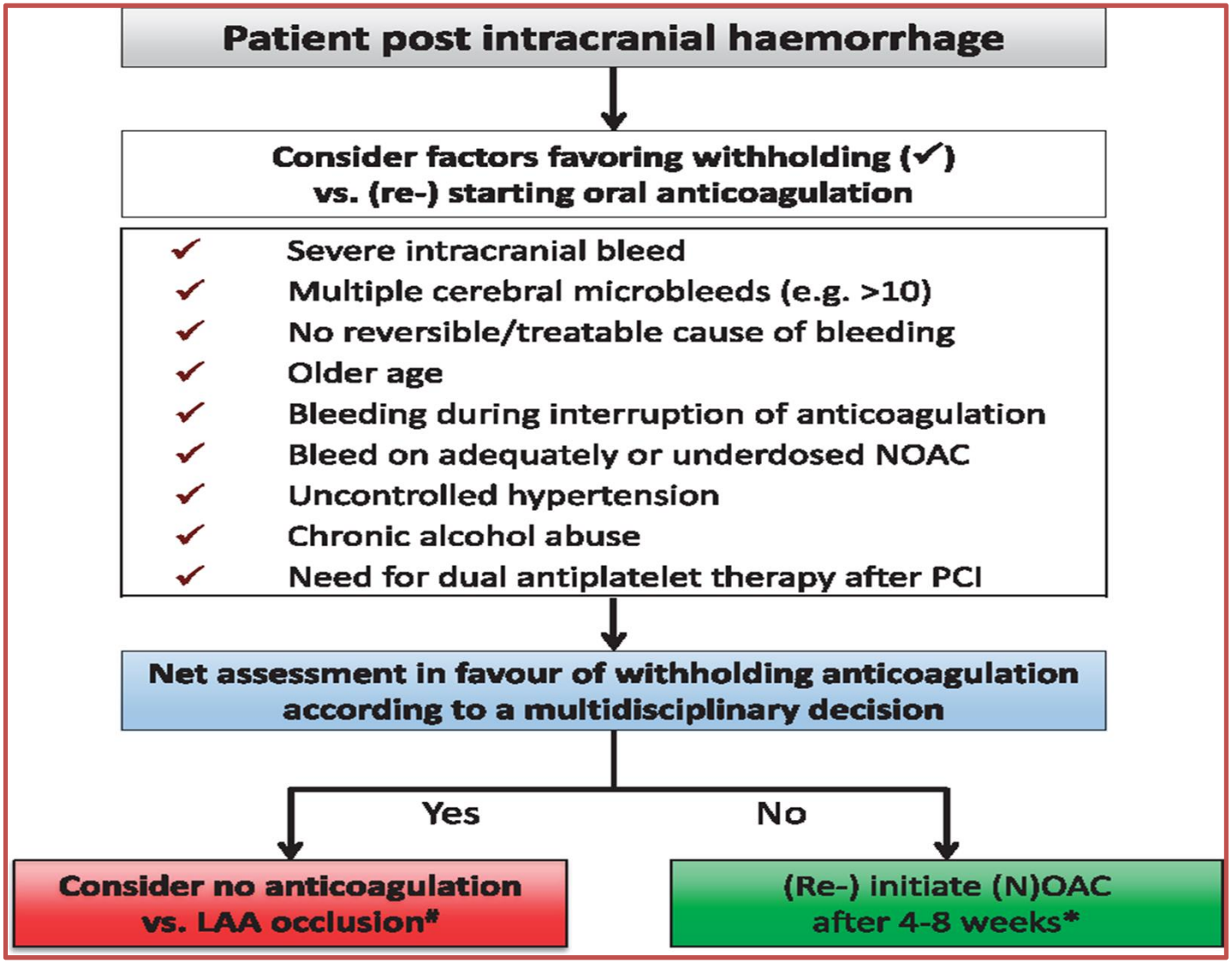
(Re-) initiation of anticoagulation post intracranial bleeding. #Without evidence



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Orchid Pharmed
Sky's the Limit

Thanks for your attention

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