Anticoagulant switching and pre operative management

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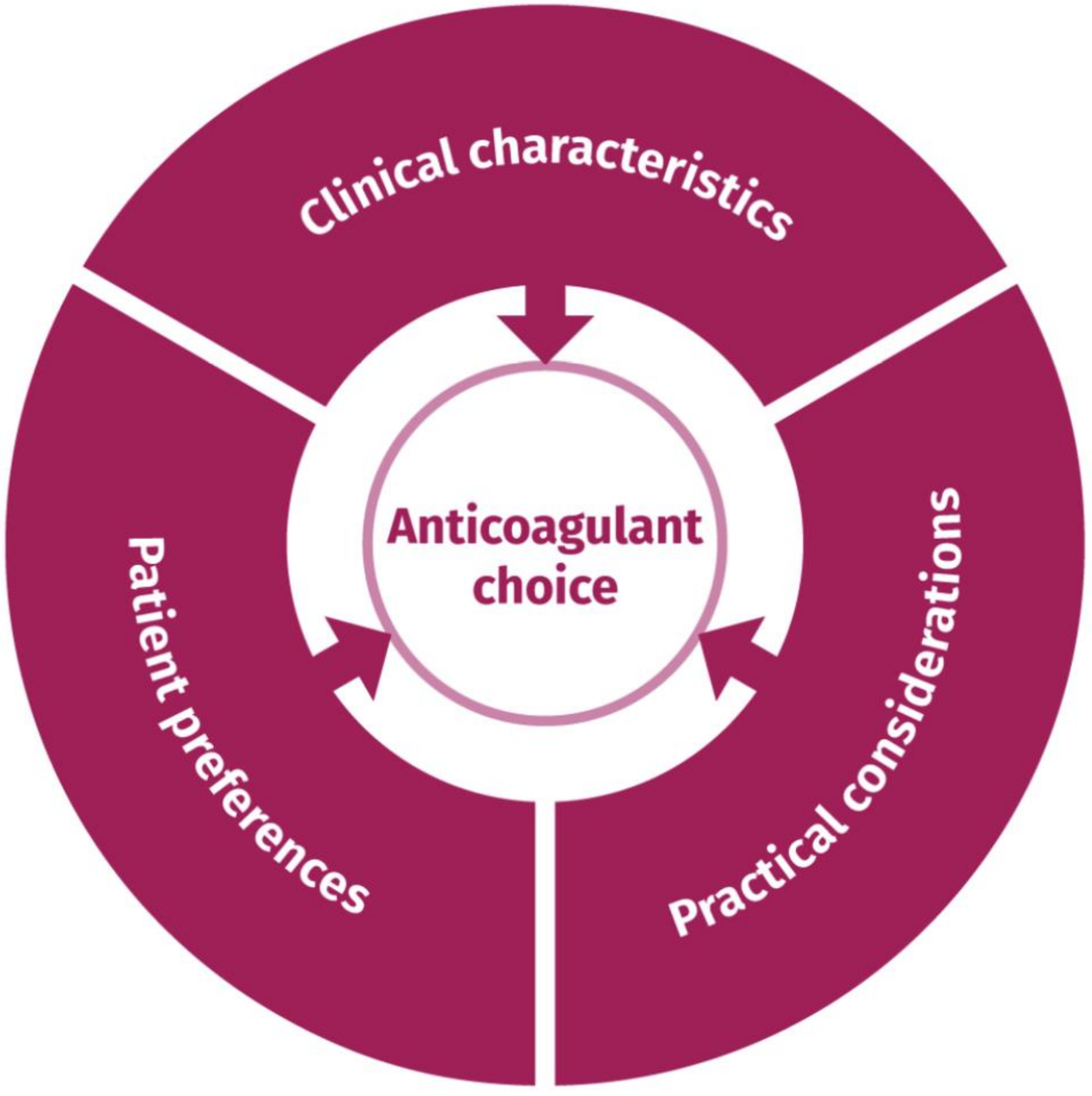
Clinical characteristics
Patient preferences
Practical considerations
Anticoagulant choice

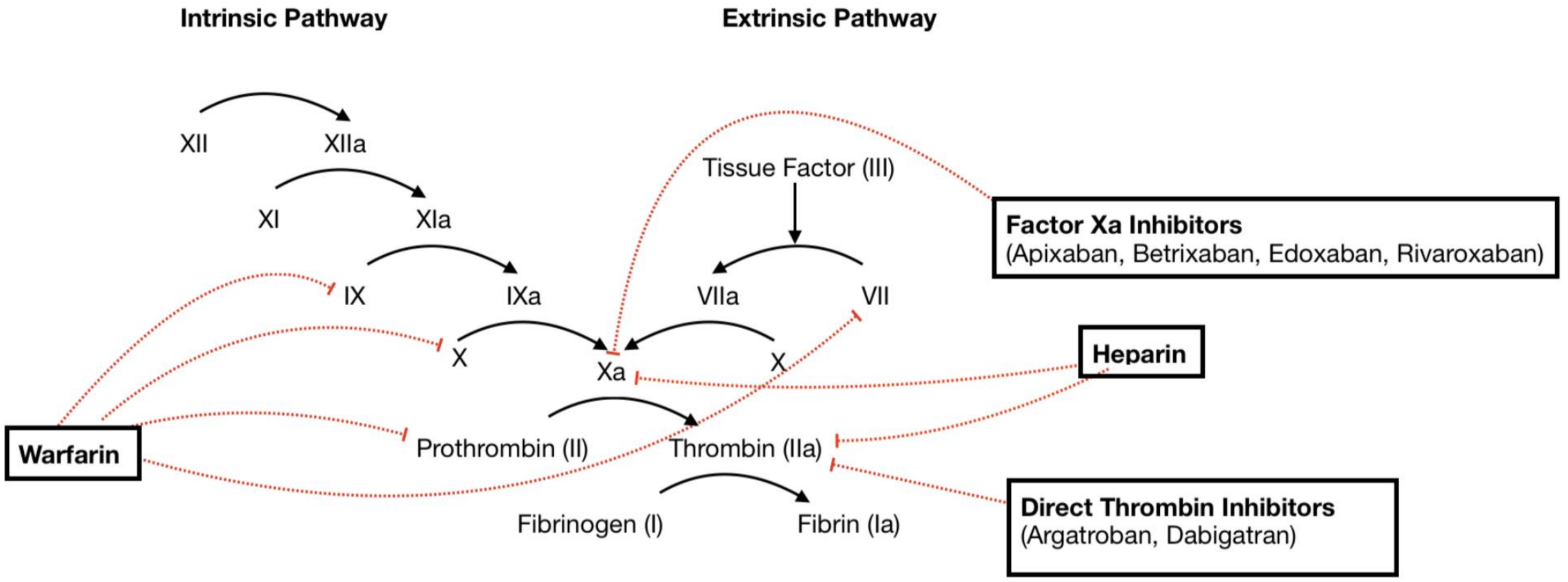
Intrinsic Pathway
Extrinsic Pathway
XII
XIIa
XI
XIa
IX
IXa
X
Xa
Tissue Factor (III)
VIIa
VII
X
Prothrombin (II)
Thrombin (IIa)
Fibrinogen (I)
Fibrin (Ia)
Factor Xa Inhibitors
(Apixaban, Betrixaban, Edoxaban, Rivaroxaban)
Heparin
Warfarin
Direct Thrombin Inhibitors
(Argatroban, Dabigatran)

Table 1. Effects of anticoagulants on various clotting tests.

Anticoagulant	aPTT	PT/INR	Elimination Half-Life	Effect of Dialysis
Warfarin	Increase or neutral	Increase	7 days	Not dialyzable
Rivaroxaban	Increase or neutral	Increase or neutral	5–9 h	Not dialyzable
Apixaban	Increase or neutral	Increase or neutral	12 h	Poorly dialyzable
Edoxaban	Neutral	Increase or neutral	10–14 h	Not dialyzable
Betrixaban	Increase	Increase	19–27 h	Not dialyzable
Argatroban	Increase	Increase	30–50 min	Poorly dialyzable
Dabigatran	Increase	Increase or neutral	12–17 h	Dialyzable
Bivalirudin	Increase	Increase or neutral	20–25 min	Poorly dialyzable
IV UFH	Increase	Neutral	30 min	Not dialyzable
LMWH	Increase or neutral	Neutral	4.5–5 h	Not dialyzable

IV: Intravenous. UFH: Unfractionated heparin. LMWH: Low-molecular-weight heparin. aPTT: Activated partial thromboplastin clotting time. PT: Prothrombin time. INR: International normalized ratio.

Characteristics	Drug Choice	Rationale
CrCl 15–30 mL/minute	Rivaroxaban, apixaban, or edoxaban	Less affected by renal impairment than dabigatran
All-oral therapy	Rivaroxaban or apixaban	Dabigatran and edoxaban require heparin bridging
Dyspepsia or upper GI complaints	Rivaroxaban, apixaban, or edoxaban	Dyspepsia with dabigatran in up to 10% of patients
Recent GI bleed	Apixaban or low-dose edoxaban	More GI bleeding with rivaroxaban and high-dose dabigatran or edoxaban than with warfarin
Significant CAD	Rivaroxaban, apixaban, or edoxaban	Possible small MI signal with dabigatran
Poor compliance with twice-daily dosing	Rivaroxaban or edoxaban	Only agents given once-daily

CAD, coronary artery disease; CrCl, creatinine clearance; GI, gastrointestinal; MI, myocardial infarction

Fitting anticoagulation in your life:

Which issue would you like to discuss first?

- Bleeding
- Anticoagulation Routine
- Reversing Anticoagulation
- Cost
- Diet & Medication Interaction

Reversing

Warfarin *Coumadin*

Medications to reverse the effects of Warfarin are:

commonly available

Direct Anticoagulants

Medications to reverse the effects of Direct Anticoagulants are:

not commonly available

Anticoagulation Routine

Warfarin *Coumadin*

- Once daily
- Regular blood tests at a clinic or possibly at home

Direct Anticoagulants

Apixaban	*Eliquis*	AM	PM
Dabigatran	*Pradaxa*	AM	PM
Edoxaban	*Savaysa*	Once daily	
Rivaroxaban	*Xarelto*	Once daily	

Are you available to do the regular blood tests that Warfarin requires?

NOACs vs. warfarin:

Pros and Cons for Patients and Providers to Consider

Advantages of NOACs

- No INR monitoring required
- No bridging required
- Easier to manage around surgical procedures
- Convenient for rural patients or those with other barriers to clinic visits
- Fewer drug/diet/disease interactions
- Potentially better efficacy & safety for patients with poor INR control on warfarin

Disadvantages of NOACs

- Higher out-of-pocket costs and copays
- No clear advantage over well-controlled warfarin
- BID dosing may have negative impact on compliance
- Missed doses place a patient at higher risk for adverse event due to short half-life
- No specific antidote
- Higher incidence of G.I. side effects & discontinuation rate
- Possible increased incidence of heart attacks with dabigatran
- Lack of monitoring may foster non-compliance
- Renal monitoring and dose adjustment required

Warfarin to DOAC Transitions

DOAC	INR to Start DOAC
Eliquis (apixaban)	<2
Pradaxa (dabigatran)	<2
Savaysa (edoxaban)	<2.5
Xarelto (rivaroxaban)	<3

Tip: Apixaban & Dabigatran are dosed TWICE daily, wait til INR <2 until initiating

DOAC to Warfarin Transitions

DOAC	When to Initiate Warfarin
Eliquis (apixaban)	D/C apixaban, initiate warfarin +/- LMWH
Pradaxa (dabigatran)	Initiate warfarin 3 days before D/C'ing dabigatran (less days for CKD pts)
Savaysa (edoxaban)	Half edoxaban dose and initiate warfarin, D/C edoxaban after INR >2
Xarelto (rivaroxaban)	D/C rivaroxaban, initiate warfarin +/- LMWH

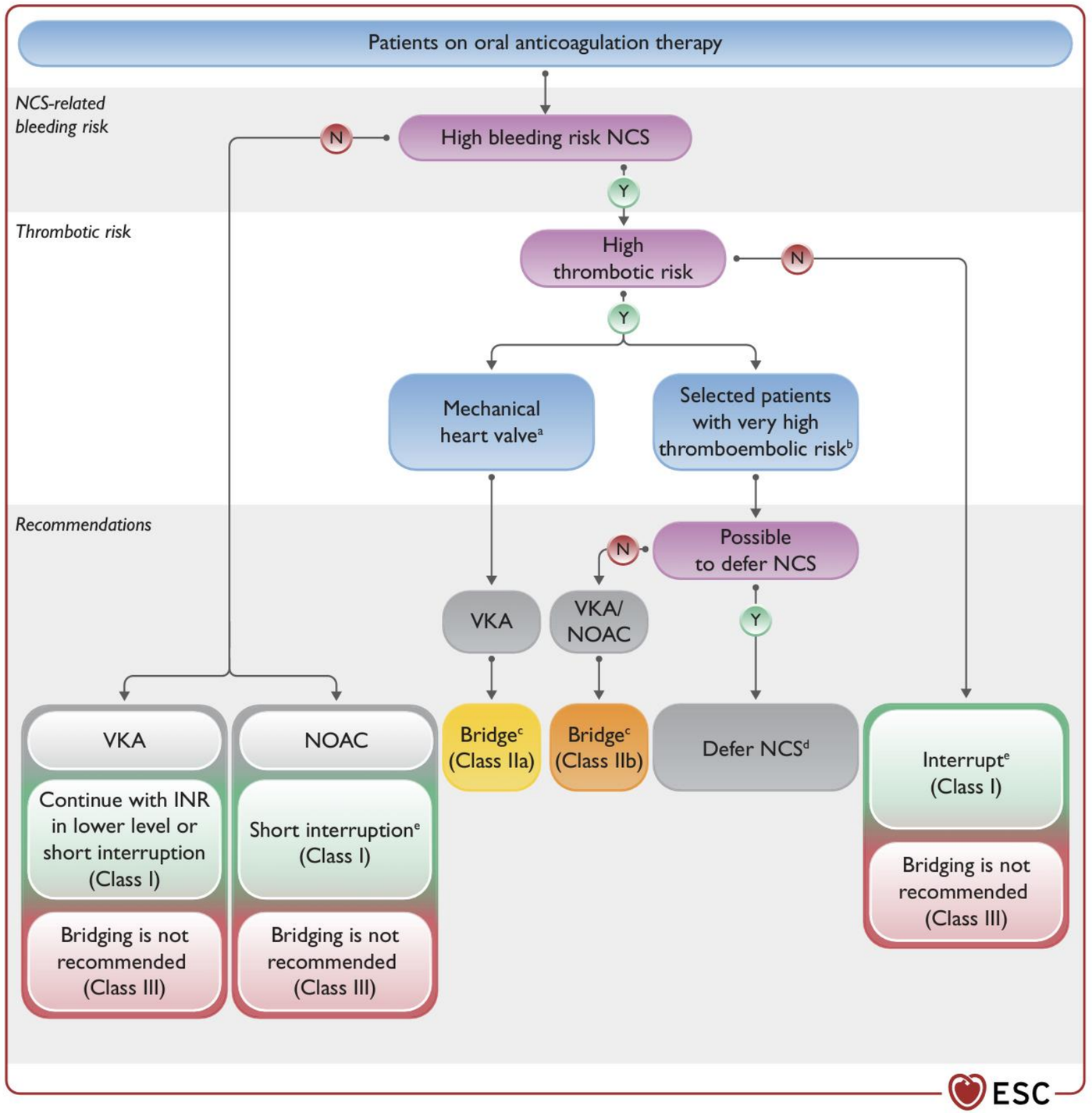

Figure 8 Recommendations for management of oral anticoagulation therapy in patients undergoing non-cardiac surgery. CHADS2-VASc, congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, stroke, vascular disease, age 65-74 years, sex category (female); N, no; NCS, non-cardiac surgery; NOAC, non-vitamin K antagonist oral anticoagulant; VKA, vitamin K antagonist; VT, venous thromboembolism. Y, yes; Mechanical aortic valve replacement (AVR) and any thromboembolic risk factor (atrial fibrillation, previous thromboembolism, severe left ventricular dysfunction, hypercoagul-able state), or older-generation mechanical AVR, or a mechanical mitral valve replacement. Recent stroke <3 months, high risk of VTE recurrences (e.g. antithrombin 3 deficiency or protein C and/or S deficiency), left ventricular apex thrombus, atrial fibrillation with a very high stroke risk. 'Bridging with unfractionated heparin or low molecular weight heparin. E.g. >3 months after stroke/TE. For NOAC management during NCS, see Figures 9 and .10

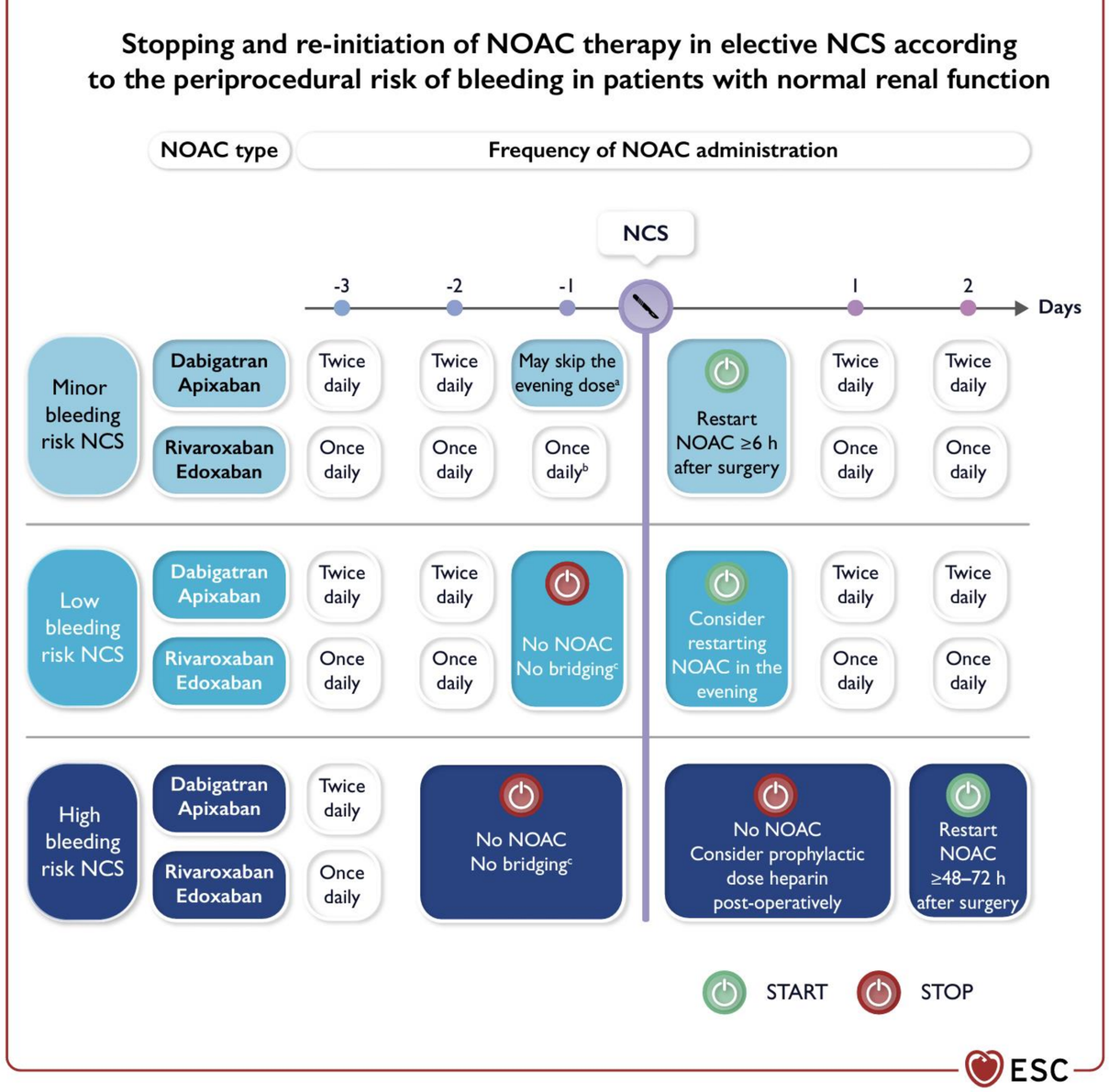

Figure 9 Peri-operative management of non-vitamin K antagonist oral anticoagulant according to the periprocedural risk of bleeding. NCS, non-cardiac surgery; NOAC, non-vitamin K antagonist oral anticoagulant. [a]In patients/circumstances favouring NOAC accumulation (e.g. renal dysfunction, older age, concomitant medication), the NOAC should be paused 12–24 h earlier. [b]In patients on rivaroxaban or edoxaban taking the dose in the evening, the evening dose may be skipped. [c]NOACs have predictable weaning of the anticoagulant effect. Owing to the increase in bleeding risk associated with bridging, it is generally not recommended to use bridging in patients taking NOACs. Very few circumstances when bridging with heparin may be considered in patients taking a NOAC include high thromboembolic risk conditions, such as: 1) patients with a recent (within 3 months) thromboembolic event (stroke, systemic embolism, or VTE); 2) patients who experienced a thromboembolic event during previous interruption of NOAC therapy.

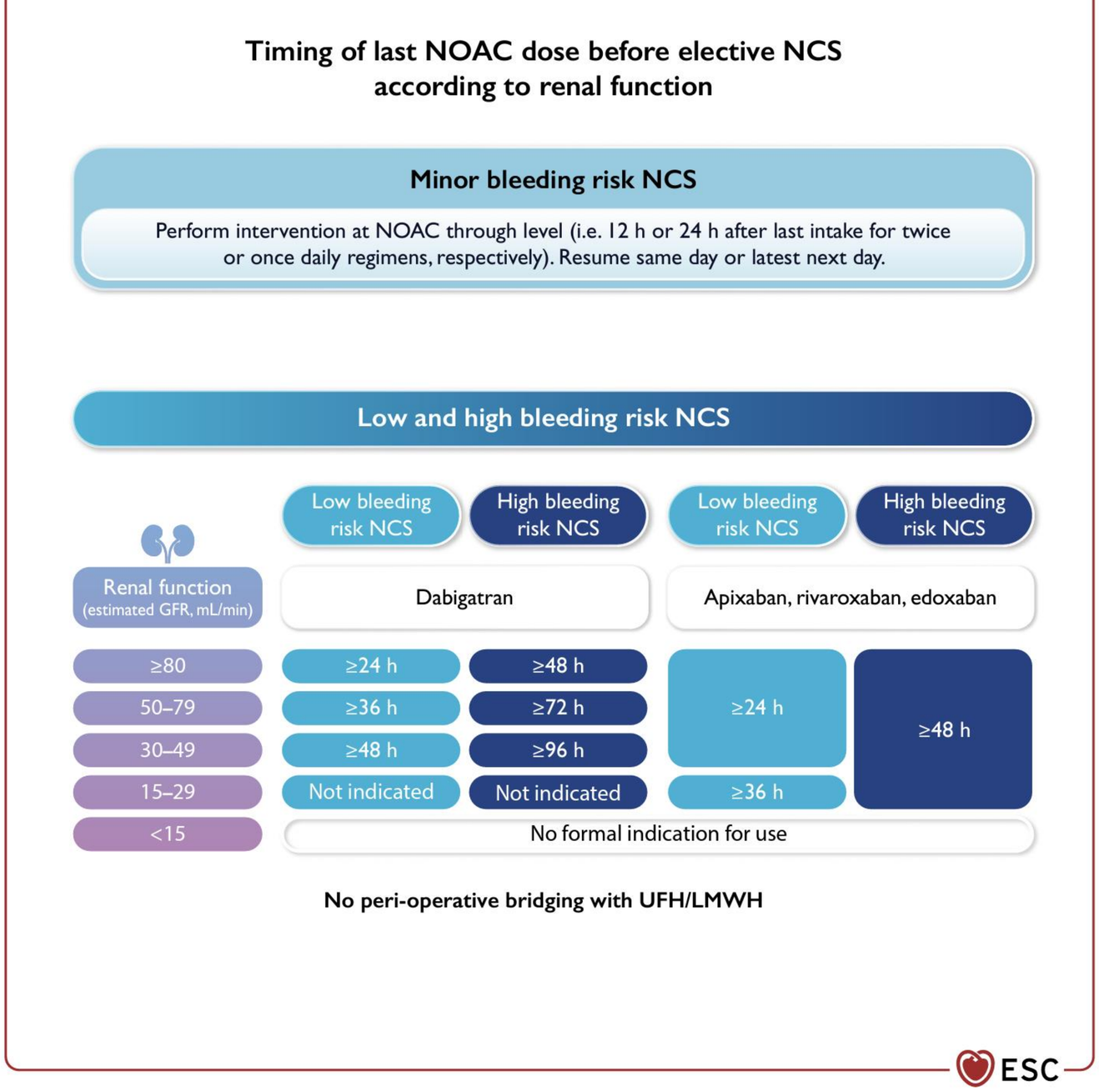

Figure 10 Timing of last non-vitamin K antagonist oral anticoagulant dose before elective NCS according to renal function. GFR, glomerular filtration rate; LMWH, low molecular weight heparin; NCS, non-cardiac surgery; NOAC, non-vitamin K antagonist oral anticoagulant; UFH, unfractionated heparin.

Table 1. Risk Classification for Surgery/Procedure-Related Bleeding.*	
High-bleed-risk surgery/procedure† (30-day risk of major bleed ≥2%)	Major surgery with extensive tissue injury Cancer surgery, especially solid tumor resection (lung, esophagus, gastric, colon, hepatobiliary, pancreatic) Major orthopedic surgery, including shoulder replacement surgery Reconstructive plastic surgery Major thoracic surgery Urologic or gastrointestinal surgery, especially anastomosis surgery Transurethral prostate resection, bladder resection, or tumor ablation Nephrectomy, kidney biopsy Colonic polyp resection Bowel resection Percutaneous endoscopic gastrostomy placement, endoscopic retrograde cholangiopancreatography Surgery in highly vascular organs (kidneys, liver, spleen) Cardiac, intracranial, or spinal surgery Any major operation (procedure duration >45 minutes) Neuraxial anaesthesia¶ Epidural injections
Low/moderate-bleed-risk surgery/procedure‡ (30-day risk of major bleed 0%–2%)	Arthroscopy Cutaneous/lymph node biopsies Foot/hand surgery Coronary angiography by femoral artery approach Gastrointestinal endoscopy ± biopsy§ Colonoscopy ± biopsy§ Abdominal hysterectomy Laparoscopic cholecystectomy Abdominal hernia repair Hemorrhoidal surgery Bronchoscopy ± biopsy
Minimal-bleed-risk surgery/procedure§ (30-day risk of major bleed ~0%)	Minor dermatologic procedures (excision of basal and squamous cell skin cancers, actinic keratoses, and premalignant or cancerous skin nevi) Ophthalmological (cataract) procedures Minor dental procedures (dental extractions, restorations, prosthetics, endodontics), dental cleanings, fillings Pacemaker or cardioverter-defibrillator device implantation Coronary angiography by radial artery approach Selected patients requiring screening gastrointestinal endoscopy and colonoscopy ± biopsy‖

Adapted from 2022 CHEST Guidelines.

†No residual anticoagulant effect at the time of the procedure (i.e., four to five drug half-life interruption preprocedure.(

‡Some residual anticoagulant effect allowed (i.e., two to three drug half-life interruption preprocedure.(

S Procedure can be safely done under full-dose anticoagulation (may consider holding direct oral anticoagulant dose the day of the procedure to avoid peak anticoagulant effects.(

"Includes spinal and epidural anesthesia or any other neuraxial (e.g., pain management) intervention; consider not only the absolute risk for major bleeding but potentially devastating consequences of epidural bleeding and associated lower limb paralysis.

I Selected patients, especially if taking a vitamin K antagonist and in whom polypectomy is not anticipated, may be classified as minimal-bleed-risk; whether they are classified as low / moderate-bleed-risk (requiring anticoagulant interruption) or minimal-bleed-risk (not requiring anticoagulant

Table 2. Risk Classification for Thromboembolism.*

Risk Category	Mechanical Heart Valve	Atrial Fibrillation	Venous Thromboembolism
High (>10%/year risk of ATE or >10%/month risk of VTE)	Mechanical mitral valve *with* risk factors for stroke† Caged ball or tilting disc valve in mitral/aortic position Recent (<3 month) stroke or TIA	CHA_2DS_2VASc score of ≥7 $CHADS_2$ score of 5 or 6 Recent (<3 month) stroke or TIA Rheumatic valvular heart disease	Recent (<3 months and especially 1 month) VTE Severe thrombophilia (deficiency of protein C, protein S or antithrombin; homozygous factor V Leiden or prothrombin gene mutation or double-heterozygous for each mutation, multiple thrombophilias) Antiphospholipid syndrome Active cancer associated with high VTE risk‡
Moderate (4%–10%/year risk of ATE or 4%–10%/month risk of VTE)	Bileaflet AVR *with* major risk factors for stroke†	CHA_2DS_2VASc score of 5 or 6 $CHADS_2$ score of 3 or 4	VTE within the past 3–12 months Recurrent VTE Nonsevere thrombophilia (heterozygous factor V Leiden or prothrombin gene mutation) Active cancer or recent history of cancer§
Low (<4%/year risk of ATE or <2%/month risk of VTE)	Bileaflet AVR *without* major risk factors for stroke†	CHA_2DS_2VASc score of 1–4 $CHADS_2$ score of 0–2 (and no prior stroke or TIA)	VTE more than 12 months ago

* Adapted from 2022 CHEST Guidelines. ATE denotes arterial thromboembolism; AVR, aortic valve replacement; TIA, transient ischemic attack; and VTE, venous thromboembolism.

† Includes atrial fibrillation, prior stroke or transient ischemic attack (including during perioperative period), prior valve thrombosis, rheumatic valvular heart disease, hypertension, diabetes, congestive heart failure, age >75 years.

‡ Includes pancreatic cancer, myeloproliferative disorders, primary brain cancer, gastric cancer, and esophageal cancer.

§ Within 5 years if history of cancer, excluding nonmelanoma skin cancer.

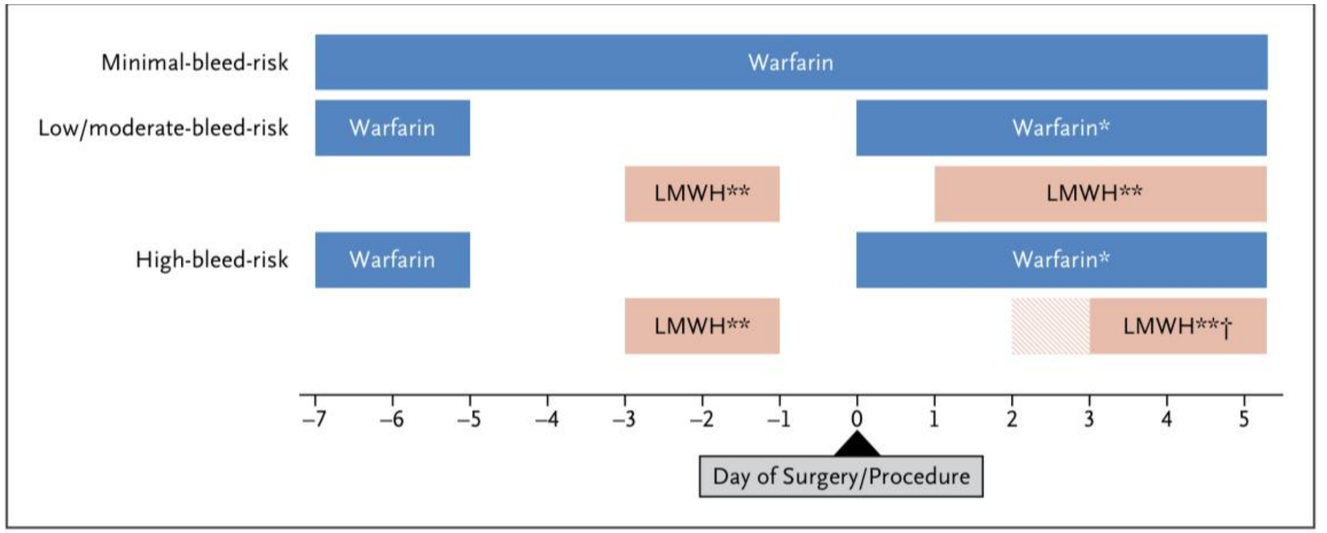

Figure 1. Perioperative Management of Vitamin K Antagonists (Warfarin), Adapted from the 2022 ACCP Guidelines.

* Warfarin can be resumed on the evening of the procedure (day 0) for most patients or the day after the procedure (i.e., day 1) at the patient's usual maintenance dose. ** Bridging suggested for high thrombotic risk populations with full-dose, subcutaneous low-molecular-weight heparin (LMWH; e.g., enoxaparin, 1 mg/kg twice a day or 1.5 mg/kg daily or dalteparin, 100 IU/kg twice a day or 200 IU/kg daily), with the last dose given the morning of the day prior to the procedure (i.e., day −1) at half the total daily dose. † Low-dose LMWH (e.g., enoxaparin, 40 mg daily or dalteparin, 5000 IU daily) can be used for venous thromboembolism prophylaxis for the first 24 to 72 hours postprocedure, with full-dose LMWH resumed 2 to 3 days postprocedure.

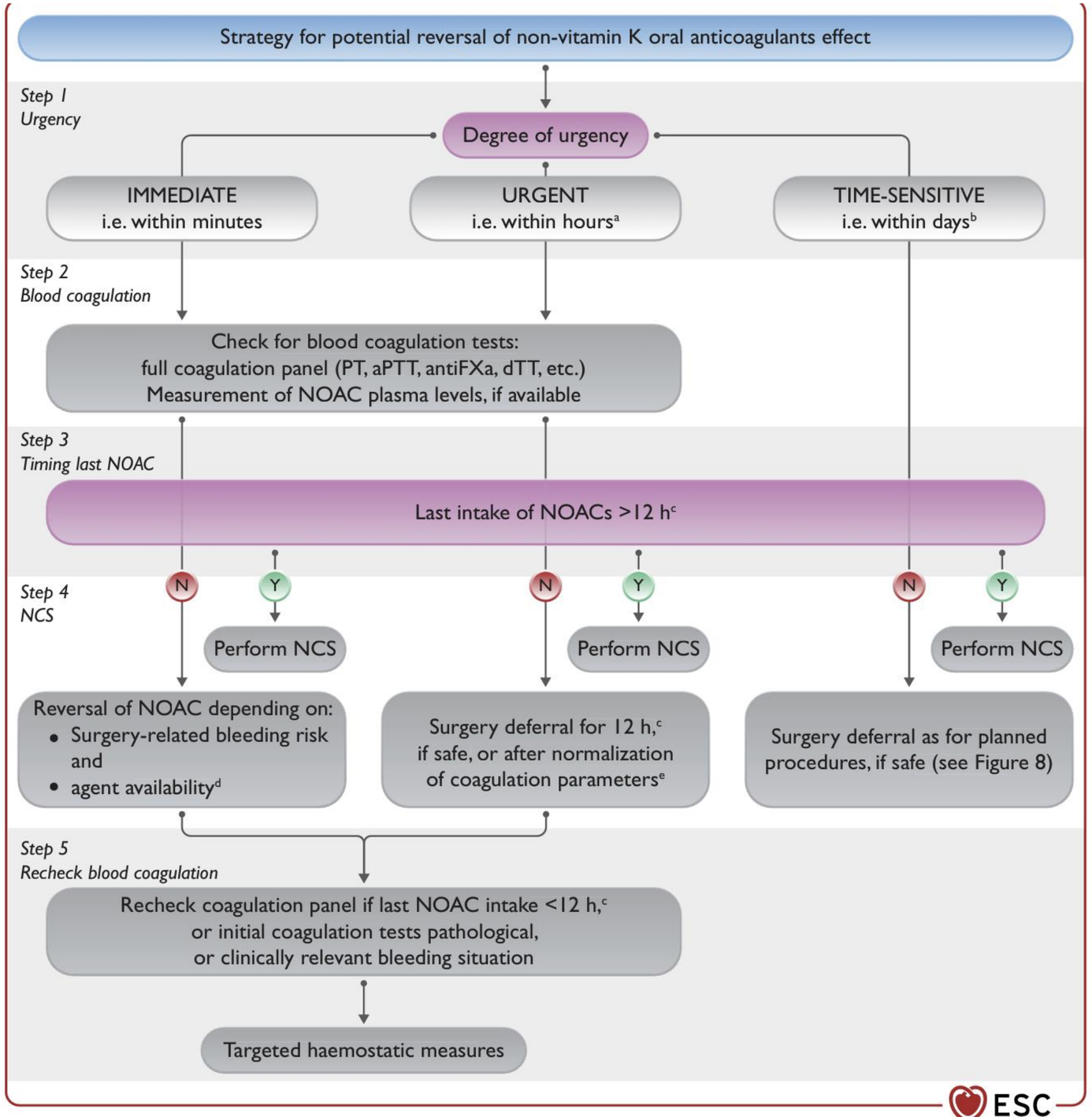

Figure 11 Suggested strategy for potential reversal of non-vitamin K oral anticoagulants effect. aPTT, activated partial thromboplastin time; dTT, diluted thrombin time; FXa, factor Xa; N, no; NOAC, non-vitamin K antagonist oral anticoagulant; PT, prothrombin time; UH, unfractionated heparin. Y, yes;

Conditions that are potentially life-threatening or that may threaten the survival of limb or organ.

•Conditions that can be managed and procedure de-

layed for several days. '>24 h in case of significantly reduced renal function (i.e. eGFR <50 mL/min). 'If specific reversal agent is unavailable, consider non-specific haemostatic agents (prothrombin complex concentrate PCC] or activated PCC [aPCCs]). Idarucizumab has only been tested in patients undergoing urgent surgery. Andexanet has not been tested in patients requiring urgent surgery. Andexanet binds all FXa inhibitors (including UFH) non specifically. Upon re-check.

Table 3. Anticoagulant Reversal Agents and Dosing.*

Reversal Agent Options	VKAs (Warfarin, Acenocoumarol, Phenprocoumon)	DOACs	
		Anti-Xa Inhibitors (Apixaban, Edoxaban, Rivaroxaban)	Anti-IIa Inhibitor (Dabigatran)
Plasma	Fresh frozen plasma, 2–6 units (depending on INR)		
PCCs	Four-factor PCC, 30 IU/kg (maximum 3000 units)†	Four-factor PCC, 30 IU/kg (maximum 3000 units)	Four-factor PCC, 30 IU/kg (maximum 3000 units) *or* FEIBA (factor VIII inhibitor bypass activity), 50 IU/kg (maximum 2000 units)
Specific reversal	n/a	Andexanet-α *Low dose*: 400 mg IV bolus, 30 mg/min, followed by 2-hour IV infusion at 4 mg/min‡ *High dose*: 800 mg IV bolus, 30 mg/min, followed by 2-hour IV infusion at 8 mg/min§	Idarucizumab 2.5 g (50 ml) IV bolus for 2 doses, 15 minutes apart

* DOAC denotes direct oral anticoagulant; INR, international normalized ratio; IV, intravenous; n/a, not applicable; PCCs, prothrombin complex concentrates; and VKA, vitamin K antagonist.

† Preferred over fresh frozen plasma.

‡ Dosing if last dose of DOAC given more than 8 hours before.

§ Dosing if last dose of DOAC given within 8 hours or unknown.