Table I Selected indications and contraindications for non-vitamin K antagonist oral anticoagulant therapy in atrial fibrillation patients

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

Hatched—limited data.
PTAV, percutaneous transluminal aortic valvuloplasty; TAVI, transcatheter aortic valve implantation.

心房細動があっても全てがNOAC服用の適応ではありません

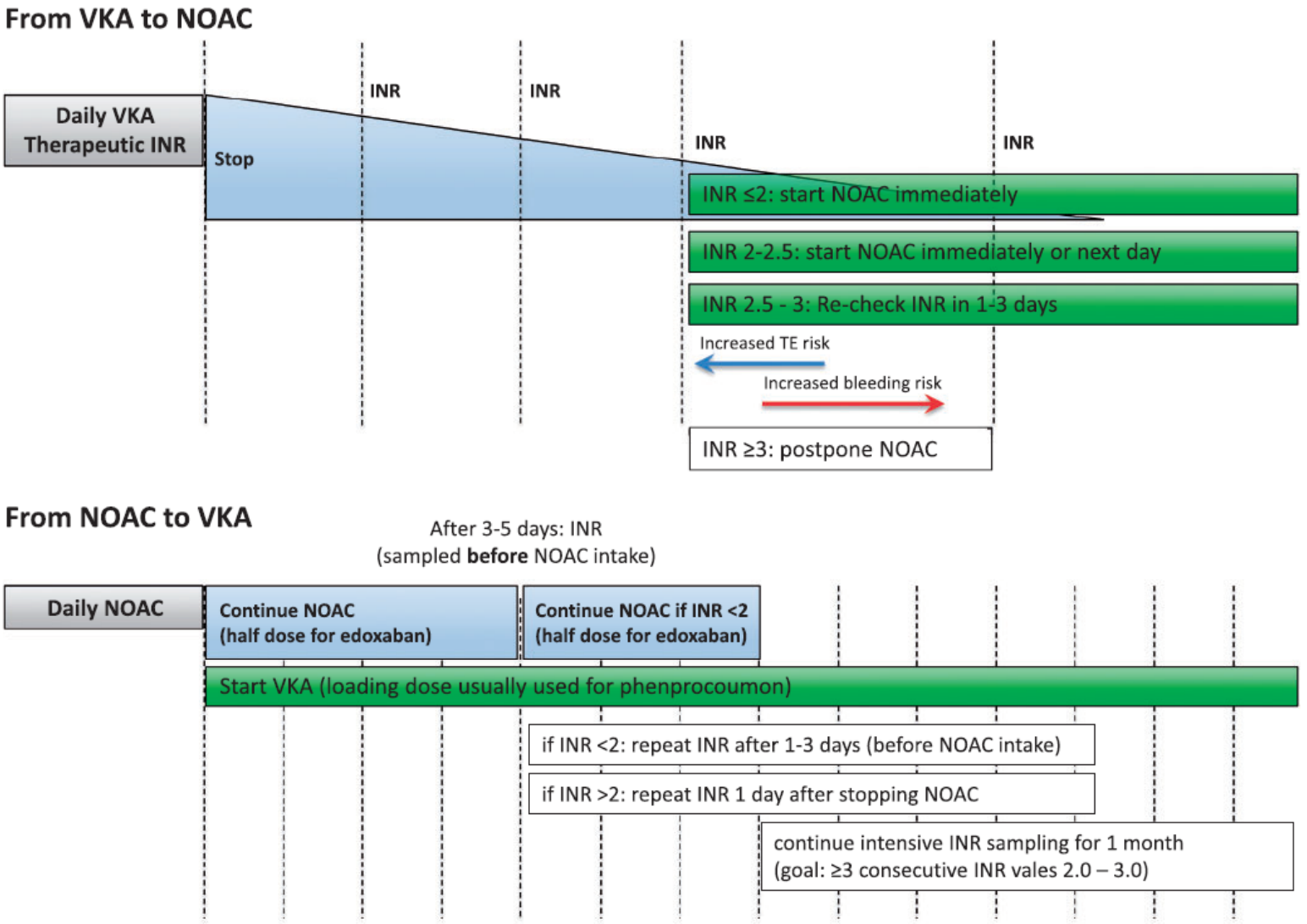

Figure 2 Switching between vitamin K antagonists and non-vitamin K antagonist oral anticoagulants and vice versa. TE, thromboembolic.

ワーファリンからNOACへの変更とNOACからワーファリンへの変更の仕方

Table 3 Effect of drug–drug interactions and clinical factors on NOAC plasma levels ('area under the curve')

	Via	Dabigatran etexilate	Apixaban	Edoxaban	Rivaroxaban
P-gp substrate		Yes	Yes	Yes	Yes
CYP3A4 substrate		No	Yes (≈25%)	No (<4%)	Yes (≈18%)[131]
Antiarrhythmic drugs					
Amiodarone	moderate P-gp competition	+12 to 60%[SmPC]	No PK data[a]	+40%[132–134]	Minor effect[a]
Digoxin	P-gp competition	No effect[SmPC]	No effect[135]	No effect	No effect[SmPC]
Diltiazem	P-gp competition and weak CYP3A4 inhibition	No effect[SmPC]	+40%[136]	No data yet	No effect
Dronedarone	P-gp competition and CYP3A4 inhibition	+70 to 100% (US: 2 × 75 mg if CrCl 30–50 mL/min)	No PK or PD data: caution	+85%[b]	Moderate effect, should be avoided
Quinidine	P-gp competition	+53%[SMPC]	No data yet	+77%[137] (no dose reduction required by label)	Extent of increase unknown
Verapamil	P-gp competition (and weak CYP3A4 inhibition)	+12 to 180%[SmPC] (if taken simultaneously)	No PK data	+53% (SR)[137,142] (no dose reduction required by label)	No effect

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Other cardiovascular drugs					
Atorvastatin	P-gp competition and CYP3A4 inhibition	No relevant interaction	No data yet	No effect	No effect
Ticagrelor	P-gp competition	+25%[SmPC] (give loading dose 2h after dabigatran)[d]	No data	No data	No data
Antibiotics					
Clarithromycin; Erythromycin	Moderate P-gp competition and strong CYP3A4 inhibition	+15 to 20%	+60% AUC +30% C_{max}	+90%[SmPC]	+34% (Erythromycin)/ +54% (Clarithromycin) SmPC129
Rifampicin	P-gp/BCRP and CYP3A4/ CYP2J2 inducers	Minus 66%[SmPC]	Minus 54%[138]	Minus 35%, but with compensatory increase of active metabolites	Up to minus 50%[SmPc]
Antiviral drugs					
HIV protease inhibitors (e.g. ritonavir)	P-gp and BCRP competition or inducer; CYP3A4 inhibition	No data yet	Strong increase[SmPC]	No data yet	Up to +153%[129]

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Fungostatics					
Fluconazole	Moderate CYP3A4 inhibition	No data yet	No data yet	No data yet	+42% (if systemically administered)[SmPC]
Itraconazole; Ketoconazole; Voriconazole	potent P-gp and BCRP competition; CYP3A4 inhibition	+140 to 150% (US: 2 x 75 mg if CrCl 30–50 mL/min)	+100%[136]	+87 to 95%[132] (reduce NOAC dose by 50%)	Up to +160%[SmPc]
Posaconasole	Mild to moderate P-gp inhibition	SmPC	SmPC		SmPC
Others					
Naproxen	P-gp competition; pharma-codynamically increased bleeding time	No data yet	+55%[139]	No effect	No data yet
H2B; PPI; Al-mg-hydroxide	GI absorption	Minus 12–30%	No effect	No effect[SmPc]	No effect[140]
St. John's wort	P-gp/BCRP and CYP3A4/CYP2J2 inducers				

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Other factors					
Age ≥80 years	Potential for Increased plasma levels		b	c	
Age ≥75 years	Potential for Increased plasma levels			c	
Weight ≤60 kg	Potential for Increased plasma levels		b	b	
Renal function	Increased plasma level	See *Figure 4*			
Other increased bleeding risk		• Concomitant antiplatelet drugs; NSAID; systemic steroid therapy; other anticoagulants • History of GI bleeding • Recent surgery on critical organ (brain; eye) • Frailty/falls risk • St.p bleeding or predisposition (anaemia, thrombocytopenia)			

The hatched colour coding indicates no clinical or PK data available, and recommendations are based on the respective NOAC SmPC (where available) or expert opinion.
White: No relevant drug–drug interaction anticipated.
Yellow: Consider dose adjustment or different NOAC if 2 or more 'yellow' factors are present (see *Figure 3*).
Orange: Consider dose adjustment or different NOAC (see *Figure 3*).
Red: contraindicated/not recommended.
Brown: Contraindicated due to *reduced* NOAC plasma levels.
Blue: The label for edoxaban mentions that co-administration is possible in these cases, despite a decreased plasma level, which are deemed not clinically relevant. Since not tested prospectively, however, such concomitant use should be used with caution, and avoided when possible.
BCRP, breast cancer resistance protein; NSAID, non-steroidal anti-inflammatory drugs; H2B, H2-blockers; PPI, proton pump inhibitors; P-gp, P-glycoprotein; GI, gastrointestinal.
[a]Based on *in vitro* investigations, comparing the IC_{50} for P-gp inhibition to maximal plasma levels at therapeutic dose, and/or on interaction analysis of efficacy and safety end-points in the Phase-3 clinical trials.[29,30] No direct PK interaction data available.
[b]Dose reduction based on published criteria (see *Table 13*, *Figure 3*).
[c]Age had no significant effect after adjusting for weight and renal function.
[d]Data from Phase I study. Evidence from Re-DUAL PCI indicate safety in the (small) subgroup on dabigatran and ticagrelor.[141]

前のグラフを参照　以下同

Table 4 Anticipated effects of common anticancer drugs on non-vitamin K antagonist oral anticoagulants plasma levels

	Via[142]	Dabigatran etexilate	Apixaban	Edoxaban	Rivaroxaban
P-gp substrate		**Yes**	**Yes**	**Yes**	**Yes**
CYP3A4 substrate		**No**	**Yes (≈25%)**	**No (<4%)**	**Yes (≈18%)**
Antimitotic agents					
Paclitaxel	Moderate CYP3A4 induction; CYP3A4/P-gp competition				
Vinblastine	Strong P-gp induction; CYP3A4/P-gp competition				
Docetaxel, Vincristine	Mild CYP3A4 induction; CYP3A4/P-gp competition				
Vinorelbine	Mild CYP3A4 induction; CYP3A4/P-gp competition				
Antimetabolites					
Metotrexate	P-gp competition; no relevant interaction anticipated				
Pemetrexed, Purine analogs, Pyrimidine analogs	No relevant interaction anticipated				
Topoisomerase inhibitors					
Topotecan	No relevant interaction anticipated				
Irinotecan	CYP3A4/P-gp competition; No relevant interaction anticipated				
Etoposide	Mild CYP3A4 inhibition; CYP3A4/P-gp competition				
Anthracyclines/Anthracenediones					
Doxorubicin	Strong P-gp induction, mild CYP3A4 inhibition; CYP3A4/P-gp competition				
Idarubicin	Mild CYP3A4 inhibition; P-gp competition				

Daunorubicin	P-gp competition; No relevant interaction anticipated				
Mitoxantrone	No relevant interaction anticipated				
Alkylating agents					
Ifosfamide	Mild CYP3A4 inhibition; CYP3A4 competition				
Ciclophosphamide	Mild CYP3A4 inhibition; CYP3A4 competition				
Lomustine	Mild CYP3A4 inhibition				
Busulfan	CYP3A4 competition; No relevant interaction anticipated				
Bendamustine	P-gp competition; No relevant interaction anticipated				
Chlorambucil, Melphalan, Carmustine, Procarbazine, Dacarbazine, Temozolomide	No relevant interaction anticipated				
Platinum-based agents					
Cisplatin, Carboplatin, Oxaliplatin	No relevant interaction anticipated				
Intercalating agents					
Bleomycin, Dactinomycin	No relevant interaction anticipated				
Mitomycin C	No relevant interaction anticipated				
Tyrosine kinase inhibitors					
Imatinib, Crizotinib	Strong P-gp inhibition, moderate CYP3A4 inhibition; CYP3A4/P-gp competition				
Nilotinib, Lapatinib	Moderate-to-strong P-gp inhibition, mild CYP3A4 inhibition; CYP3A4/P-gp competition				
Vemurafenib	Moderate CYP3A4 induction; CYP3A4/P-gp competition				

Dasatinib	Mild CYP3A4 inhibition; CYP3A4/P-gp competition				
Vandetanib, Sunitinib	Strong P-gp induction; CYP3A4 competition				
Erlotinib, Gefitinib	CYP3A4 competition; No relevant interaction anticipated				
Monoclonal antibodies					
Brentuximab	CYP3A4 competition; No relevant interaction anticipated				
Rituximab, Alemtuzumab, Cetuximab, Trastuzumab, Bevacizumab	No relevant interaction assumed				
Hormonal agents					
Abiraterone	Moderate CYP3A4 inhibition, strong P-gp inhibition; CYP3A4/P-gp competition				
Enzalutamide	Strong CYP3A4 induction, strong P-gp inhibition; CYP3A4/P-gp competition				
Bicalutamide	Moderate CYP3A4 inhibition				
Tamoxifen	Strong P-gp inhibition, mild CYP3A4 inhibition; CYP3A4 competition				
Anastrozole	Mild CYP3A4 inhibition				
Flutamide	CYP3A4 competition; No relevant interaction anticipated				
Letrozole, Fulvestrant	CYP3A4 competition; No relevant interaction anticipated				
Raloxifene, Leuprolide, Mitotane	No relevant interaction anticipated				
Immune-modulating agents					
Cyclosporine	Strong-to-moderate P-gp inhibition, moderate CYP3A4 inhibition; CYP3A4/P-gp competition	SmPC	SmPC	+73%[143]	

Dexamethasone	Strong CYP3A4/P-gp induction; CYP3A4/P-gp competition				
Tacrolimus	Strong-to-moderate P-gp inhibition, mild CYP3A4 inhibition; CYP3A4/P-gp competition	SmPC			
Prednisone	Moderate CYP3A4 induction; CYP3A4 competition				
Temsirolimus, Sirolimus	Mild CYP3A4 inhibition; CYP3A4/P-gp competition				
Everolimus	CYP3A4 competition; No relevant interaction anticipated				

Purine analogs: Mercaptopurine, Thioguanine, Pentostatin, Cladribine, Clofarabine, Fludarabine.
Pyrimidine analogs: Fluorouracil, Capeticabine, Cytarabine, Gemcitabine, Azacitadine, Decitabine.
Anticipated effects of common anticancer drugs on NOACs plasma levels.[144]
The hatched colour coding indicates no clinical or PK data available, and recommendations are based on the respective NOAC SmPC (where available) or expert opinion. Some of the colour codes will likely require adaptation as more data become available over time.
White: No relevant drug–drug interaction anticipated.
Yellow (light): Caution is needed in case of polypharmacy or in the presence of ≥2 bleeding risk factors.
Yellow: Consider dose adjustment or different NOAC if 2 or more 'yellow' factors are present (see *Figure 3*).
Orange: Consider dose adjustment or different NOAC (see *Figure 3*).
Red: contraindicated/not recommended.
Brown (dark): Contraindicated due to reduced NOAC plasma levels.
Brown (light): Use with caution or avoid. Either expert opinion or the NOAC label mentions that co-administration is possible despite a decreased plasma level, which is deemed not clinically relevant (nevertheless, since not tested prospectively, such concomitant use should be used with caution, and avoided when possible).
Where no data or SmPC instructions were available, expert opinion was based on the following principles:

- Strong CYP3A4 and/or P-gp inducer—should not be used (dark brown).
- Moderate CYP3A4 or P-gp inducer—use with caution or avoid (light brown).
- Strong CYP3A4 and/or inhibitor—should not be used (red).
- Moderate CYP3A4 or P-gp inhibitor—use with caution, consider dose reduction or different NOAC (orange).
- Mild CYP3A4 and/or P-gp inducers or inhibitors—caution is needed with polypharmacy or in the presence of ≥2 bleeding risk factors (yellow).

Table 5 **Anticipated effects of common antiepileptic drugs on non-vitamin K antagonist oral anticoagulants plasma levels**

	Via[142,145,146]	Dabigatran etexilate	Apixaban[130]	Edoxaban	Rivaroxaban
P-gp substrate		Yes	Yes	Yes	Yes
CYP3A4 substrate		No	Yes (≈25%)	No (<4%)	Yes (≈18%)
Drug					
Carbamazepine	Strong CYP3A4/P-gp induction; CYP3A4 competition	SmPC	−50%[SmPC]	−35%[SmPC]	SmPC, Ref.[147]
Ethosuximide	CYP3A4 competition; No relevant interaction known/assumed				
Gabapentin	No relevant interaction known/assumed				
Lamotrigine	P-gp competition; No relevant interaction known/assumed				
Levetiracetam	P-gp induction; P-gp competition				
Oxcarbazepine	CYP3A4 induction; P-gp competition				
Phenobarbital	Strong CYP3A4/P-gp induction; P-gp competition		SmPC	SmPC	SmPC
Phenytoin	Strong CYP3A4/P-gp induction; P-gp competition	SmPC, Ref.[148]	SmPC	SmPC	SmPC
Pregabalin	No relevant interaction known/assumed				
Topiramate	CYP3A4 induction; CYP3A4 competition				
Valproic acid	CYP3A4/P-gp induction				Ref.[149]
Zonisamide	CYP3A4 competition; No relevant interaction known/assumed				

Anticipated effects of common antiepileptic drugs on NOACs plasma levels.[147,150]
The hatched colour coding indicates no clinical or PK data available, and recommendations are based on the respective NOAC SmPC, where available, or expert opinion. Some of the colour codes will likely require adaptation as more data become available over time.
White: No relevant drug–drug interaction anticipated.
Brown (dark): Contraindicated due to *reduced* NOAC plasma levels.
Brown (light): Use with caution or avoid—either the label for the respective NOAC mentions that co-administration is possible despite a decreased plasma level, which are deemed not clinically relevant (nevertheless, since not tested prospectively, such concomitant use should be used with caution, and avoided when possible) or expert opinion.
Where no data or SmPC instructions were available, expert opinion was based on the following principles:

- Strong CYP3A4 and/or P-gp inducer—should not be used (dark brown).
- Moderate CYP3A4 or P-gp inducer—use with caution or avoid (light brown).
- Strong CYP3A4 and/or inhibitor—should not be used (red).
- Moderate CYP3A4 or P-gp inhibitor—use with caution, consider dose reduction or different NOAC (orange).
- Mild CYP3A4 and/or P-gp inducers or inhibitors—caution is needed with polypharmacy or in the presence of ≥2 bleeding risk factors (yellow).

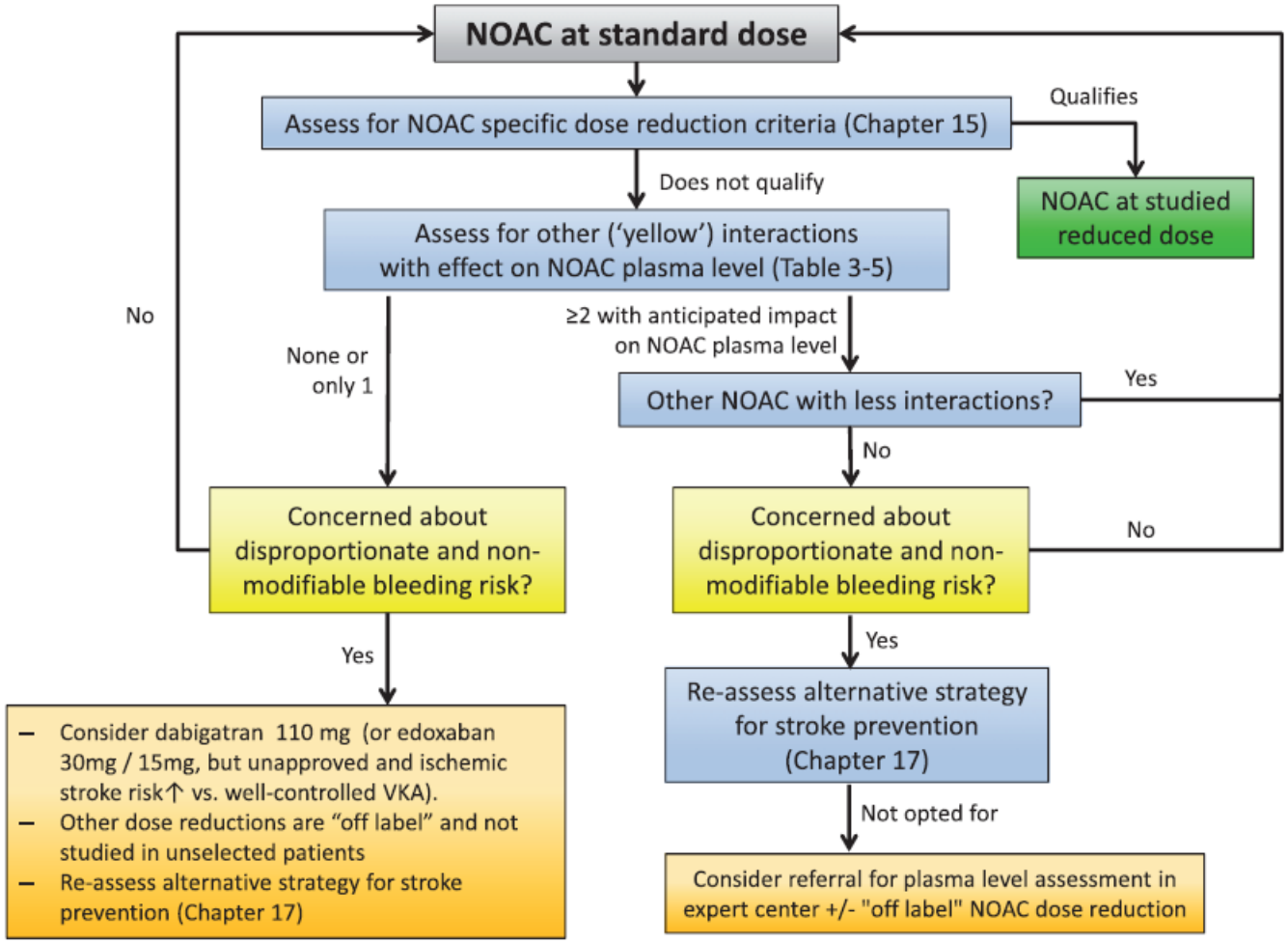


Figure 3 NOAC selection based on drug–drug interactions and/or risk of bleeding. Use of plasma level measurements to guide dosing is generally discouraged and should only be used in rare cases of potentially substantial interactions or special situations, and only in centres with great experience in the performance and interpretation of such assays as well as the care of NOAC-treated patients.

Table 6 Absorption and metabolism of the different NOACs

	Dabigatran[158,182]	Apixaban[183]	Edoxaban[184]	Rivaroxaban[185,186]
Bioavailability	3–7%	50%	62%	15 mg/20 mg: 66% without food, 80–100% with food
Prodrug	Yes	No	No	No
Clearance non-renal/renal of absorbed dose	20%/80%	73%/27%	50%/50%	65%/35%
Plasma protein binding	35%	87%	55%	95%
Dialysability	50–60% (in part dialysable)	14% (in part dialysable)	n.a. (in part dialysable)	n.a. (in part dialysable)
Liver metabolism: CYP3A4 involved	No	Yes [elimination, moderate contribution (≈25%)[a]]	Minimal (<4% of elimination)	Yes (hepatic elimination ≈18%)[131]
Absorption with food	No effect	No effect	6-22% more; minimal effect on exposure	+39% more (see above)
Absorption with H2B/PPI	-12% to 30% (not clinically relevant)	No effect	No effect	No effect
Asian ethnicity	+25%[166]	No effect	No effect	No effect
Elimination half-life	12–17 h	12 h	10–14 h	5–9 h (young)
				11–13 h (elderly)
Other	Dyspepsia (5–10%)			Intake of 15 mg/20 mg with food mandatory

[a]Hepatic metabolism in total of ≈25%, mostly via CYP3A4, with minor contributions of CYP1A2, 2J2, 2C8, 2C9, and 2C19.

吸収と代謝について

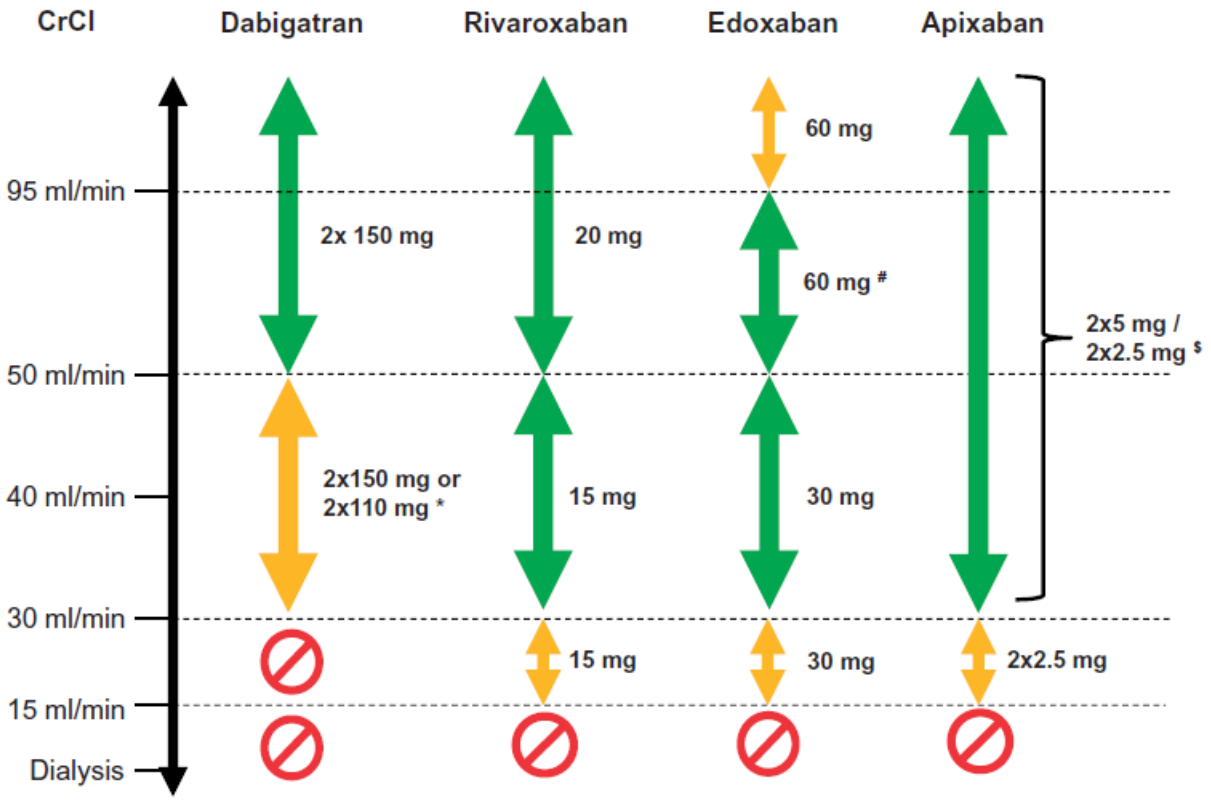


Figure 4 Use of non-vitamin K antagonist oral anticoagulants according to renal function. *2 × 110 mg in patients at high risk of bleeding (per SmPc). #Other dose reduction criteria may apply (weight ≤60 kg, concomitant potent P-Gp inhibitor therapy). $2 × 2.5 mg only if at least two out of three fulfilled: age ≥80 years, body weight ≤60 kg, creatinine ≥1.5 mg/dL (133 µmol/L). Orange arrows indicate cautionary use (dabigatran in moderate renal insufficiency, FXa inhibitors in severe renal insufficiency, edoxaban in 'supranormal' renal function); see text for details.

腎機能に対する対応

Table 8 Calculation of the Child-Turcotte-Pugh score and use of NOACs in hepatic insufficiency

Parameters	1 point	2 points	3 points
Encephalopathy	No	Grade 1–2 (suppressed with medication)	Grade 3–4 (refractory/chronic)
Ascites	No	Mild (diuretic-responsive)	Moderate–severe (diuretic-refractory)
Bilirubin	<2 mg/dL	2–3 mg/dL	>3 mg/dL
	<34 μmol/L	34–50 μmol/L	>50 μmol/L
Albumin	>3.5 g/dL	2.8–3.5 g/dL	<2.8 g/dL
	>35 g/L	28–35 g/L	<28 g/dL
INR	<1.7	1.71–2.30	>2.30

Child–Pugh category	Dabigatran	Apixaban	Edoxaban	Rivaroxaban
A (5–6 points)	No dose reduction	No dose reduction	No dose reduction	No dose reduction
B (7–9 points)	Use with caution	Use cautiously	Use cautiously	Do not use
C (10–15 points)	Do not use	Do not use	Do not use	Do not use

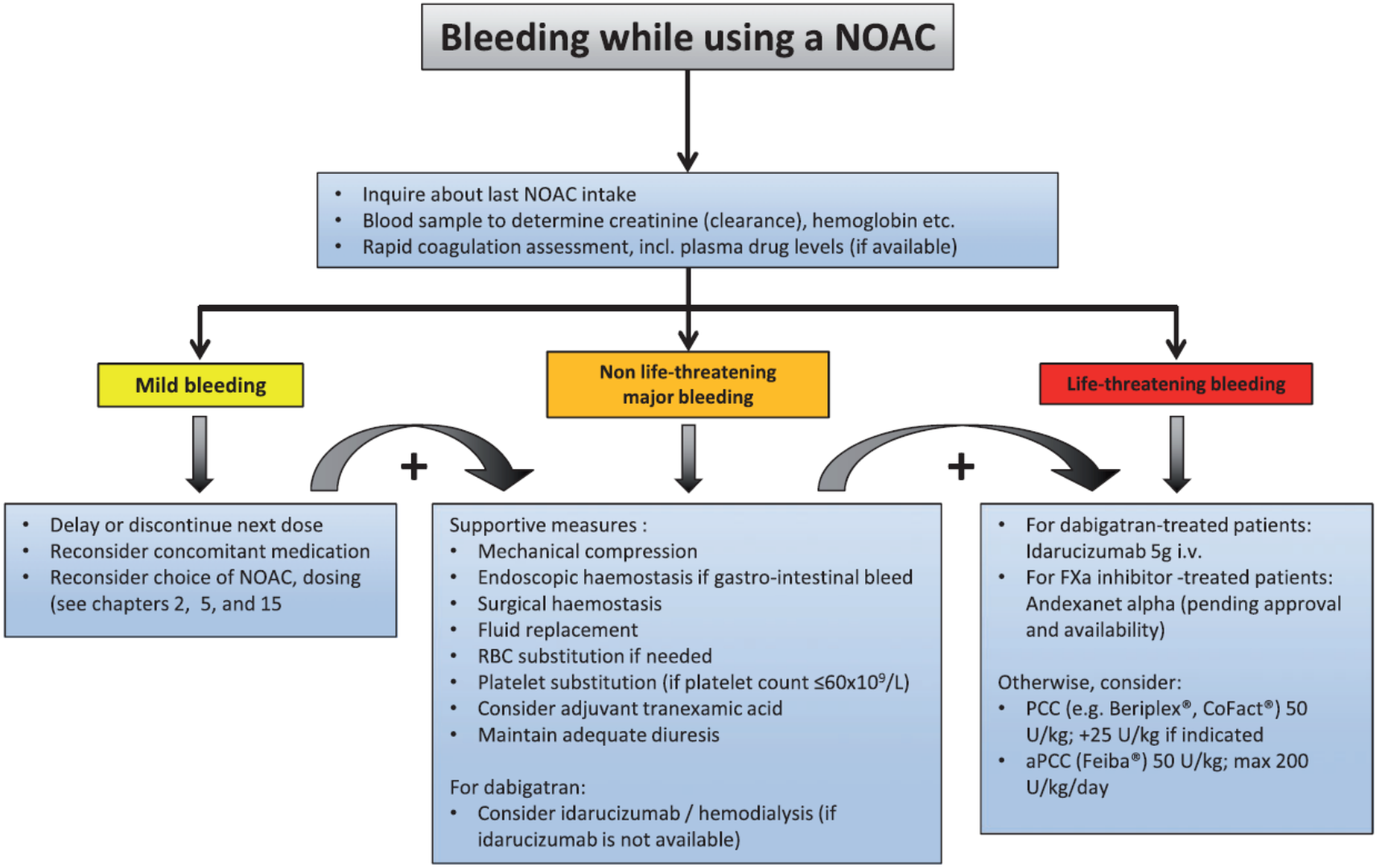
肝機能に対するスコアー

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.

凝固検査の有効性


Bleeding while using a NOAC
Inquire about last NOAC intake
Blood sample to determine creatinine (clearance), hemoglobin etc.
Rapid coagulation assessment, incl. plasma drug levels (if available)
Mild bleeding
Non life-threatening major bleeding
Life-threatening bleeding
+
+
Delay or discontinue next dose
Reconsider concomitant medication
Reconsider choice of NOAC, dosing (see chapters 2, 5, and 15
Supportive measures :
Mechanical compression
Endoscopic haemostasis if gastro-intestinal bleed
Surgical haemostasis
Fluid replacement
RBC substitution if needed
Platelet substitution (if platelet count ≤60x10⁹/L)
Consider adjuvant tranexamic acid
Maintain adequate diuresis
For dabigatran:
Consider idarucizumab / hemodialysis (if idarucizumab is not available)
For dabigatran-treated patients: Idarucizumab 5g i.v.
For FXa inhibitor -treated patients: Andexanet alpha (pending approval and availability)
Otherwise, consider:
PCC (e.g. Beriplex®, CoFact®) 50 U/kg; +25 U/kg if indicated
aPCC (Feiba®) 50 U/kg; max 200 U/kg/day

出血時の対応

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.

出血時の腎機能による対応の仕方

Table 12 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; . . .)
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 setting, e.g. congenital heart disease)
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)
Interventions with high bleeding risk AND increased thromboembolic risk
Complex left-sided ablation (pulmonary vein isolation; some VT ablations)

For each patient, individual factors relating to bleeding and thromboembolic risk need to be taken into account, and be discussed with the operating physician.

処置に関するリスクの層別化

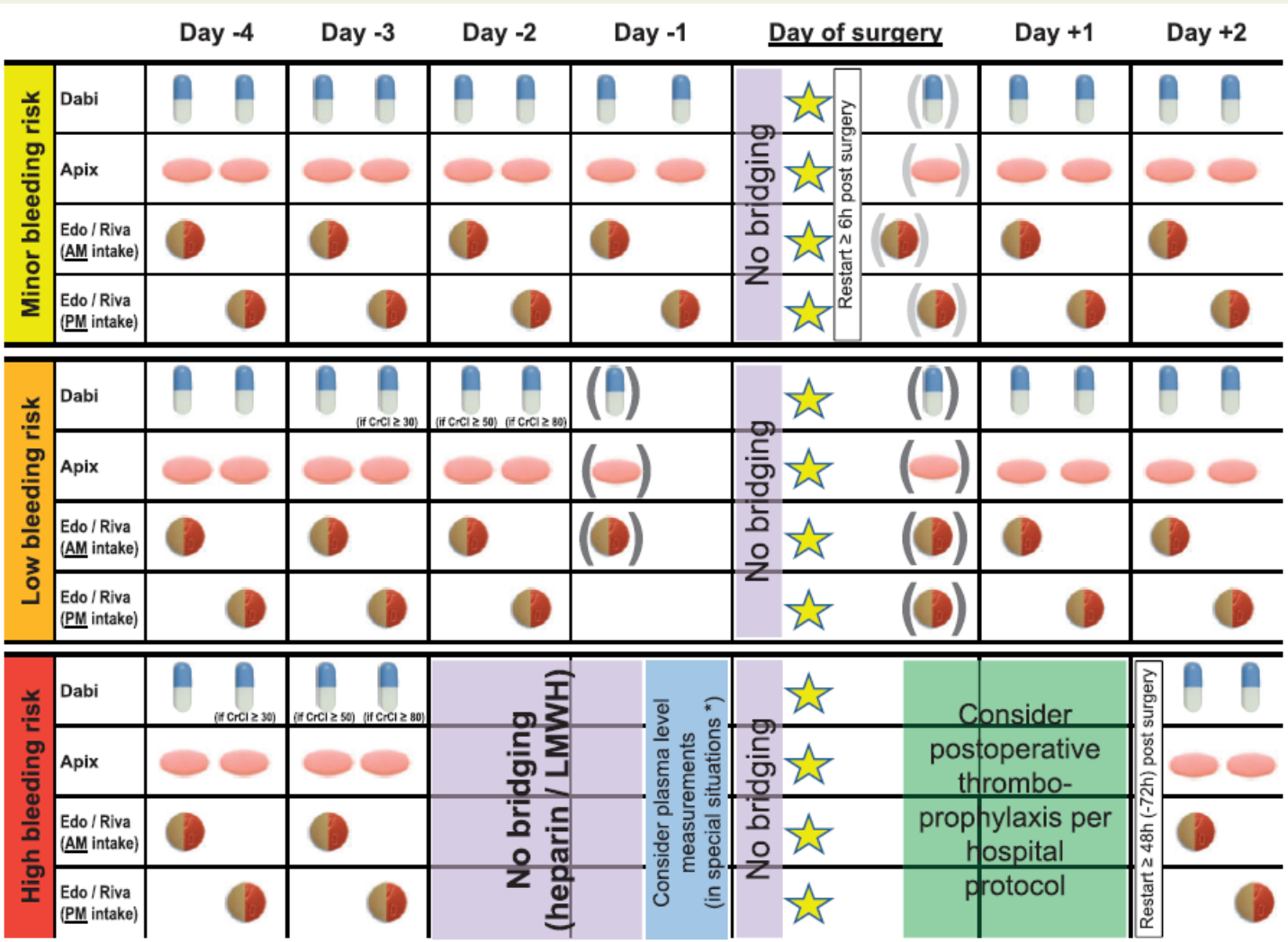
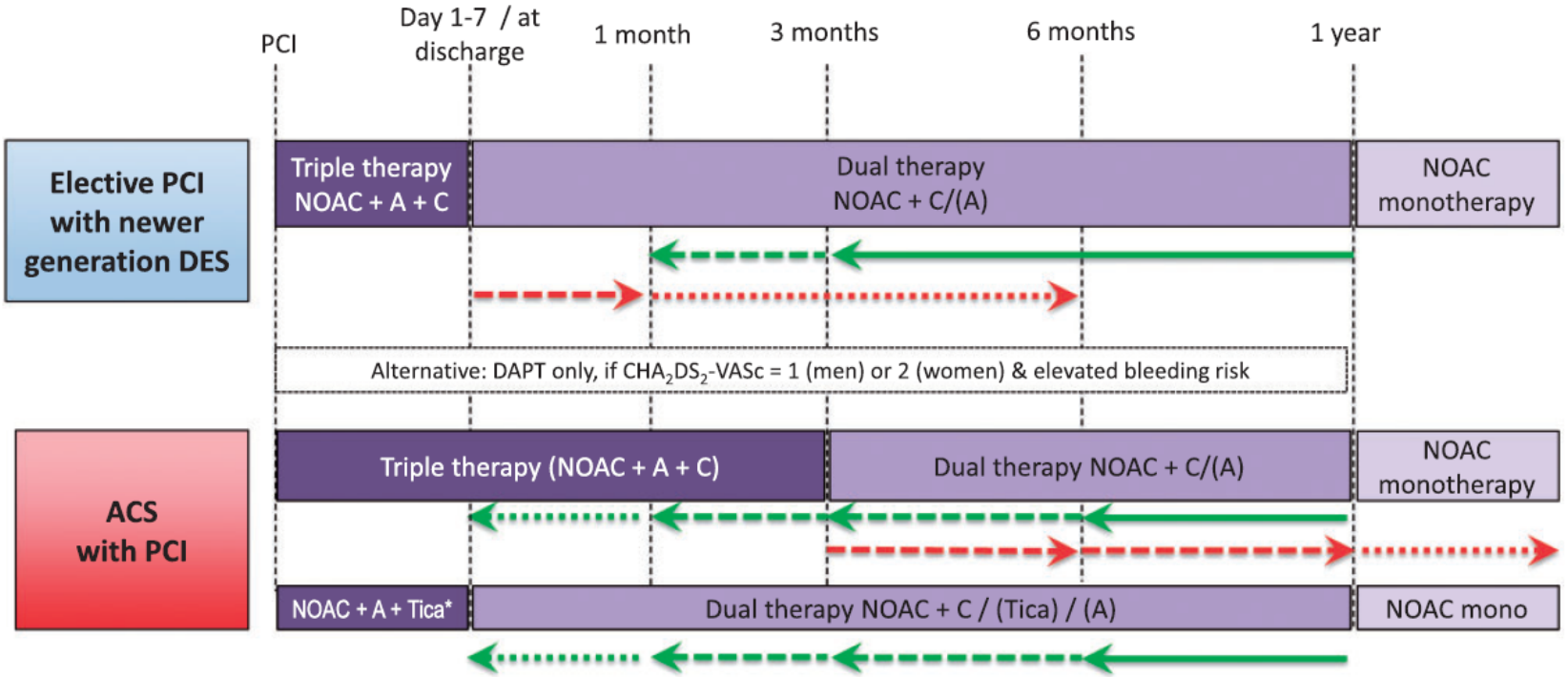


Figure 8 Stopping and re-initiation of non-vitamin K antagonist oral anticoagulant therapy in elective surgery. Yellow star, time point of the intervention/operation. Consider +24 h of interruption in situations likely resulting in increased plasma levels [e.g. patients taking verapamil, body weight <50 kg, significant interactions (see **chapter 5**)]. *Consider measurement of plasma levels (see **chapter 7**) in very special situations, e.g. highest risk neurosurgery/cardiac surgery, severe renal insufficiency, and combination of factors predisposing to higher non-vitamin K antagonist oral anticoagulant levels (see **chapter 5**). Rivaroxaban needs to be taken with food for stroke prevention in atrial fibrillation, which needs to be looked after (also) in the post-operative setting. Apix, apixaban; CrCl, creatinine clearance; Dabi, dabigatran; Edo, edoxaban; LMWH, low molecular weight heparin; Riva, rivaroxaban.



Factors to shorten combination therapy

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

Factors to lengthen combination therapy

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

冠疾患時の対応

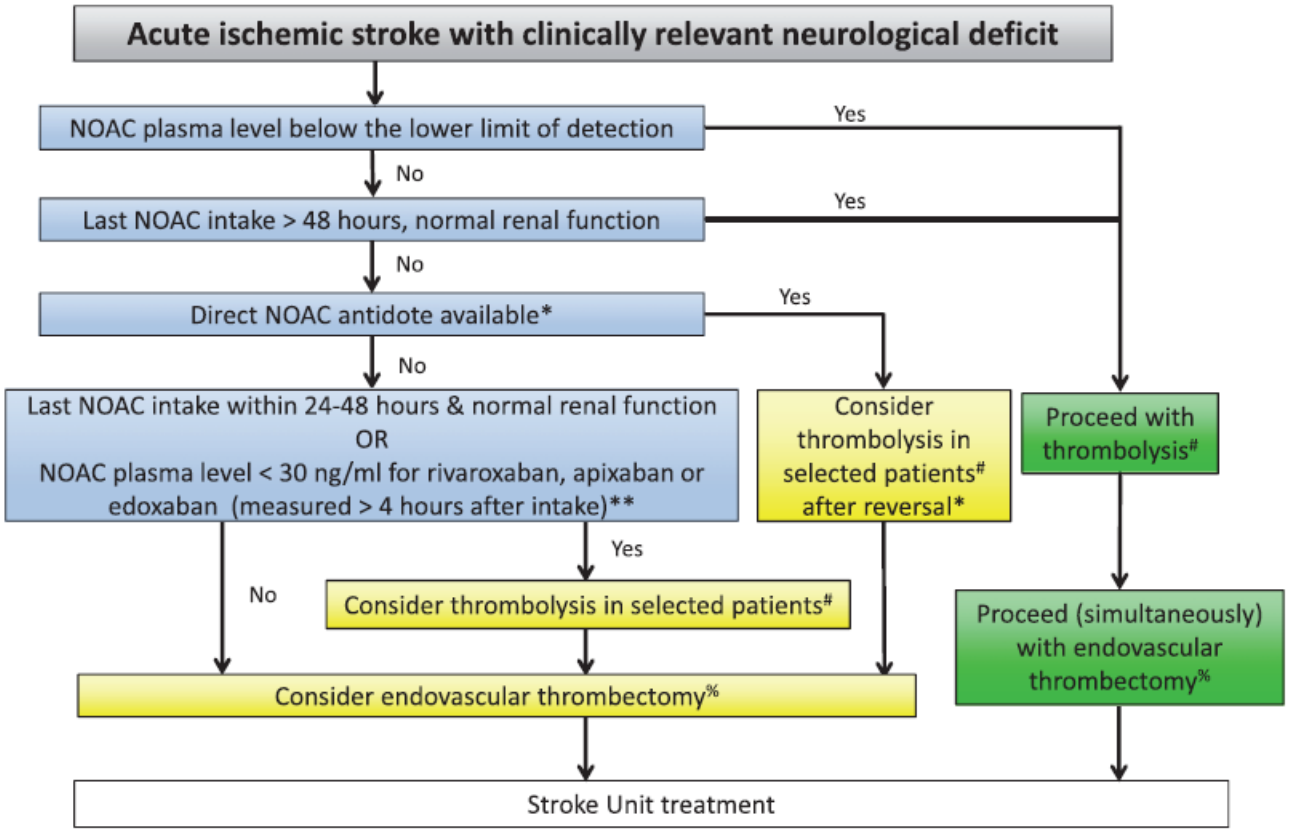


Figure 13 Acute management of acute ischaemic stroke in a patient on non-vitamin K antagonist oral anticoagulant. *Currently only available for dabigatran (idarucizumab). #Perform systemic thrombolysis only if there are no (other) contraindications for intravenous application of recombinant tissue plasminogen activator according to its label. %Perform endovascular thrombectomy only if there is a target vessel occlusion and procedure is indicated and feasible according to present evidence. **According to expert consensus.[370]

脳梗塞後の対応、本院ではとくにTIAが問題