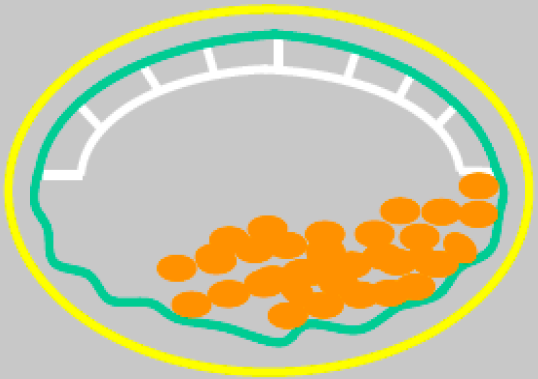
GESTION PERI-OPÉRATOIRE DES ANTICOAGULANTS

Cliniques universitaires SAINT-LUC UCL BRUXELLES

Bernard le Polain, Bamako 11.2019

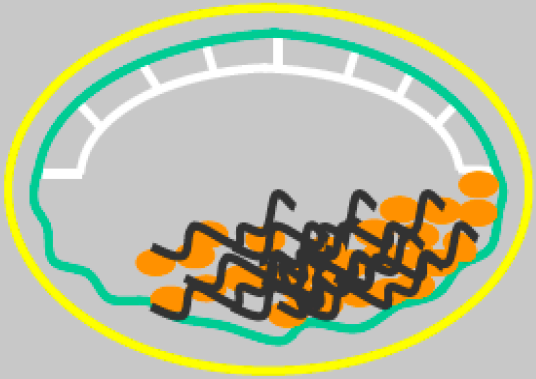
Le triptyque de la coagulation



1. Platelets plug

Primary Haemostasis

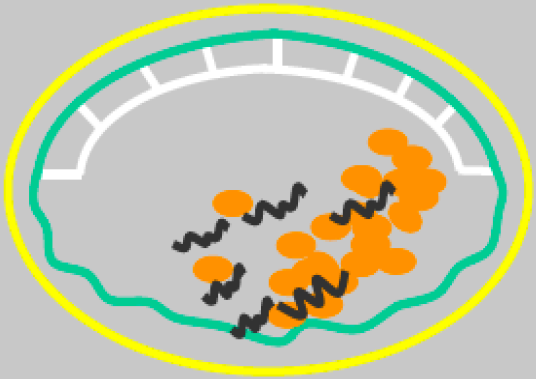
Platelets
Von Willebrand F



2. Fibrin Formation

Coagulation cascade

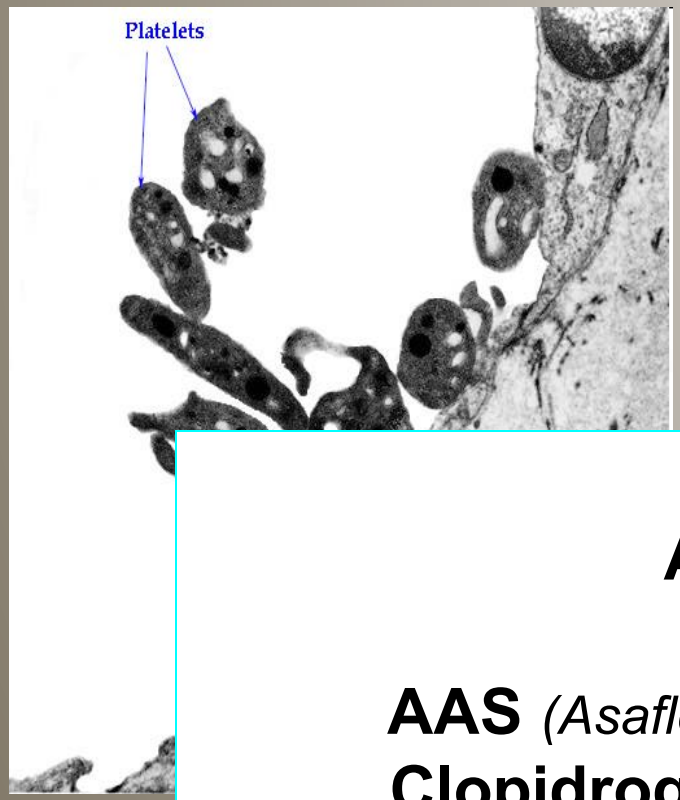
Coagulation factors



3. Clot destruction

Fibrinolysis

D'après prof C Hermans, 2019



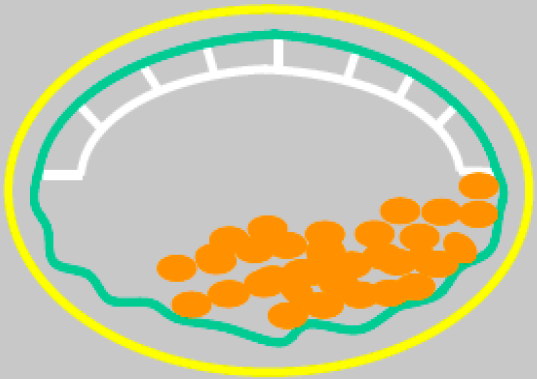
Hémostase primaire:
agrégation des plaquettes

Antiagrégants

AAS *(Asaflow)*
Clopidrogel *(Plavix)*
Nouveaux: Prasugrel *(Efient),* Ticagrelor*(Brilique)…*

Prévention primaire et secondaire

Le triptyque de la coagulation



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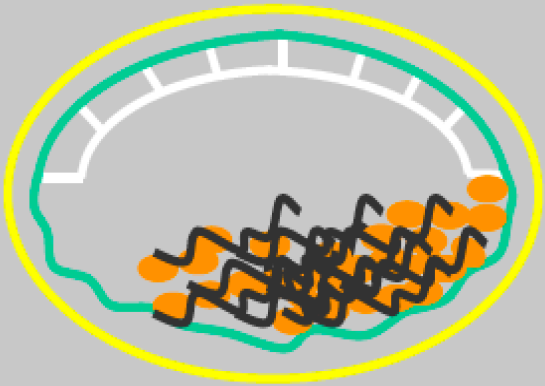

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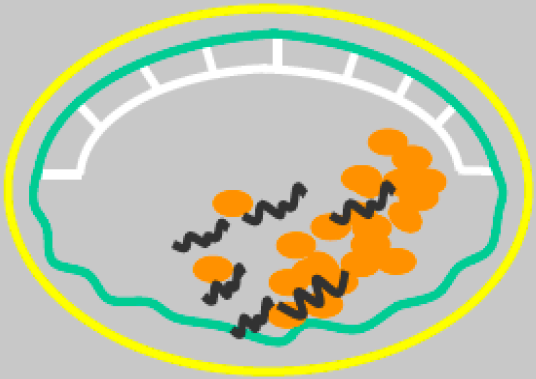
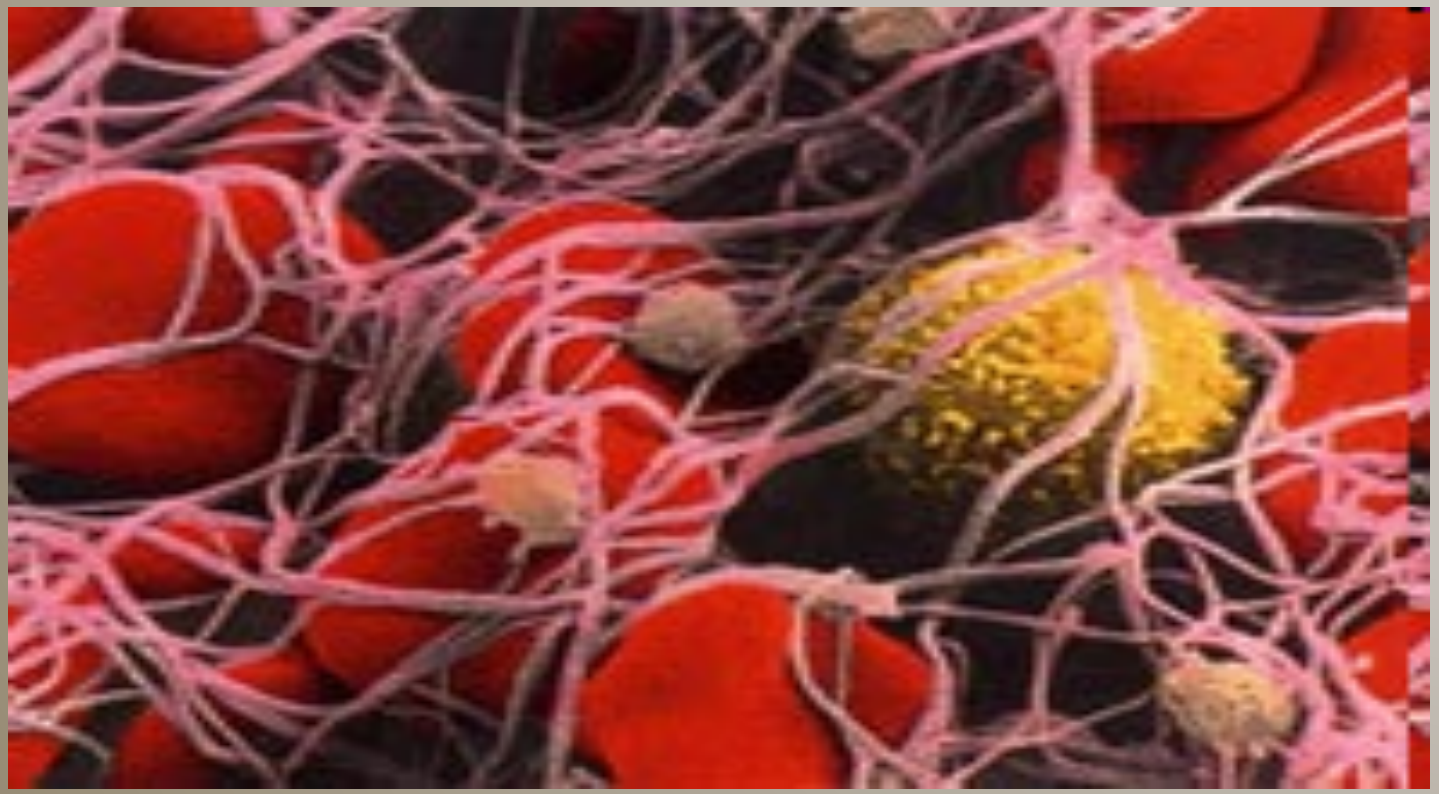


3. Clot destruction

Fibrinolysis

D'après prof C Hermans, 2019

FORMATION DU CAILLOT, HÉMOSTASE SECONDAIRE: CRÉATION D'UN RÉSEAU DE FIBRINE



COAGULATION

Anticoagulants

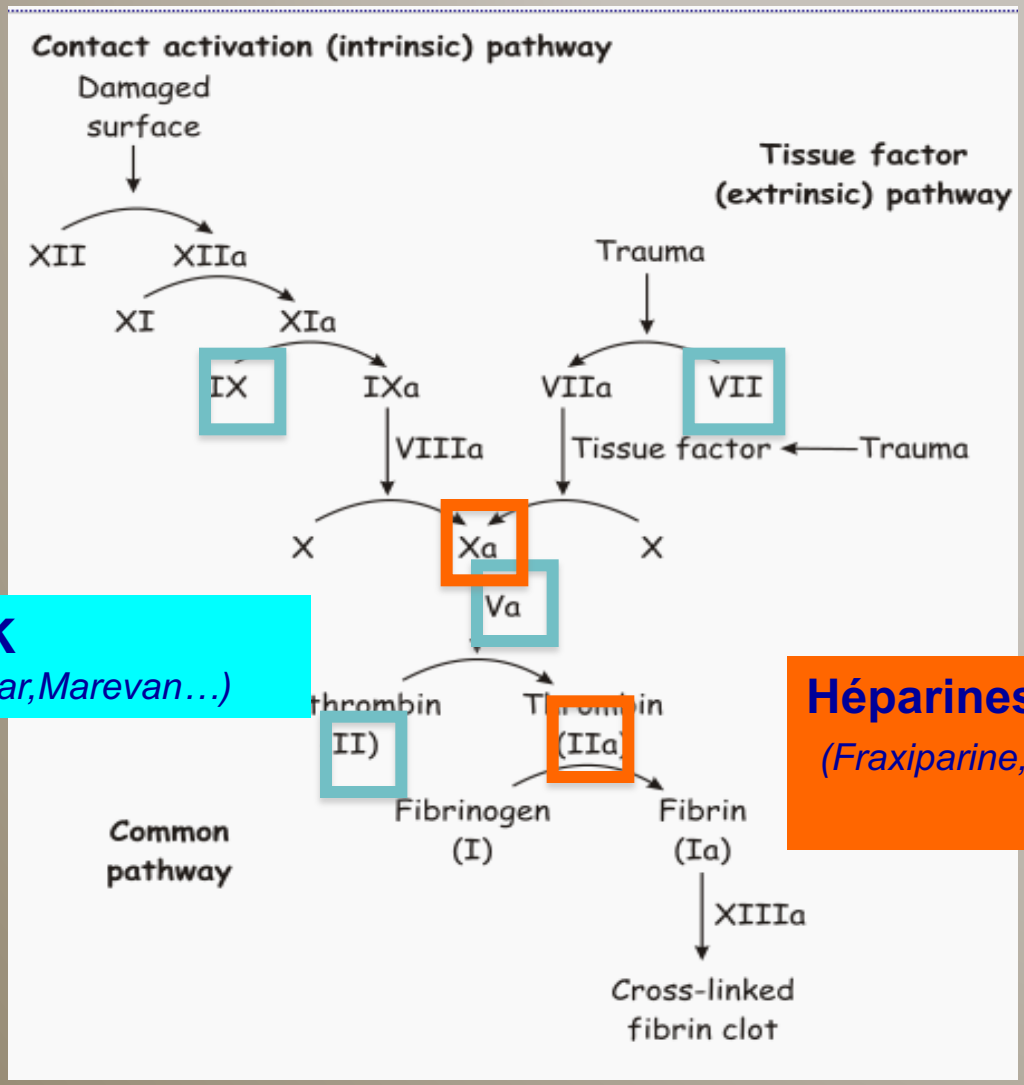
Héparines et HBPM (*Fraxiparine, Fraxodi, Clexane, Innohep…)*
Antivitamine K *(Sintrom, Marcoumar,Marevan…)*
Nouveaux Inhibiteurs

Xa Rivaroxaban *(Xarelto),* Apixaban *(Eliquis),* Edoxaban *(Lixiania)*

IIa Dabigatran *(Pradaxa)*

Maladie thromboembolique, FA, Valve mécanique…

D'après prof C Hermans, 2019



Antivitamine K
(Sintrom, Marcoumar,Marevan…)

Héparines et HBPM
(Fraxiparine, Fraxodi, Clexane, Innohep…)

Tableau 5

Patient sous antivitK (Acénocoumarol, Sintrom® ,phenprocoumone, Marcoumar®,Warfarine Marevan®), si une intervention nécessite une normalisation INR

	HBPM (1mg/kg) 2x/J Attention insuffisance rénale	HBPM 1mg/kg 1x/J Attention insuffisance rénale
J-8	Dernière prise Marcoumar	Dernière prise Marcoumar
J-6	Dernière prise Marevan	Dernière prise Marevan
J-4	Dernière prise de Sintrom	Dernière prise de Sintrom
J-3	Matin : HBPM Soir : HBPM	Matin : HBPM Soir : 0
J-2	Matin : HBPM Soir : HBPM	Matin : HBPM Soir : 0
J-1	Matin : HBPM Soir : 0 Si INR > 1,5 vitamine K 5 mg per os et contrôle INR à J0	Matin : HBPM Soir : 0 Si INR > 1,5 vitamine K 5 mg per os et contrôle INR à J0
J0	Matin : 0	Matin : 0
Fin de l'intervention + 6-8 heures Voir avec chir	Reprise HBPM	Reprise HBPM

RISQUE THROMBO-EMBOLIQUE EN CAS D'INTERRUPTION DE L'ANTICOAGULANT [1]

INDICATION DU TRAITEMENT AUX AVK

- Prothèse valvulaire cardiaque

Risque ELEVE (>10%)	• Prothèse mitrale • Ancienne prothèse aortique • AVC/AIT récent (< 6 mois)
Risque MODERE (5-10%)	• Prothèse aortique mécanique à ailettes avec facteurs de risque supplémentaires (FA, antécédents AVC/AIT, hypertension, diabète, insuffisance cardiaque, âge > 75)
Risque FAIBLE (2-5%)	• Prothèse aortique mécanique à ailettes sans facteurs de risque supplémentaires

- Fibrillation auriculaire

Risque ELEVE (>10%)	• Antécédent AVC/AIT récent (< 3 mois) • Score $CHADS_2$ 5 ou 6 • Maladie valvulaire rhumatismale
Risque MODERE (5-10%)	• Score $CHADS_2$ 3 of 4
Risque FAIBLE (2-5%)	• Score $CHADS_2$ ≤ 2

- Maladie veineuse thrombo-embolique

Risque ELEVE (>10%)	• TVP/EP récente (< 3 mois) • Thrombophilie sévère
Risque MODERE (5-10%)	• TVP ou EP endéans les 3 à 12 mois • TVP ou EP récidivante • Cancer actif • Thrombophilie légère
Risque FAIBLE (2-5%)	• TVP ou EP unique il y a plus de 12 mois et pas de thrombophilie

Relais par HBPM

	Risque ELEVE	Risque MODERE ou FAIBLE
Dernière prise de l'AVK	• Sintrom® : Jour - 4 • Marcoumar® : Jour - 8 • Marevan® : Jour - 6	
Dose d'HBPM		
JOUR DE L'		
	• Reprendre l'AVK 12-24h après l'intervention • HBPM jusqu'à INR > 2	

Réduire la dose de moitié en cas d'insuffisance rénale sévère (clearance de la créatinine < 30 ml/min).

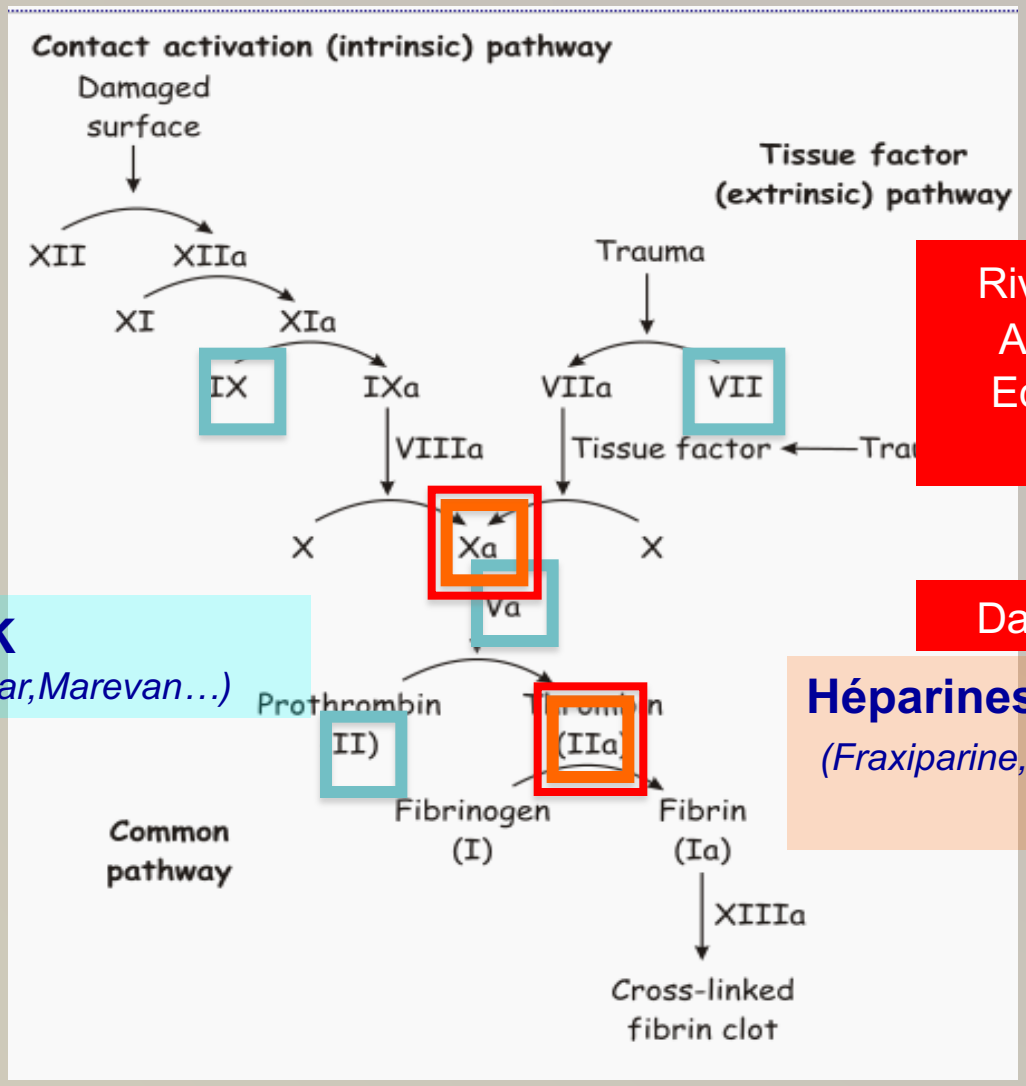
AVK= Anti-vitamine K; HBPM= Héparine de bas poids moléculaire

Score de $CHADS_2$

Congestion heart failure	1 point
Hypertension	1 point
Age > 75 ans	1 point
Diabetes	1 point
S_2 : stroke or TIA	2 point
TOTAL	**/ 6 points**

Maladie thrombo-embolique veineuse : reporter chirurgie au minimum 1 mois après épisode , de préférence 3 mois ; si chirurgie nécessaire avant un mois, discuter filtre cave.

D'après C Hermans



Antivitamine K
(Sintrom, Marcoumar,Marevan…)

Rivaroxaban *(Xarelto)*,
Apixaban *(Eliquis…)*
Edoxaban *(Lixiana)*

Dabigatran *(Pradaxa)*

Héparines et HBPM
(Fraxiparine, Fraxodi, Clexane, Innohep…)

Table 1: Properties of DOACs [13–16, 28].

	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Class	Oral thrombin inhibitor	Oral factor Xa inhibitor	Oral factor Xa inhibitor	Oral factor Xa inhibitor
FDA-approved indication	Reduction of stroke and SEE risk for patients with NVAF; treatment of DVT and PE following 5–10 days of parenteral anticoagulant; and reduction of recurrence risk for DVT and PE	Reduction of stroke and SEE risk for patients with NVAF; treatment of DVT and PE and reduction of recurrence risk for DVT and PE; prophylaxis of DVT in patients undergoing knee or hip replacement surgery	Reduction of stroke and SEE risk for patients with NVAF; treatment of DVT and PE and reduction of recurrence risk for DVT and PE; prophylaxis of DVT in patients undergoing knee or hip replacement surgery	Reduction of stroke and SEE risk for patients with NVAF and treatment of DVT and PE following 5–10 days of parenteral anticoagulant[a]
Time to C_{max} (h)	1-2	2–4	3-4	1-2
Half-life (h)	12–17	5–13	12	10–14
Renal elimination	80% of absorbed dose	66% of oral dose	27% of absorbed dose	50% of absorbed dose
Transporters[b]	P-gp	P-gp/BCRP	P-gp/BCRP	P-gp
Cytochrome P450 metabolism	No	Yes	Yes	Minimal
Bioavailability (%)	3–7	≥80[c]	50[d]	62
Potential drug interactions	Potent P-gp inhibitors and P-gp/CYP3A4 dual inducer rifampin	Potent dual CYP3A4 and P-gp inhibitors or inducers	Potent dual CYP3A4 and P-gp inhibitors or inducers	Potent P-gp inhibitors and P-gp/CYP3A4 dual inducer rifampin

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GIHP Groupe d'intérêt en hémostase péri-opératoire	Risque hémorragique faible	Risque hémorragique élevé		
Avant le geste	Pas de prise la veille au soir ni le matin de l'acte invasif	rivaroxaban apixaban edoxaban	Cockcroft ≥ 30 ml/mn	Dernière prise à J-3
		dabigatran	Cockcroft ≥ 50 ml/mn	Dernière prise à J-4
			Cockcroft 30-49 ml/mn	Dernière prise à J-5
	Pas de relai Pas de dosage			
Après le geste	Reprise à l'heure habituelle et au moins 6 h après la fin de l'acte invasif	Anticoagulant à dose « prophylactique » au moins 6 heures après l'acte invasif, si une thromboprophylaxie veineuse est indiquée		
		Anticoagulant à dose « curative » dès que l'hémostase le permet (à titre indicatif: entre 24 et 72 heures)		

Figure 1. Gestes invasifs à faible risque hémorragique

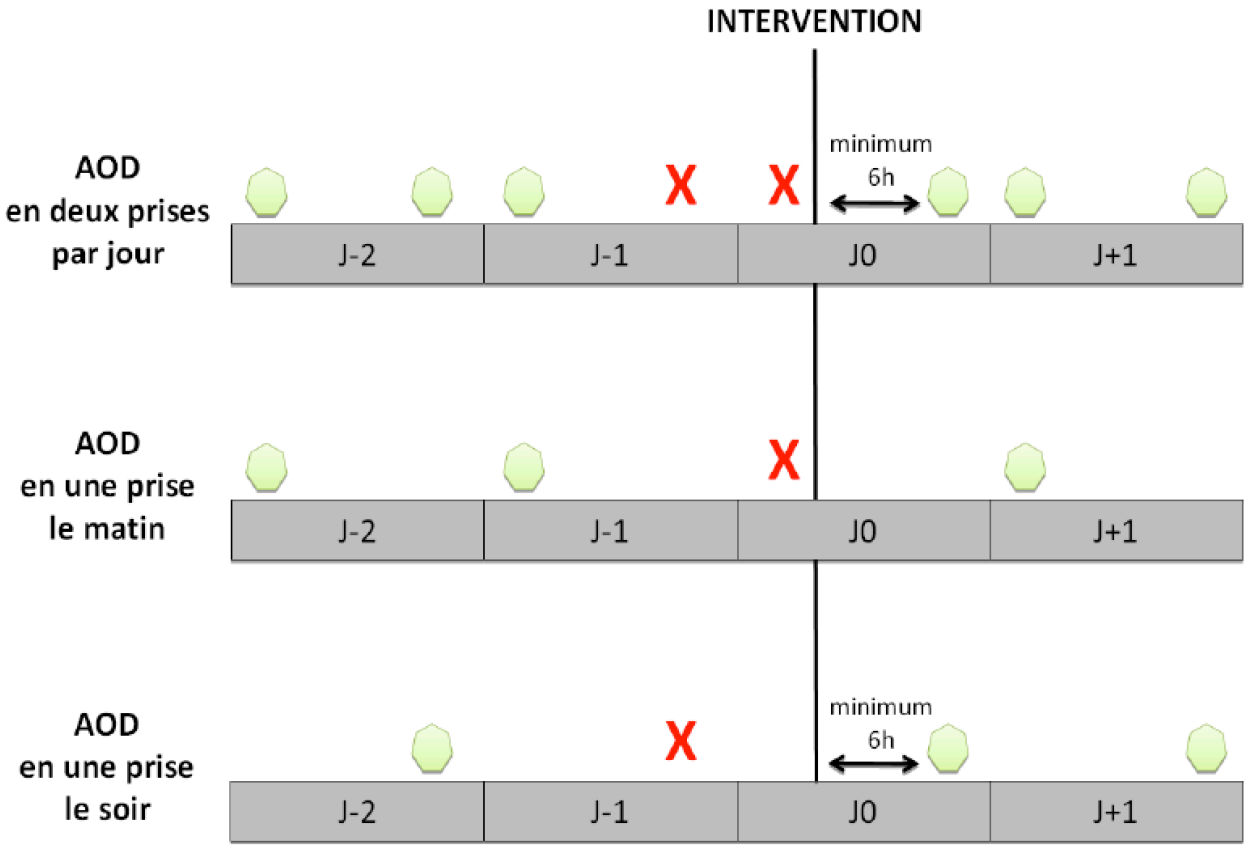


Tableau II – Règles d'interruption avant des interventions invasives de confort ou des opérations chirurgicale			
Fonction rénale CLCr (ml/min)	Demi-vie estimée (h)	Arrêter la prise de dabigatran avant la chirurgie de confort	
		Risque de saignement élevé ou acte chirurgical important	Risque normal
≥ 80	~ 13	2 jours avant	24 heures avant
≥ 50-< 80	~ 15	2-3 jours avant	1-2 jours avant
≥ 30-< 50	~ 18	4 jours avant	2-3 jours avant (> 48 heures)

C Hermans Louvain médical 2012

URGENCE

- Stop dabigatran
- Si avant 4 heures: charbon de bois
- Hydratation pour élimination rénale (80%)
- Hémodialyse (risque ponction)
- Antidote : Idarucizumab (Praxbind®)

Andexanet: reverse apixaban, rivaroxaban, edoxabanheparine et LMWH
Ciraparantag: tous les NOAC

Acide tranexamique (Exacyl®), pas cher, utile

$ $ $

Gestes invasifs

Tableau 5

Anticoagulants fonction intervention			
Intervention		Complication	Maintien/suppression
Chirurgie	en général	Saignement	Stop AVK Stop clopidrogel Maintien AAS
	Segment post oeil	Compression	Stop AVK Stop Clopidrogel Stop AAS
	Neurochirurgie	Compression intracranienne déçès	
	Prostate par voie transuréthrale	Saignement	
Anesthésie rachi ou péridurale (SFAR 2006)		Risque d'hématome, compression médullaire	Stop AVK Stop Clopidrogel * Maintien AAS
Blocs paravertébraux Sympatholyse (Welti 1951!)		Hématome rétropéritonéal Décès	?
Procédures dentaires mineures (Chest 2008)		Saignement	Continuer AVK Continuer AAS Clopidrogel Fct patient Agent prohémostatique oral
Procédures dermatologiques mineures (Chest 2008)		Saignement	Continuer AVK, AAS Clopidrogel fct patient
Cataracte (Chest 2008)		-	
Infiltration épaule corticoïdes (Goupille 2008)		Saignement/ hématome AAS 1%, AVK 10%	Continuer AVK,AAS, Clopidrogel ?
Angiographie artérielle (Meis 2009)		Hématome important 1,4% (f ≥ 5F, > 60 ans)	

* 5 jours suffisent d'après Berzon

ALR- RACHI- PERI

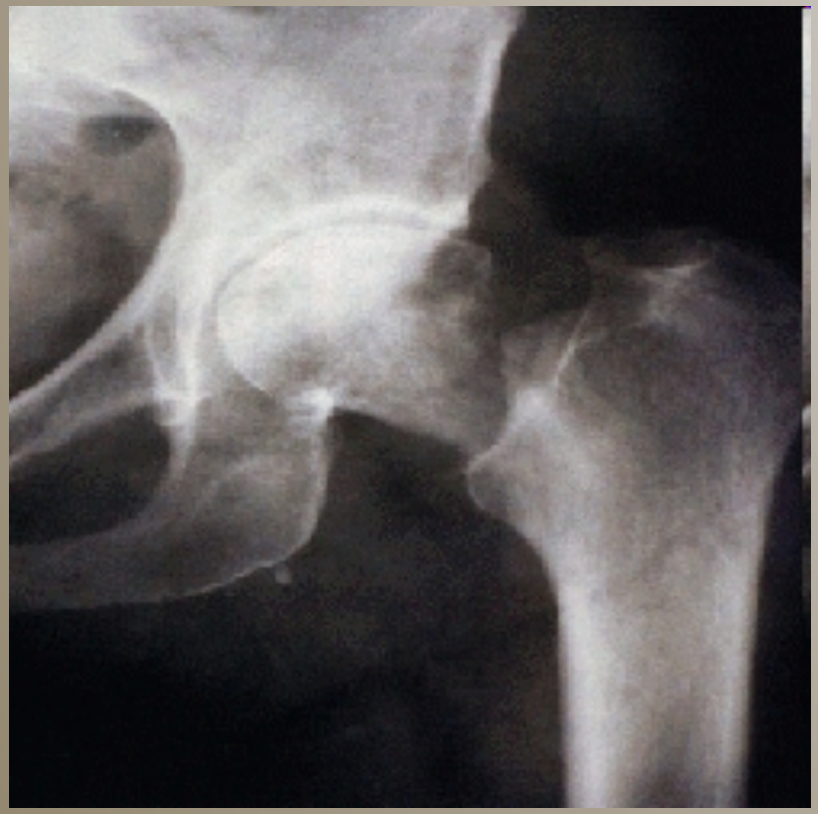
TABLE 6. Risk Factors and Estimated Incidence for Spinal Hematoma and Neuraxial Anesthesia

	Relative Risk of Spinal Hematoma	Estimated Incidence for Epidural Anesthesia	Estimated Incidence for Spinal Anesthesia
No heparin			
Atraumatic	1.00	1:220,000	1:320,000
Traumatic	11.2	1:20,000	1:29,000
With aspirin	2.54	1:150,000	1:220,000
Heparin anticoagulation following neuraxial procedure			
Atraumatic	3.16	1:70,000	1:100,000
Traumatic	112	1:2000	1:2900
Heparin >1 h after puncture	2.18	1:100,000	1:150,000
Heparin <1 h after puncture	25.2	1:8700	1:13,000
With aspirin	26	1:8500	1:12,000

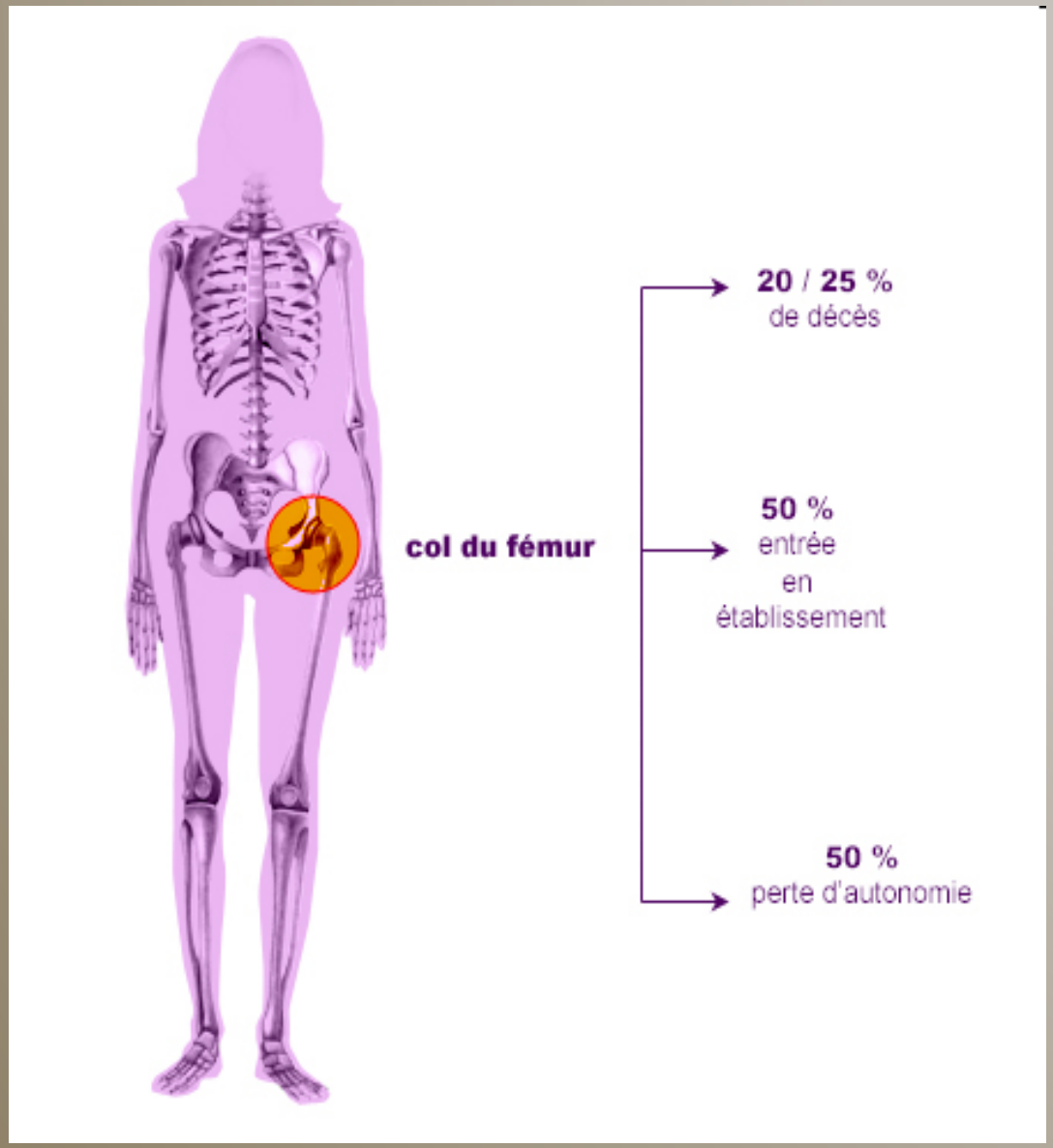
ALR RACHI- PÉRI

TABLE 7. European Society of Anaesthesiology's Recommended Time Intervals Before and After Neuraxial Puncture or Catheter Removal*

	Time Before Puncture/Catheter Manipulation or Removal	Time After Puncture/Catheter Manipulation or Removal	Laboratory Tests
UFHs (for prophylaxis, ≤15,000 IU/d)	4–6 h	1 h	Platelets during treatment for >5 d
UFHs (for treatment)	IV 4–6 h	1 h	aPTT, ACT, platelets
	SC 8–12 h	1 h	
LMWHs (for prophylaxis)	12 h	4 h	Platelets during treatment for >5 d
LMWHs (for treatment)	24 h	4 h	Platelets during treatment for >5 d
Fondaparinux (for prophylaxis, 2.5 mg/d)	36–42 h	6–12 h	(Anti–factor Xa, standardized for specific agent)
Rivaroxaban (for prophylaxis, 10 mg daily)	22–26 h	4–6 h	(Anti–factor Xa, standardized for specific agent)
Apixaban (for prophylaxis, 2.5 mg BID)	26–30 h	4–6 h	(Anti–factor Xa, standardized for specific agent)
Dabigatran (for prophylaxis, 150–220 mg)	Contraindicated according to the manufacturer	6 h	TT
Coumarins	INR ≤1.4	After catheter removal	INR



Personnes âgées
comorbidités



Intervention sans délai

Récupération meilleure

Orthop Traumatol Surg Res. 2016 Nov 15. pii: S1877-0568(16)30163-3. doi: 10.1016/j.otsr.2016.08.022. [Epub ahead of print]

Discontinuation of Plavix® (clopidogrel) for hip fracture surgery. A systematic review of the literature.

Mattesi L[1], Noailles T[1], Rosencher N[1], Rouvillain JL[2].

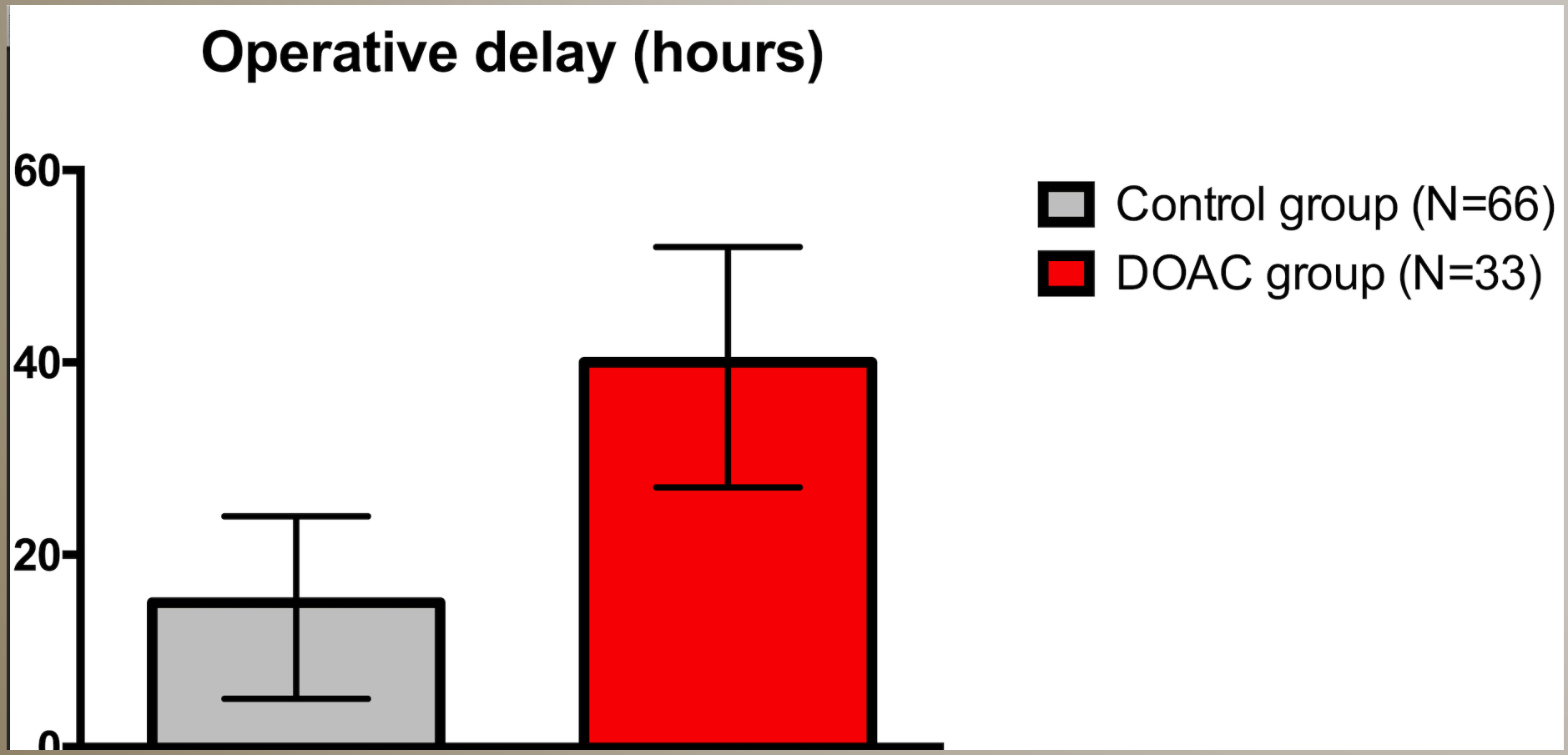
Safety of Clopidogrel in Hip Fracture Surgery

Molly A. Feely, MD, **Tad M. Mabry, MD**, **Christine M. Lohse, MS**, **Stephen A. Sems, MD**, and **Karen F. Mauck, MD, MSc**
Division of General Internal Medicine (M.A.F., K.F.M.), Department of Orthopedic Surgery (T.M.M., S.A.S.), and Division of Biomedical Statistics and Informatics (C.M.L.), Mayo Clinic, Rochester, Minnesota

Table

Preop variables	Control group	DOAC group	P value	Outcome variables	Control group	DOAC group	P value
Age (years)	87 (82 to 90)	85 (83 to 89)	0.784	Operative time (min)	48 (35 to 67)	50 (34 to 72)	0.859
Gender (M/F)	10 / 56	9 / 24	0.149	Hb POD1 (g/dl)	10.4 ±1.3	10.1 ± 1.5	0.303
BMI (kg/m2)	23 ± 4	24 ± 5	0.044	Hb end (g/dl)	10.0 ± 1.1	9.9 ± 1.4	0.675
ASA (II/III)	50 / 16	7 / 25	0.000	Blood loss (ml)	501 (364 to 856)	553 (299 to 1032)	0.484
CAD (%)	9	31	0.005	Patients transfused (%)	36	58	0.045
CKD (%)	23	58	0.001	RBC (units)	2 (1 to 2)	2 (1 to 2)	0.788
Hb (g/dl)	12.4 ± 1.4	12.5 ± 1.6	0.861	Complications (%)	30 (45)	19 (58)	0.255
Plts (10^3/mm^3)	239 (216 to 289)	226 (193 to 276)	0.335	Hospital LOS (days)	9 (5 to 23)	17 (8-28)	0.197
PT (%)	95 (86 to 100)	66 (52 to 85)	0.000	In op mortality (%)	3 (5)	5 (15)	0.068
aPTT (s)	23 (22 to 25)	28 (24 to 35)	0.000	30-day mortality (%)	3 (5)	5 (15)	0.068
Fibrinogen (mg/dl)	349 ± 68	385 ± 85	0.032	90-day mortality (%)	4 (6)	8 (24)	0.009

BMI: body mass index; ASA: American Society of Anesthesiologists score; CAD: coronary artery disease; CKD: chronic kidney disease; Hb: hemoglobin; Plts: platelets; PT: prothrombin time, aPTT: activated partial prothrombin time; POD1: postoperative day one; RBC: red blood cell; LOS: length of stay; in op mortality: in hospital mortality.



N Gautier, 2019

COMMENT JE FAIS ?

- Risque d'arrêter les anticoagulants?
- Héparine (HBPM) à disposition?

- Urgent: vitamine K à disposition?
- Accès à la transfusion? Au PFC? Autre?

- Compétence du chirurgien?

- Acide tranexamique (Exacyl)?

REGIONAL ANESTHESIA AND ACUTE PAIN

SPECIAL ARTICLE

Regional Anesthesia in the Patient Receiving Antithrombotic or Thrombolytic Therapy

American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Fourth Edition)

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TABLE 2. Recommendations for Thromboprophylaxis in Nonorthopedic Surgical Patients

	Risk of Major Bleeding Complications	
Risk of Symptomatic VTE	**Average Risk (~1%)**	**High Risk (~2%) or Severe Consequences**
Very low (<0.5%)	No specific prophylaxis	
Low (~1.5%)	Mechanical prophylaxis, preferably with IPC	
Moderate (~3.0%)	LDUH, LMWH, *or* mechanical prophylaxis, preferably with IPC	Mechanical prophylaxis, preferably with IPC
High (~6.0%)	LDUH *or* LMWH *plus* mechanical prophylaxis with ES *or* IPC	Mechanical prophylaxis, preferably with IPC, until risk of bleeding diminishes and pharmacologic prophylaxis can be added
High-risk cancer surgery	LDUH *or* LMWH *plus* mechanical prophylaxis with ES *or* IPC *and* extended-duration prophylaxis with LMWH postdischarge	Mechanical prophylaxis, preferably with IPC, until risk of bleeding diminishes and pharmacologic prophylaxis can be added
High risk, LDUH, and LMWH contraindicated or not available	Fondaparinux *or* low-dose aspirin (160 mg); mechanical prophylaxis, preferably with IPC; or both	Mechanical prophylaxis, preferably with IPC, until risk of bleeding diminishes and pharmacologic prophylaxis can be added

ES indicates elastic stockings; IPC, intermittent pneumatic compression; LDUH, low-dose UFH.
Adapted from Gould et al,[28] with permission.

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Table 2

Summary of recommended minimum time intervals or clotting times before and after central neuraxial needle puncture/catheter insertion, manipulation or removal of catheters*

Antithrombotic agent	Before puncture/catheter insertion/manipulation or removal	After puncture/catheter insertion/manipulation or removal	Laboratory investigations
LMWH (prophylactic dose)#	12 h	4 h	Platelet count if LMWH > 5 d
LMWH (intermediate or therapeutic dose)£	24 h	4 h	Platelet count if LMWH > 5 d
UH (therapeutic dose)	aPTT and/or ACT within normal range	1 h	aPTT, ACTPlatelet count if UH > 5 d
Fondaparinux	36-42 h	6-12 h	Anti-Xa activity – assay standardized for specific agent§
Rivaroxaban (≤ 10 mg/d)	22-26 h	6 h	Anti-Xa activity – assay standardized for specific agent§
Rivaroxaban (>10 mg/d)	3 d	6 h	Anti-Xa activity – assay standardized for specific agent§
Apixaban (≤ 2.5 mg bid)	26-30 h	6 h	Anti-Xa activity – assay standardized for specific agent§
Apixaban (> 2.5 mg bid)	3 d	6 h	Anti-Xa activity – assay standardized for specific agent§
Lepirudin	8-10 h	2-4 h	aPTT, ECT
Dabigatran (≤ 220 mg/d)	Contraindicated according to manufacturer	6 h	TT, ECT
Dabigatran (> 220 mg/d)	4 d	6 h	TT, ECT
Vitamin K antagonists	INR ≤ 1.4	After catheter removal	INR
NSAIDs	None	None	
Dipyridamole	None	None	
Acetylsalicylic acid	None	None	
Ticlopidin	10 d	After catheter removal	
Clopidogrel	7 d	After catheter removal	
Prasugrel	10 d	6 h	
Ticagrelor	7 d	6 h	
Eptifibatide / tirofiban	8-10 h	2-4 h	Platelet count
Abciximab	48 h	2-4 h	Platelet count

ACT, Activated clotting time ; aPTT, activated partial thromboplastin time ; ECT, ecarin clotting time ; INR, international normalised ratio ; NSAIDs, non-steroidal anti-inflammatory drugs ; TT, thrombin time. *All time intervals apply to patients with normal body weight and normal hepatic/renal function. #Maximum prophylactic dosages of low molecular weight heparins are listed in Table 4. £ Intermediate and therapeutic doses of LMWH are listed in Table 4. § Under development.

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- Acénocoumarol sintron 6.72 100 co 1mg 0.067 €/J
- Acénocoumarol sintron 6.25 20 co 4 mg
- Phenprocoumone Marcoumar 6.17 25 co 3 mg

- Rivaroxaban Xarelto 94,80 28 x 15 ou 20 mg 3.38 €/J
- Dabigatran Pradaxa 240,83 180 X 110 mg 1.33 €/j