

iCMP, ICH, invaze antiagregace, antikoagulace

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Liberec 24.4.2024



- ischemie / krvácení
- restart antikoagulační terapie
- Operace / LP a antikoagulační a antiagregační terapie

Mozková ischemie



iCMP

20-30% FiS
16-38% OACs
25% FiS de-novo

ICH

22-25% FiS
25-70% OACs assoc ICH

FiS

roční riziko ischemie

permanentní, persistentní	3%
paroxysmální	2%
subklinická (device detected)	1%

iCMP riziko recidivy 1% denně během 10 dnů

FiS preventabilní

Restart OACs po iCMP

1-2-3-4

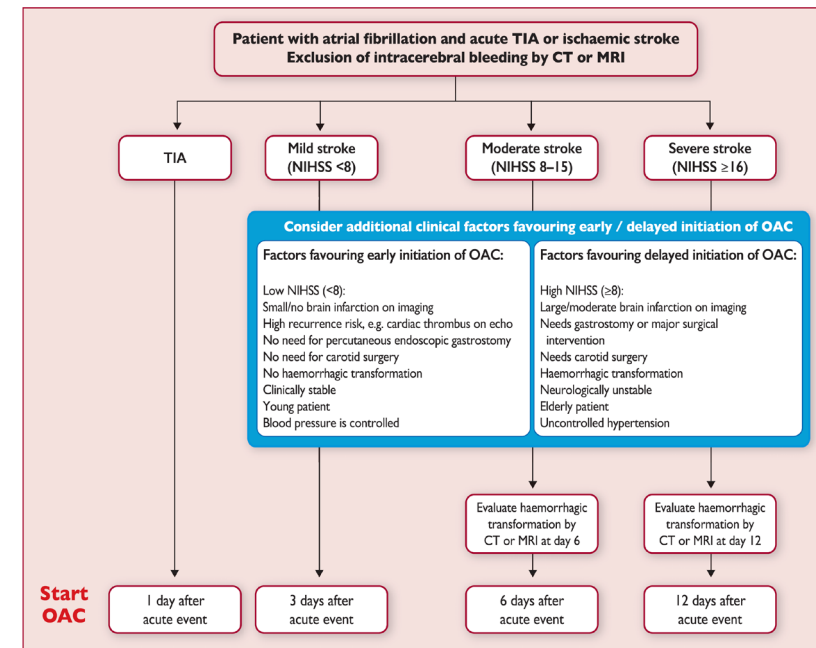
registr SAMURAI-NVAF

TIA - mild - moderate - severe stroke

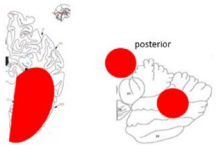
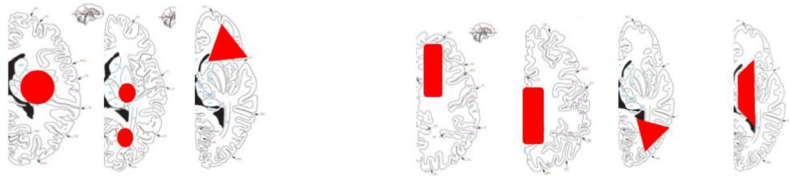
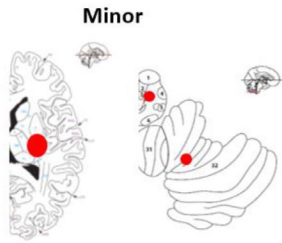
CMP/ systémová embolie
iCMP
Významné krvácení
Intrakraniální krvácení

Early vs late
NS

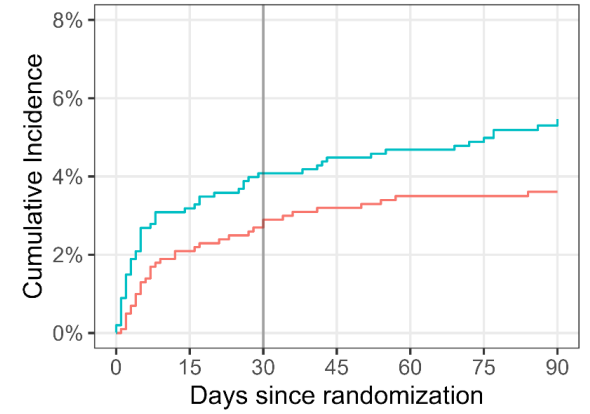
1-3-6-12



minor moderate major **ELAN**
EARLY LATE



	minor moderate	major
EARLY	<48h	6-7D
LATE	3-4D	12-14D



At Risk

Early	1006	975	957	946	940	933	583
Late	1007	969	949	938	929	919	558

		early	late
30D	composite	2,90%	4,10%
	iCMP	1,40%	2,50%
	ICH	0,20%	0,20%

„Imaging-based“ stratifikace - bezpečná pro restart DOACs po iCMP

Intracerebrální krvácení



Spontánní ICH

APT

incidence ICH	+/-
redukce SAH	
dávka ASA	bez vlivu
délka terapie	protektivní?
CMB	- vznik během terapie APT? - riziko ICH? - lobární vs hluboké - velikost
PLT transfuse	- nezlepšuje outcome

OACs

incidence	0,3-3,7%/rok	(10-15x vyšší)
OAC-ICH	- vyšší věk - extenzivnější morbidita - 60% významná invalidita - 40-50% mortalita	
FiS	22-25%	
	2/3	OACs
VKA	≈25% ICH	
DOAC vs VKA	- riziko ICH - mortalita	(40-65%) +/-

Restart APT po ICH

	EARLY < 30 D	LATE ≥ 31 D
recurrent ICH (1 rok)	3,12%	3,27%
iCMP	4,80%	4,18%
systémová embolie	8,02%	9,12%
velké krvácení	4,86%	6,11%
mortalita	9,17%	7,19%
	1-14D	15-30D
rICH	3,63%	3,94%
iCMP	4,83%	4,68%
mortalita	4,53%	9,06%

RESTART	APT	no-APT
Velké krvácení:	7%	9%
Velká ischemie	14%	20%

Medián nasazení APT: 76 dní

etiologie - spont / trauma
 lokalizace - hluboké / lobární
 nálezy na MRI - CMB

Restart APT ≤ 30 D
Vysoké riziko TE ≤ 14 D

Restart OACs po ICH

Multiparametrické zhodnocení

ischemický profil

rizika krvácení

etiologie, lokalizace

nálezy na MRI

CAA

DOAC vs VKA	- riziko ICH	(40-65%)
	- mortalita	+/-

Efekt OACS po ICH:

- snížení mortality a tromboembolismu 3x
- nevýznamný vliv na zvýšení ICH



Timing OACs

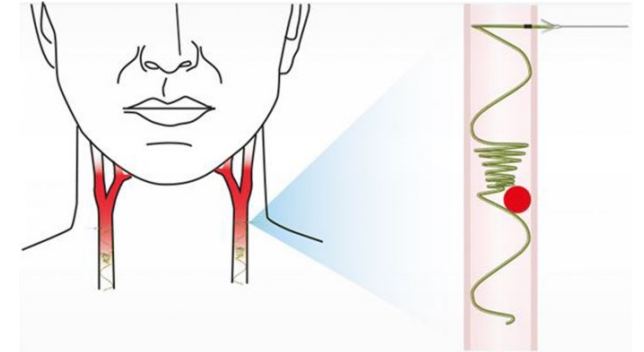
ANO / NE ?
timing
DOAC / VKA ?

Důležité faktory:

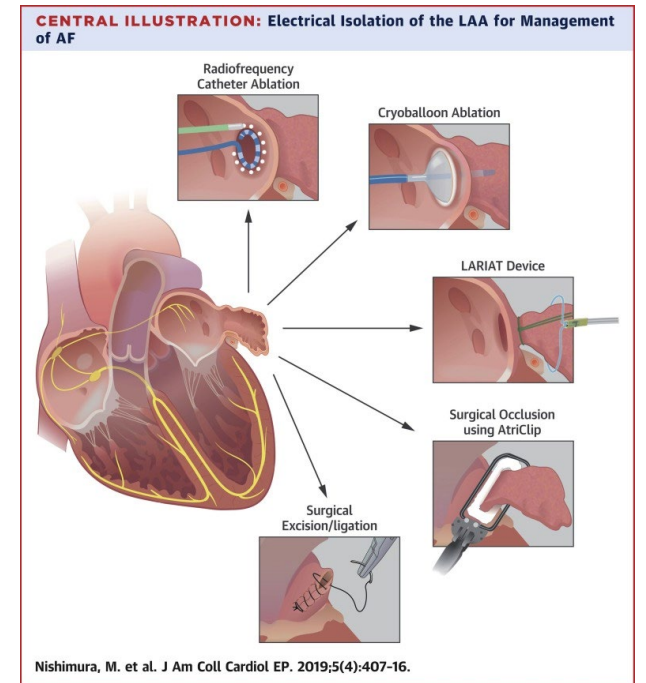
lokalizace ICH
mechanismus vzniku
OAC třída (VKA, DOAC, LMWH)
„reversal“
MHV
trombofilní stav
mozkové malignity
APOE

Alternativní řešení:

LAAO - noninferior (invazivita)
VCI - not applicable
INTERCEPT - RCT (superiority over OACs alone ?)



De Potter T et al. Current Cardiology Reports (2020) 22: 144



Nishimura, M. et al. J Am Coll Cardiol EP. 2019;5(4):407-16.

Timing OACs po ICH

ANO / NE
timing
DOAC / VKA ?

72h až 10-30T

- „optimální interval“ znovunasazení OACs

10-30 T
7-8 T

nejnižší kombinované riziko rICH a IS
maximální redukce iktu a vaskulární smrti

Guidelines	Year	Class of Recommendation (Level of evidence)	Resumption Recommendations
ACC Expert Consensus (158)	2017	-	Multidisciplinary approach for high-risk cases, 4-week waiting for DOACs
CHEST Guideline (117)	2018	Ungraded consensus-based statement	From 48 h to 4 weeks based on individual risk/benefit evaluation. DOAC preferred. LAA occlusion for high recurrent ICH risk
ESO-Karolinska Stroke Update (159)	2019	C	4-8 week waiting, individual decision-making, DOACs for NVAf
ESC Guidelines (82)	2020	Ila (C) Iib (B)	OACs re-initiation (2-4 weeks), after careful evaluation of individual risks and benefits, DOACs preferred. LAA occlusion for high recurrent ICH risk.
EHRA Practical Guide (160)	2021	-	4-8 week waiting after multidisciplinary team assessment, consider no anticoagulation or LAAO

ESC GDL 2020

4-8 wks

After ICH oral anticoagulation in patients with AF may be reinitiated after **4-8 weeks** provided the cause of bleeding or the relevant risk factor has been treated or controlled.

Iib

AHA/ASA GDL 2022

7-8 wks

posouzení individuálních benefitů a rizik

2022 Guideline for the Management of Spontaneous ICH

clinician and patient preferences. Therefore, timing should be considered on a **case-by-case basis** of individual risk assessments of thromboembolism, recurrent ICH, and late ICH expansion.

Greenberg SM, et al. Stroke. 2022 Jul;53(7):e282-e361.
Hindricks G, et al. Eur Heart J. 2021 Feb 1;42(5):373-498.

Restart OACs po ICH

ANO / NE
6-8 T (VKA)
DOAC / VKA

- 1) kompenzace HT
- 2) MRI - high-risk stavy - (cSS, cSAH)
- occurrence, recurrence
- 3) DOAC > VKA - riziko ICH (40-65%)
- mortalita +/-

OACs při CAA - nedostatek dat pro jednoznačný závěr

Lobární ICH + (CMB, cSS, cSAH) - OACs i LAA možné

LAAO - bezpečná alternativa, kde není jiná možnost

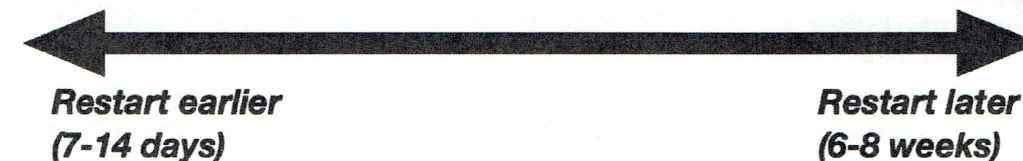
Restart OACs

ANO / NE ?
6-8 T (VKA)
DOAC / VKA

kompence RF - HT, DM, ...

důležité faktory

DOACs dříve, než VKA



1 ICH location	Deep	Lobar* (including CAA)
2 Mechanism of bleed	Traumatic	Spontaneous
3 Anticoagulant class	DOAC	Warfarin
4 Other considerations	Risk factors for thromboembolism: <ul style="list-style-type: none"> Mechanical prosthetic heart valves Malignancy AF with CHA₂DS₂-VASc ≥5 Previous stroke or TIA (< 3 months) Recent VTE (<3 months) High-risk thrombophilia† Risk factors for bleeding: <ul style="list-style-type: none"> Advanced age (>75 years) Uncontrolled hypertension (sBP >180 mmHg) Heavy alcohol use Labile or supratherapeutic INR (≥3.0) Thrombocytopenia (platelet count <50 x 10⁹/L) Concomitant antiplatelet or NSAID use Chronic kidney disease (CrCl <30 ml/min) Apolipoprotein E ε2 and ε4 polymorphisms 	

Z restartu OACs mohou těžit i pacienti s nepříznivým rizikovým profilem.



Operace / LP vs OACs, APTs



i. m. injekce - OACs

EMG, BoNT

trombotická rizika > rizika krvácení

INR v den aplikace - 2-3 (INR: 1,2-4,2)

kalibr jehly - co nejtenčí (25G a výše)

svaly - povrchové < hluboké

počet vpichů - co nejméně

hematom 0-5,2% vs 0-2,9%

kompartment sy 1 (konz)

Minor risk interventions (i.e. infrequent bleeding and with low clinical impact)

Dental extractions (1–3 teeth), paradental surgery, implant positioning, subgingival scaling/cleaning

Cataract or glaucoma intervention

Endoscopy without biopsy or resection

Superficial surgery (e.g. abscess incision; small dermatologic excisions, skin biopsy)

Pacemaker or ICD implantation (except complex procedures)

Electrophysiological study or catheter ablation (except complex procedures)

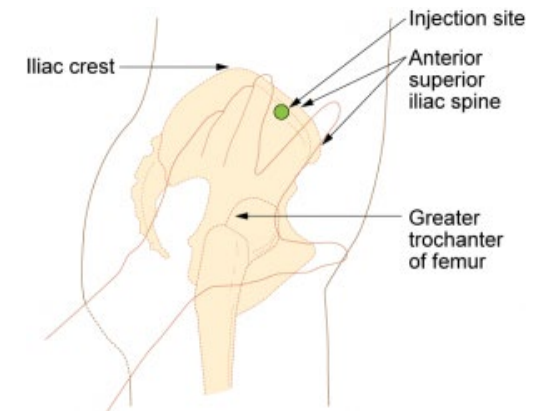
Routine elective coronary/peripheral artery intervention (except complex procedures)

Intramuscular injection (e.g. vaccination)

i.m. injekce

- vakcíny 0,6%
- PNC 0%
- muskuloskeletální injekce podlitiny: 8,2% (INR 3,2)
- analgetika?

ventrogluteální !!
deltoideus
vastus lateralis (stř 1/3)



American Association of Neuromuscular & Electrodiagnostic Medicine, 2017. Position statement: risks in diagnostic medicine. In: Medicine, A.A.o.N.E. (Ed.), American Association of Neuromuscular & Electrodiagnostic Medicine. <https://www.aanem.org/Advocacy/Position-Statements/Risks-in-Electrodiagnostic-Medicine>.

Tan YL, Wee TC. PM R. 2021 Aug;13(8):880-889.
Fox E et al. J Thromb Thrombolysis. 2020 Jul;50(1):237-238.
Schrader Ch et al. J Neural Transm (2018) 125:173–176

Operace a OACs - profil rizik

Tromboembolie

CHA₂DS₂-VASc
MHV
CMP/TIA
VTE

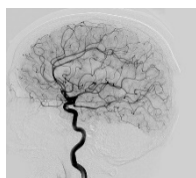
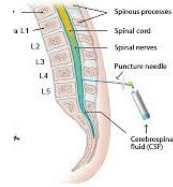
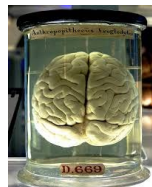
Risk Category	Mechanical Heart Valve	Atrial Fibrillation	VTE
High (> 10%/y risk of ATE or > 10%/mo risk of VTE)	Mitral valve <i>with</i> major risk factors for stroke ^b Caged ball or tilting-disc valve in mitral/aortic position Recent (< 3 mo) stroke or TIA	CHA ₂ DS ₂ VASc score ≥ 7 or CHADS ₂ score of 5 or 6 Recent (< 3 mo) stroke or TIA Rheumatic valvular heart disease	Recent (< 3 mo and especially 1 mo) VTE Severe thrombophilia (deficiency of protein C, protein S or antithrombin; homozygous factor V Leiden or prothrombin gene G20210A mutation or double heterozygous for each mutation, multiple thrombophilias) Antiphospholipid antibodies Active cancer associated with high VTE risk ^c
Moderate (4%-10%/y risk of ATE or 4%-10%/mo risk of VTE)	Mitral valve <i>without</i> major risk factors for stroke ^b Bileaflet AVR <i>with</i> major risk factors for stroke ^b	CHA ₂ DS ₂ VASc score of 5 or 6 or CHADS ₂ score of 3 or 4	VTE within past 3-12 mo Recurrent VTE Non-severe thrombophilia (heterozygous factor V Leiden or prothrombin gene G20210A mutation) Active cancer or recent history of cancer
Low (< 4%/y risk of ATE or < 2%/mo risk of VTE)	Bileaflet AVR <i>without</i> major risk factors for stroke ^b	CHA ₂ DS ₂ VASc score of 1-4 or CHADS ₂ score of 0-2 (and no prior stroke or TIA)	VTE > 12 mo ago

Operační riziko krvácení

High-bleed-risk surgery/procedure ^a (30-d 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 GI 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 min) Neuraxial anesthesia^b Epidural injections
Low-to-moderate-bleed-risk surgery/procedure ^c (30-d risk of major bleed 0%-2%)	Arthroscopy Cutaneous/lymph node biopsies Foot/hand surgery Coronary angiography ^d GI endoscopy ± biopsy Colonoscopy ± biopsy Abdominal hysterectomy Laparoscopic cholecystectomy Abdominal hernia repair Hemorrhoidal surgery Bronchoscopy ± biopsy
Minimal-bleed-risk surgery/procedure ^e (30-d risk of major bleed approximately 0%)	Minor dermatologic procedures (excision of basal and squamous cell skin cancers, actinic keratoses, and premalignant or cancerous skin nevi) Ophthalmologic (cataract) procedures Minor dental procedures (dental extractions, restorations, prosthetics, endodontics), dental cleanings, fillings Pacemaker or cardioverter-defibrillator device implantation



krvácení



BRIDGING

„patient-centric approach“

VKA

12 M
3

6 M
5

3 M
7

CMP, VTE
CHA₂DS₂-VASc

tromboembolie



bikus AoV

MHV, APLS, Ca, trombofilie



Minor-risk surgery



+ TnxA - výplach komprese

VKA

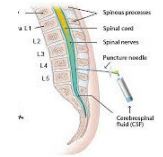


DOAC



delayed dose
omitted dose

High-risk surg/patient



← před

po →

VKA

5D OFF

věk
INR > 3,0



LMWH

ON +36h ; OFF -24h (12h)

< 24h ON



ON

12h



OFF

5D

DOAC



24h / 48h (72h) OFF

1D (30-36h)

2D (60-68h)

anti Xa - NO
drug level - NO

24h
(48-72h) ON

(LMWH 12h - 3D)

Operace a OACs

minimum risk: OACs bez vysazení!

low/moderate-risk:

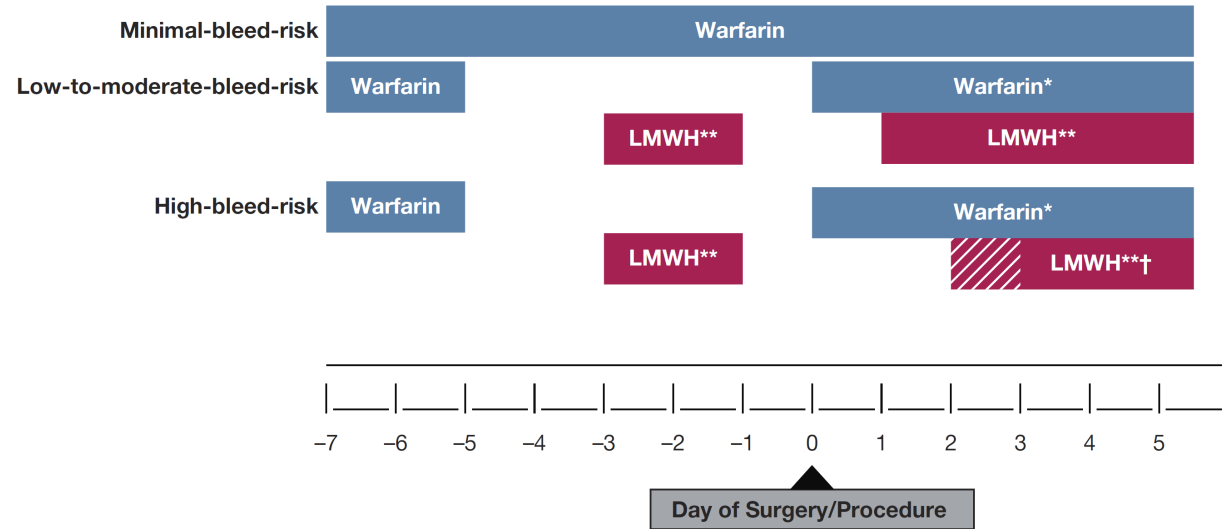
VKA: vysadit: -5D , INR ≤ 1,4
 restart: D0: večer (24h)
 (200% první dávka)

DOAC: vysadit: D-1 (D-2)
 restart: 24h (48-72h moderate/high risk)

LMWH bridging rutinně NE!

VKA: moderate/high risk 24h - (48-72h)
 postop - profylaxe 3-5D

DOAC: high-risk VTE profylaxe



Direct Oral Anticoagulant	Procedure Bleeding Risk	Pre-Procedure DOAC Interruption						Surgery/Procedure (Day 0)	Post-Procedure Resumption*			
		Day -6	Day -5	Day -4	Day -3	Day -2	Day -1		Day +1	Day +2	Day +3	Day +4
Apixaban	High							Surgery/Procedure (Day 0)				
	Low/Mod											
Dabigatran (CrCl ≥ 50 ml/min)	High											
	Low/Mod											
Dabigatran (CrCl < 50 ml/min)	High											
	Low/Mod											
Edoxaban	High											
	Low/Mod											
Rivaroxaban	High											
	Low/Mod											

□ No DOAC administered that day



APT / DAPT



Perioperační APT

ASA

Pokles efektu ASA

10% / D

„users“ < „non-users“

Perioperačně:

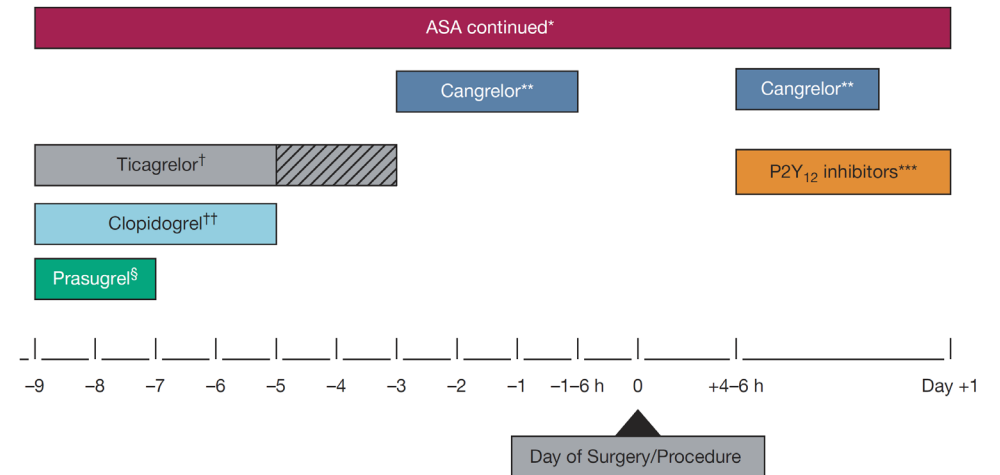
ASA - ponechat - users
- vysadit 2 D - high risk (NCH intraaxial)
- restart 3D (NCH intraaxial)

P2Y₁₂ - vysadit 3-7 D

DAPT - ASA ponechat
- P2Y₁₂ vysadit 3-7 D

Urgentní operace (CABG, ...)

Trombonáplavy - hemostatický efekt?



Obnova plného antiagregačního efektu:

ASA	minuty
ticagrelol	2h
prasugrel	3D
clopidogrel	4-5D

Operace po koronárních stentech

10-15% pacientů / 2 roky po implantaci

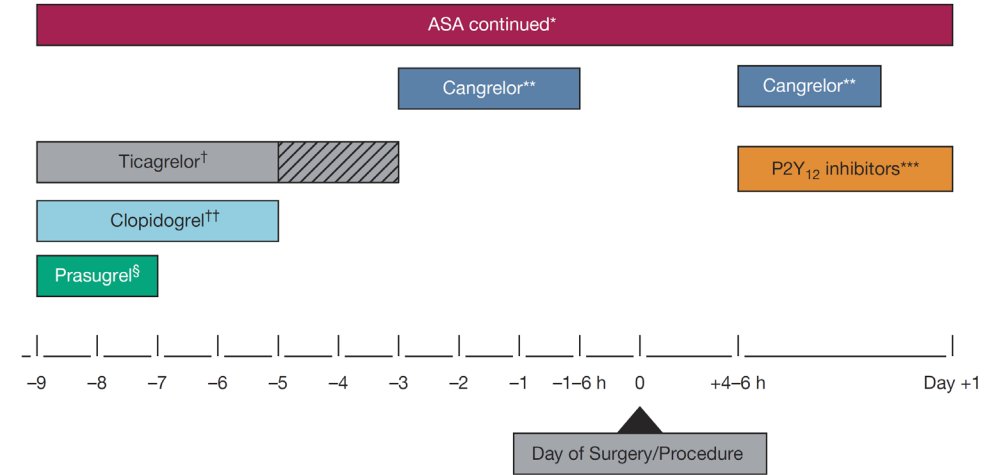
Důležité faktory:

- typ
 - DES (6-12 mth)
 - BMS (1 mth)
- uložení
 - dominantní CA
- počet
- délka

High-risk (TE): 2-4T po implantaci stentů!

Velká extrakardiální operace

	ASA	no-ASA
AIM:	5,1% vs	11,0%
velké krvácení:	4,6% vs	3,8%



Perioperačně:

- ASA - ponechat
- P2Y12 - vysadit na 3-10 D
- bridging
 - cangrelol (0,75ug.kg⁻¹.min⁻¹)
 - GPI (tirofiban, eptifibatide)

high-risk

Lumbální punkce ED a spinální anestezie/ intervence

Spinální ED hematom



Incidence 1:1341 - 1:200 000

Outcome - paraplegie, sfinktery
- 43% invalidita
- 23% smrt

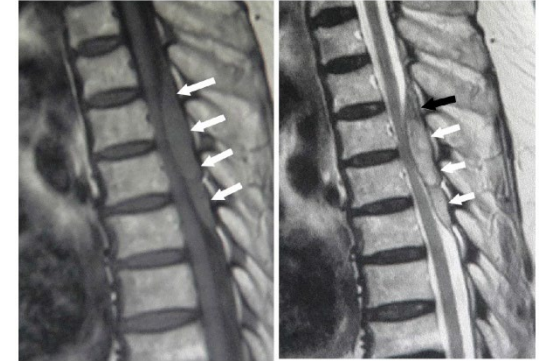
Rizika krvácení

- koagulopatie
- věk
- kalibr jehly
- opakovaná inserce
- páteřní patologie
- ED > spinální anestezie
- L > Th

Spinální hematom

- progresivní motorický deficit
- sfinkterová dysfunkce
- absence bolestí
- LP (spinální intervence) před několika dny
- dynamika 10-15h

MRI nejvyšší priorita
NCH intervence < 8h!!



LP a spinální anestezie - PŘED

KO, koagulace

- obligatorně NE

(známé krvácivé komplikace, genetika, jaterní, renální onemocnění)

hematolog

Normy: PLT > 40 x 10⁹/L
PT, INR < 1,5
APTT norma

Bridging: - high-risk tromboembolie

„high-risk“
- mortalita 3% vs 40%

VTE Patients with a VTE within the previous 3 months.
Very high-risk patients such as patients with a previous VTE while on therapeutic anticoagulation who now have a target INR of 3.5.

AF Patients with a previous stroke/transient ischaemic attack in last 3 months.
Patients with a previous stroke/transient ischaemic attack and three or more of the following risk factors:

- ▶ Congestive heart failure;
- ▶ Hypertension (>140/90 mm Hg or on medication);
- ▶ Age > 75 years;
- ▶ Diabetes mellitus.

MHV Mechanical heart valve patients other than those with a bileaflet aortic valve and no other risk factors.

LP - speciální situace

	Podmínka	Timing
VKA - urgence LP	Vit-K 5 mg i.v. PCC 30-50 IU/kg	> 6-8h dříve
dočasná antikoagulace	LP odložit (pokud lze)	ukončení AK > 3 měsíce
IVT - (před)	Fibrinogen > 1g/l	OK
IVT - (po)		> 10D
APT - urgence LP	PLT transfuze ?	?

Lumbar Puncture and Bleeding Risk

A brief guide to managing antiplatelets and anticoagulation in patients requiring lumbar puncture (LP).

Patient requires lumbar puncture

Consider Bleeding Risk

Performing an LP with coagulopathy increases the risk of spinal haematoma

- Routine coagulopathy testing in unselected patients is not recommended
- Consider a patient's risk of haemorrhage on an individual basis
- Consider checking platelet count is >40 x10⁹ and PT/APTT within normal range if high risk for coagulopathy:
 - liver or renal failure
 - heparin treatment for >5 days
 - haematological disorder
 - disseminated intravascular coagulation
 - personal/family history of unexplained bleeding

If at high risk for bleeding discuss with haematology team or consider postponing LP

Consider Thrombosis Risk

Suspending antithrombotic treatment comes with an increased risk of thrombosis

High risk for stopping anticoagulants:

- mechanical heart valves (apart from bileaflet aortic valves with no other risk factors)
- AF with stroke/TIA <3 months, or CHA₂DS₂-VASc score of ≥3
- VTE <3 months or previous VTE on therapeutic anticoagulation

→ Give bridging therapy with treatment dose low molecular weight heparin (LMWH)

Very high risk for stopping antiplatelets:

- drug eluting stent <12 months
- bare metal stent <1 month

→ Consider postponing LP

Intermediate risk:

- on dual antiplatelets or complex cardiac history

→ Consider aspirin bridging and discuss with cardiology

Urgent LPs: Patients may require an urgent LP outside of these time frames. Discuss with haematology about reversing warfarin and some DOACs. In other situations it may be decided that the benefit of an LP outweighs the increased bleeding risk, but the patient must be informed of this risk and be carefully monitored for new neurological symptoms or signs.

Discontinuing medications in patients with normal renal function

Medication	Withhold prior to LP	First dose after LP
Antiplatelets		
Aspirin low dose 75mg	Continue	No delay
Clopidogrel	7 Days consider aspirin cover	6 Hours
Prasugrel	7 Days	6 Hours
Ticagrelor	7 Days	6 Hours
Dipyridamole	24 Hours	6 Hours
Tirofiban + Eptifibatide	4-8 Hours	24 Hours
Abciximab	48 Hours	24 Hours
Anticoagulants		
Warfarin	5 Days check INR ≤1.4	12 Hours
LMWH prophylaxis	12 Hours	4 Hours
LMWH treatment	24 Hours	4 Hours (24 hours if traumatic)
Fondaparinux prophylaxis	36 Hours	6-12 Hours
Fondaparinux treatment	Avoid LP	Avoid LP
Unfractionated heparin IV	4-6 Hours	1 Hour
Rivaroxaban + Apixaban	24 Hours	6 Hours
Dabigatran	48 Hours	6 Hours

Bridging Protocol for High Risk Patients

Day	-5	-4	-3	-2	-1	LP	+1	+2	+3
Warfarin	X	X	X	X	X	X Check INR ≤1.4	Usual or double usual dose	Usual or double usual dose	Check INR
LMWH	X	Once INR subtherapeutic	✓	✓	Withhold at least 24hrs before	4 hours after	✓	✓	? Stop once INR in target range

Periprocedural antithrombotic management for lumbar puncture: Association of British Neurologists clinical guideline

Katherine Claire Dodd,^{1,2} Hedley C A Emsley,^{1,3} Michael J R Desborough,^{4,5} Suresh K Chhetri^{1,6}

Pract Neurol. 2018 Dec;18(6):436-446.

ESA
ACCP
ASRA
AAGBI
OAA
RA-UK
BSH

- European Society of Anaesthesiology
- American College of Chest Physicians
- American Society of Regional Anesthesia and Pain Medicine
- Association of Anaesthetists of Great Britain and Ireland
- Obstetric Anaesthetists' Association
- Regional Anaesthesia UK
- British Society of Haematology



Periprocedurální OACs - summary

			vysazení			bridging		restart			CAVE	
VKA			5D			high-risk TE		24h			Tranexamic wash/compress	
			INR < 1,3-1,4			postop 3-5D		48-72h			high-risk bleed	
						36h po VKA / pod th INR		12-24h	ACCP	LP	double dose/2D	ACCP
								cath removal	ESA	LP	usual dose	
											routine anti-Xa - ?	
UFH			2-4h	ASRA		0						
			4-6h	ESA		0						
			APTT ≤1,4	ASRA RA-UK		0						
LMWH	enoxaparin	prophylax	12h					2-4h	ESA			ESA
		treat	24h					24h	ACCP			ACCP
								4-24h	OAA			OAA
fondaparinux		2,5mg	36-42h					6-12h				
		5-10 mg	avoid									
DOAC	- xaban		24h (48h)			0		6h			anti Xa, hladiny - ??	
	dabigatran		48-72h			0		6h			high risk TE	

Periprocedurální APTs - summary

		vysazení		bridging		restart		CAVE
ASA		0		0		1-2h		high-bleed-risk
dipyridamol		10-12h	LP			6h		
		24h		0				
cilostazol		42h		0		5-6h		
P2Y ₁₂	clopidogrel	5D		0		0 LP; < 24h		
	ticagrelol	3-5D		0		0 LP; < 24h		
	prasugrel	7-10D		0		6h LP; < 24h		
	cangrelol	1-6h		0		6h		high-risk , 2-4Wks after coronary stent
GPI	eptifibatide	4-8h		0		24h		high-risk , 2-4Wks after coronary stent
	tirofiban	4-8h		0		24h		
	abciximab	48h		0		24h		

