

# Antitrombotická léčba po CMP: antikoagulancia či antiagregancia?

Petr Widimský

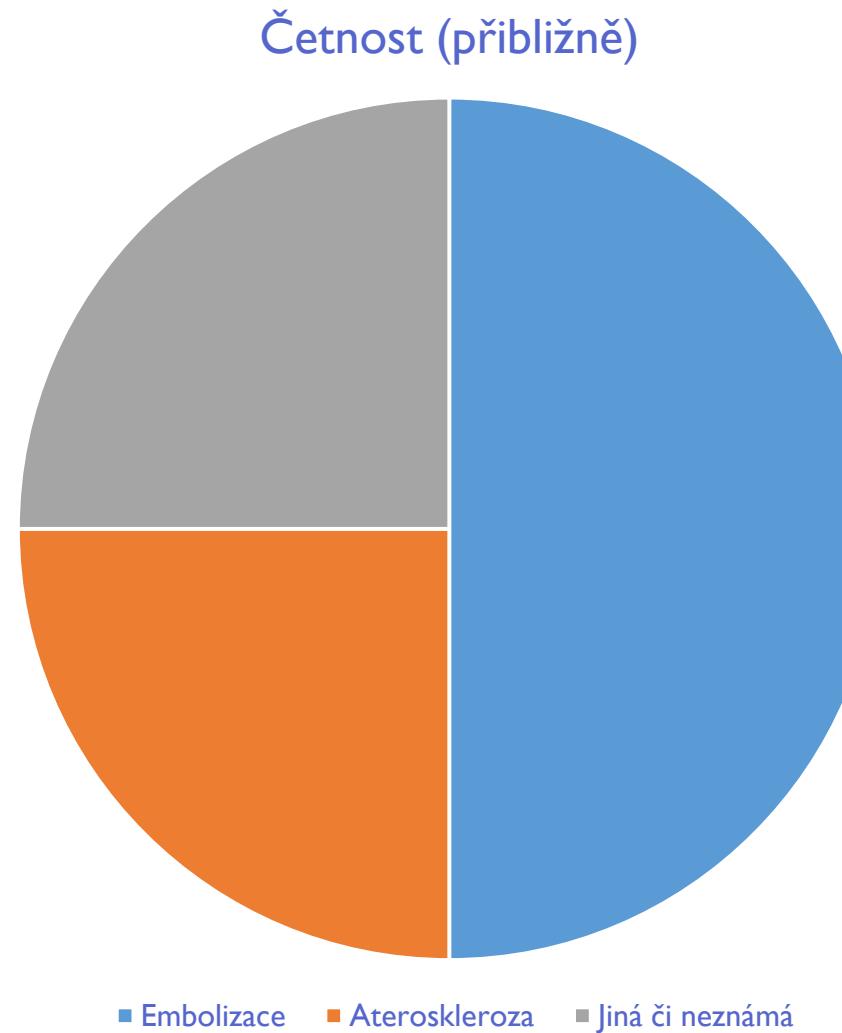
Kardiocentrum

FNKV a 3. LF UK Praha

**XXXI.** VÝROČNÍ SJEZD  
ČESKÉ KARDIOLOGICKÉ  
SPOLEČNOSTI



# Jaké jsou příčiny ischemických CMP ?



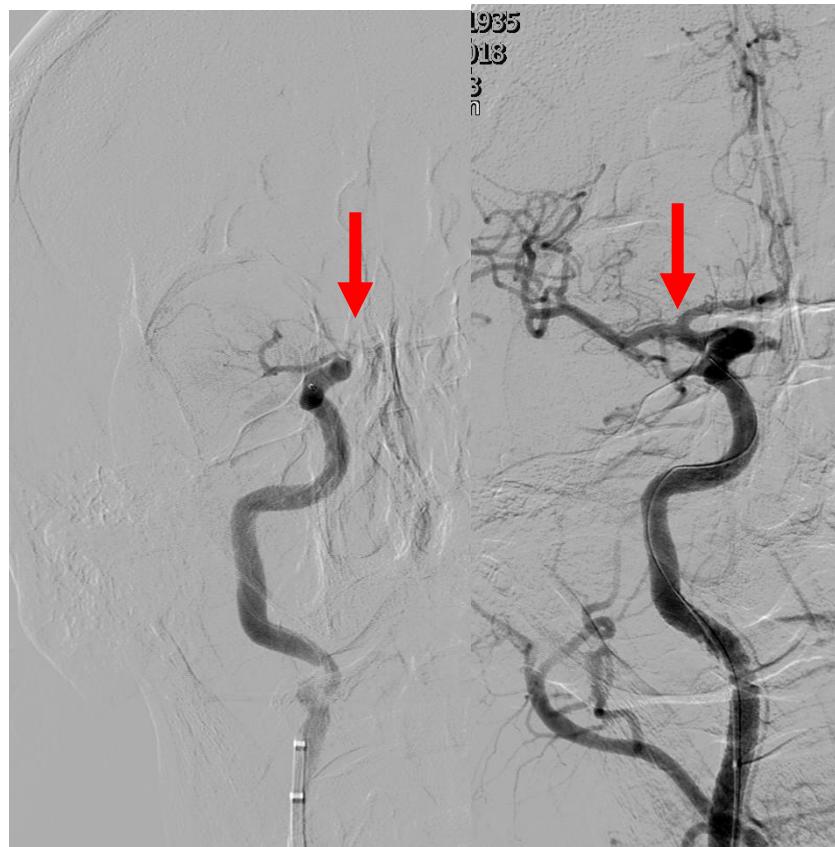
**Extrakran. stenóza ACI:  
ateroskleroza / aterotromboza**



**Intrakran. uzávěr ACM:  
embolus**



**T-uzávěr ACI: embolus**



**Uzávěr AB: aterotromboza**



# Guideline on pharmacological interventions for long-term secondary prevention after ischaemic stroke or transient ischaemic attack

Jesse Dawson, Yannick Bejot, Louisa Christensen, Gian Marco de Marchis, Martin Dichgans, Guri Hagberg, Mirjam Heldner, Haralampus Milionis, Linxin Li, Martin Taylor-Rowan, Cristina Tiu, Alastair Webb

6<sup>th</sup> May, 2022, 10.30am

European Stroke Organisation Conference, Lyon

# Antithrombotics

PICO 8: Does long-term antiplatelet therapy (compared to no antiplatelet therapy) reduce the risk of recurrent stroke?

## Evidence-based Recommendation

**Previous ischaemic stroke or TIA: recommend long-term use of antiplatelet therapy to reduce the risk of recurrent stroke.**

Quality of evidence: **Moderate** ⊕⊕⊕

Strength of recommendation: **Strong for intervention** ↑↑

# Supporting Information

## Recurrent Stroke

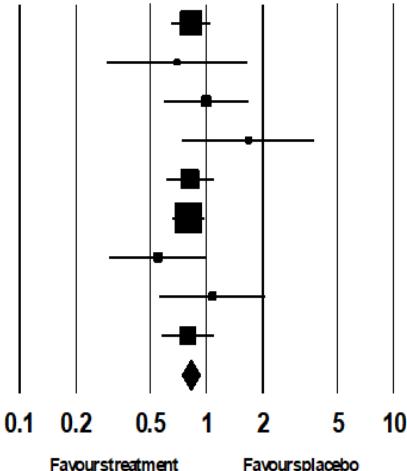
### Study name

#### Statistics for each study

	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
UK-TIA	0.827	0.648	1.055	-1.528	0.127
AITIA	0.696	0.291	1.663	-0.816	0.415
A Swedish Cooperative Study	0.995	0.589	1.682	-0.017	0.986
A Danish Cooperative Study	1.674	0.742	3.780	1.240	0.215
The SALT Collaborative Group	0.815	0.605	1.098	-1.347	0.178
ESPS2(aspirin)	0.799	0.655	0.974	-2.217	0.027
AICLA	0.550	0.301	1.004	-1.946	0.052
The Canadian Cooperative Study	1.073	0.557	2.068	0.210	0.833
CATS	0.789	0.571	1.090	-1.436	0.151
	0.821	0.731	0.922	-3.329	0.001

#### Odds ratio and 95% CI

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## MACE

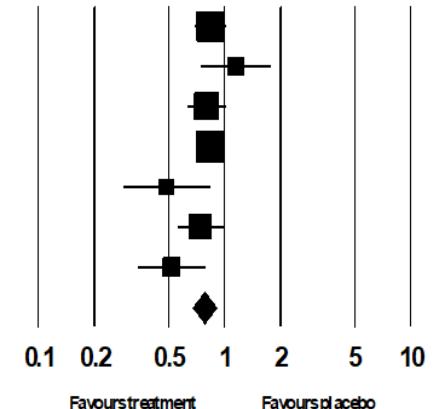
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#### Odds ratio and 95% CI

UK-TIA	0.835	0.686	1.018	-1.784	0.074
A Swedish Cooperative Study	1.153	0.746	1.782	0.642	0.521
The SALT Collaborative Group	0.801	0.628	1.022	-1.788	0.074
ESPS2(aspirin)	0.841	0.702	1.007	-1.883	0.060
AICLA	0.487	0.284	0.836	-2.608	0.009
CATS	0.744	0.557	0.994	-2.003	0.045
CSPS	0.518	0.340	0.790	-3.058	0.002
	0.778	0.673	0.900	-3.371	0.001



### Meta Analysis

## Meta Analysis

- Significant benefits for ischaemic stroke (0.67, 0.54-0.85), MACE (0.78, 0.67-0.90), MI (0.77, 0.61-0.98); NS for death, CV death, functional outcome
- Significant harms from any major bleeding (2.51, 1.42 – 4.43); NS increase for ICH.
- Mostly studies with aspirin. Later studies suggest at least equivalent efficacy with other single antiplatelets

PICO 9: Does DAPT (ASA + clopidogrel or dipyridamole) longer than 90 days (compared to a single antiplatelet) reduce the risk of recurrent stroke?

## Evidence-based Recommendation

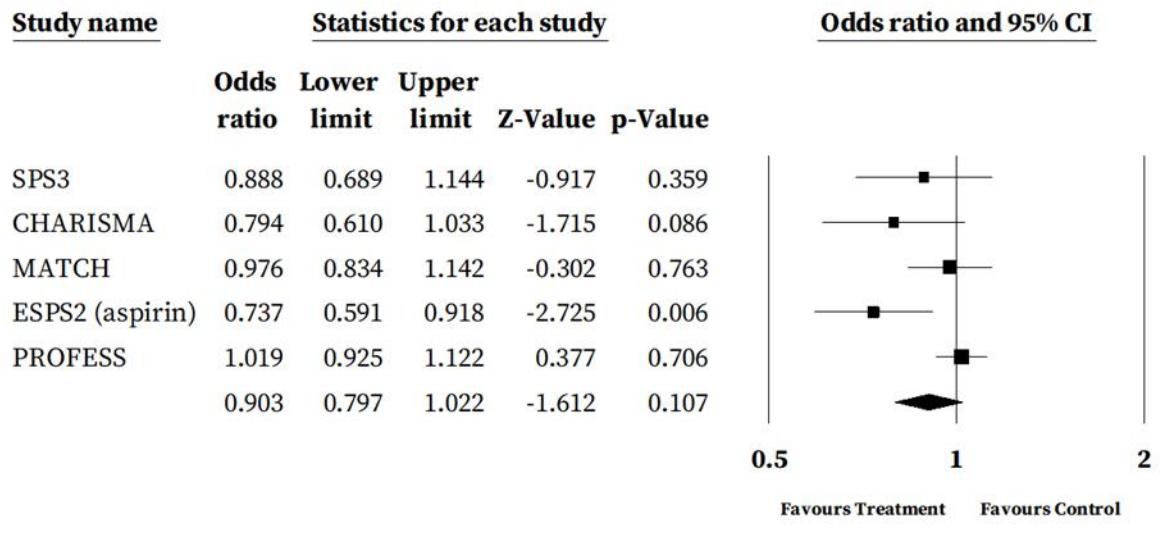
Recommend against long-term DAPT and recommend **single antiplatelet** after **90 days post-stroke** to reduce the risk of recurrent stroke.

Quality of evidence: **Very Low** 

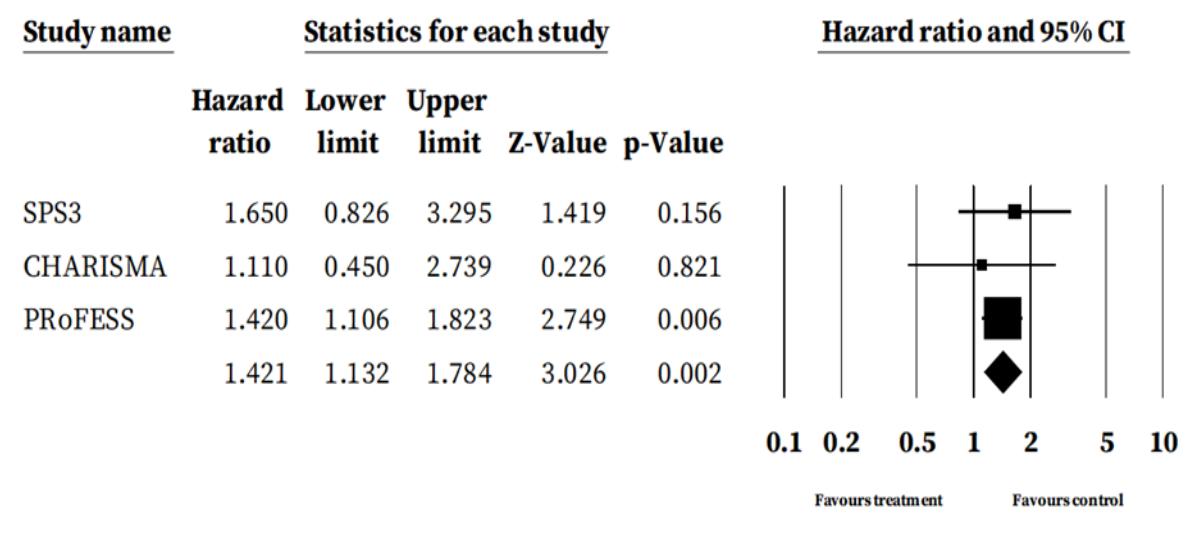
Strength of recommendation: **Weak against intervention ↓?**

# Supporting Information

## Recurrent Stroke



## ICH



Meta Analysis

- Non-significant reduction in recurrent stroke → NNT 8 per 1000
- Significant increase in intracerebral haemorrhage → NNH 4 per 1000

# Alternative Strategies: NOACs

## PICO 10 Expert Consensus Statement: Low dose NOAC + Antiplatelet

Antiplatelet therapy combined with low-dose rivaroxaban can be considered in CAD or PAD with a history of ischaemic stroke or TIA.

## PICO 11 Evidence-based Recommendation: NOAC vs Antiplatelet in ESUS

In people with an embolic stroke of undetermined source, we suggest use of antiplatelet therapy and not a DOAC to reduce the risk of recurrent stroke.

Quality of evidence: Low  $\oplus\oplus$

Strength of recommendation: Weak against intervention  $\downarrow?$

# European Stroke Organisation (ESO) guidelines on treatment of patients with intracranial atherosclerotic disease (ICAD)

Marios Psychogios; Elena López-Cancio; Gian Marco De Marchis ; Elena Meseguer; Aristeidis H. Katsanos; Christine Kremer; Peter Sporns; Marialuisa Zedde; Adam Kobayashi,; Jildaz Caroff; Daniel Bos, Sabrina Lémeret, Avtar Lal and Juan F. Arenillas

06.05.2022, Lyon, ESOC

# Symptomatic intracranial atherosclerosis

PICO 6:

In patients with an ischemic stroke or transient ischemic attack related to a high-grade stenosis related to ICAD and without any formal indication for anticoagulation, **does anticoagulant therapy, as compared to antiplatelet therapy, improve outcome?**

## Evidence-based Recommendation

In patients with an ischemic stroke or transient ischemic attack due to high-grade stenosis related to ICAD we recommend **against oral anticoagulation over aspirin** unless there is another formal indication for it.

Quality of evidence: Moderate ⊕⊕⊕

Strength of recommendation: **Strong against intervention ↓**

## PICO 7:

In patients with an ischemic stroke or transient ischemic attack related to intracranial stenosis related to ICAD, **does dual antiplatelet therapy, as compared to single antiplatelet therapy, improve outcome?**

### Evidence-based Recommendation

In patients with an ischemic stroke or transient ischemic attack related to intracranial stenosis due to ICAD **we suggest dual antiplatelet therapy over single antiplatelet therapy.** Regarding the duration of the dual antiplatelet therapy, we refer to the additional information.

Quality of evidence: Very low 

Strength of recommendation: Weak for intervention 

# Antitrombotika v akutní fázi iCMP

ASA: léčbu zahájit během 24-48 h po začátku příznaků (IA)

ASA + clopidogrel u malých (NIHSS<4) iCMP po vyloučení kardioembolické příčiny zahájit během 24 h a pokračovat 3 týdny až 3 měsíce (IA)

Role akutní antikoagulace při těsné stenóze ACI není jasná (IIbB)

Role NOAK v akutní fázi iCMP není jasná (IIbB)

Benefit profylaktické dávky LMWH (prevence ŽT/PE) u iCMP není přesvědčivě prokázán (IIbA)

Akutní antikoagulace není doporučenou léčbou akutní iCMP (IIIA)

# Antitrombotika po propuštění (sekundární prevence)

Non-kardioembolická iCMP: protidestičkové léky (IA)

Non-kardioembolická iCMP vzniklá při léčbě ASA: role změny protidestičkového léku na jiný není jasná (IIbB)

Non-kardioembolická iCMP vzniklá při léčbě kterýmkoli protidestičkovým lékem: výměna za warfarin není indikována (IIIB)

iCMP + FS: Zahájit OAC mezi 4.-14.dnem po začátku iktu (IIaB)

iCMP v anamnéze + FS + ICHS: role přidání protidestičkových léků k OAC není jasná (IIbC)

AKS a/nebo PCI + anamnéza iCMP + FS: trojkombinace (DAPT + OAC) může být vhodná (IIbC)

Akutní iCMP způsobená disekcí mozkové tepny artery (ACI či AV): protidestičková nebo antikoagulační léčba po dobu 3-6 měsíců (IIaB)

AIS

Day 1-3 search for  
ethiology

Cardioembolic  
ethiology

Non-  
cardioembolic  
stroke

Oral  
anticoagulants

Antiplatelet drugs

# Head-to-head efficacy and safety of rivaroxaban, apixaban, and dabigatran in an observational nationwide targeted trial

Yeela Talmor-Barkan  <sup>1,2,3,4,†</sup>, Nancy-Sarah Yacovzada <sup>3,5,6,†</sup>, Hagai Rossman <sup>3,4</sup>,  
Guy Witberg <sup>1,2</sup>, Iris Kalka <sup>3,4</sup>, Ran Kornowski  <sup>1,2,‡</sup> and Eran Segal <sup>3,4,\*‡</sup>

Data from 141 992 individuals with AF was used to emulate a target trial for head-to-head comparison of DOACs therapy.  
Final cohort: 56 553 patients (apixaban = 35 101; rivaroxaban = 15 682; dabigatran = 5 770).

# Graphical Abstract Six-years follow-up of 56,553 patients who were treated with apixaban, rivaroxaban or dabigatran for ...



A retrospective, nationwide, propensity matched-based observational study from Clalit Health Services.

## 56,553 PATIENTS

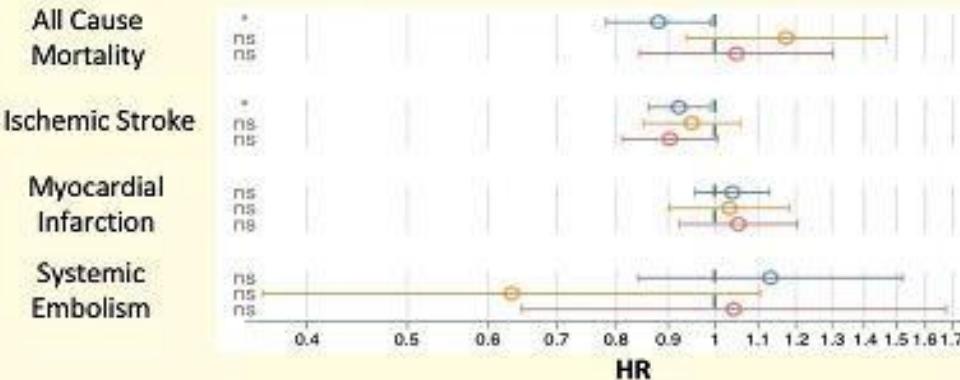
- Non-valvular atrial fibrillation
- eGFR>30mL/min/1.73m<sup>2</sup>
- Newly assigned to DOACs

Apixaban n=35,101	12.8%	1.0%
	28.9%	57.1%
Rivaroxaban n=15,682	9.3%	2.2%
	29.3%	59.1%
Dabigatran n=5,770	30.2%	2.8%
	21.9%	45.0%

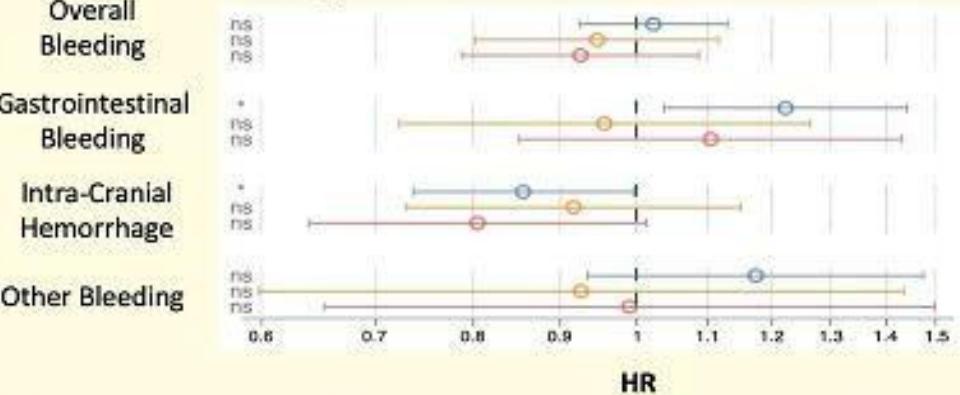
- Appropriate full dose
- Appropriate reduced dose
- Inappropriate full dose
- Inappropriate reduced dose

Rivaroxaban, compared to Apixaban and Dabigatran, was associated with better effectiveness and safety.

### HR PSM, pairwise



### HR PSM, pairwise



■ Rivaroxaban (vs. Apixaban) ■ Apixaban (vs. Dabigatran) ■ Rivaroxaban (vs. Dabigatran)

ns p>0.05; \*p≤0.05

# Conclusions.

- 6 years follow-up revealed differences in *mortality risk in favor of rivaroxaban* that were not demonstrated in previous studies in which the follow-up period was shorter.
- The *bleeding rates were higher in the dabigatran group* in patients with impaired renal function and in elderly (80 years and above).
- A comparison between apixaban and rivaroxaban revealed *decreased GI bleeding in the apixaban group*, and on the other hand, *decreased ICH in the rivaroxaban group.*