Strategie protidestičkové léčby u pacienta s indikací k antikoagulaci

Petr Kala
FN Brno

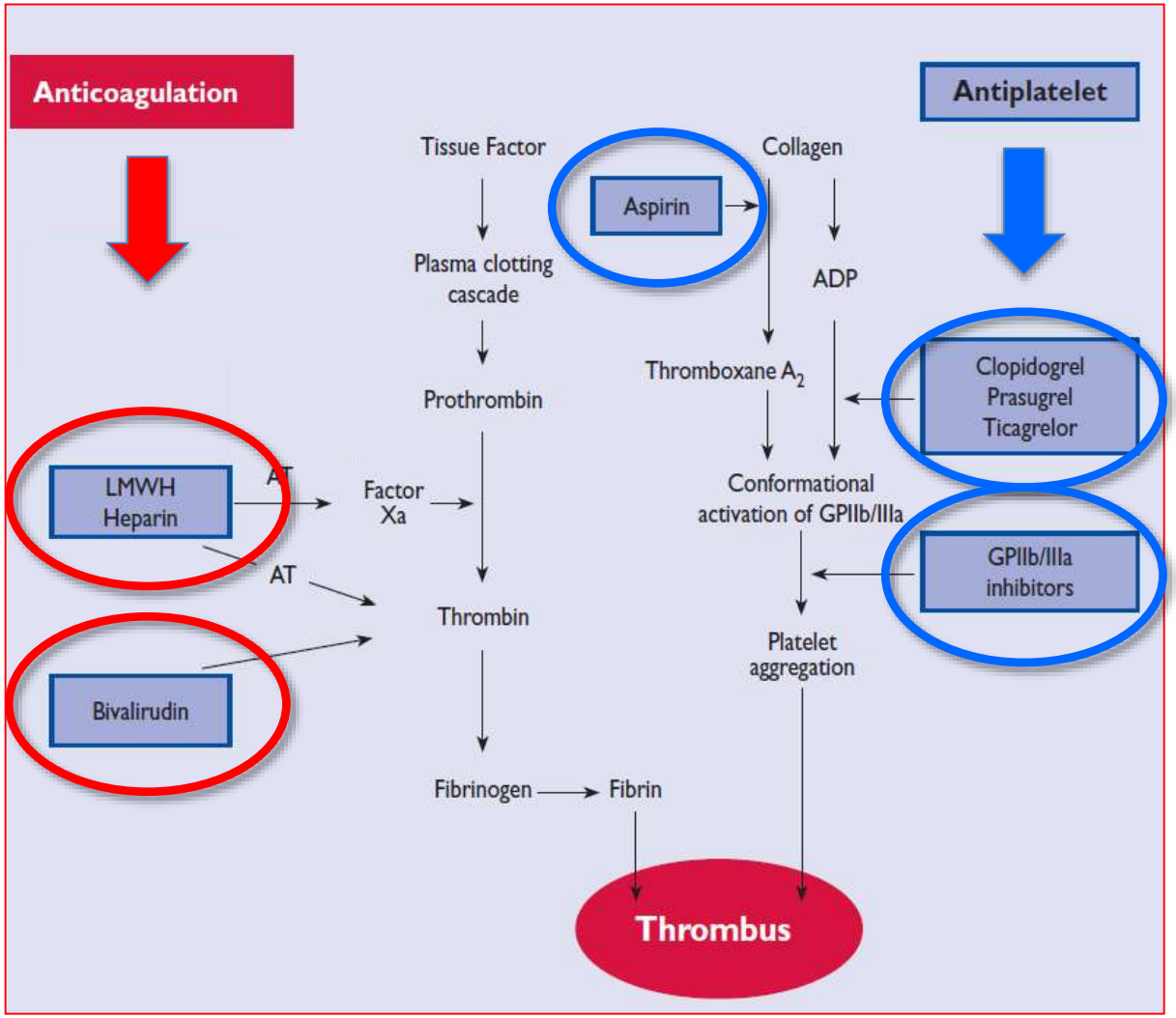
14. Konference akutní kardiologie, Karlovy Vary, 4.12. 2016

ČESKÁ ASOCIACE INTERVENČNÍ KARDIOLOGIE

Intervenční kardiologie
IKK FN Brno

Antitrombotická léčba

Přednemocniční **Periprocedurální** Nemocniční **Dlouhodobá**



Abciximab

Eptifibatide

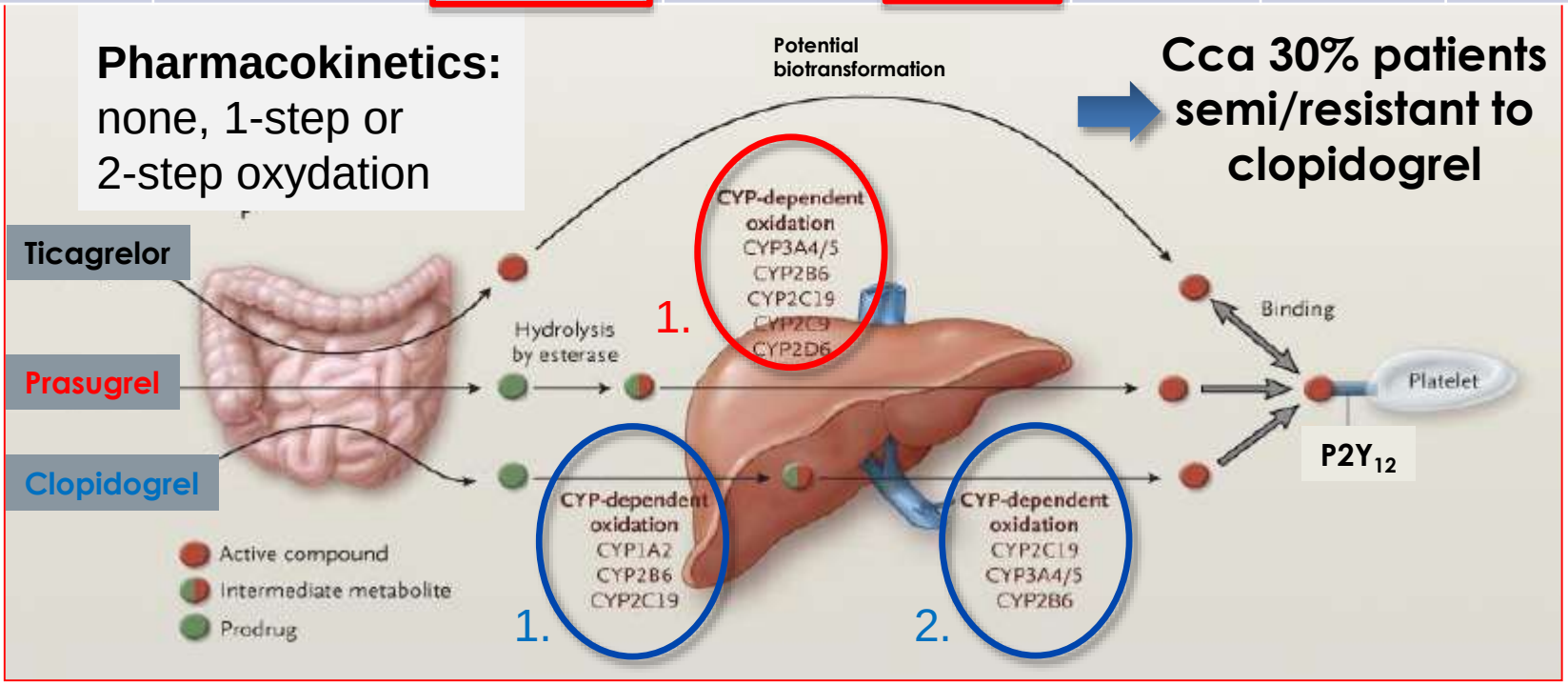
Tirofiban

2. P2Y12 inhibitors: Farmakokinetika a farmakodynamika

Drug	Administration	Activation (CYP dependant)	Receptor binding	Onset of action	Offset of action	Loading dose	Maintenance dose
Clopidogrel	oral	sensitive to inhibition	irreversible	2-8 hrs	7-10 days	600mg	1x75mg
Prasugrel	oral	**resistant to inhibition**	irreversible	**0,5-4 hrs**	7-10 days	60mg	1x10mg (5mg)
Ticagrelor	oral	**not needed**	reversible	**0,5-2 hrs**	3-5 days	180mg	2x90mg

Pharmacokinetics:
none, 1-step or
2-step oxydation

Cca 30% patients semi/resistant to clopidogrel



Ferreiro JL, Circ Cardiovasc Interv 2012;5:433-445

Management OAK u AKS/PCI

Intervenční kardiologie
IKK FN Brno

2014 ESC Consensus Document	2015 ESC NSTE-ACS Guidelines	2016 ESC A-Fib Guidelines Nová

European Heart Journal Advance Access published August 25, 2014

CURRENT OPINION

Management of antithrombotic therapy in atrial fibrillation patients presenting with acute coronary syndrome and/or undergoing percutaneous coronary or valve interventions: a joint consensus document of the European Society of Cardiology Working Group on Thrombosis, European Heart Rhythm Association (EHRA), European Association of Percutaneous Cardiovascular Interventions (EAPCI) and European Association of Acute Cardiac Care (ACCA) endorsed by the Heart Rhythm Society (HRS) and Asia-Pacific Heart Rhythm Society (APHRS)

Task Force Members: Gregory Y.H. Lip* (UK, Chairman), Stephan Windecker (Switzerland)[†], Kurt Huber (Austria)[‡], Paulus Kirchhof (UK)[§], Francisco Marin (Spain), Jurriën M. Ten Berg (Netherlands), Karl Georg Haeusler (Germany), Giuseppe Boriani (Italy), Davide Capodanno (Italy), Martine Gilard (France), Uwe Zeymer (Germany), Deirdre Lane (UK, Patient Representative).

Document Reviewers: Robert F. Storey (Review Co-ordinator), Hector Bueno, Jean-Philippe Collet, Laurent Fauchier, Sigrun Halvorsen, Maddalena Lettino, Joao Morais, Christian Mueller, Tatjana S. Potpara, Lars Hvilsted Rasmussen, Andrea Rubboli, Juan Tamargo, Marco Valgimigli, and Jose L. Zamorano

European Heart Journal Advance Access published August 29, 2015

ESC GUIDELINES

2015 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC)

Authors/Task Force Members: Marco Roffi* (Chairperson) (Switzerland), Carlo Patrono* (Co-Chairperson) (Italy), Jean-Philippe Collet[†] (France), Christian Mueller[†] (Switzerland), Marco Valgimigli[†] (The Netherlands), Felicita Andreotti (Italy), Jeroen J. Bax (The Netherlands), Michael A. Borger (Germany), Carlos Brotons (Spain), Derek P. Chew (Australia), Baris Gencer (Switzerland), Gerd Hasenfuss (Germany), Keld Kjeldsen (Denmark), Patrizio Lancellotti (Belgium), Ulf Landmesser (Germany), Julinda Mehilli (Germany), Debabrata Mukherjee (USA), Robert F. Storey (UK), and Stephan Windecker (Switzerland)

Document Reviewers: Helmut Baumgartner (CPG Review Coordinator) (Germany), Oliver Gaemperli (CPG Review Coordinator) (Switzerland), Stephan Achenbach (Germany), Stefan Agewall (Norway), Lina Badimon (Spain), Colin Baigent (UK), Hector Bueno (Spain), Raffaele Bugiardini (Italy), Stéphane Carron (Italy), Filip Casselman (Belgium), Thomas Cuisset (France), Çetin Erol (Turkey), Donna Fitzsimons (UK), Martin Halle (Germany),

European Heart Journal Advance Access published August 27, 2016

ESC GUIDELINES

2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS

The Task Force for the management of atrial fibrillation of the European Society of Cardiology (ESC)

Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC

Endorsed by the European Stroke Organisation (ESO)

Authors/Task Force Members: Paulus Kirchhof* (Chairperson) (UK/Germany), Stefano Benussi[†‡] (Co-Chairperson) (Switzerland), Dipak Kotecha (UK), Anders Ahlsson[§] (Sweden), Dan Atar (Norway), Barbara Casadei (UK), Manuel Castella[¶] (Spain), Hans-Christoph Diener[#] (Germany), Hein Heidbuchel (Belgium), Jeroen Hendriks (The Netherlands), Gerhard Hindricks (Germany), Antonis S. Manolis (Greece), Jonas Oldgren (Sweden), Bogdan Alexandru Popescu (Romania), Ulrich Schotten (The Netherlands), Bart Van Putte[†] (The Netherlands), and Panagiotis Vardas (Greece)

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PCI a antikoagulační léčba
ESC Guidelines pro revaskularizace 2014

Recommendations for antithrombotic treatment in patients undergoing PCI who require oral anticoagulation

Recommendations	Class[a]	Level[b]	Ref[c]
In patients with a firm indication for oral anticoagulation (e.g. atrial fibrillation with CHA_2DS_2-VASc score ≥2, venous thromboembolism, LV thrombus, or mechanical valve prosthesis), oral anticoagulation is recommended in addition to antiplatelet therapy.	I	C	
New-generation DES are preferred over BMS among patients requiring oral anticoagulation if bleeding risk is low (HAS-BLED ≤2).	IIa	C	
In patients with SCAD and atrial fibrillation with CHA_2DS_2-VASc score ≥2 at low bleeding risk (HAS-BLED ≤2), initial triple therapy of (N)OAC and ASA (75–100 mg/day) and clopidogrel 75 mg/day should be considered for a duration of at least one month after BMS or new-generation DES followed by dual therapy with (N)OAC and aspirin 75–100 mg/day or clopidogrel (75 mg/day) continued up to 12 months.	IIa	C	
DAPT should be considered as alternative to initial triple therapy for patients with SCAD and atrial fibrillation with CHA_2DS_2-VASc score ≤1.	IIa	C	
In patients with ACS and atrial fibrillation at low bleeding risk (HAS-BLED≤2), initial triple therapy of (N)OAC and ASA (75–100 mg/day) and clopidogrel 75 mg/day should be considered for a duration of 6 months irrespective of stent type followed by (N)OAC and aspirin 75–100 mg/day or clopidogrel (75 mg/day) continued up to 12 months.	IIa	C	
In patients requiring oral anticoagulation at high bleeding risk (HAS BLED ≥3), triple therapy of (N)OAC and ASA (75–100 mg/day) and clopidogrel 75 mg/day should be considered for a duration of one month followed by (N)OAC and aspirin 75–100 mg/day or clopidogrel (75 mg/day) irrespective of clinical setting (SCAD or ACS) and stent type (BMS or new-generation DES).	IIa	C	
Dual therapy of (N)OAC and clopidogrel 75 mg/day may be considered as an alternative to initial triple therapy in selected patients.	IIb	B	865,870
The use of ticagrelor and prasugrel as part of initial triple therapy is not recommended	III	C	
Anticoagulation therapy after PCI in ACS patient			
In selected patients who receive ASA and clopidogrel, low-dose rivaroxaban (2.5 mg twice daily) may be considered in the setting of PCI for ACS if the patient is at low bleeding risk.	IIb	B	855
Anticoagulation during PCI in patients on oral anticoagulation			
It is recommended to use additional parenteral anticoagulation, regardless of the timing of the last dose of (N)OAC.	I	C	
Periprocedural parenteral anticoagulants (bivalirudin, enoxaparin or UFH) should be discontinued immediately after primary PCI.	IIa	C	

[a]Class of recommendation.
[b]Level of evidence.
[c]References.
ACS = acute coronary syndrome; ASA = acetylsalicylic acid; BMS = bare-metal stent; CHA_2DS_2-VASc = Cardiac failure, Hypertension, Age ≥75 [Doubled], Diabetes, Stroke [Doubled]–Vascular disease, Age 65–74 and Sex category [Female]); DAPT = dual antiplatelet therapy; DES = drug-eluting stent; (N)OAC = (non-vitamin K antagonist) oral anticoagulant; HAS-BLED = hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile INR, elderly, drugs/alcohol; INR = international normalized ratio; LV = left ventricular; PCI = percutaneous coronary intervention; SCAD = stable coronary artery disease; UFH = unfractionated heparin.

Management OAK u AKS/PCI

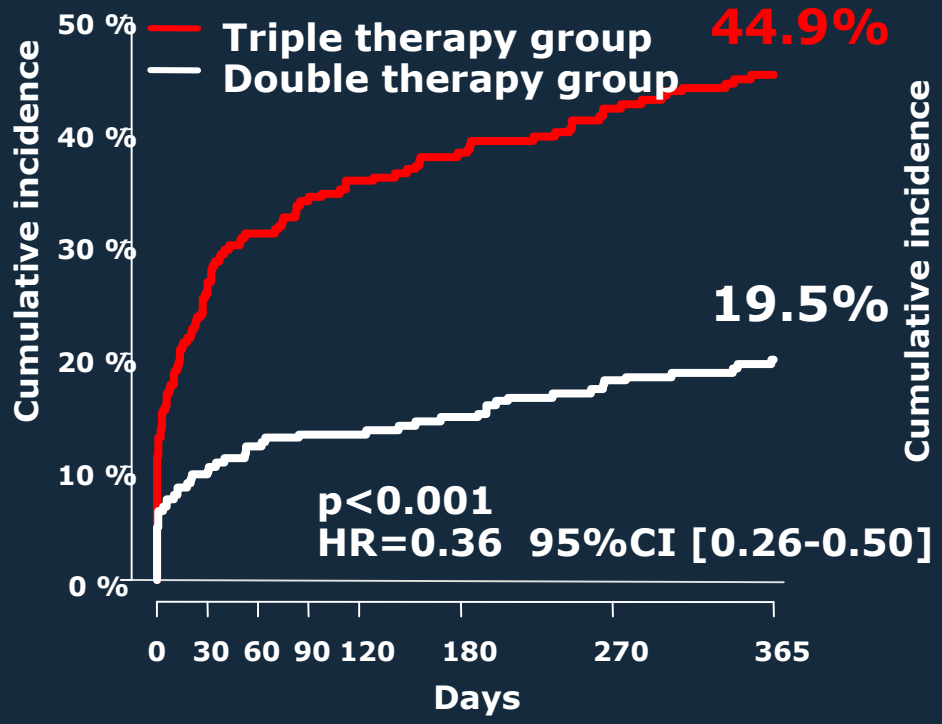
1. Využití CHA_2-DS_2-VASc a HAS-BLED (Class IC)
2. INR 2.0-2.5 v případě, že pacient užívá VKA + clopidogrel a/nebo aspirin (Class IIaC)
3. Nižší dávka NOAK (Class IIbC)
4. Single OAK u pacientů se stabilní ICHS (Class IIaB)
5. Radiální přístup (Class IIaC)
6. DES u pacientů s nízkým rizikem krvácení (Class IIbC)
7. Prasugrel a/nebo ticagrelor nejsou doporučeny do trojkombinace (Class **IIIC**)

- Lip GY et al. Eur Heart J. 2014;35:3155-79

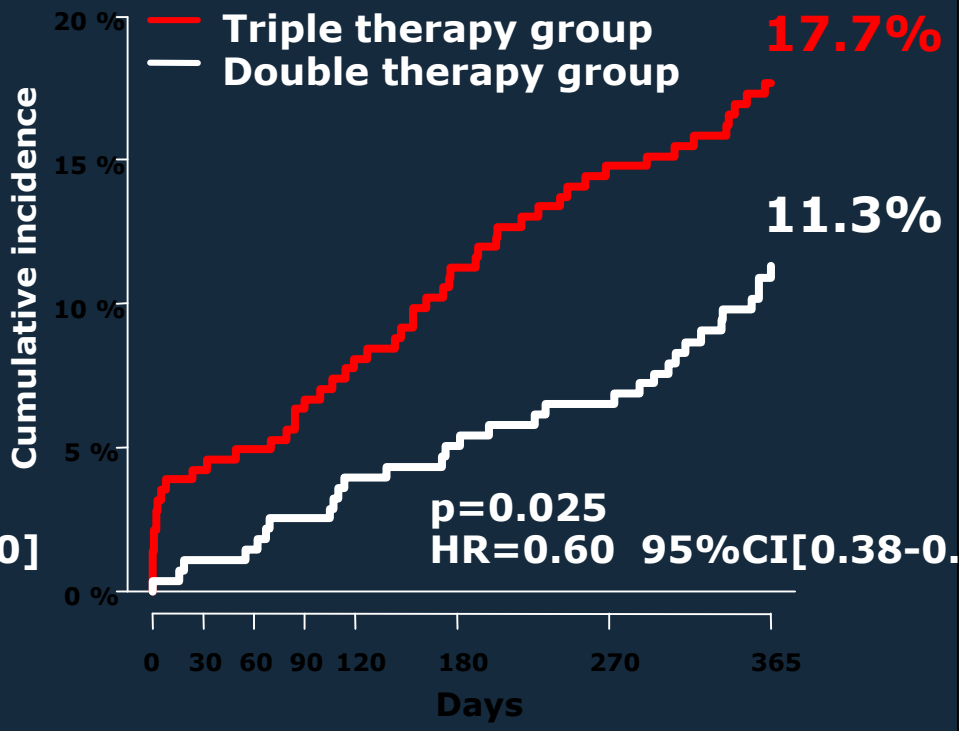
Studie WOEST

573 pacientů s PCI na OAK

Any TIMI Bleeding (Primary Endpoint)



Death, MI, TVR, Stroke, ST (Secondary Endpoint)

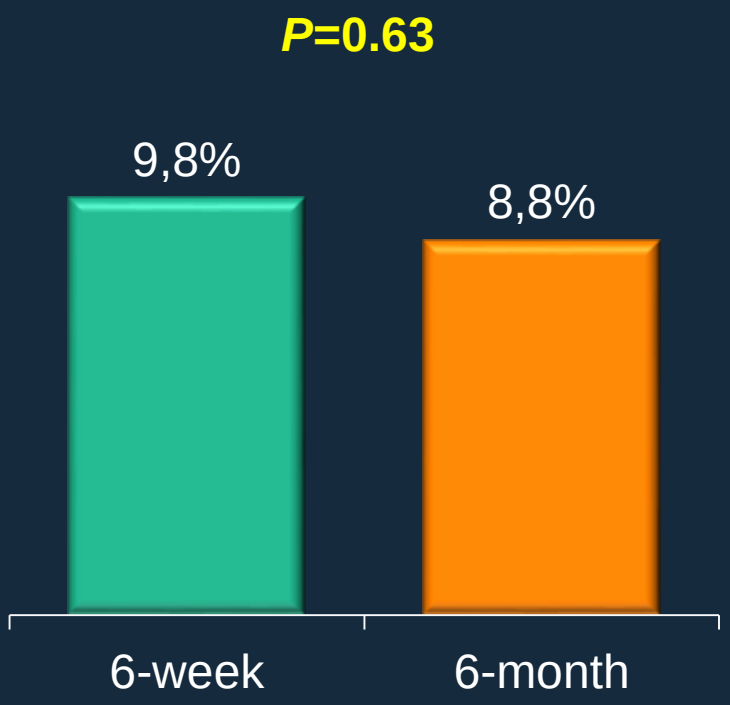


- Dewilde WJ et al. Lancet. 2013;381:1107-15

ISAR-TRIPLE

- 614 PCI pacientů s DES na OAK (32% s AKS)

Úmrtí, IM, ST, CMP nebo TIMI Velké krvácení



	6-týdnů	6-měs	*P* value
KV úmrtí	1.7%	3.0%	0.29
IM	2.0%	0	0.03
Definitivní ST	0.7%	0	0.50
Ischemická CMP	1.0%	1.3%	0.99
TIMI velké krvácenig	5.3%	4.0%	0.44

•Fiedlrer KA, et al. J Am Coll Cardiol 2015;65:1619–29

Doporučení pro kombinaci protidestičkové léčby s NOAK

	RE-LY Dabigatran	ROCKET-AF Rivaroxaban	ARISTOTLE Apixaban	ENGAGE Edoxaban
Concomitant use of aspirin alone	32%	≈37%	≈31%	≈29%
Concomitant use of clopidogrel alone	≈2%	<2%	≈2%	≈2%
Concomitant use of DAPT	≈5%	Excluded	Excluded	Excluded

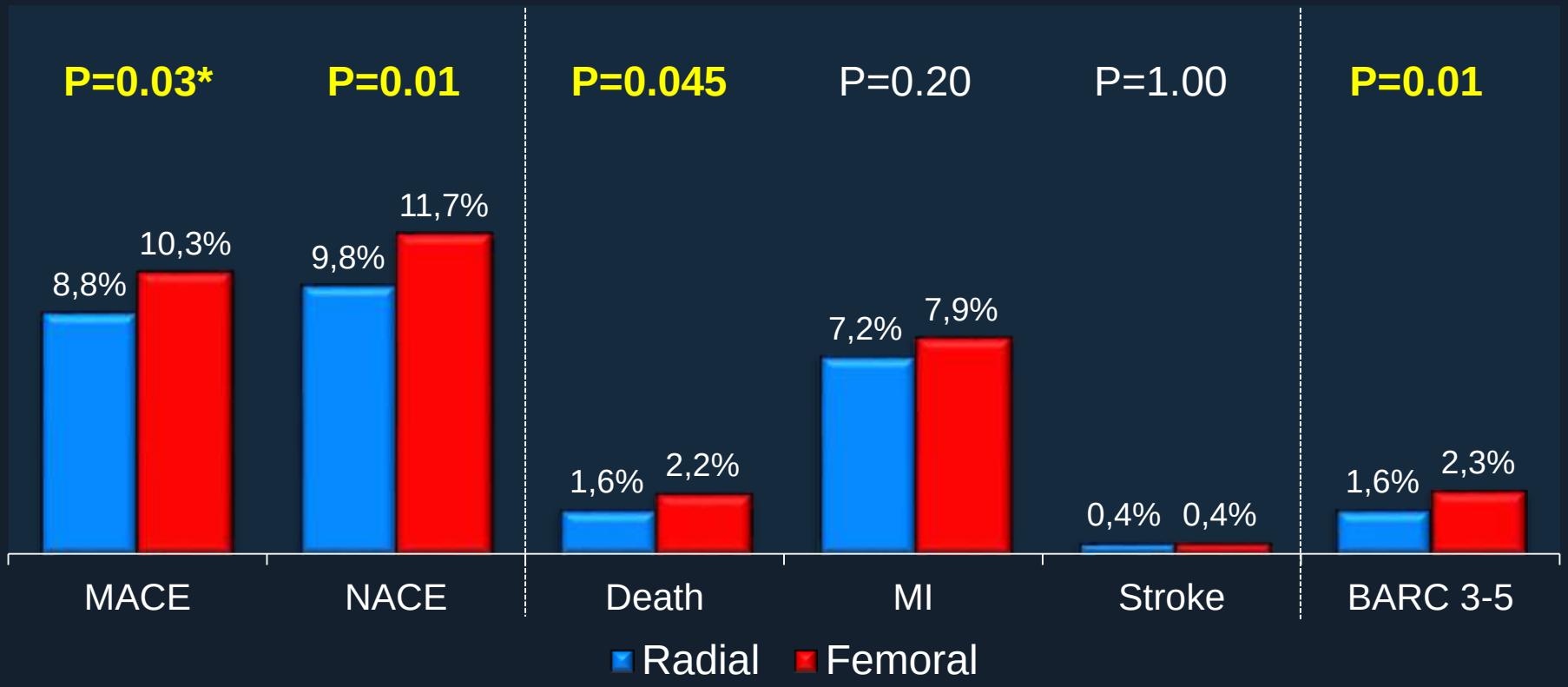
•Percentages refer to use of antiplatelet drugs at some time during the study period, including discontinuation at enrollment and non-consecutive use

- **Capodanno D, et al. EuroIntervention. 2015;10:1015-21**

MATRIX: Radiální přístup (z IIaC na IA)

8,404 AKS pacientů k radiální vs femorální PCI

30-denní výsledky



*15% significant reduction at nominal 5% alpha which is however NOT significant at the pre-specificed alpha of 2.5%

UNIVERSITÀ degli STUDI di CATANIA
Ferrarotto Hospital
A.O.U. Policlinico-Vittorio Emanuele
Catania, Italy

Valgimigli M, et al. Lancet. 2015;385:2465-76

TR přístup v České republice

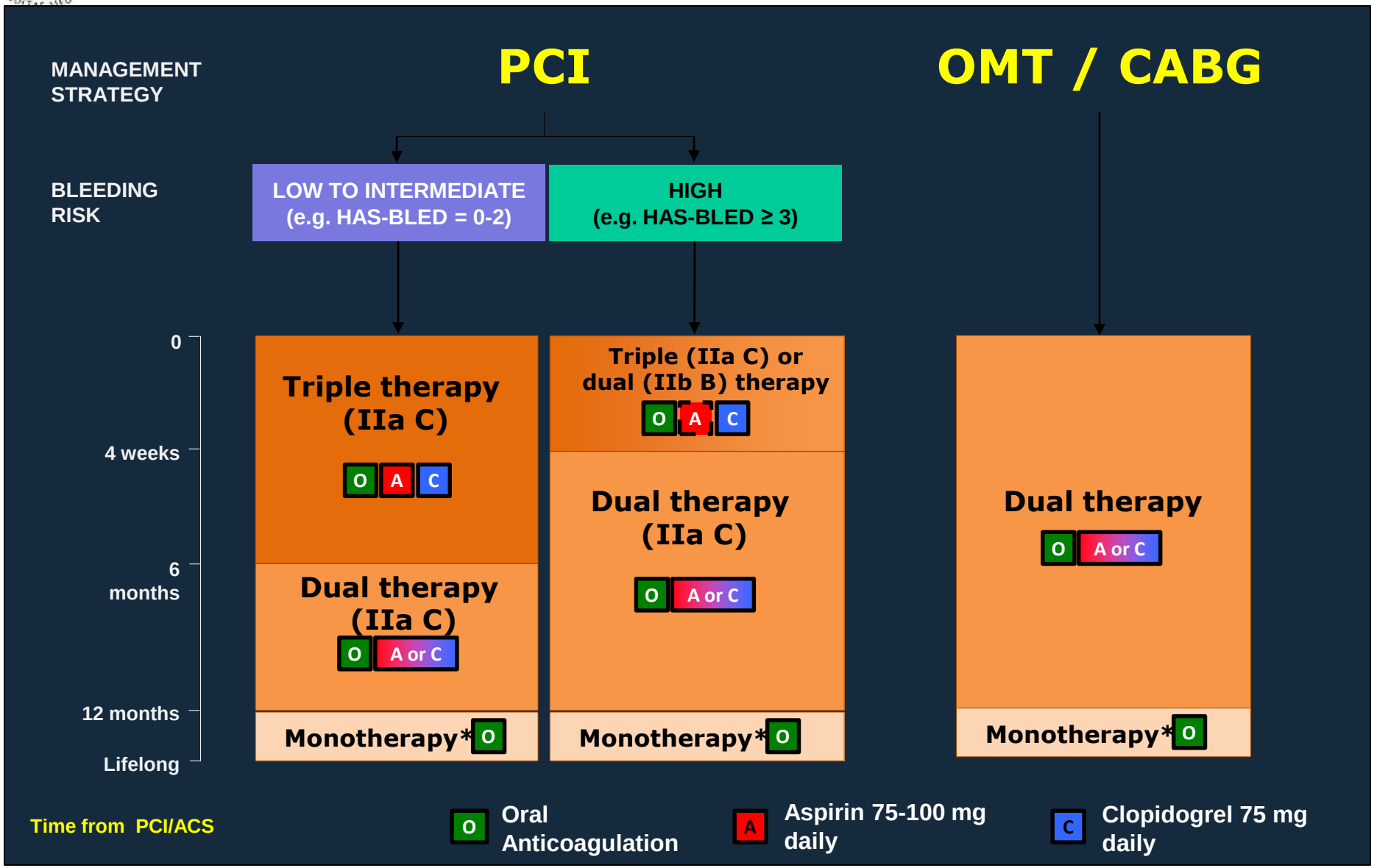
2012	2013	2014	2015
52%	68%	75%	76,0%
14%	38%	62%	58,6%
11%	34%	31%	40,0%
10%	15%	30%	61,0%
30%	20%	25%	25,0%
85%	77%	85%	85,0%
92%	89%	86%	88,0%
85%	80%	82%	86,0%
80%	83%	85%	87,0%
84%	81%		90,0%
89%		94%	95,0%
9%	9%	8%	4,0%
88%	95%	96%	97,0%
95%	95%	96%	96,0%
50%	78%	89%	90,0%
75%	79%	89%	92,0%
95%	95%	95%	95,0%
90%	87%	91%	92,0%
96%	96%	97%	96,0%
66%	92%	96%	94,0%
82%	91%	91%	90,0%
87%		89%	87,0%
67%	**70%**	**76%**	**78%**

2015

11/22 katetrizačních laboratoří využívá TR přístup ve >90%

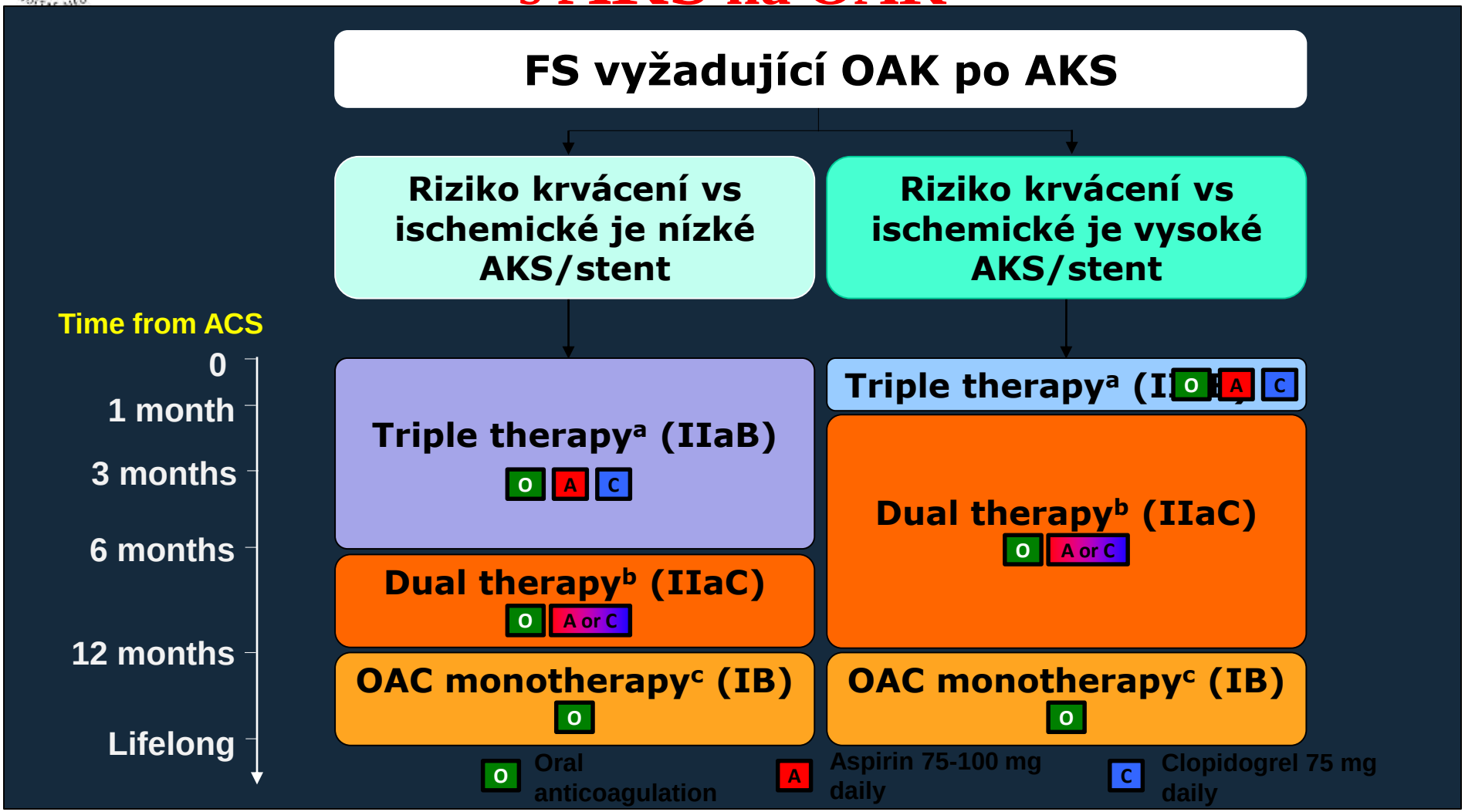
3/22 v < 50%

Antithrombotická léčba pacientů s nevalv. FS a NSTE-AKS



- Roffi M, et al. Eur Heart J. 2016;37:267-315

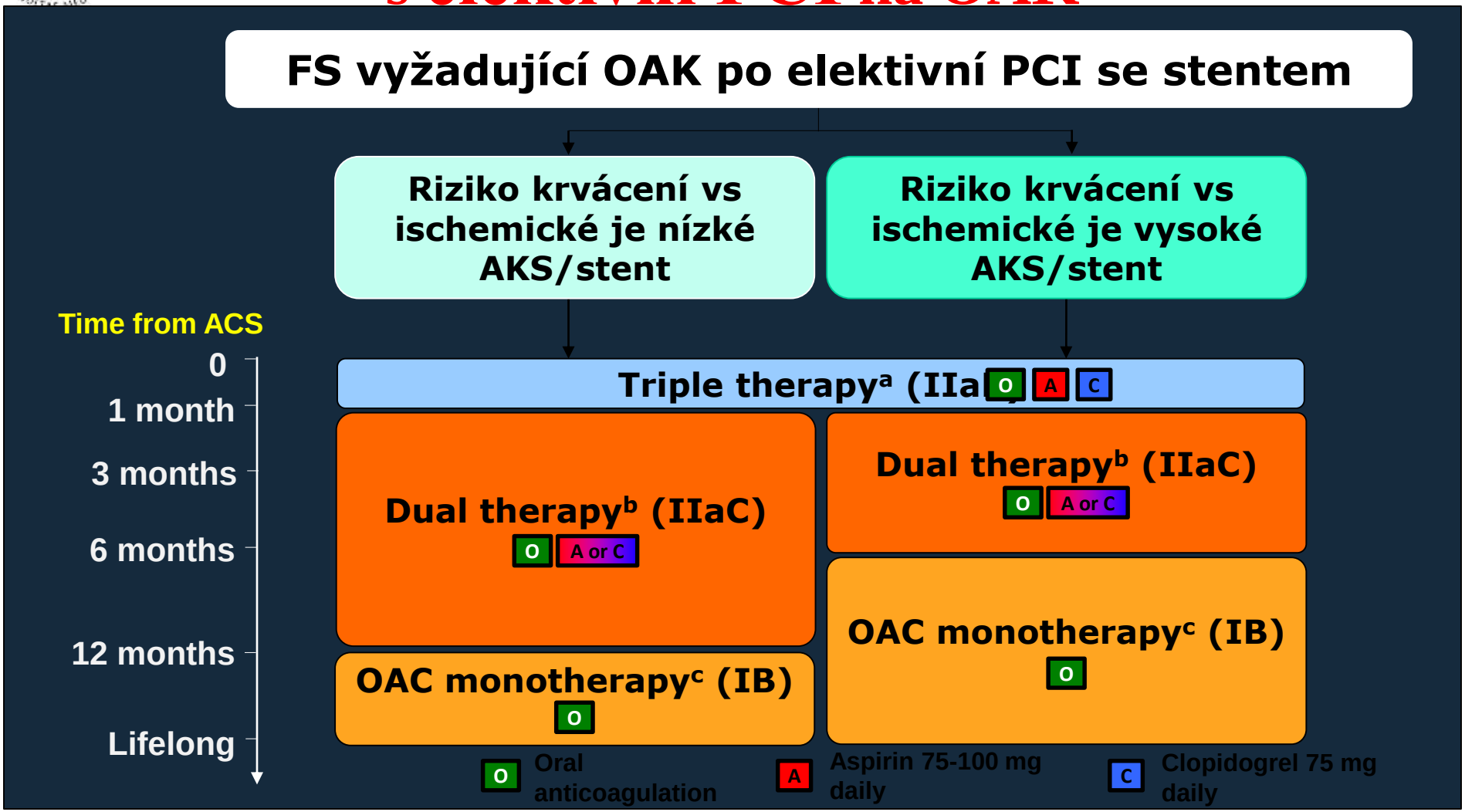
Antitrombotická léčba pacientů s AKS na OAK



[a]Dual therapy with OAC and aspirin or clopidogrel may be considered in selected patients, especially those not receiving a stent or patients at a longer time from the index event. [b]OAC plus single antiplatelet. [c]Dual therapy with OAC and an antiplatelet agent (aspirin or clopidogrel) may be considered in patients at high risk of coronary events.

- Kirchhof P et al. Eur Heart J. 2016 [ePub Ahead of print]

Antitrombotická léčba pacientů s elektivní PCI na OAK



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- Kirchhof P et al. Eur Heart J. 2016 [ePub Ahead of print]

Definice vysokého rizika krvácení po PCI (vstupní kritéria studie LEADERS FREE)

- **Věk ≥ 75 let**
- **Plánovaná léčba OAK po PCI**
- **Hb < 11g / dl nebo transfuze v posledních 4 týdnech**
- **Plánovaná velká nekardiální operace (během 12 měsíců)**
- **Nádorové onemocnění ≤ 3 years**
- **Clearance kreatininu < 40 ml / min**
- **Hospitalizace pro krvácení v posledním roce**
- **Thrombocytopenie (< 100.000 / mm3)**
- **Jakékoliv intracerebrální krvácení**
- **Jakákoliv CMP v posledním roce**
- **Těžká hepatopathie**
- **NSAID nebo steroidyi po PCI**

Antiagregační/antikoagulační příprava pacienta před ELEKTIVNÍ SKG a/nebo PCI

DOPORUČENÍ IKK LF MU a FN BRNO

1. Neužívá antiagregaci

Při nízké pravděpodobnosti ICHS ponechat bez léčby
Při střední a vysoké pravděpodobnosti ICHS nasadit ASA 100 mg p.o. denně (event. sytící dávku 400 mg p.o.) a zvážit podání clopidogrelu 300 mg
V případě elektivní PCI je nutná předléčba clopidogrelem VŽDY v dávce 300 - 600 mg minim. 24 hod před výkonem

2. Užívá ASA/clopidogrel/ticagrelor/prasugrel

Nevysazovat!

3. Užívá warfarin

Nevysazovat při INR ≤ 3 (max. 3 dny staré)
Pokud je nutné přerušení:
- **před výkonem zahájit ASA event. spolu s clopidogrelem (viz 1.)**
- **LMWH jen u vysokého rizika trombembolismu**

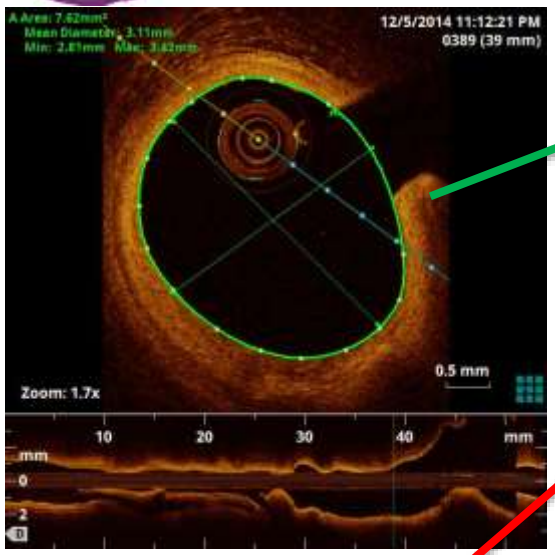
4. Užívá NOAK (rivaroxaban, apixaban, dabigatran)

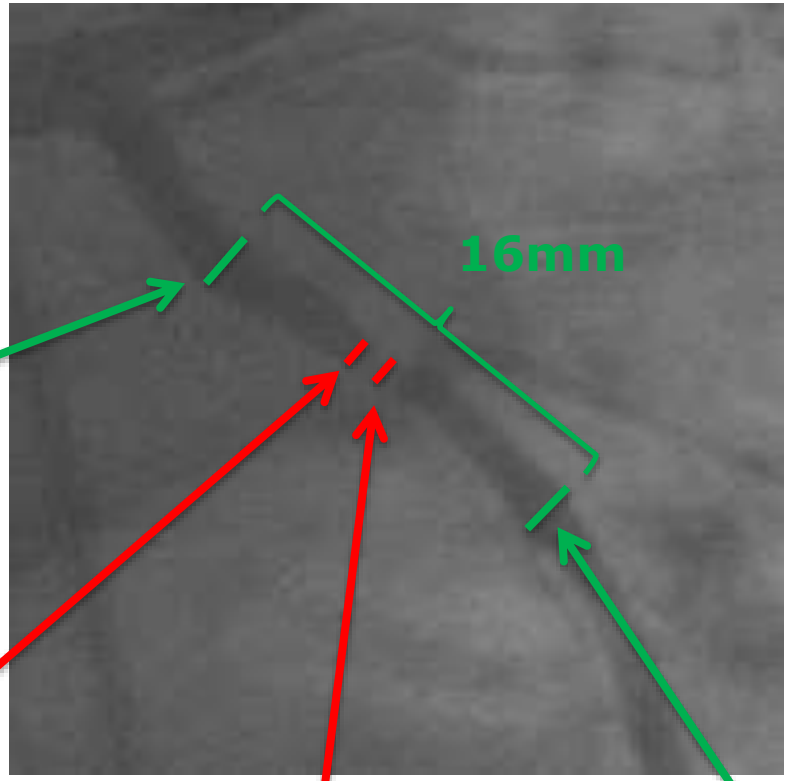
Přerušit 24 hod před výkonem, zahájit ASA +/- clopidogrel (viz 1.)

(v případě CHRI a léčbě dabigatranem až 48 hod)

STENT FOR LIFE

Intervenční kardiologie
IKK FN Brno





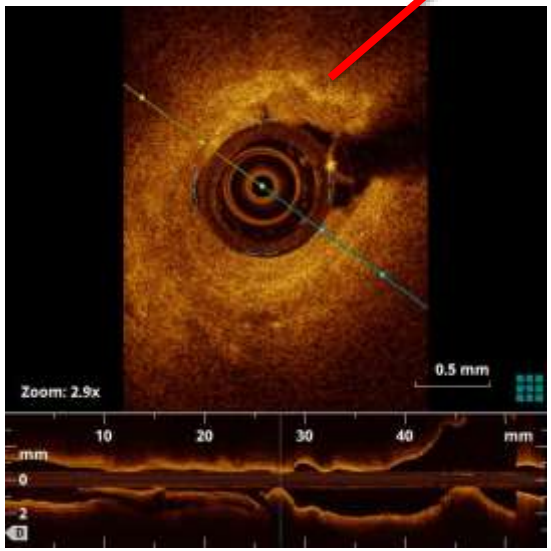
STEMI

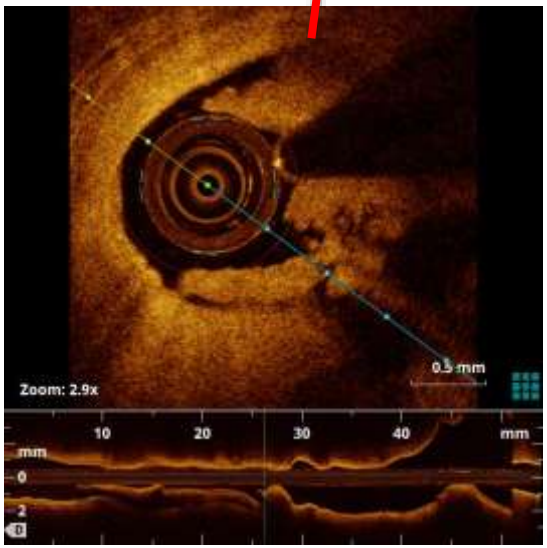
1VD – RC s

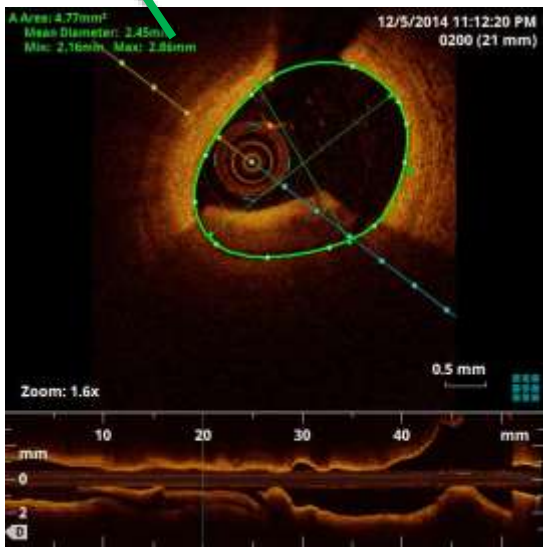
TIMI 1

OCT:

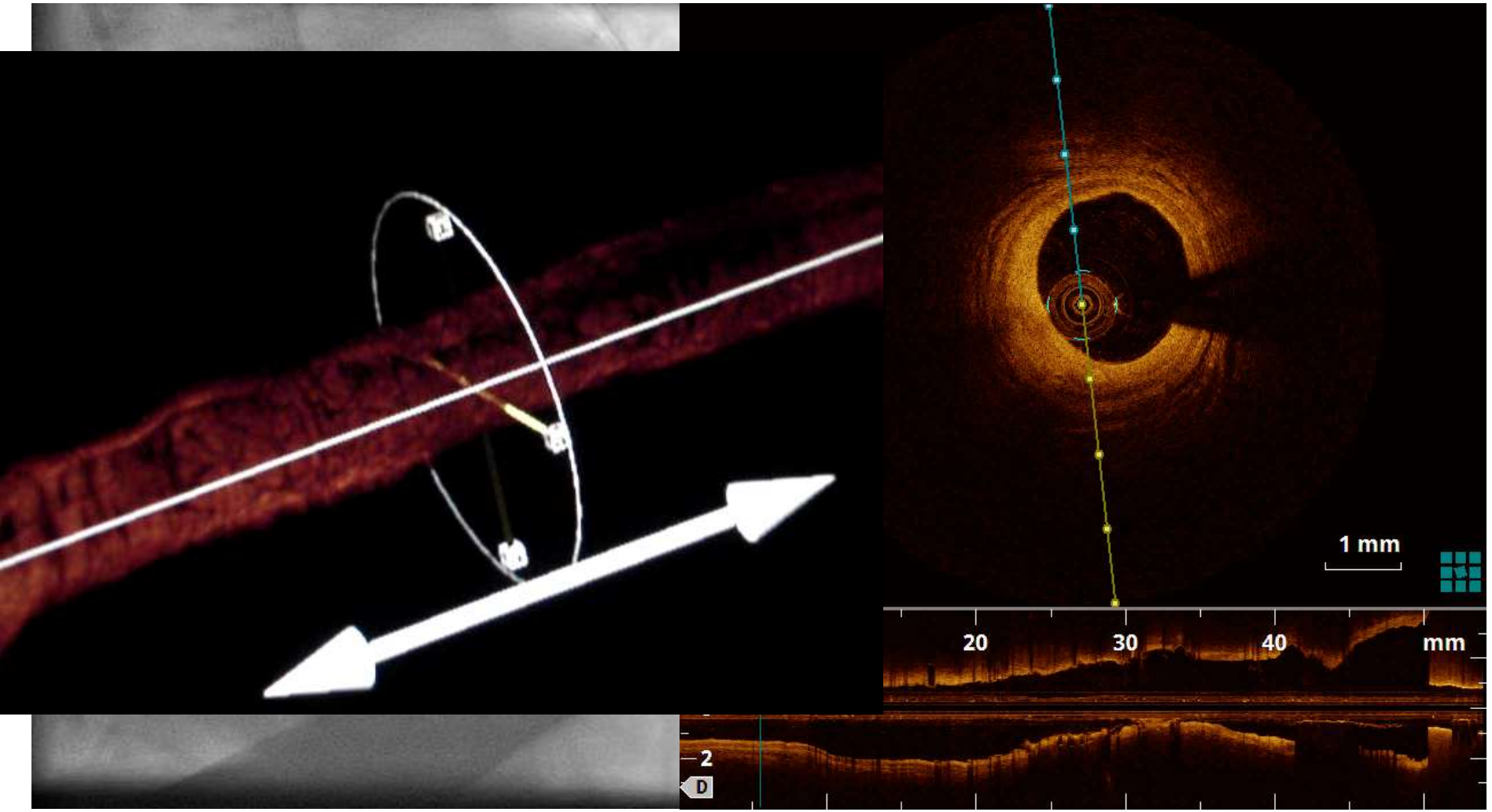
ruptura plátu bohatého na lipidy s trombózou







Optimální výsledek po 2. vysokotlaké postdilataci



Závěry

1. **Antitrombotická léčba pacientů vyžadujících OAK se liší v závislosti na základní diagnóze, typu stentu a poměru rizika ischemie/krvácení.**
2. **Optimální kombinace a délka trvání kombinované antitrombotické léčby není přesně určena, ale především u pacientů ve vyšším věku / s vysokým rizikem krvácení by měla být zvážena kratší doba léčby.**
3. **Této problematice se věnují studie s NOAK - PIONEER-AF, RE-DUAL, AUGUSTUS, ENTRUST AF, GLOBAL-LEADERS, TWILIGHT.**

Děkuji za pozornost.