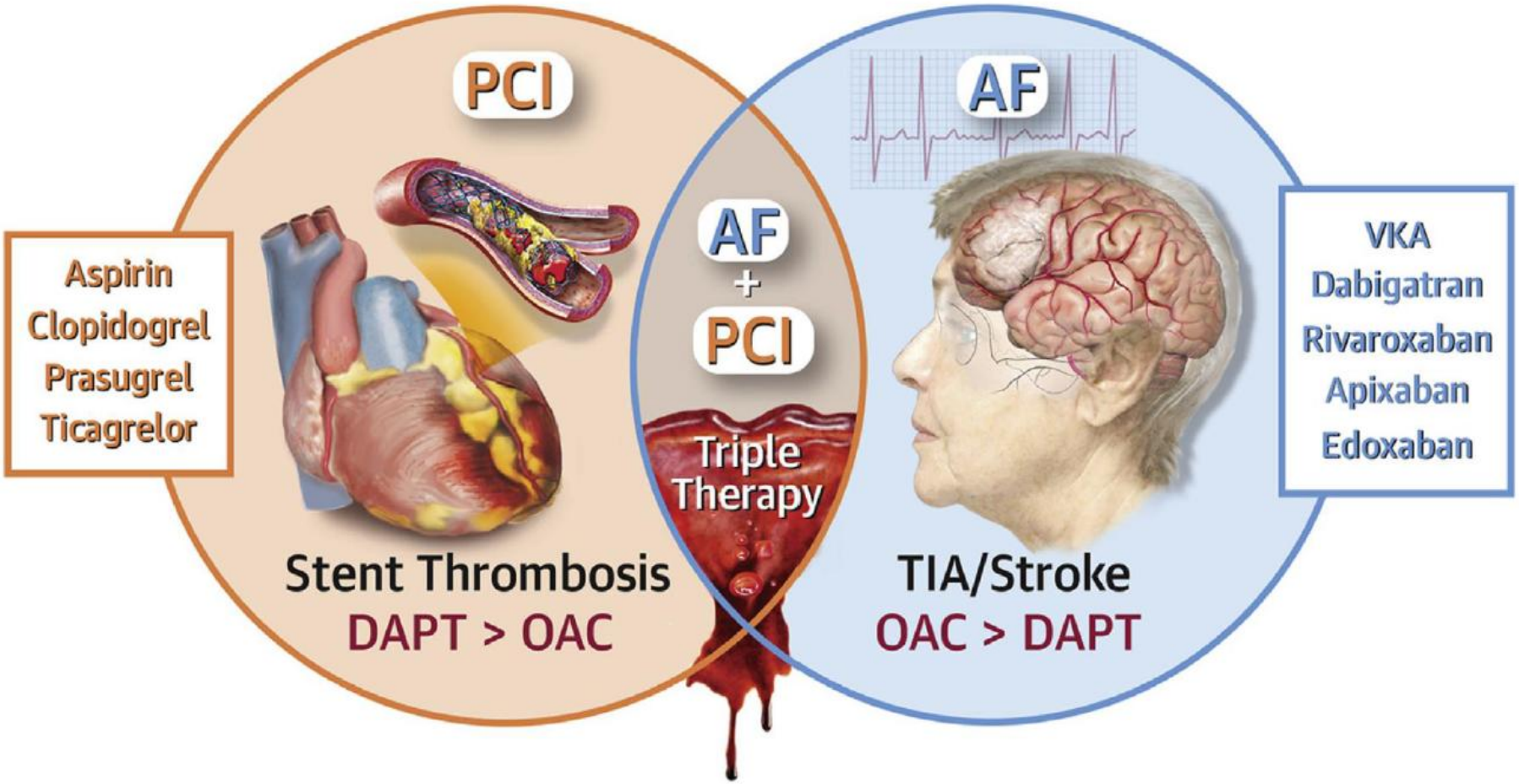
Individualizace AT léčby po AKS při nutnosti OAK

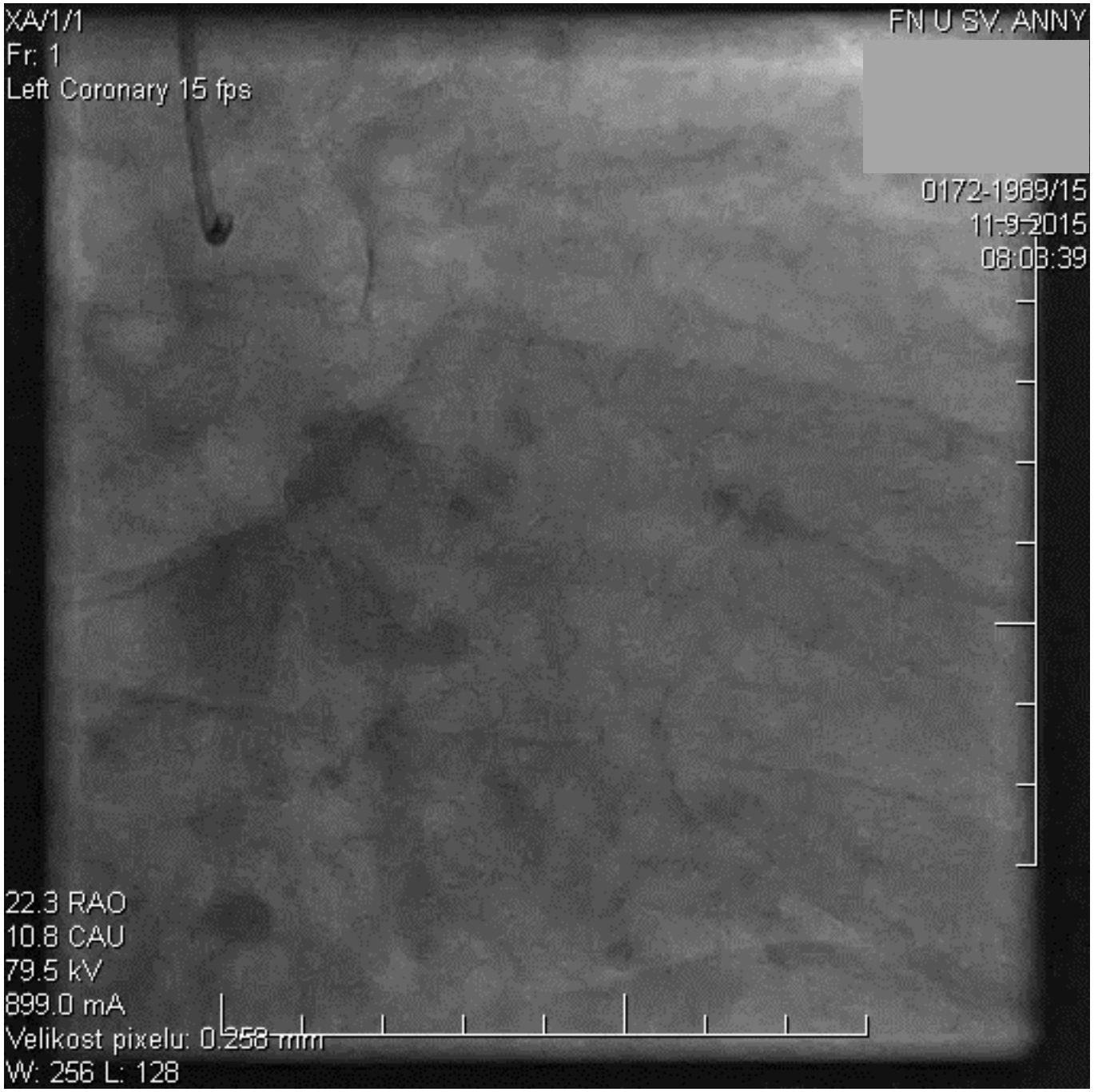
O. Hlinomaz

I. IKAK, ICRC, FN u sv. Anny, Brno
CINRE, Bratislava

DAPT vs OAK



Capodanno et al.: JACC Card Interv. 2017;10:1086-8

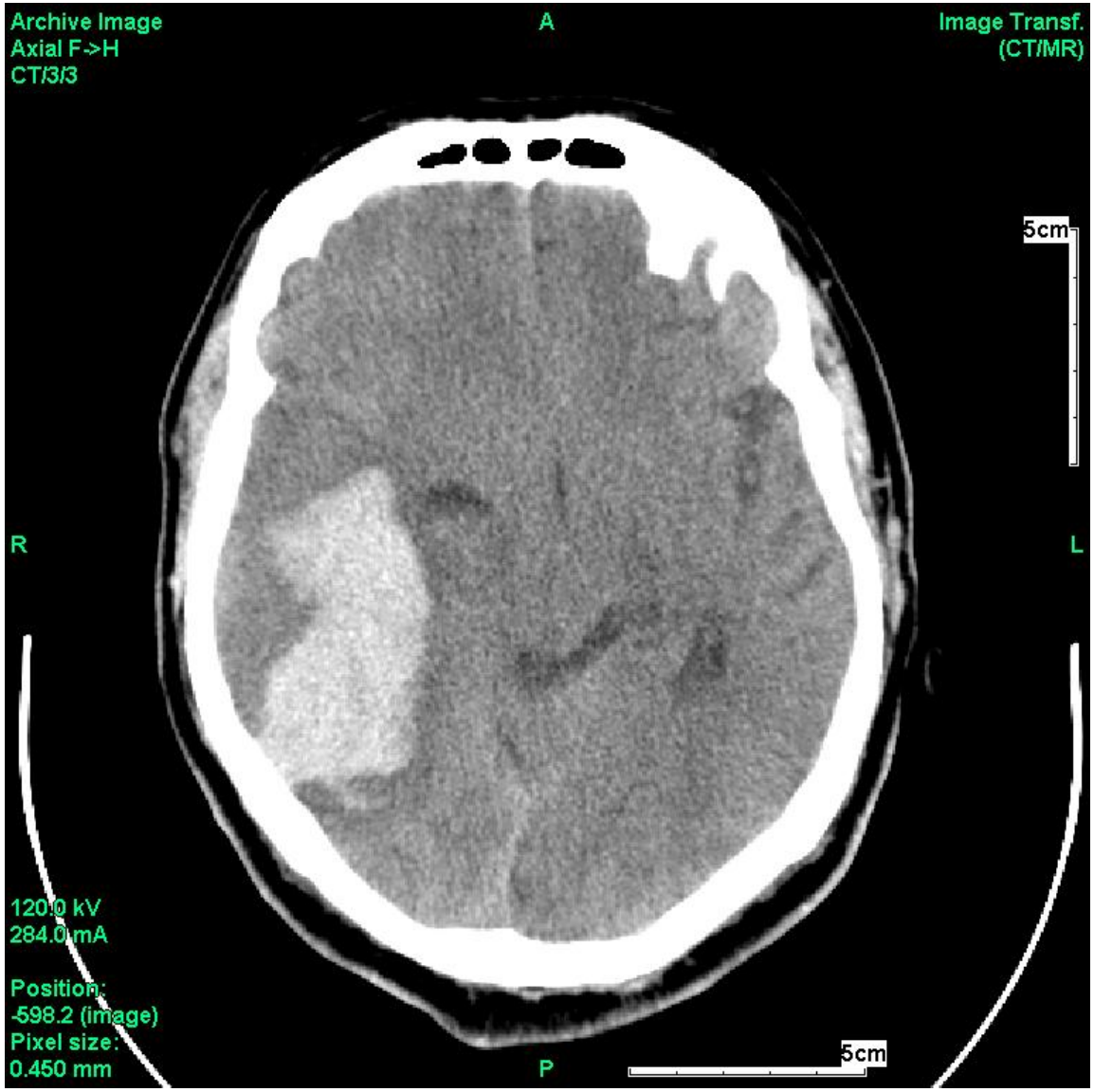


M, 69 let

NSTEMI
Preterminal neg. II,III,aVF,V4-6

DM II 5 let
Hypertenze
Obezita
Kolorektální Ca 2014- CH,R

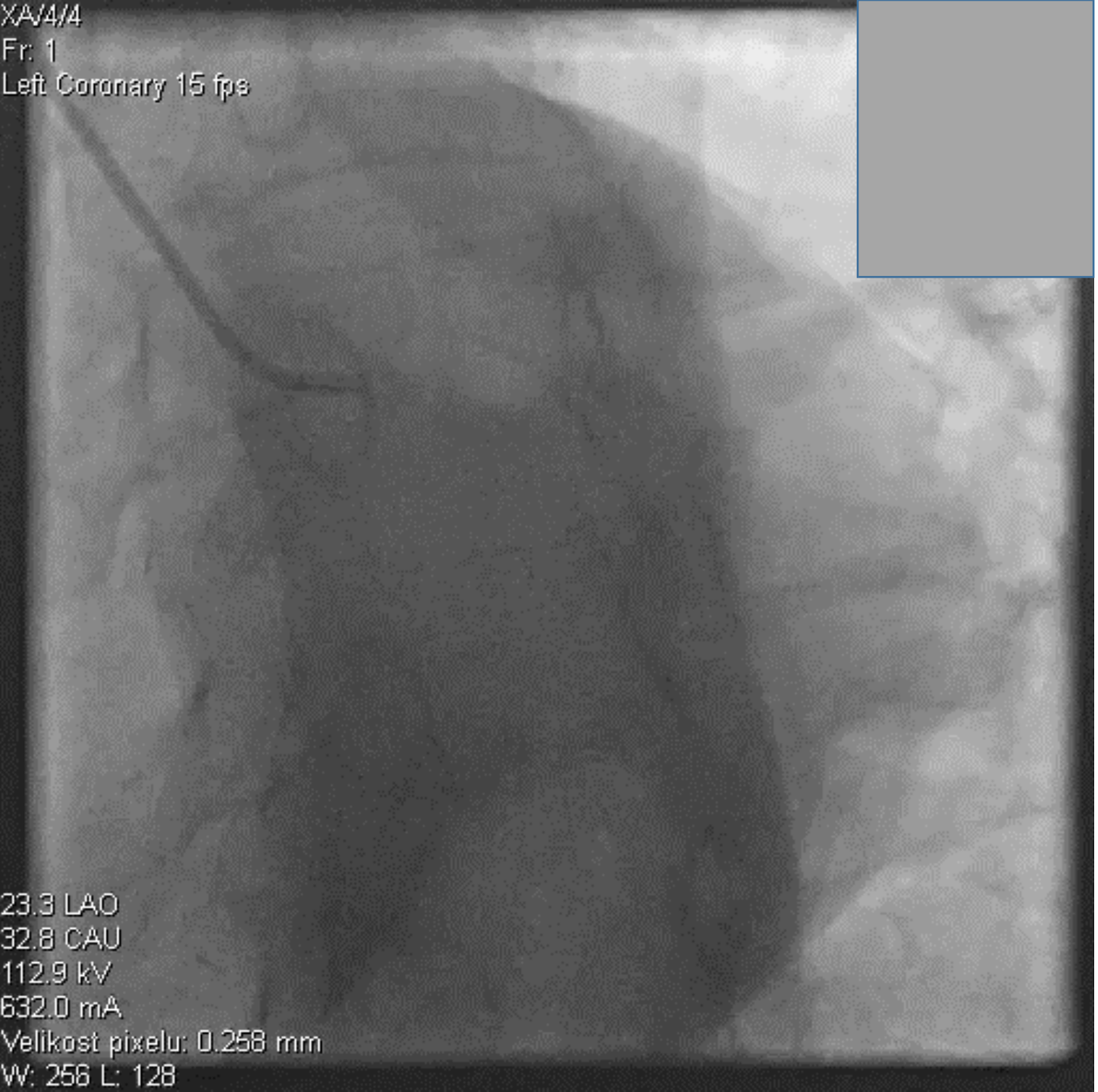
Mozkové krvácení



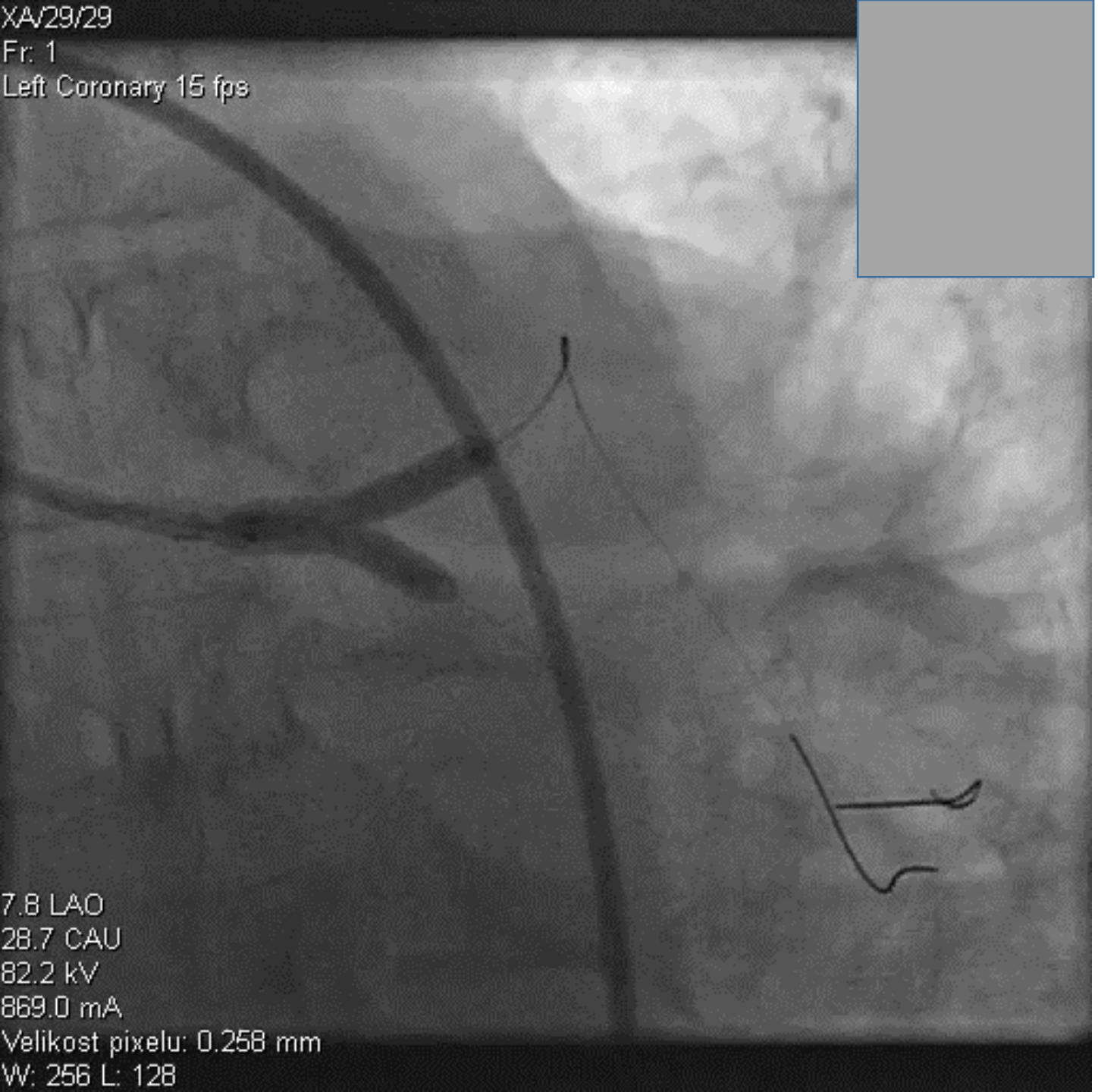
Perfektní práce intervenčního kardiologa

KVALITA NA 1. MÍSTĚ

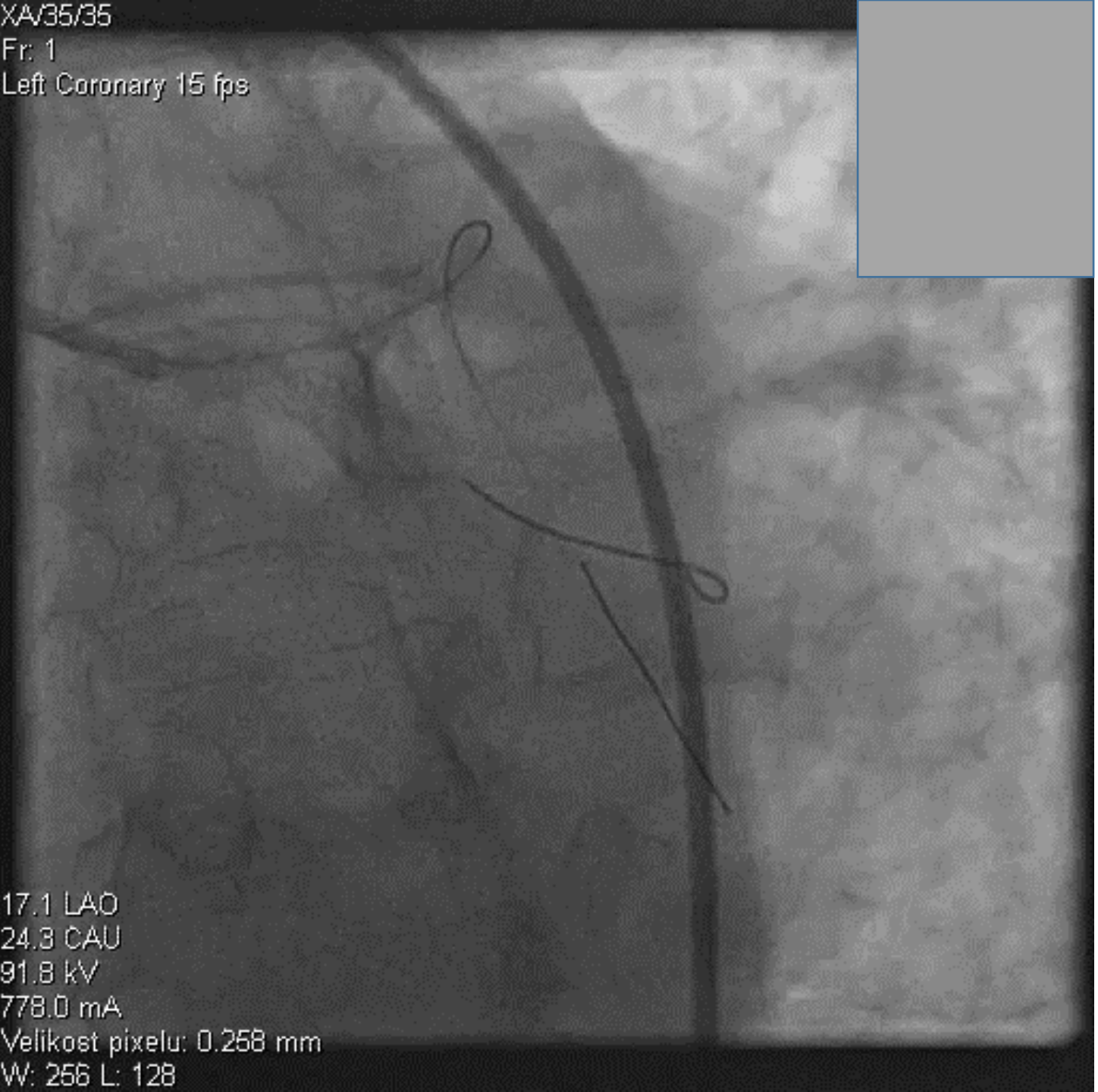
Příprava léze
DES 1:1, nová generace, výsl. studií
Vysotlaká postdilatace
OCT, IVUS


XA/4/4
Fr: 1
Left Coronary 15 fps
23.3 LAO
32.8 CAU
112.9 kV
632.0 mA
Velikost pixelu: 0.258 mm
W: 256 L: 128

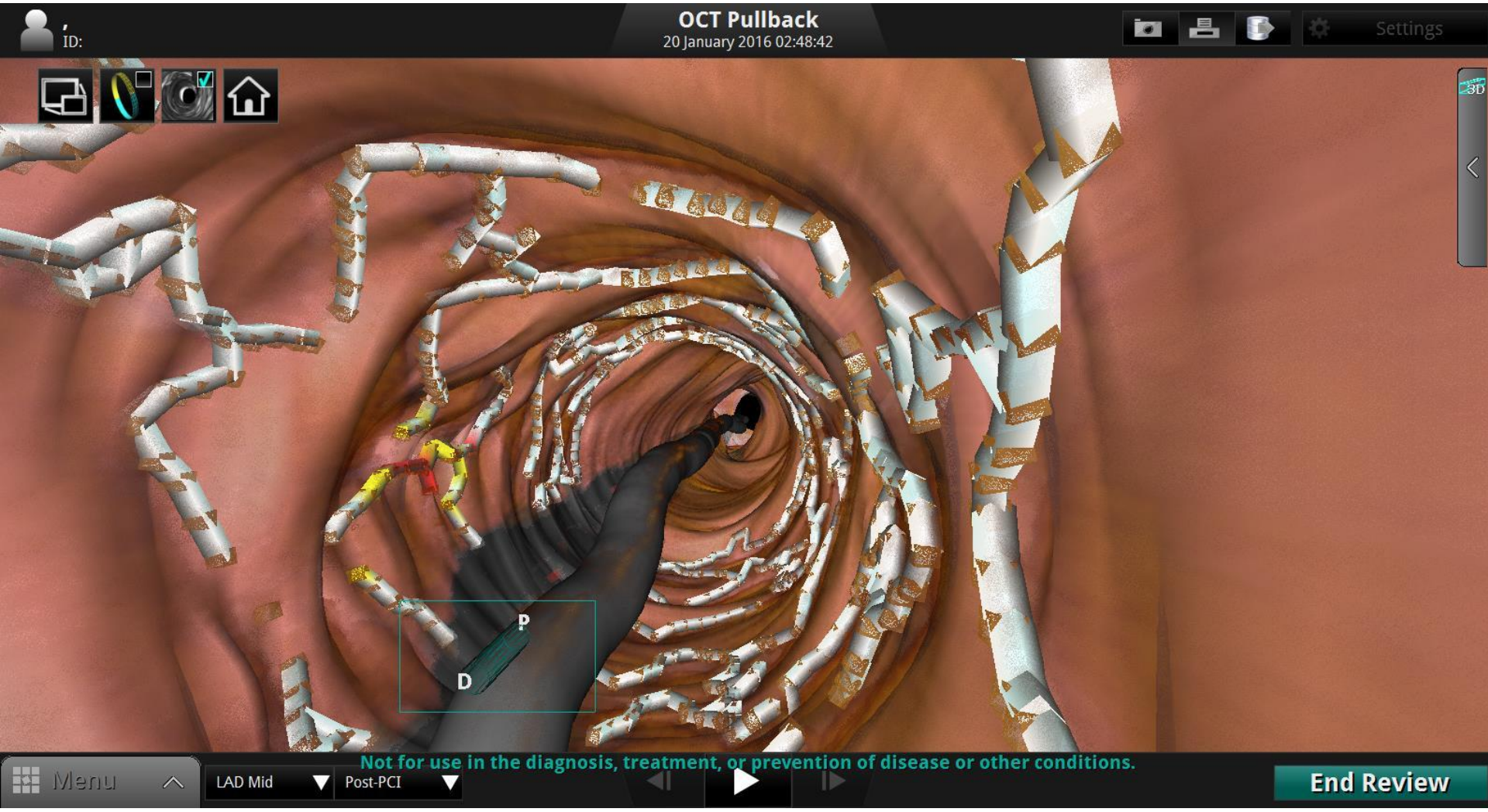
M, 40 let
NAP



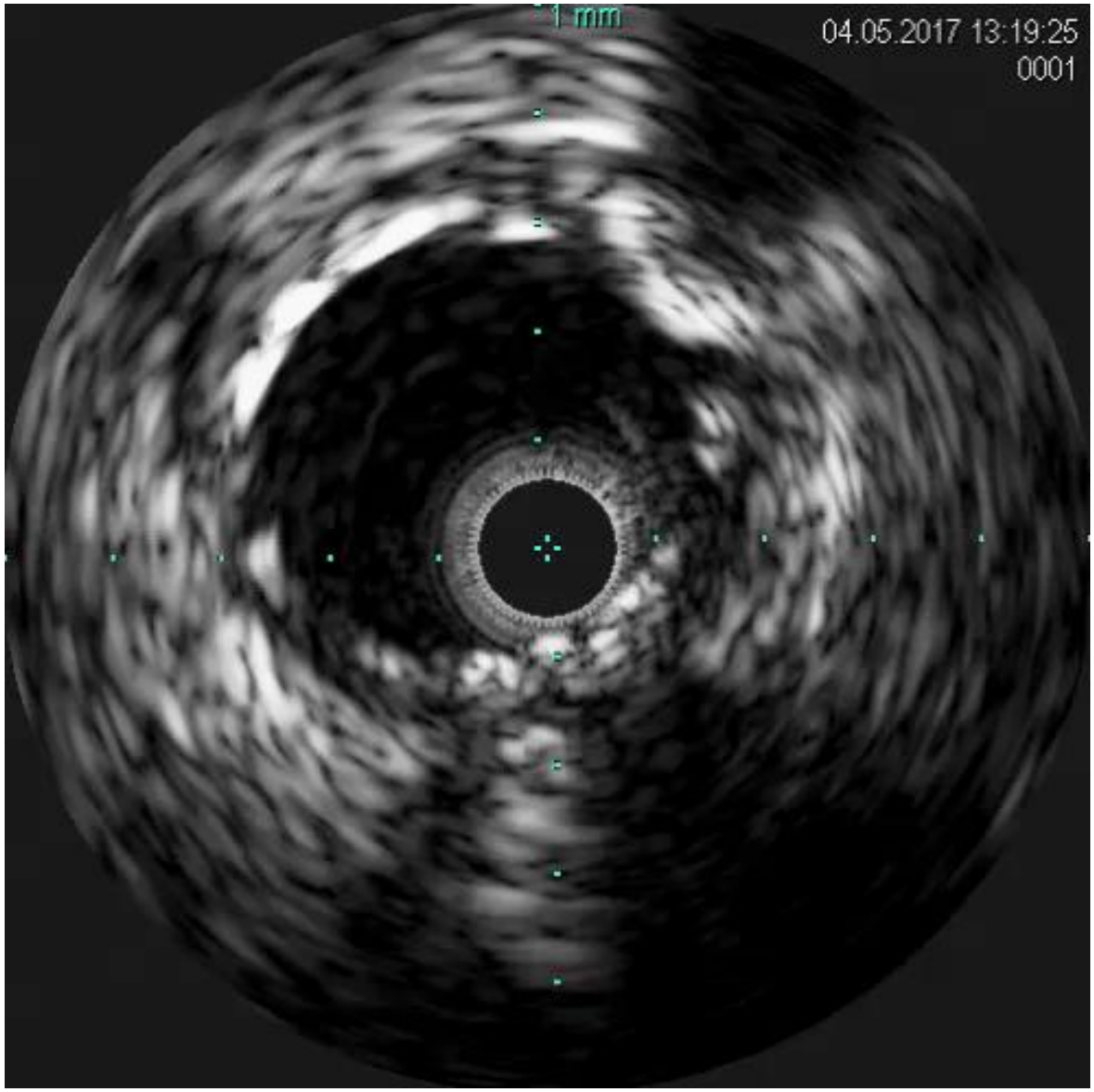
RIA (TAP)
DES 3,0 18
kissing


XA/35/35
Fr: 1
Left Coronary 15 fps
17.1 LAO
24.3 CAU
91.8 kV
778.0 mA
Velikost pixelu: 0.258 mm
W: 256 L: 128

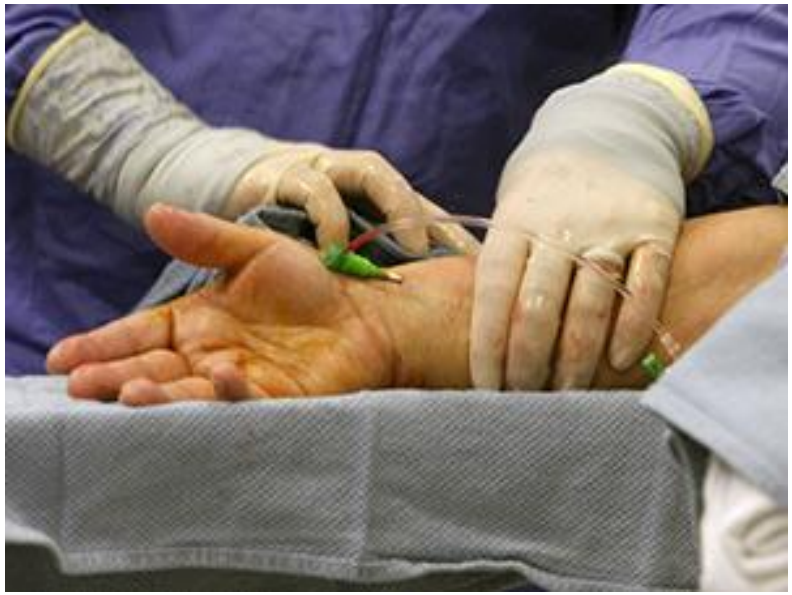
Velmi dobrá apozice stentu

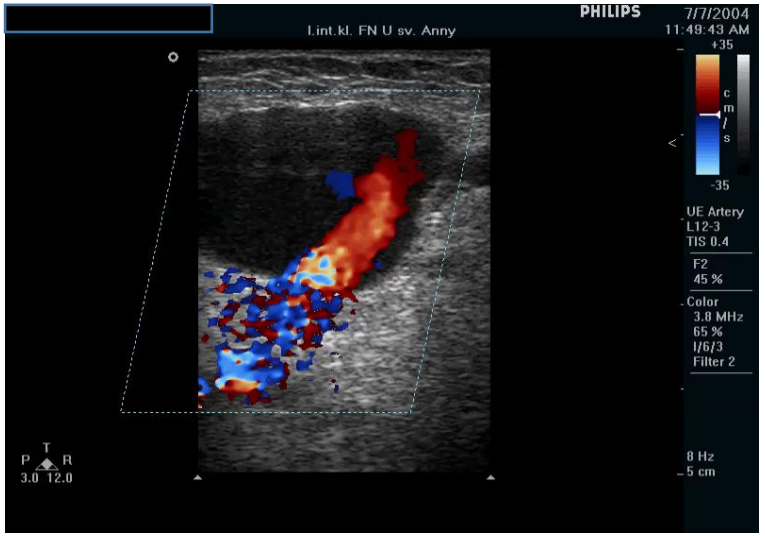


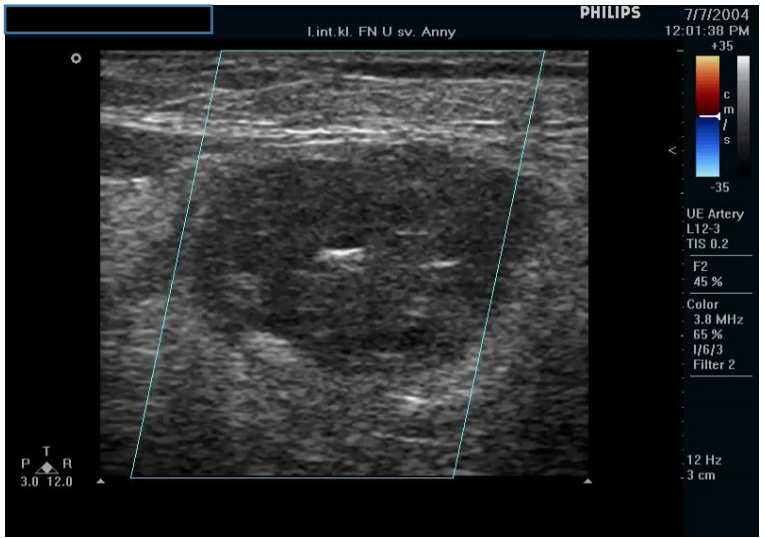
Intrakoronární ultrazvuk - IVUS



Radiální přístup - lepší než femorální







96% (5-25-47%)

CHA_2DS_2-VASc

• Congestive heart failure, ↓EF	1
• Hypertension	1
• Age ≥75	2
• Diabetes mellitus	1
• Stroke/TIA, TE	2
• Vascular disease	1
• Age 65-74	1
• Sex (female)	1
Risk of STROKE/SE	**max. 9**

www.chadsvasc.org

HAS-BLED

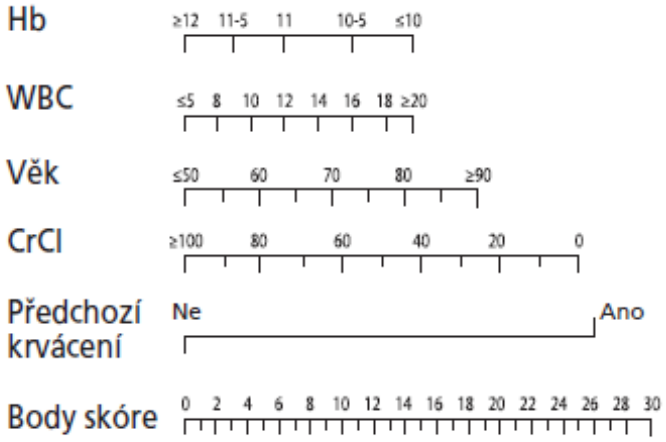
• **Hypertension**	**1**
• **Abnormal liver or renal function**	**1+1**
• **Stroke**	**1**
• **Bleeding disposition**	**1**
• **Labile INR with warfarin**	**1**
• **Elderly >65 yrs**	**1**
• **Drugs (ASA, NSAID) + alcohol**	**1+1**

BLEEDING **max. 9**

www.chadsvasc.org

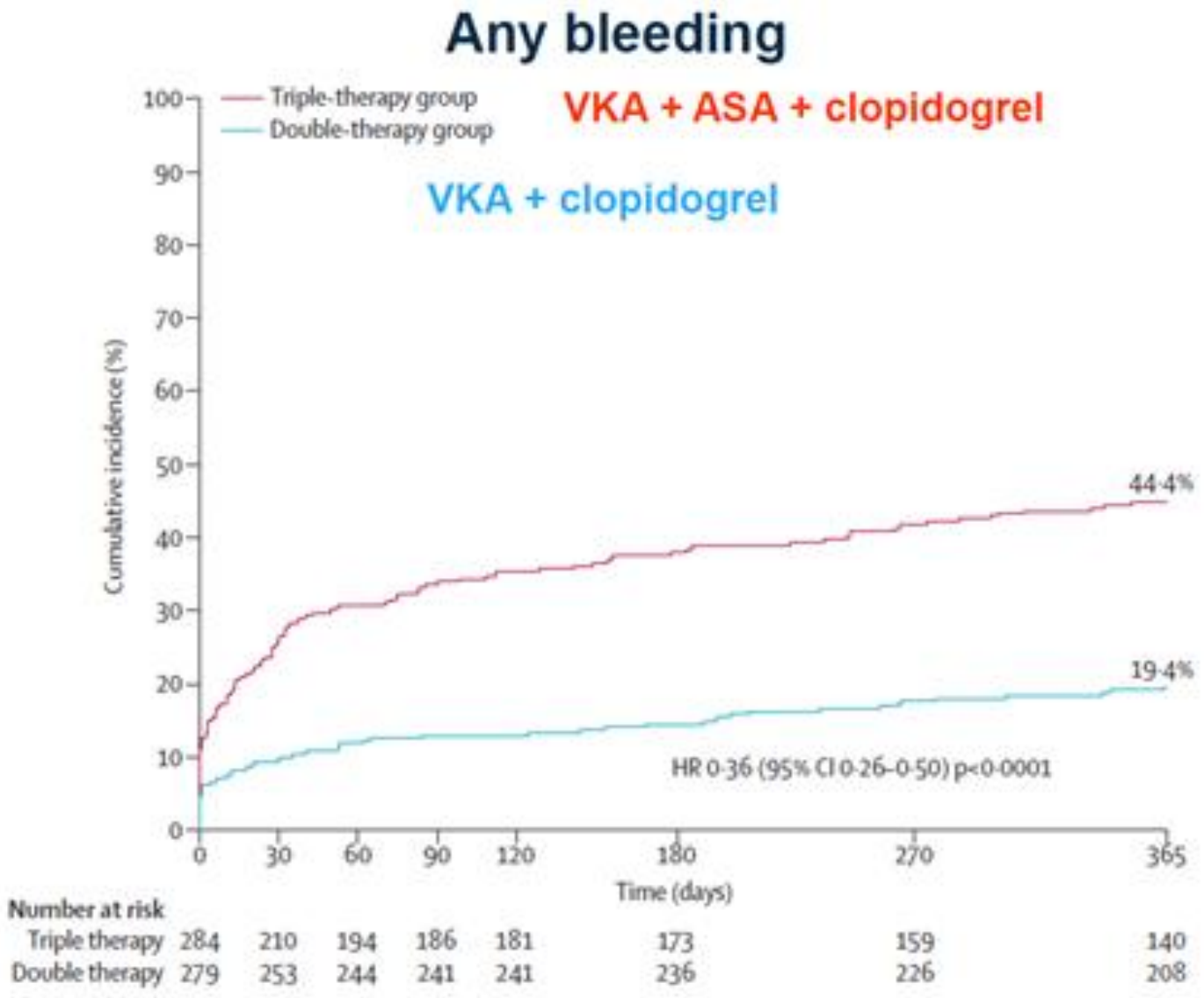
PRECISE-DAPT a DAPT

Tabulka 3 – Riziková skóre validovaná pro rozhodování o délce trvání duální protidestičkové léčby

	Skóre PRECISE-DAPT	Skóre DAPT	
Doba uplatnění	V době koronárního stentingu	Po 12 měsících DAPT bez komplikací	
Hodnocené strategie délky trvání DAPT	Krátkodobá DAPT (3–6 měsíců) oproti standardní/dlouhodobé DAPT (12–24 měsíců)	Standardní DAPT (12 měsíců) oproti dlouhodobé DAPT (30 měsíců)	
Výpočet skóre[a]		Věk ≥ 75 65 až < 75 < 65 Kouření cigaret Diabetes mellitus IM vstupně Předchozí PCI nebo předchozí IM Stent uvolňující paclitaxel Průměr stentu < 3 mm CHF nebo EFLK < 30 % Stent z žilního štěpu	 –2 body –1 bod 0 bodů +1 bod +1 bod +1 bod +1 bod +1 bod +1 bod +2 body +2 body
Rozmezí skóre	0 až 100 bodů	–2 až 10 bodů	
Navrhovaná hraniční hodnota pro rozhodování	Skóre ≥ 25 → krátkodobá DAPT Skóre < 25 → standardní/dlouhodobá DAPT	Skóre ≥ 2 → dlouhodobá DAPT Skóre < 2 → standardní DAPT	
Kalkulátor	www.precisedaptscore.com	www.daptstudy.org	

DAPT ESC Guidelines 2017

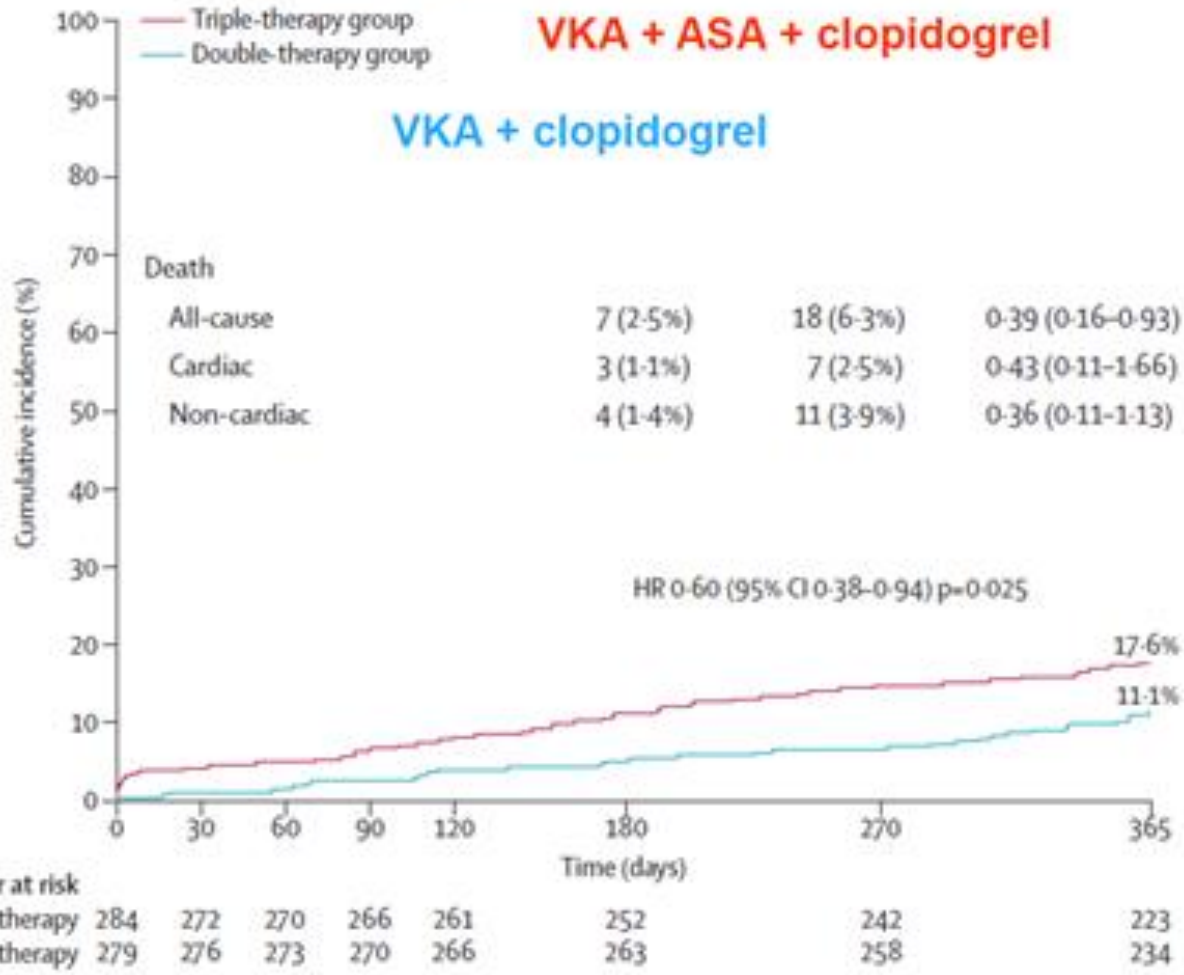
WOEST



Dewilde W et al.: Lancet 2013;381:1107-1115

WOEST

Death, MI, stroke, TVR, ST



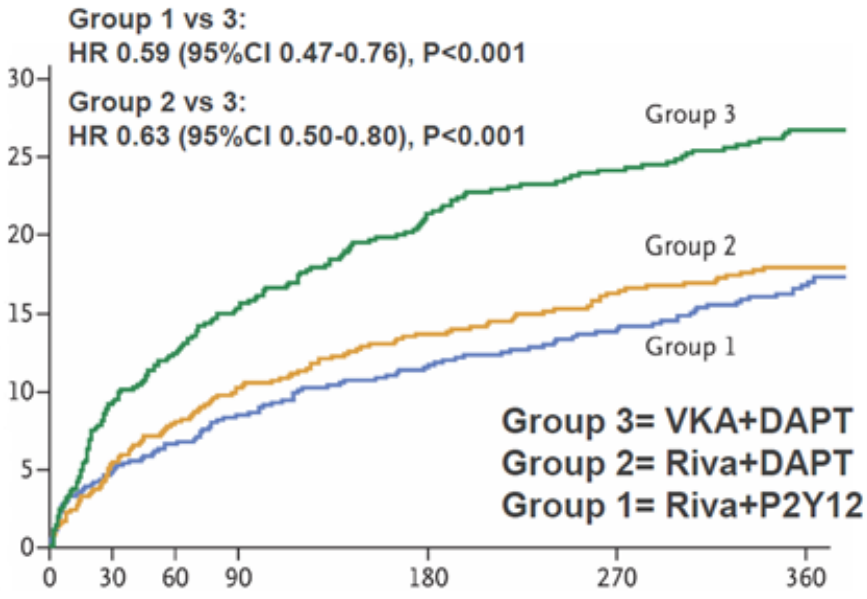
Death				
All-cause	7 (2·5%)	18 (6·3%)	0·39 (0·16–0·93)	0·027
Cardiac	3 (1·1%)	7 (2·5%)	0·43 (0·11–1·66)	0·207
Non-cardiac	4 (1·4%)	11 (3·9%)	0·36 (0·11–1·13)	0·069

Number at risk								
Triple therapy	284	272	270	266	261	252	242	223
Double therapy	279	276	273	270	266	263	258	234

Dewilde W et al.: Lancet 2013;381:1107-1115

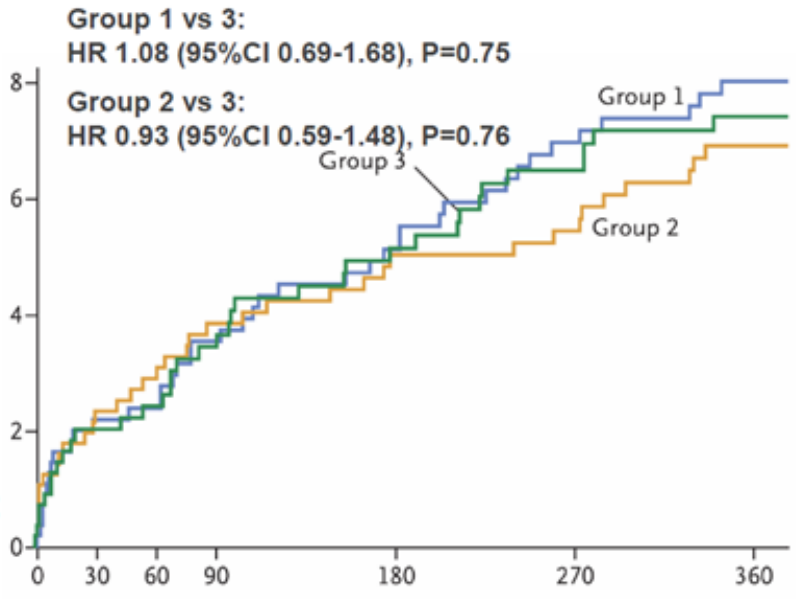
PIONEER AF-PCI

Primary Safety Endpoint



Clinically relevant TIMI bleeding (major, minor or bleeding requiring medical attention)

Secondary Efficacy Endpoint

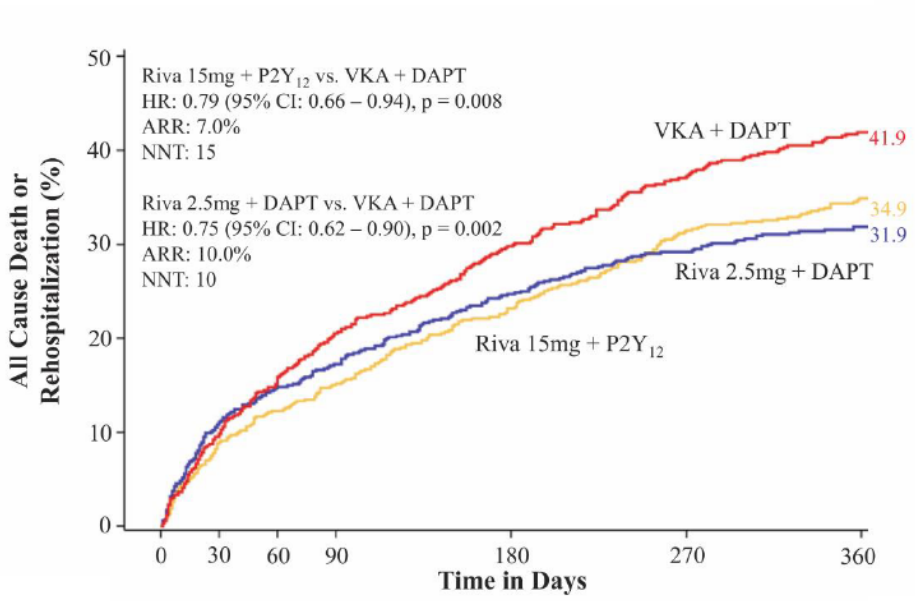


CV death, MI or stroke

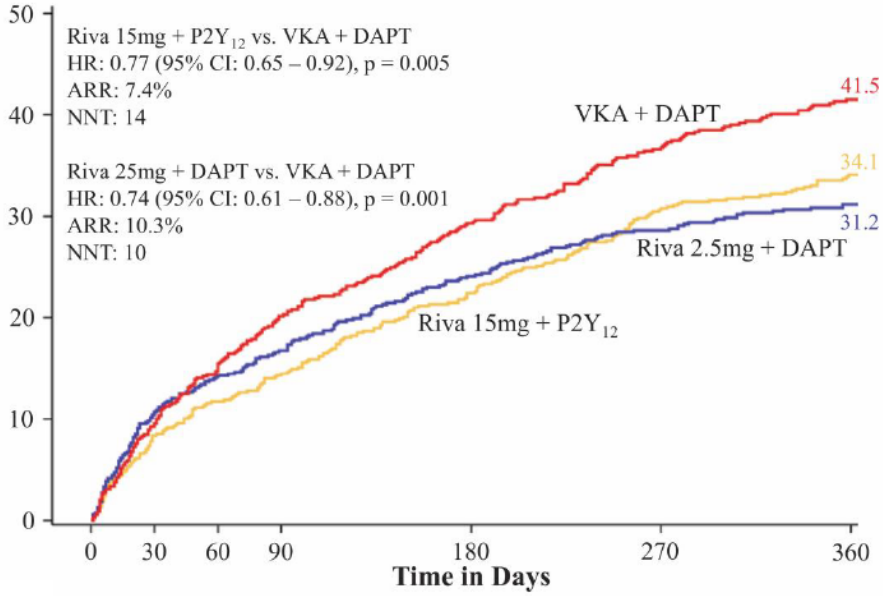
Gibson MC et al.: NEJM 2016;375:2423-34

PIONEER AF-PCI

Death or Rehospitalization



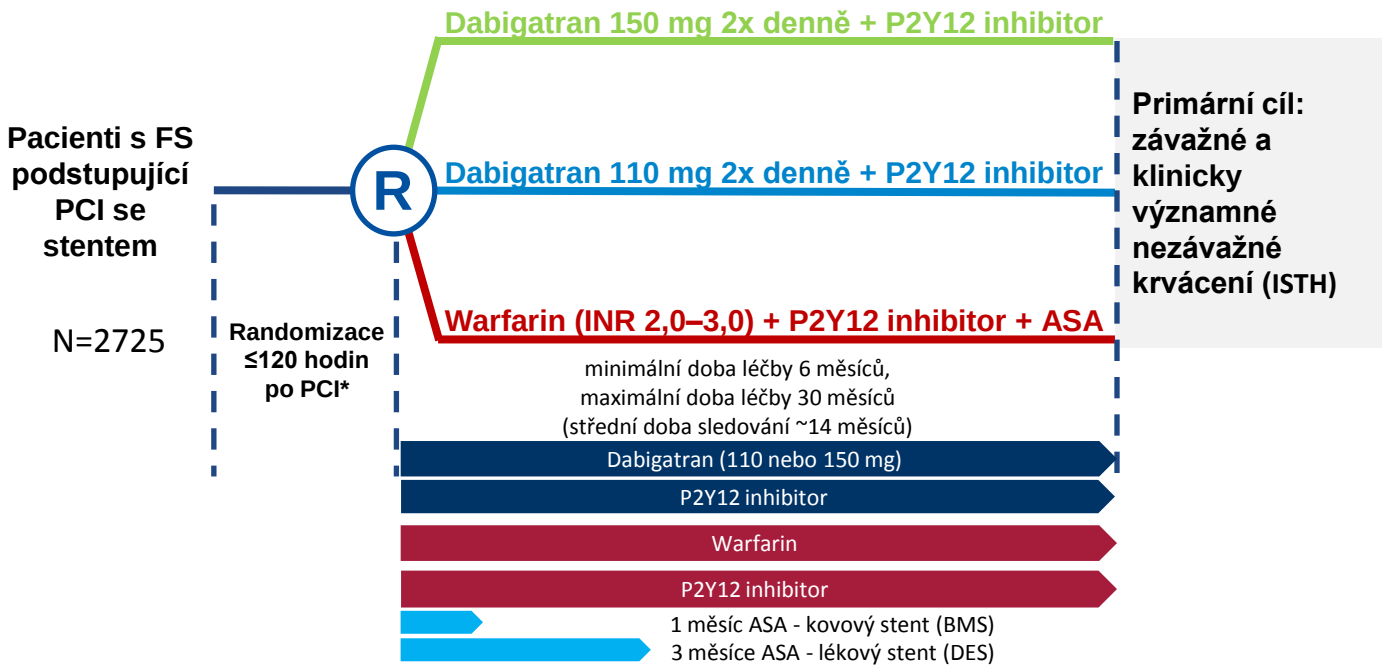
Rehospitalization



Rivaroxaban 10-15 mg daily+$P2Y_{12}$ inhibitor x12M
Rivaroxaban 2.5 mg BID+DAPT x1, 6, or 12M
Warfarin+DAPT x1, 6, or 12M

Gibson MC et al.: NEJM 2016;375:2423-34

RE-DUAL PCI



RE-DUAL PCI - multicentrická, prospektivní, randomizovaná, otevřená studie se zaslepenými end-pointy; *Studijní medikace byla podána 6 hodin po vytažení sheathu ne později než 120 hodin po PCI (≤72 hodin preferováno); ASA - kyselina acetylsalicylová; R - randomizace;

Cannon et al. Clin Cardiol 2016; Cannon et al. N Engl J Med 2017

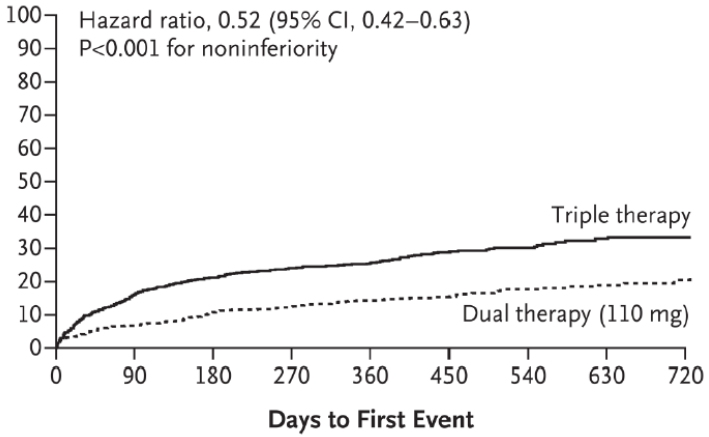
RE-DUAL PCI

MAJOR OR CLINICALLY RELEVANT BLEEDING

Cannon et al. *N Engl J Med* 2017;377:1513-24.

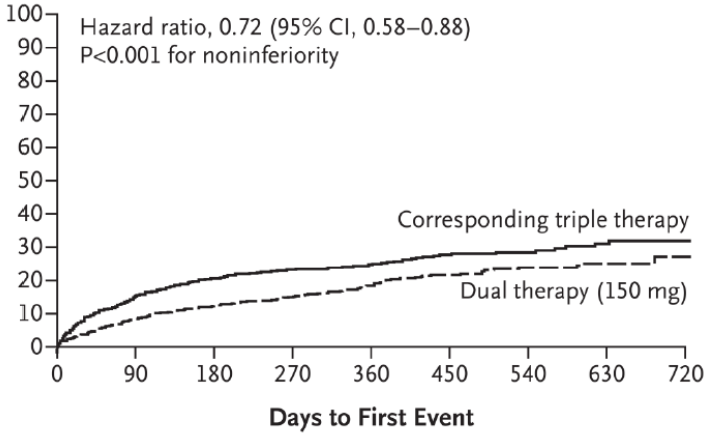
2,725 patients with atrial fibrillation undergoing PCI

Dual-Therapy (110mg) vs. Triple-Therapy



↓48% RRR

Dual-Therapy (150mg) vs. Triple-Therapy



↓28% RRR

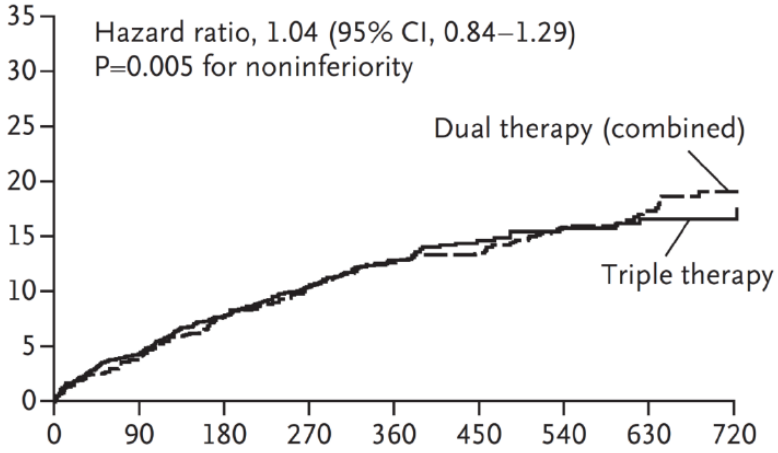
Cannon et al. Clin Cardiol 2016; Cannon et al. N Engl J Med 2017

RE-DUAL PCI

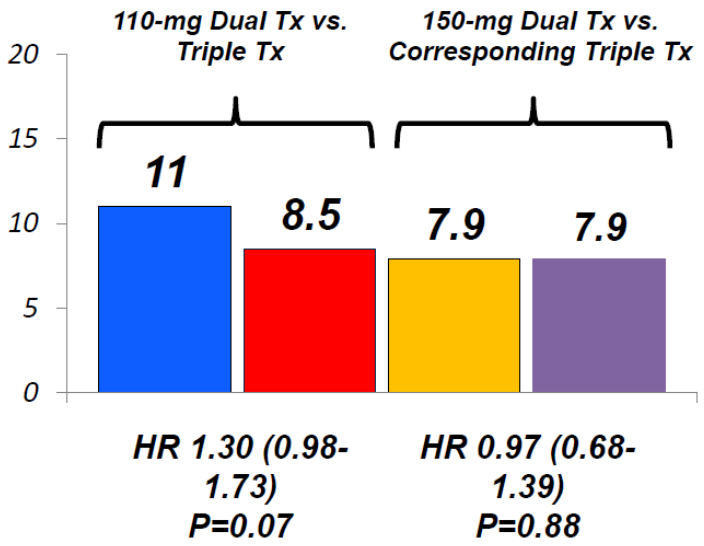
SECONDARY EFFICACY ENDPOINTS

Cannon et al. *N Engl J Med* 2017;377:1513-24.

Thromboembolic events (MI, Stroke, Systemic Embolism), death, or unplanned revascularizazion

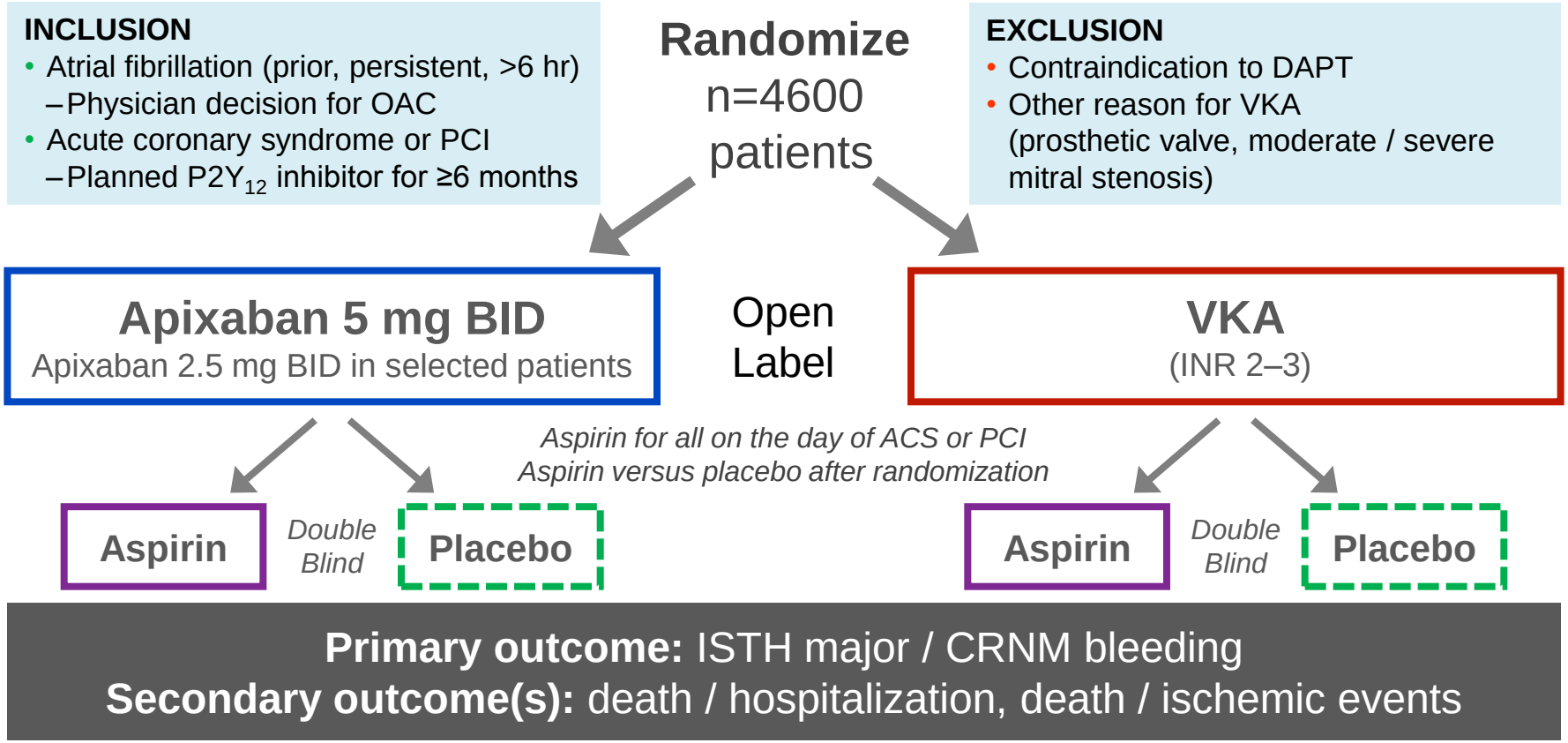


Thromboembolic events (MI, Stroke, Systemic Embolism) or death,



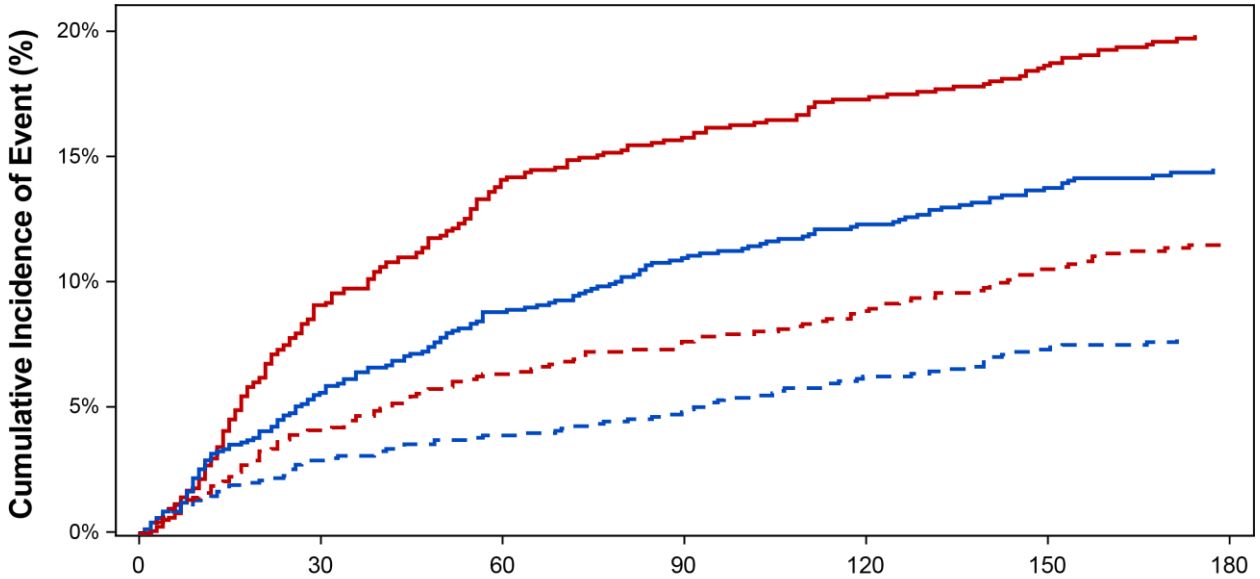
Cannon et al. Clin Cardiol 2016; Cannon et al. N Engl J Med 2017

Trial Design



Lopes RD, et al. Am Heart J. 2018;200:17-23.

Major / CRNM Bleeding



Number at Risk							
Apixaban and Aspirin	1145	1036	975	937	903	880	485
Apixaban and Placebo	1143	1075	1044	1007	975	947	536
VKA and Aspirin	1123	962	881	838	800	776	467
VKA and Placebo	1126	1007	947	917	883	851	528

VKA + Aspirin (18.7%)

Apixaban + Aspirin (13.8%)

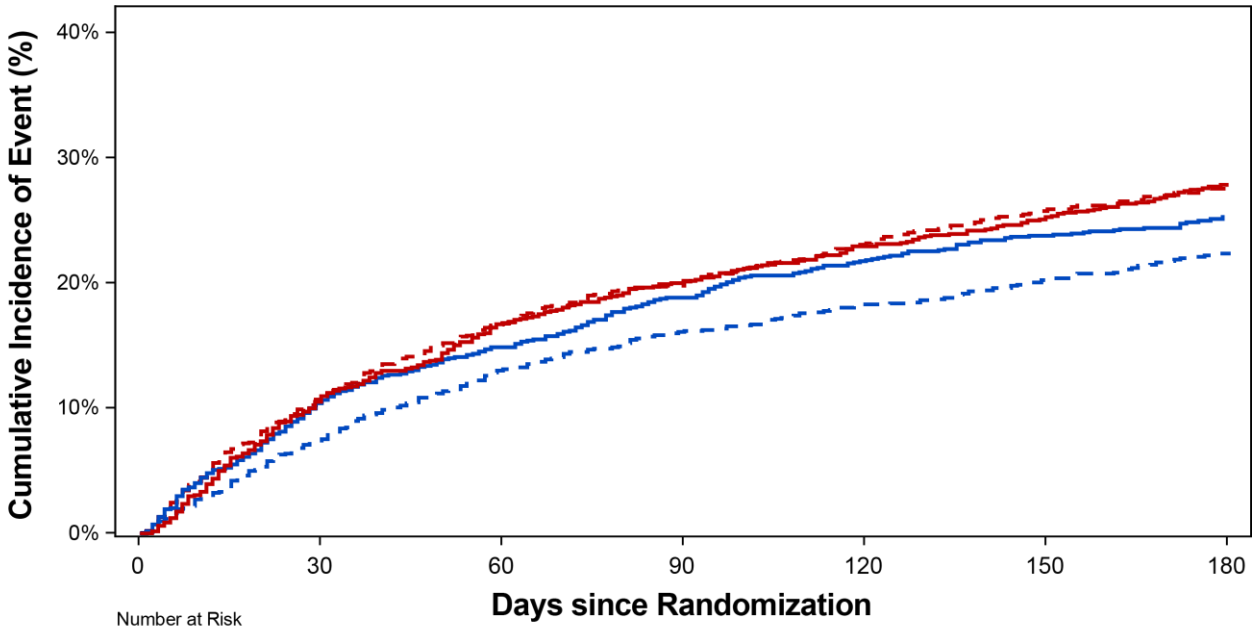
VKA + Placebo (10.9%)

Apixaban + Placebo (7.3%)

Apixaban + Placebo vs. VKA + Aspirin: 11.4% absolute risk reduction (NNT=9)

NEJM 2019

Death / Hospitalization



Number at Risk

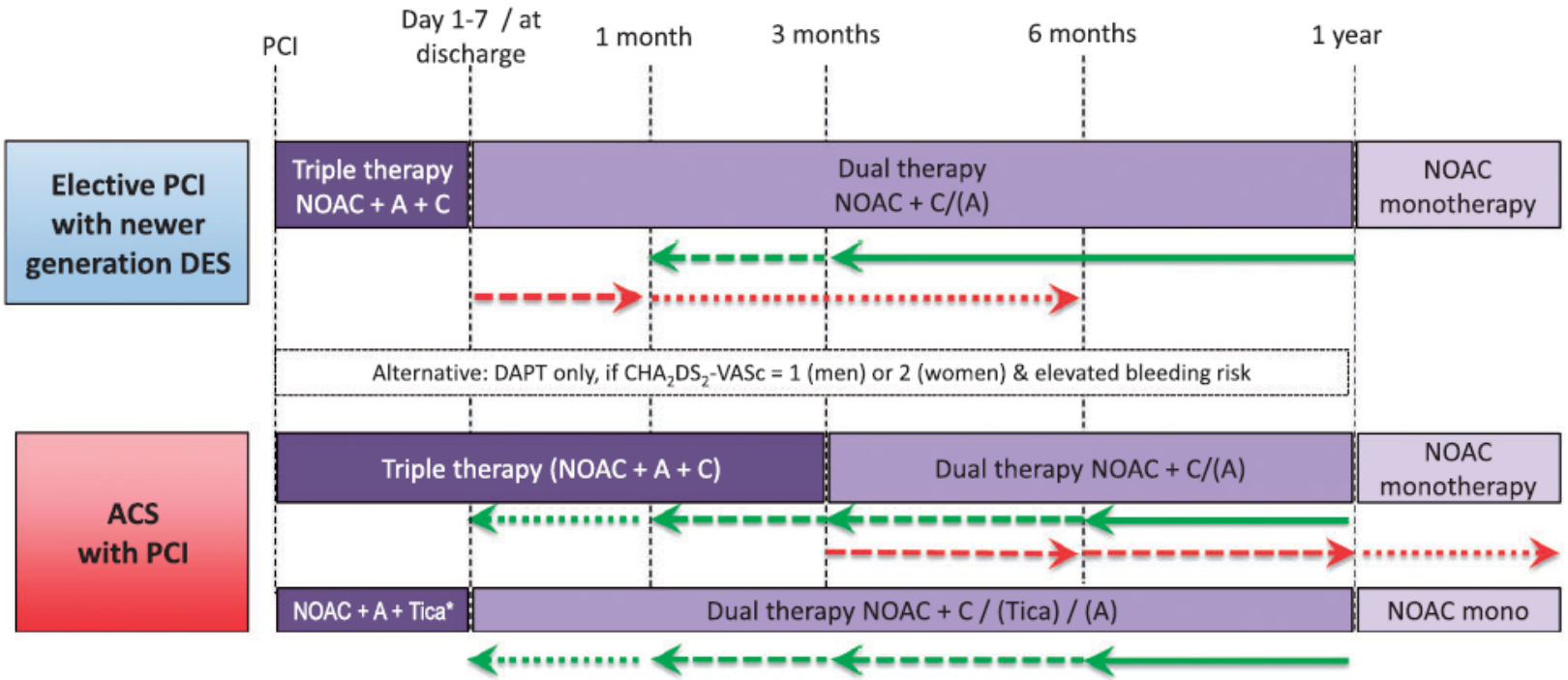
Apixaban and Aspirin	1153	1026	970	923	888	863	459
Apixaban and Placebo	1153	1064	995	958	933	909	488
VKA and Aspirin	1154	1016	939	899	864	836	492
VKA and Placebo	1154	1019	946	906	868	837	509

VKA + Aspirin (27.5%)
VKA + Placebo (27.3%)
Apixaban + Aspirin (24.9%)
Apixaban + Placebo (22.0%)

Apixaban + Placebo vs. VKA + Aspirin:
5.5% absolute risk reduction (NNT=18)

NEJM 2019

NOAK a PCI



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

EHRA Guidelines, EHJ 2018

NOAK – DES - AKS

Triple

- 3M — CHA_2DS_2-VASc ≥ HAS-BLED a PRECISE-DAPT < 25
- 1M — CHA_2DS_2-VASc < HAS-BLED nebo PRECISE-DAPT ≥ 25
- Za hosp. — CHA_2DS_2-VASc < HAS-BLED a PRECISE-DAPT ≥ 25

Individuální posouzení rizika ischémie vs krvácení

NOAK – DES - AKS

Dual

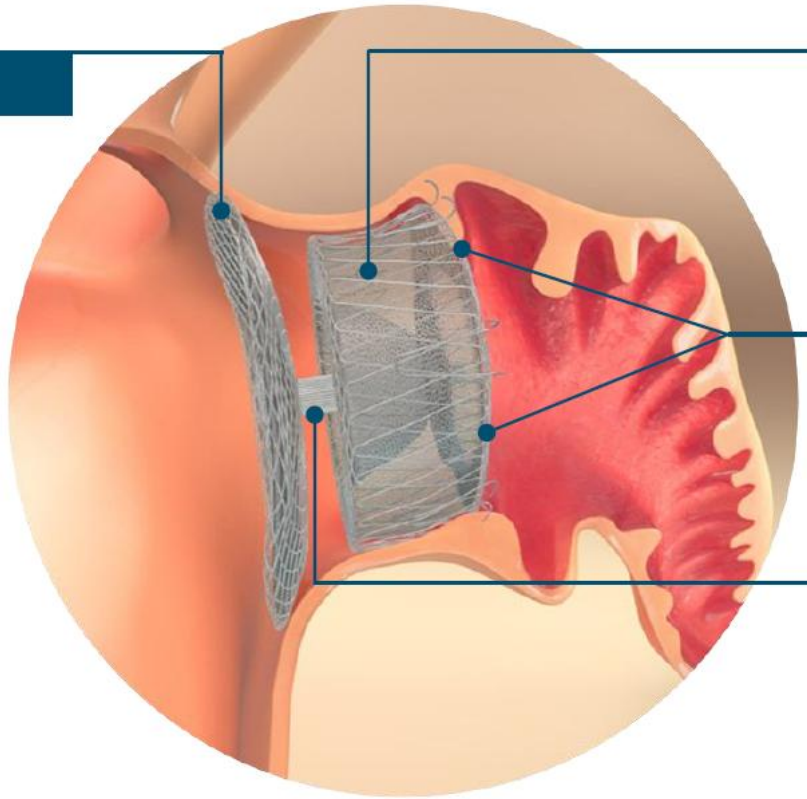
- 12M — CHA_2DS_2-VASc ≥ HAS-BLED a PRECISE-DAPT < 25
- 6M — CHA_2DS_2-VASc < HAS-BLED nebo PRECISE-DAPT ≥ 25
- 3M — CHA_2DS_2-VASc < HAS-BLED a PRECISE-DAPT ≥ 25

Individuální posouzení rizika ischémie vs krvácení

Uzávěr ouška levé síně

DISC

- Designed to completely seal the LAA at the orifice



LOBE

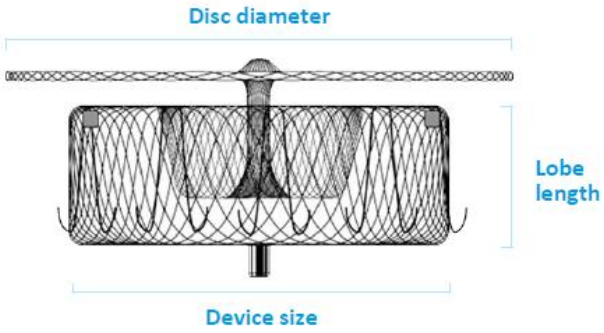
- Positioned inside the LAA neck
- Designed to conform to different sizes and shapes of LAA anatomy

STABILIZING WIRES

- Engage with the wall of the LAA
- Help hold the device in place

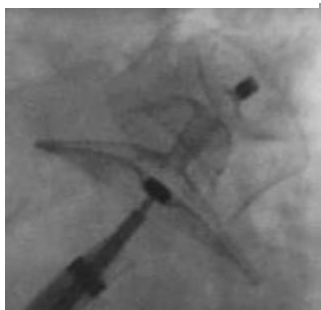
WAIST

- Maintains tension between lobe and disc
- Flexible connection allows device to self-orient



LAA occlusion may be considered for stroke prevention in patients with AF and contra-indications for long-term anticoagulant treatment (e.g. those with a previous life-threatening bleed without a reversible cause).

IIb	B



Závěry

- Počítejme skóre (CHA_2Ds_2-VASc2, HAS-BLED, PRECISE-DAPT)
- Výsledný efekt PCI

- Triple th. - co nejkratší dobu
- NOAK lepší než warfarin s výjimkou KI
- Warfarin INR o 0,5 níže než norm.
- Clopidogrel nejvhodnější z P2Y12 inh.
- ASA ≤ 100mg tbl.
- PPI rutinně
- Uzávěr ouška LS při KI OAK

Individualizace ANO

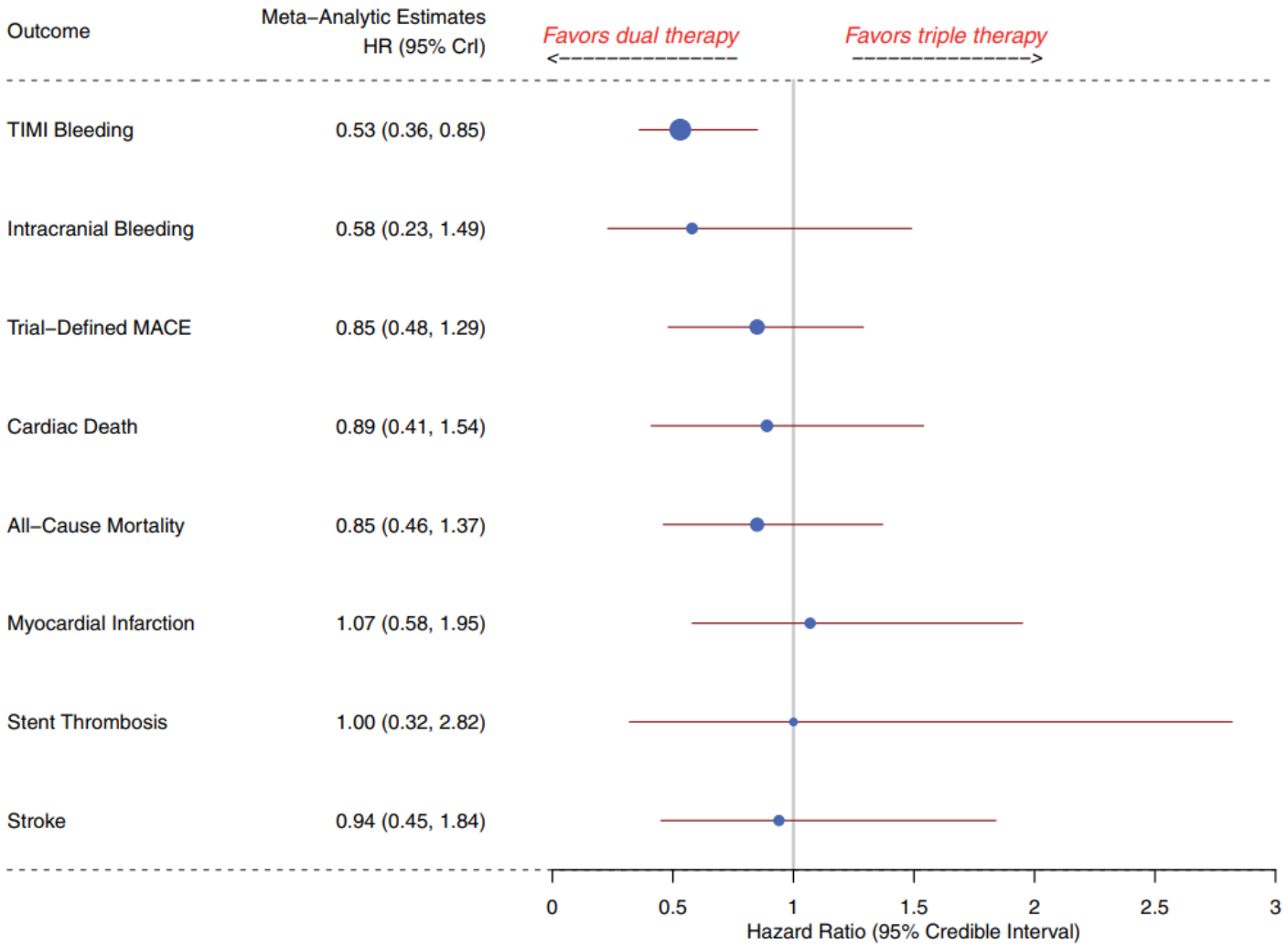
- Evidence based medicine
- Selský rozum
- Pocity lékaře

Pro každé rozhodnutí nutné vědecky podložené zdůvodnění

Medicína za 100 let – GENETIKA (GDPR?)

Metaanalýza

WOEST, ISAR-Triple, Pioneer-AF PCI, Re-Dual PCI (n=5317)



Golwala HB et al.: Eur Heart J 2018;39:1726-1735

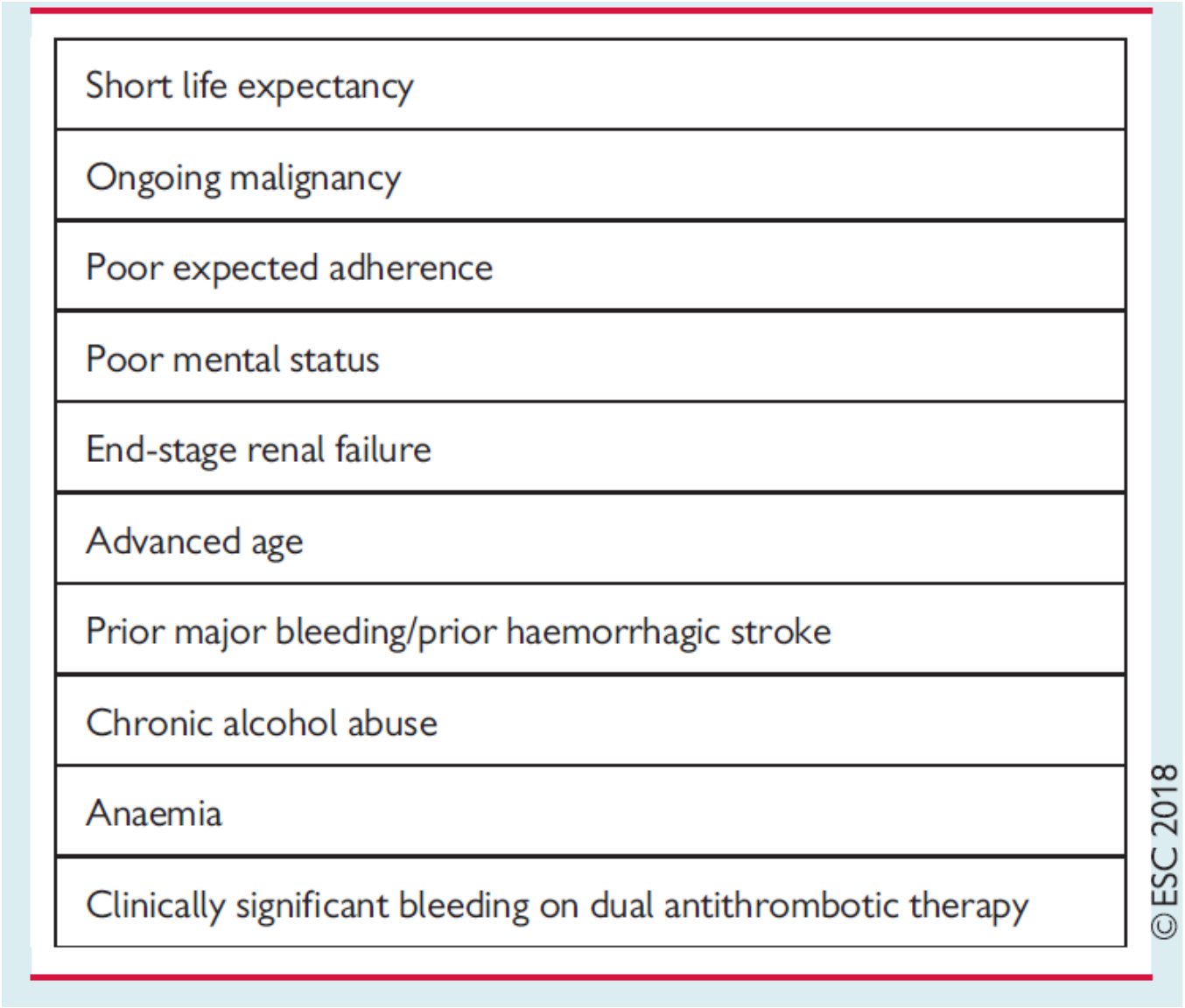
Kdy chronická OA léčba?

- Umělá chlopeň — warfarin
- Fibrilace síní
  - Mi stenóza — warfarin
  - Ostatní — NOAK
- Trombus v srdci — warfarin, NOAK
- Stp. PE — NOAK
- Trombóza žil DKK — NOAK

Vysoké riziko ischemické příhody

Prior stent thrombosis on adequate antiplatelet therapy
Stenting of the last remaining patent coronary artery
Diffuse multivessel disease, especially in diabetic patients
Chronic kidney disease (i.e. creatinine clearance <60 mL/min)
At least three stents implanted
At least three lesions treated
Bifurcation with two stents implanted
Total stented length >60 mm
Treatment of a chronic total occlusion
History of STEMI

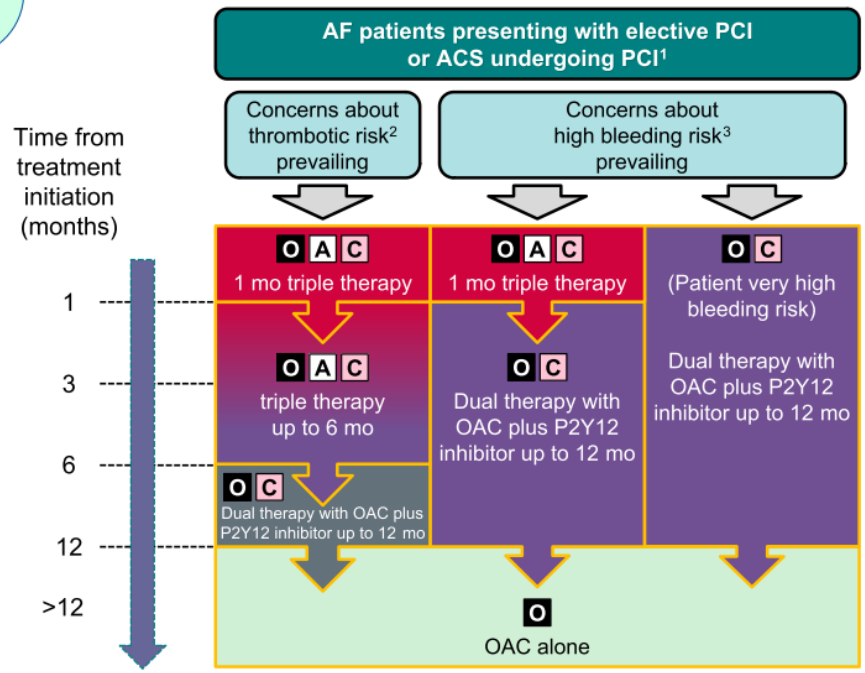
Málo vhodní pacienti pro kombinovanou antikoagulační a protidestičkovou léčbu



Now, with new evidence, expert consensus statements have been updated

Aug 2018

Joint European Consensus document



'Low dose dabigatran 110 mg BID and full dose apixaban 5 mg BID and edoxaban 60 mg OD should be selected to optimize risk-benefit ratio, if part of a TAT regime.'

'…safety of reduced-dose apixaban 2.5 mg BID and edoxaban 30 mg OD is likely higher, true efficacy in stroke prevention is unknown when […] used in the absence of factors qualifying patients for dose reduction, and should therefore generally not be used, even when DAPT […] is given in conjunction.'

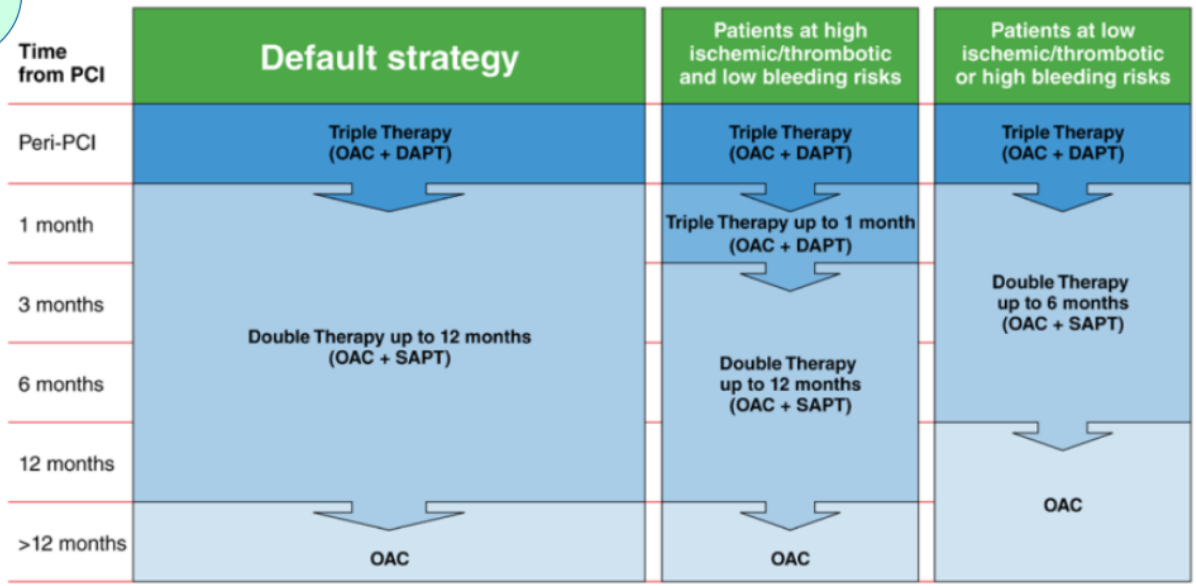
'With DAT, **dabigatran 150 mg plus P2Y12 is preferred**, unless dose reduction criteria for dabigatran are present.'

1. Periprocedural administration of aspirin and clopidogrel during PCI is recommended irrespective of the treatment strategy; as dual therapy, potent P2Y12 inhibitors (ticagrelor) may be combined with dabigatran; 2: High atherothrombotic risk (For Elective PCI, use SYNTAX score; for ACS, GRACE score >140; stenting of the left main, proximal LAD, proximal bifurcation; recurrent MIs; stent thrombosis etc.) and low bleeding risk; 3: Bleeding risk can be estimated using the HAS-BLED score; correct modifiable bleeding risk factors. DAT, dual antithrombotic therapy; LAD, left anterior descending; TAT, triple antithrombotic therapy. Lip GYH et al. Europace 2018;doi:10.1093/europace/euy174.

Now, with new evidence, expert consensus statements have been updated

2018

North American expert consensus document



'A **double therapy** approach (OAC + P2Y12 inhibitor) should represent the **default strategy** for most patients…'

'An NOAC (rather than VKA) should generally be preferred..'

'If ticagrelor is chosen as the P2Y12 agent, concomitant aspirin should not be given (i.e. avoid triple therapy), as was done in the RE-DUAL PCI trial'

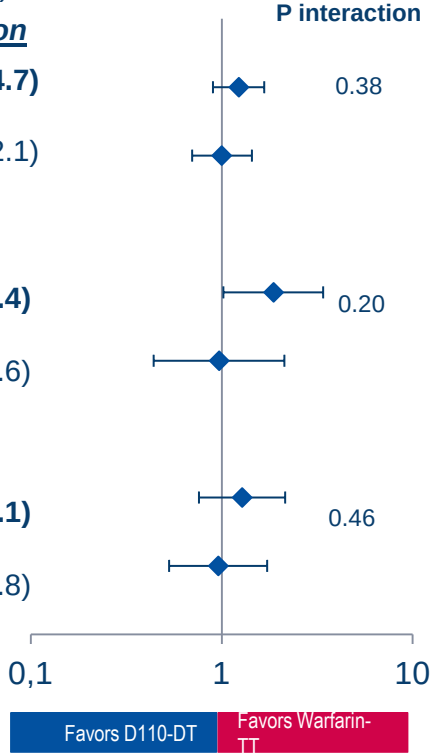
'When different therapeutic dosing options (i.e. dabigatran 110 and 150 mg) are available, the intensity of anticoagulant treatment should be tailored according to the bleeding and thrombotic risk profiles of the patient'

Angiolillo DJ et al. Circulation 2018;138:527–36

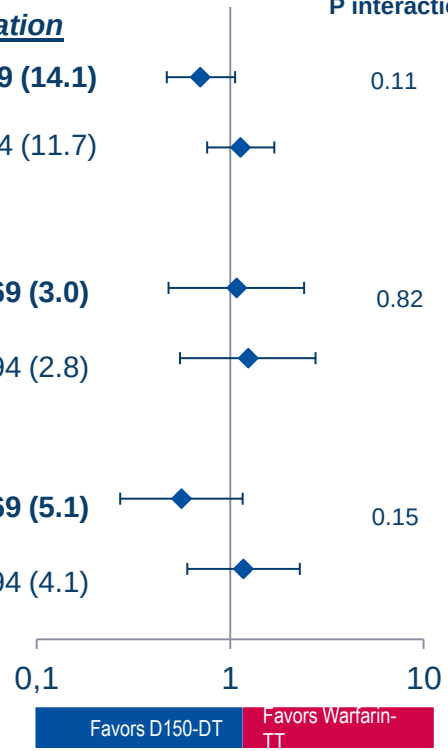
Death and thromboembolic events: ACS vs non-ACS

RE-DUAL PCI
Study in NVAF patients undergoing PCI

	D110-DT n/N (%)	Warfarin-TT n/N (%)	P interaction
DTE or Unplanned Revascularization			
ACS	**92/509 (18.1)**	**70/475 (14.7)**	0.38
Non-ACS	57/472 (12.1)	61/505 (12.1)	
Myocardial Infarction			
ACS	**32/509 (6.3)**	**16/475 (3.4)**	0.20
Non-ACS	12/472 (2.5)	13/505 (2.6)	
All-cause Death			
ACS	**34/509 (6.7)**	**24/475 (5.1)**	0.46
Non-ACS	21/472 (4.4)	24/505 (4.8)	



	D150-DT n/N (%)	Warfarin-TT n/N (%)	P interaction
DTE or Unplanned Revascularization			
ACS	**41/391 (10.5)**	**52/369 (14.1)**	0.11
Non-ACS	49/372 (13.2)	46/394 (11.7)	
Myocardial Infarction			
ACS	**13/391 (3.3)**	**11/369 (3.0)**	0.82
Non-ACS	13/372 (3.5)	11/394 (2.8)	
All-cause Death			
ACS	**12/391 (3.1)**	**19/369 (5.1)**	0.15
Non-ACS	18/372 (4.8)	16/394 (4.1)	



ACS, acute coronary syndrome; D, dabigatran; DT, dual therapy; DTE, death or thromboembolic event (myocardial infarction, stroke or systemic embolism); TT, triple therapy.

Summary

In the RE-DUAL PCI trial

- The index indication for PCI was an ACS in 50% of the patients
- DES alone were used in 83% of the patients, similarly in patients with ACS and non-ACS
- The majority of patients received clopidogrel; 12% of the patients received ticagrelor either as part of dabigatran dual therapy or warfarin triple therapy
- Patients who received ticagrelor more often had ACS as the index event, were oral anticoagulation naïve, and had DAPT clinical complexity factors; and ticagrelor was associated with higher bleeding risk than clopidogrel
- There were no significant interactions in any of the presented outcomes for any of the presented subgroups

ACS, acute coronary syndrome; DAPT, dual antiplatelet therapy; DES, drug-eluting stent; PCI, percutaneous coronary intervention.

GRACE skóre a GRACE2 RISK CALCULATOR – NSTE ACS

- Věk
- sTK
- TF
- Kreatinin
- Killip třída
- Srdeční zástava
- ↑ ukazatelů nekrózy myokardu
- Změny ST úseků

Mortalita hosp., 6M, 1Y, 3Y; mortalita nebo IM 1Y

www.gracescore.org

CRUSADE bleeding risc score - NSTEMI

- INTRODUCTION
- CALCULATOR
- ABOUT
- REFERENCES
- LINKS
- DISCLAIMER
- DOWNLOADS

Last Updated:
March 2008

Enter values in drop-down boxes below:

Baseline Hematocrit	HCT (%)	Prior Vascular Disease	-Select-
GFR: Cockcroft-Gault	mL/min (Calculate GFR)	Diabetes Mellitus	-Select-
Heart rate on admission	bpm	Signs of CHF on admission	-Select-
Systolic blood pressure on admission	mmHg	Sex	-Select-

Clear Selections

CRUSADE Bleeding Score	Risk of In-Hospital Major Bleeding
--	--
Enter all fields above	Enter all fields above

www.crusadebleedingscore.org

Závažné krvácení

↑riziko mortality bez ohledu na místo krvácení

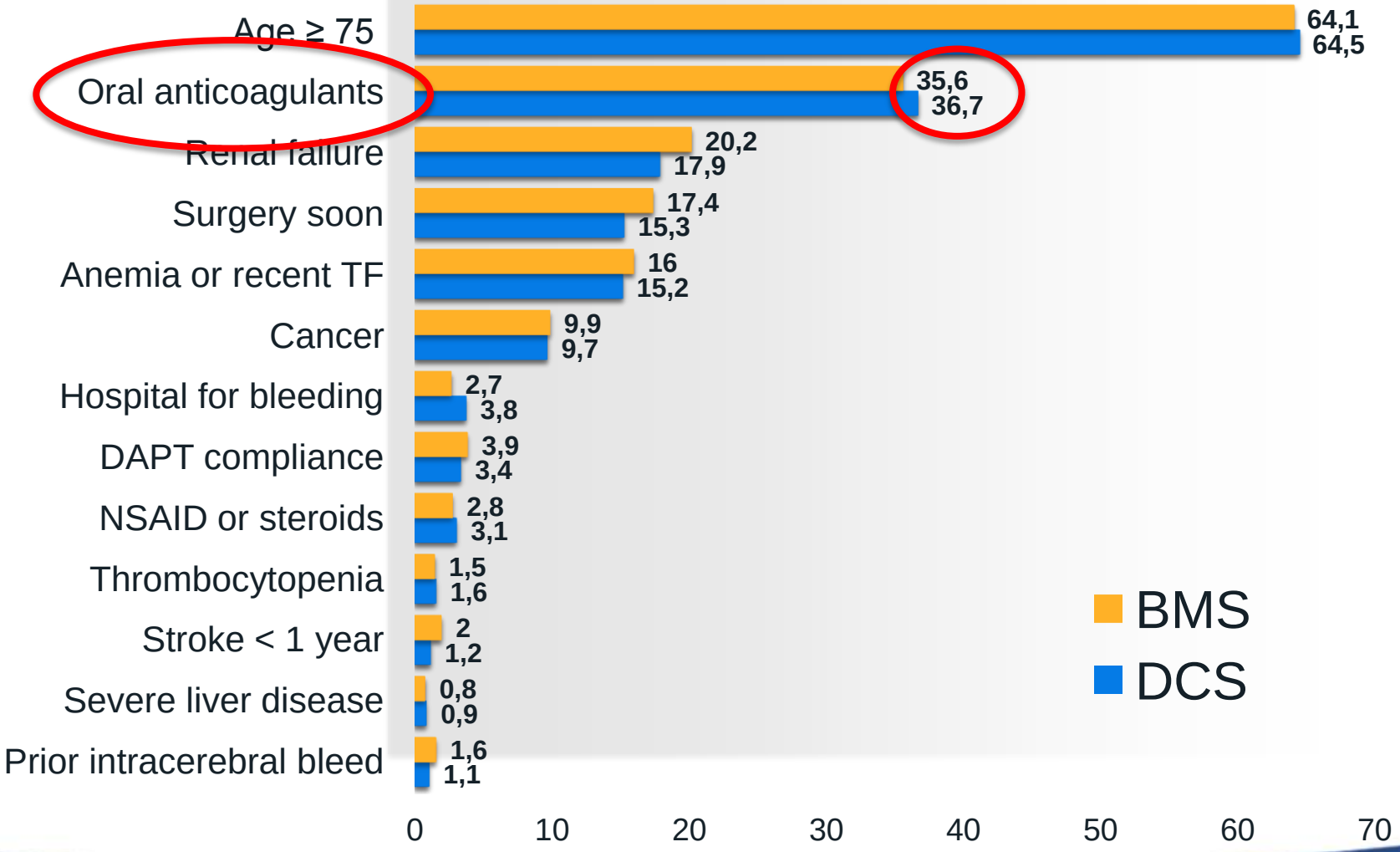
Analýza 17 393 pacientů podstupující PCI jako součást studií REPLACE-2, ACUITY, a HORIZONS-AMI

	Jednoroční úmrtnost (%)	Relativní riziko: s krvácením vs bez krvácení (95% CI)	P hodnota
Bez krvácení	2,54	–	–
Krvácení pouze z cévního přístupu	6,16	2,33 (1,53–3,53)	<0,001
Všechna krvácení mimo cévní přístup	14,4	5,40 (4,32–6,74)	<0,0001
Pouze krvácení mimo cévní přístup	14,1	5,52 (3,62–8,40)	<0,001
Krvácení z cévního přístupu i jiného zdroje	14,5	5,70 (3,78–8,61)	<0,001
Nejasného původu	14,6	5,18 (3,82–7,03)	<0,001

Neupravená jednoroční úmrtnost a relativní riziko spojené s třicetidenním krvácením TIMI

Verheugt et al. JACC 2001

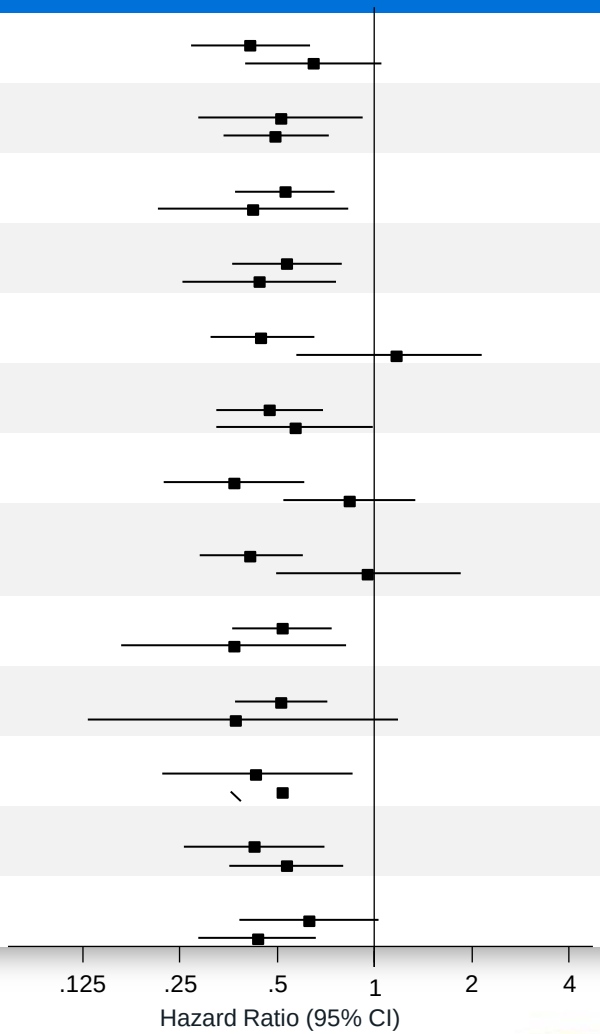
LEADERS FREE
(1.7 HBR incl. criteria / patient)



Subgroups

Efficacy endpoint (clinically driven TLR)

Category		N	DCS: Events (%)	BMS: Events (%)	P-value for interaction
Age >80	No	1602	31 (4.0)	72 (9.4)	0.17
	Yes	830	28 (7.1)	41 (10.6)	
Male	No	738	17 (5.0)	33 (9.3)	0.92
	Yes	1694	42 (5.1)	80 (10.0)	
ACS at admission	No	1773	47 (5.5)	86 (10.1)	0.55
	yes	659	12 (3.9)	27 (9.0)	
Diabetes	No	1622	40 (5.3)	74 (9.4)	0.57
	Yes	805	19 (4.7)	39 (10.7)	
Renal failure at admission	No	1754	42 (4.9)	88 (10.6)	0.02
	Yes	466	16 (7.9)	15 (6.7)	
Planed OAC at randomization	No	1553	39 (5.3)	80 (10.7)	0.61
	Yes	879	20 (4.7)	33 (8.2)	
Crusade score > median (35)	No	1061	21 (4.1)	56 (10.7)	0.02
	Yes	962	33 (7.5)	39 (8.7)	
Anemia, transfusion or bleeding leading to hospitalization	No	2007	41 (4.2)	95 (9.9)	0.03
	Yes	425	18 (9.2)	18 (9.6)	
Planned major surgery in following year	No	2002	49 (5.1)	89 (9.5)	0.43
	yes	404	8 (4.3)	23 (11.5)	
Cancer in last 3 years*	No	2193	55 (5.2)	102 (9.8)	0.59
	yes	239	4 (3.5)	11 (9.8)	
Multi-vessel disease at admission	No	906	12 (2.8)	28 (6.4)	0.64
	yes	1493	46 (6.5)	84 (12.0)	
Total stent length > 30 mm	No	1409	21 (3.2)	51 (7.4)	0.48
	Yes	999	38 (7.6)	61 (13.6)	
Minimal stent diameter < 3 mm	No	1195	26 (4.5)	41 (7.2)	0.26
	Yes	1213	33 (5.7)	71 (12.4)	



2018 ESC/EACTS Guidelines on myocardial revascularization

Recommendations	Class[a]	Level[b]
IVUS or OCT should be considered in selected patients to optimize stent implantation.[603,612,651–653]	IIa	B
IVUS should be considered to optimize treatment of unprotected left main lesions.[35]	IIa	B

EHJ 2018

Není stent jako stent - DES

DES	Stent platform	Polymer coating	Drug
Based on durable polymer coatings			
Promus element	Platinum–chrome	PBMA and PVDF-HFP	Everolimus
Resolute	Cobalt–chrome	PBMA, PHMA, PVP, and PVA	Zotarolimus
Xience	Cobalt–chrome	PBMA and PVDF-HFP	Everolimus
EluNIR (BioNIR)	Cobalt–chrome	PBMA and TSPCU	Ridaforolimus
Based on biodegradable polymer coatings			
Biomatrix	Stainless steel	PDLLA	Biolimus A9
Nobori	Stainless steel	PDLLA	Biolimus A9
Orsiro	Cobalt–chrome	PLLA	Sirolimus
Synergy	Platinum–chrome	PLGA	Everolimus
Ultimaster	Stainless steel	PDLLA/PCL	Sirolimus
Yukon Choice PC	Stainless steel	PDLLA	Sirolimus
Polymer-free			
BioFreedom	Stainless steel	–	Biolimus A9
Yukon Choice PF	Stainless steel	–	Sirolimus

Supraflex, Biomime

EHJ 2018, EuroPCR 2018, TCT 2018

ABC stroke and bleeding risk

ABC-Stroke and ABC-Bleeding risk calculation:

Prior stroke:	○ Yes ◉ No	
Prior Bleeding:	○ Yes ◉ No	
Age (years):	68	Accepted range 22 - 95 (years)
hs-troponin T (ng/L):	100	Accepted range 3.0 - 200 (ng/L)
NT-proBNP (ng/L):	2000	Accepted range 5 - 21000 (ng/L)
GDF-15 (ng/L):	690	Accepted range 400 - 20000 (ng/L)
Hemoglobin (g/dL):	12	Accepted range 9.0 - 20 (g/dL)
	Calculate estimated risk	

Result

You entered:

Variables for ABC-Stroke score: Prior stroke = No, age = 68, cTnT = 100, NT-proBNP = 2000

Variables for ABC-Bleeding score: Prior bleeding = No, age = 68, cTnT = 100, GDF-15 = 690, HB = 12

The ABC-stroke risk score[1]: Predicted one year stroke/SE risk = 2.03%

Without oral anticoagulation the estimated stroke risk is approximately 3 times higher; based on estimated OAC vs no treatment risk[3]

The ABC-bleeding risk score[2]: Predicted one year bleeding risk = 3.37%

http://www.ucr.uu.se/en/services/abc-risk-calculators