Koronární stent-návod k použití

Kdo má prospěch z prodloužené duální léčby?

P. Červinka
Krajská zdravotní a.s., Masarykova nemocnice v Ústí nad Labem o.z
a UJEP Ústí nad Labem

(XXVI. sjezd ČKS, Brno, 6.-9.5. 2018)

Kdo má prospěch z prodloužené DAPT?

➢ Kdo má prospěch z prodloužené DAPT?

Individualizace trvání DAPT na základě bedlivého posouzení ischemického a krvácivého rizika a přání nemocného“

➢ Kdo má prospěch z prodloužené DAPT?

- "So far, there is no 'free lunch'. If you interfere with coagulation in any manner, it will be associated with excess bleeding."

Eugene Braunwald

Kdo má prospěch z prodloužené DAPT?

- ***Klasifikace krvácení***

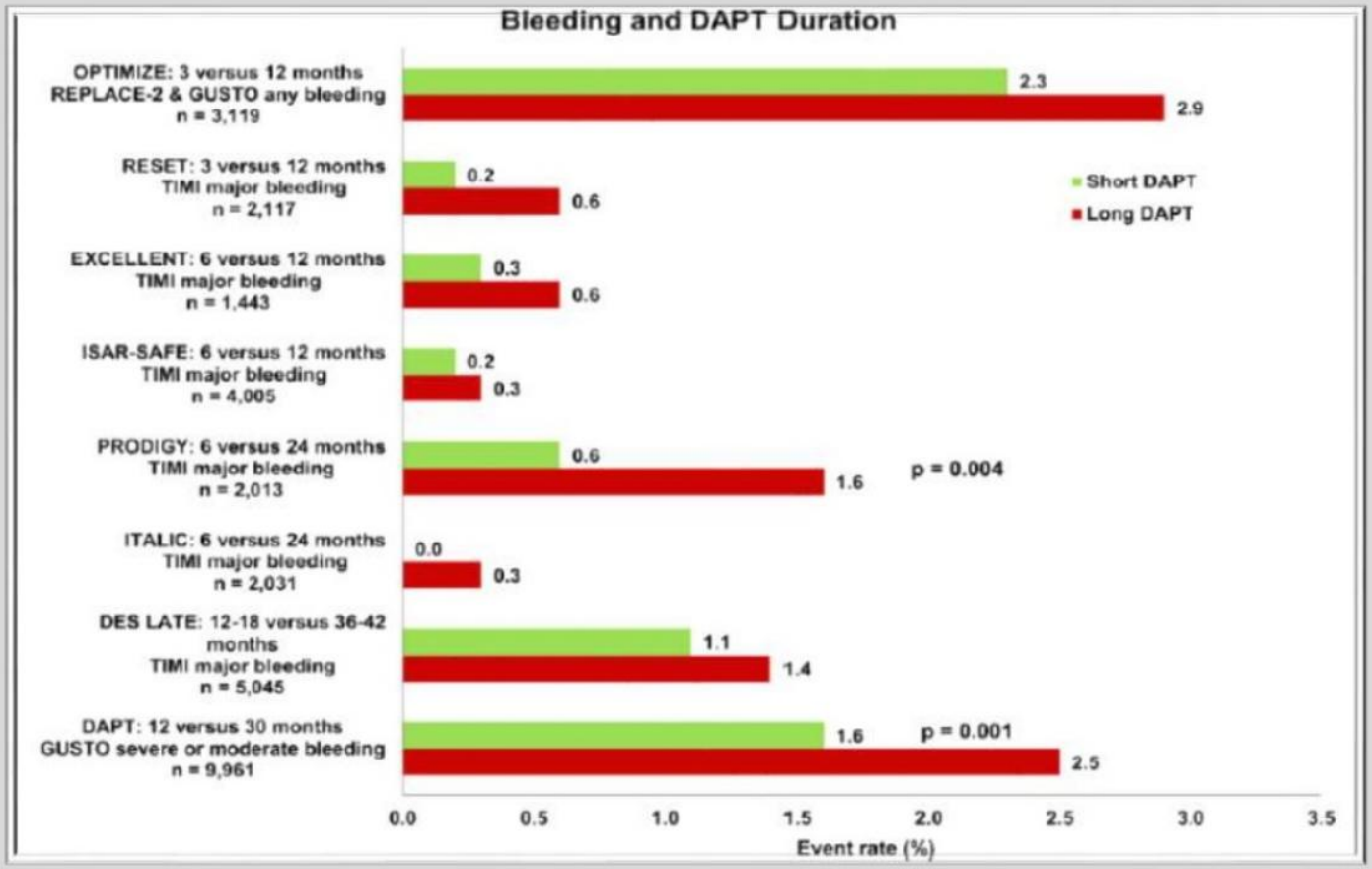
Table 1. BARC Definitions

Type 0	No bleeding
Type 1	Bleeding that is not actionable and does not cause the patient to seek treatment
Type 2	Any clinically overt sign of hemorrhage that "is actionable" and requires diagnostic studies, hospitalization, or treatment by a health care professional
Type 3	a. Overt bleeding plus hemoglobin drop of 3 to < 5 g/dL (provided hemoglobin drop is related to bleed); transfusion with overt bleeding b. Overt bleeding plus hemoglobin drop < 5 g/dL (provided hemoglobin drop is related to bleed); cardiac tamponade; bleeding requiring surgical intervention for control; bleeding requiring IV vasoactive agents c. Intracranial hemorrhage confirmed by autopsy, imaging, or lumbar puncture; intraocular bleed compromising vision
Type 4	CABG-related bleeding within 48 hours
Type 5	a. Probable fatal bleeding b. Definite fatal bleeding (overt or autopsy or imaging confirmation)

TIMI Bleeding Classification	
Major	Intracranial haemorrhage or clinically overt bleeding (including imaging) ≥ 5 g/dL decrease in the haemoglobin concentration
Minor	Clinically overt bleeding (including imaging) with 3 to < 5 g/dL decrease in the haemoglobin concentration
Minimal	Clinically overt bleeding (including imaging) with a < 3 g/dL decrease in the haemoglobin concentration
GUSTO Bleeding Classification	
Severe or life threatening	Either intracranial haemorrhage or bleeding that causes haemodynamic compromise and requires intervention
Moderate	Bleeding that requires blood transfusion but does not result in haemodynamic compromise
Mild	Bleeding that does not meet criteria for either severe or moderate bleeding

➢ Kdo má prospěch z prodloužené DAPT?

- ***Krvácení a DAPT***



Rates of bleeding are consistently higher for prolonged DAPT, reaching statistical significance in some studies

European Heart Journal (2015) 36, 1207–1211

➢ Kdo má prospěch z prodloužené DAPT?

- **Závažná krvácení jsou spojena s významným zvýšením hospitalizační úmrtnosti bez ohledu na místo krvácení**

In the CathPCI registry, analysing data from 3.3 million PCI procedures (2004–11):

1.87%
in-hospital mortality rate:
non-bleeding

risk difference = 3.39%
(95% CI: 3.20–3.59)
P<0.001

5.26%
in-hospital mortality rate:
major bleeding

Bleeding is the most common non-cardiac complication of PCI

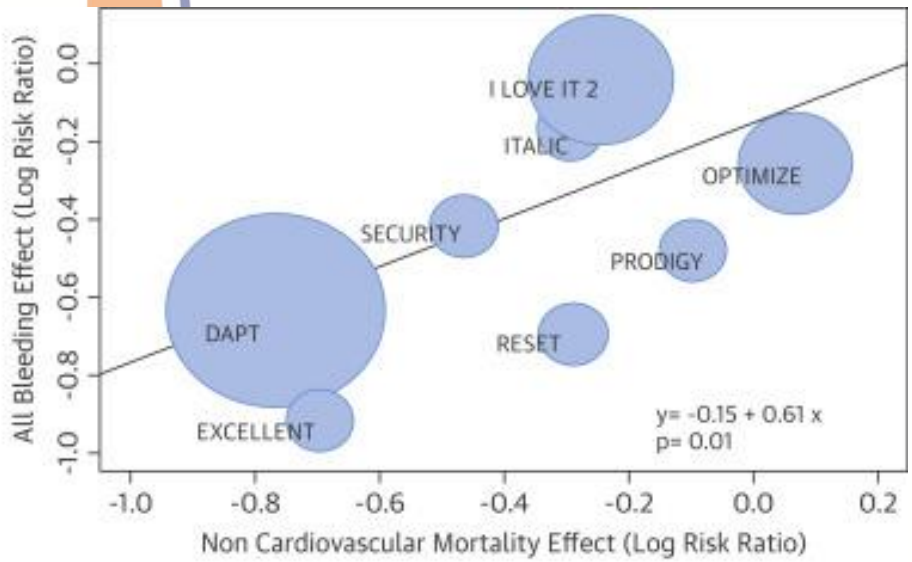
Antithrombotic therapy that minimizes the risk of bleeding complications therefore might be expected to result in better short- and long-term clinical outcomes after PCI

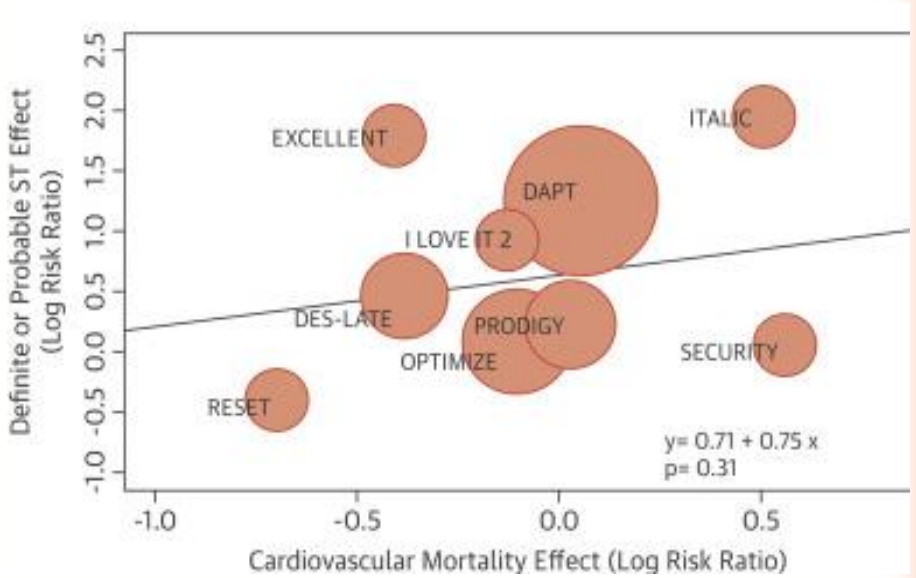
PCI, percutaneous coronary intervention; Chhatriwalla et al. JAMA 2013

Kdo má prospěch z prodloužené DAPT?

- ***Meta-Analyses of Dual Antiplatelet Therapy Following Drug-Eluting Stent Implantation : Do Bleeding and Stent Thrombosis Weigh Similar on Mortality***?

Association Between Log-Transformed Risk of All Bleeding and ST With Noncardiovascular and Cardiovascular Mortality, RespectivelyThe size of each circle represents the precision of each estimate ...



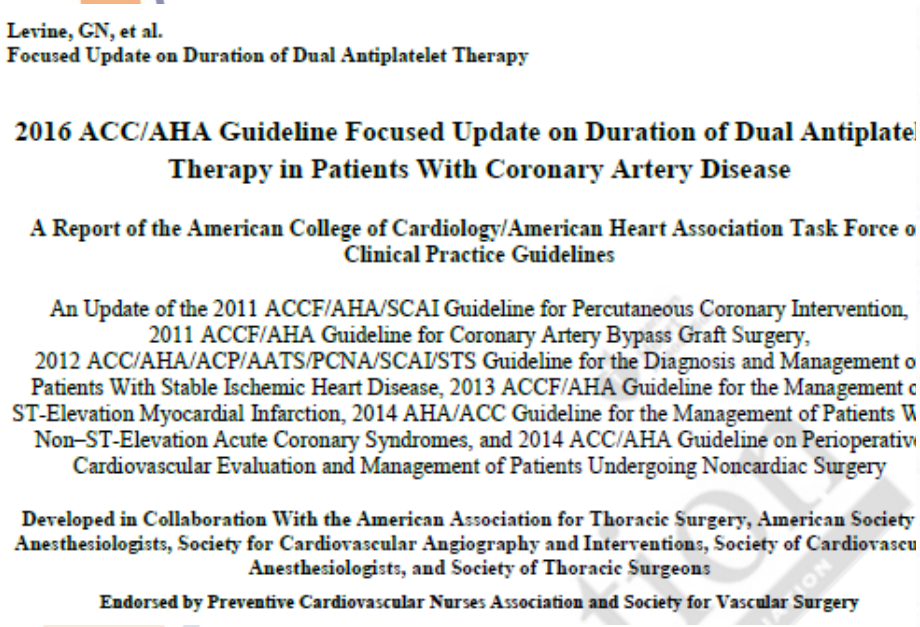


In conclusion, in drug-eluting stent trials of DAPT duration, bleeding seems to be significantly associated with noncardiovascular mortality, whereas ST does not seem to be significantly associated with cardiovascular mortality. Therefore, DAPT prolongation over current recommendations should only be undertaken after careful consideration of the benefit-risk balance.

(Capodanno D, et al. JACC, Volume 66, Issue 14, 2015, 1639–1640)

➢ Kdo má prospěch z prodloužené DAPT?

- ***Doporučení ACC/AHA (2016) a ESC/EACTS (2017)***



Levine, GN, et al.
Focused Update on Duration of Dual Antiplatelet Therapy

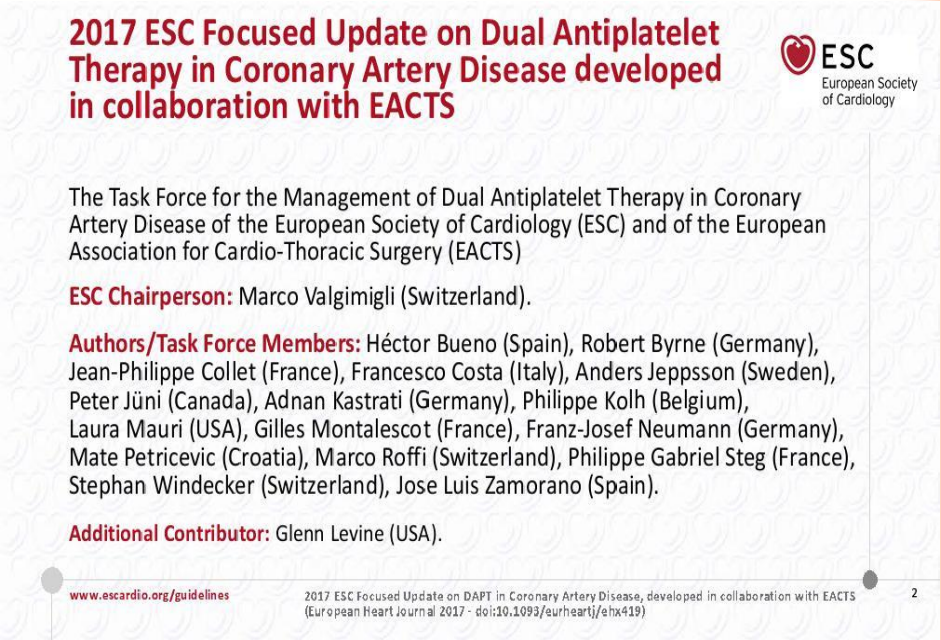
2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatel Therapy in Patients With Coronary Artery Disease

A Report of the American College of Cardiology/American Heart Association Task Force o Clinical Practice Guidelines

An Update of the 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention, 2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery, 2012 ACC/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the Diagnosis and Management o Patients With Stable Ischemic Heart Disease, 2013 ACCF/AHA Guideline for the Management c ST-Elevation Myocardial Infarction, 2014 AHA/ACC Guideline for the Management of Patients W Non–ST-Elevation Acute Coronary Syndromes, and 2014 ACC/AHA Guideline on Perioperativ Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery

Developed in Collaboration With the American Association for Thoracic Surgery, American Society Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascu Anesthesiologists, and Society of Thoracic Surgeons

Endorsed by Preventive Cardiovascular Nurses Association and Society for Vascular Surgery



2017 ESC Focused Update on Dual Antiplatelet Therapy in Coronary Artery Disease developed in collaboration with EACTS

ESC European Society of Cardiology

The Task Force for the Management of Dual Antiplatelet Therapy in Coronary Artery Disease of the European Society of Cardiology (ESC) and of the European Association for Cardio-Thoracic Surgery (EACTS)

ESC Chairperson: Marco Valgimigli (Switzerland).

Authors/Task Force Members: Héctor Bueno (Spain), Robert Byrne (Germany), Jean-Philippe Collet (France), Francesco Costa (Italy), Anders Jeppsson (Sweden), Peter Jüni (Canada), Adnan Kastrati (Germany), Philippe Kolh (Belgium), Laura Mauri (USA), Gilles Montalescot (France), Franz-Josef Neumann (Germany), Mate Petricevic (Croatia), Marco Roffi (Switzerland), Philippe Gabriel Steg (France), Stephan Windecker (Switzerland), Jose Luis Zamorano (Spain).

Additional Contributor: Glenn Levine (USA).

www.escardio.org/guidelines

2017 ESC Focused Update on DAPT in Coronary Artery Disease, developed in collaboration with EACTS (European Heart Journal 2017 - doi:10.1093/eurheartj/ehx419)

2

Kdo má prospěch z prodloužené DAPT?

- ***Klinické a procedurální charakteristiky spojené se zvýšeným ischemickým rizikem nebo krvácením***

Increased Ischemic Risk/Risk of Stent Thrombosis (may favor longer-duration DAPT)	Increased Bleeding Risk (may favor shorter-duration DAPT)
Increased ischemic risk • Advanced age • ACS presentation • Multiple prior MIs • Extensive CAD • Diabetes mellitus • CKD	• History of prior bleeding • Oral anticoagulant therapy • Female sex • Advanced age • Low body weight • CKD • Diabetes mellitus • Anemia • Chronic steroid or NSAID therapy
Increased risk of stent thrombosis • ACS presentation • Diabetes mellitus • Left ventricular ejection fraction <40% • First-generation drug-eluting stent • Stent undersizing • Stent underdeployment • Small stent diameter • Greater stent length • Bifurcation stents • In-stent restenosis	

Kdo má prospěch z prodloužené DAPT?

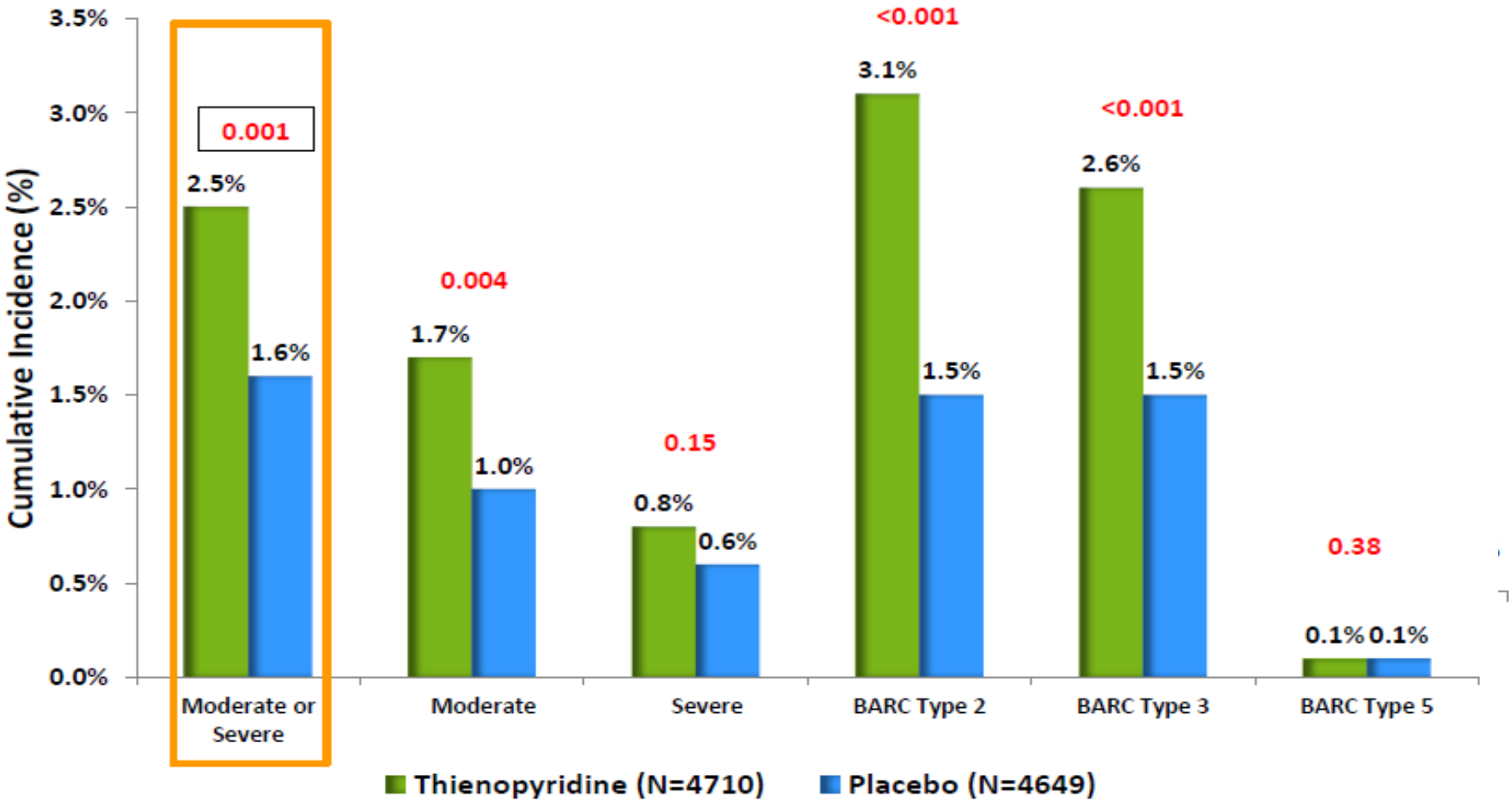
RCTs of DAPT Duration After Implantation of DES

(N=33051)

Observed Proportion

Primary Safety End Point (Moderate or Severe Bleeding): 12-30 Months

DAPT STUDY

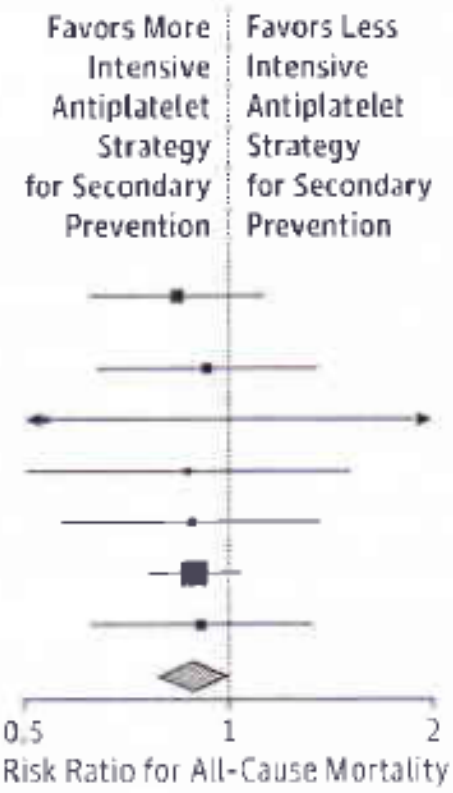


➢ Kdo má prospěch z prodloužené DAPT?

Endpoints After Prolonged Versus 6 to 12 Months of DAPT After DES Implantation

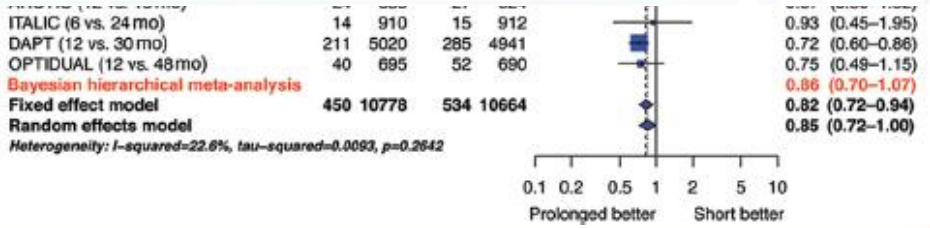
Figure. Risk of All-Cause Mortality With More Intensive Antiplatelet Therapy for Long-term Secondary Prevention in Patients With Prior Myocardial Infarction

Trial	More Intensive No./Total No.	Less Intensive No./Total No.	Hazard Ratio (95% CI)
CHARISMA (prior myocardial infarction cohort)	82/1903	99/1943	0.84 (0.63-1.13)
PRODIGY	52/732	56/733	0.93 (0.64-1.35)
ARCTIC	1/156	2/167	0.54 (0.05-5.87)
DAPT MI	24/1805	27/1771	0.87 (0.50-1.50)
DES-LATE	37/1512	43/1551	0.88 (0.57-1.37)
PEGASUS-TIMI 54 (60 mg twice daily)	289/7045	326/7067	0.89 (0.76-1.04)
TRA2P-TIMI 50 MI (no stroke/TIA)	238/8458	259/8439	0.91 (0.62-1.33)
Total	723/21611	812/21671	0.89 (0.79-0.99)
			P = .04



(Bonaca MP, Sabatine MS. JACC;2016,Vol.1, 627-8)

- ***Zvýšení závažných krvácení***
- ***Snížení IM a ST***



➢ Kdo má prospěch z prodloužené DAPT?

6-month versus 12-month or longer dual antiplatelet therapy after percutaneous coronary intervention in patients with acute coronary syndrome (SMART-DATE): a randomised, open-label, non-inferiority trial

Joo-Yong Hahn, Young Bin Song*, Ju-Hyeon Oh, Deok-Kyu Cho, Jin Bae Lee, Joon-Hyung Doh, Sang-Hyun Kim, Jin-Ok Jeong, Jang-Ho Bae, Byung-Ok Kim, Jang Hyun Cho, Il-Woo Suh, Doo-il Kim, Hoon-Ki Park, Jong-Seon Park, Woong Gil Choi, Wang Soo Lee, Jihoon Kim, Ki Hong Choi, Taek Kyu Park, Joo Myung Lee, Jeong Hoon Yang, Jin-Ho Choi, Seung-Hyuk Choi, Hyeon-Cheol Gwon, for the SMART-DATE investigators†*

Summary

Background Current guidelines recommend dual antiplatelet therapy (DAPT) of aspirin plus a P2Y12 inhibitor for at least 12 months after implantation of drug-eluting stents (DES) in patients with acute coronary syndrome. However, available data about the optimal duration of DAPT in patients with acute coronary syndrome undergoing percutaneous coronary intervention are scant. We aimed to investigate whether a 6-month duration of DAPT would be non-inferior to the conventional 12-month or longer duration of DAPT in this population.

Methods We did a randomised, open-label, non-inferiority trial at 31 centres in South Korea. Patients were eligible if they had unstable angina, non-ST-segment elevation myocardial infarction, or ST-segment elevation myocardial infarction, and underwent percutaneous coronary intervention. Enrolled patients were randomly assigned, via a web-based system by computer-generated block randomisation, to either the 6-month DAPT group or to the 12-month or longer DAPT group, with stratification by site, clinical presentation, and diabetes. Assessors were masked to treatment allocation. The primary endpoint was a composite of all-cause death, myocardial infarction, or stroke at 18 months after the index procedure in the intention-to-treat population. Secondary endpoints were the individual components of the primary endpoint; definite or probable stent thrombosis as defined by the Academic Research Consortium; and Bleeding Academic Research Consortium (BARC) type 2–5 bleeding at 18 months after the index procedure. The primary endpoint was also analysed per protocol. This trial is registered with ClinicalTrials.gov, number NCT01701453.

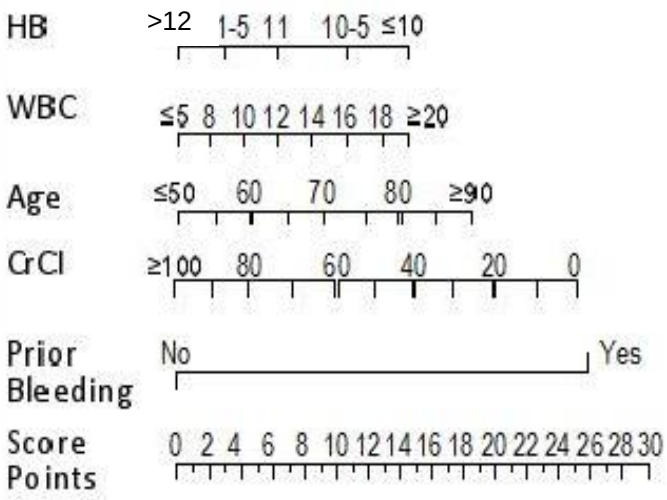
Findings Between Sept 5, 2012, and Dec 31, 2015, we randomly assigned 2712 patients; 1357 to the 6-month DAPT group and 1355 to the 12-month or longer DAPT group. Clopidogrel was used as a P2Y12 inhibitor for DAPT in 1082 (79·7%) patients in the 6-month DAPT group and in 1109 (81·8%) patients in the 12-month or longer DAPT group. The primary endpoint occurred in 63 patients in the 6-month DAPT group and in 56 patients in the 12-month or longer DAPT group (cumulative event rate 4·7% *vs* 4·2%; absolute risk difference 0·5%; upper limit of one-sided 95% CI 1·8%; $p_{non\text{-}inferiority}$=0·03 with a predefined non-inferiority margin of 2·0%). Although all-cause mortality did not differ significantly between the 6-month DAPT group and the 12-month or longer DAPT group (35 [2·6%] patients *vs* 39 [2·9%]; hazard ratio [HR] 0·90 [95% CI 0·57–1·42]; p=0·90) and neither did stroke (11 [0·8%] patients *vs* 12 [0·9%]; 0·92 [0·41–2·08]; p=0·84), myocardial infarction occurred more frequently in the 6-month DAPT group than in the 12-month or longer DAPT group (24 [1·8%] patients *vs* ten [0·8%]; 2·41 [1·15–5·05]; p=0·02). 15 (1·1%) patients had stent thrombosis in the 6-month DAPT group compared with ten (0·7%) in the 12-month or longer DAPT group (HR 1·50 [95% CI 0·68–3·35]; p=0·32). The rate of BARC type 2–5 bleeding was 2·7% (35 patients) in the 6-month DAPT group and 3·9% (51 patients) in the 12-month or longer DAPT group (HR 0·69 [95% CI 0·45–1·05]; p=0·09). Results from the per-protocol analysis were similar to those from the intention-to-treat analysis.

Interpretation The increased risk of myocardial infarction with 6-month DAPT and the wide non-inferiority margin prevent us from concluding that short-term DAPT is safe in patients with acute coronary syndrome undergoing percutaneous coronary intervention with current-generation DES. Prolonged DAPT in patients with acute coronary syndrome without excessive risk of bleeding should remain the standard of care.

Lancet 2018; 391: 1274

➢ Kdo má prospěch z prodloužené DAPT?

▪ *Trvání DAPT?: Riziková skóre k ohodnocení rizika krvácení při DAPT po PCI*

	PRECISE-DAPT score	DAPT score	
Time of use	At the time of coronary stenting	After 12 months of uneventful DAPT	
DAPT duration strategies assessed	Short DAPT (3–6 months) vs. Standard/long DAPT (12–24 months)	Standard DAPT (12 months) vs. Long DAPT (30 months)	
Score calculation		Age ≥75 65 to <75 <65 Cigarette smoking Diabetes mellitus MI at presentation Prior PCI or prior MI Paclitaxel-eluting stent Stent diameter <3 mm CHF or LVEF <30% Vein graft stent	 −2 pt −1 pt 0 pt +1 pt +1 pt +1 pt +1 pt +1 pt +1 pt +2 pt +2 pt
Score range	0 to 100 points	−2 to 10 points	
Decision making cut-off suggested	Score ≥25 → Short DAPT Score <25 → Standard/long DAPT	Score ≥2 → Long DAPT Score <2 → Standard DAPT	
Calculator	www.precisedaptscore.com	www.daptstudy.org	

➢ Kdo má prospěch z prodloužené DAPT?

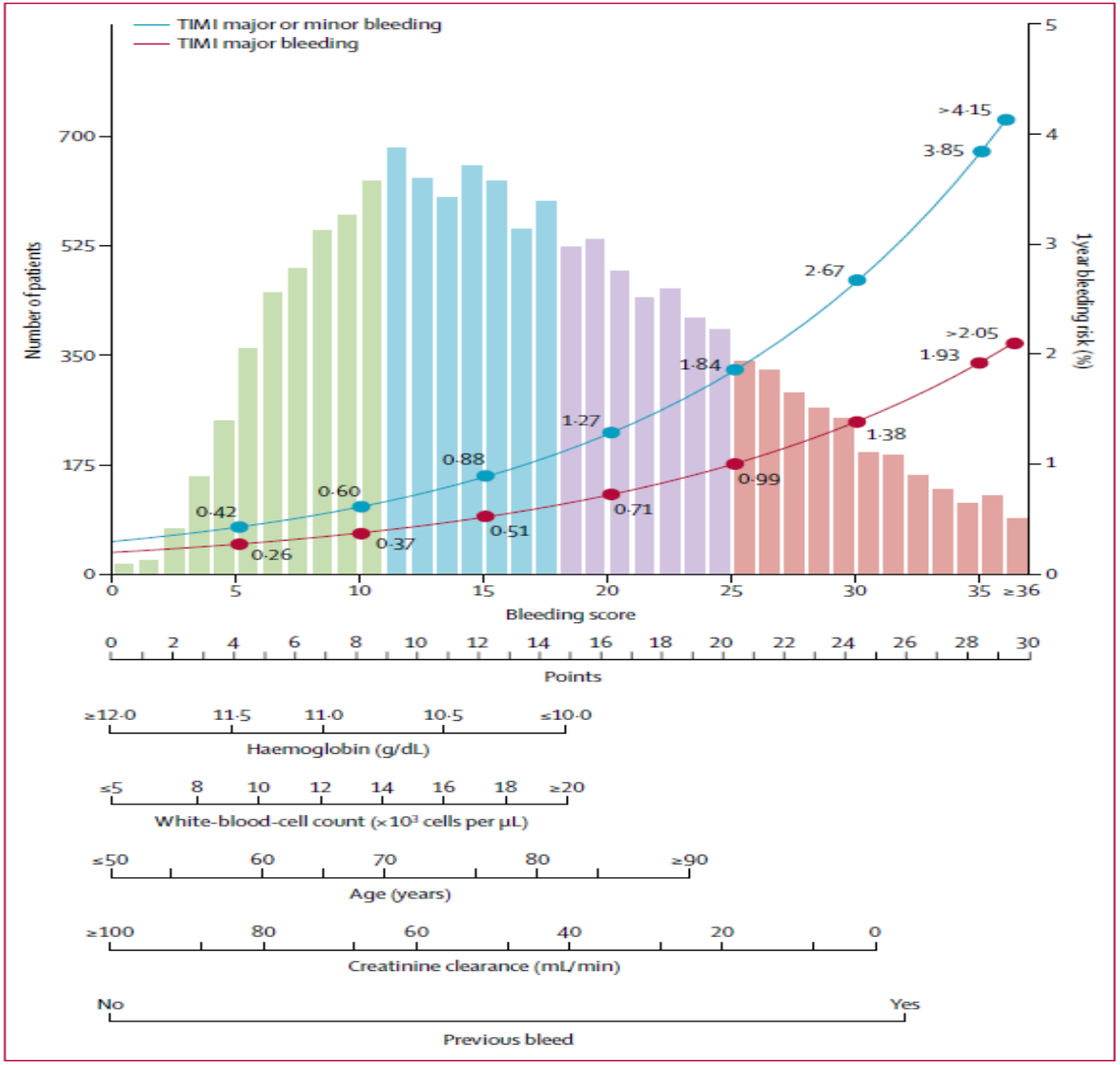


Figure 1: **The PRECISE-DAPT score nomogram for bedside application**
Risk curves refer to out-of-hospital Thrombosis in Myocardial Infarction (TIMI) major or minor bleeding and TIMI major bleeding at 12 months while on-treatment with dual antiplatelet therapy (DAPT). Histogram refers to the PRECISE-DAPT score distribution in the derivation cohort: green bars, the first score quartile (very low risk); blue bars, the second score quartile (low risk); purple bars, the third score quartile (moderate risk); and red bars, the

➢ Kdo má prospěch z prodloužené DAPT?

ICHS

PCI with DES

HIGH BLEEDING RISK	LOW ISCHEMIC RISK	INTERMEDIATE ISCHEMIC RISK	HIGH ISCHEMIC RISK
• Clinically significant bleeding on DAPT • Bleeding diathesis • Prior bleeding • Female gender • Elderly • Liver disease • Chronic renal dysfunction • Anemia or thrombocytopenia • Chronic anticoagulation therapy • Diabetes • Second generation DES	• Stable CAD • Troponin negative ACS • Single vessel disease • Simple stenting (single, short, large stent)	• Troponin positive ACS	• High-risk ACS • Recurrent ischemic events on DAPT • Peripheral vascular disease • Prior MI • Diabetes • Chronic renal dysfunction • Complex/multivessel CAD • Stent-related factors (multiple stents, overlapping stents, long stents, small-sized stents, double stents in bifurcations) • First generation DES
Favors 3-or 6-month DAPT		Favors 1-year DAPT	Favors >1-year DAPT

CONCLUSIONS

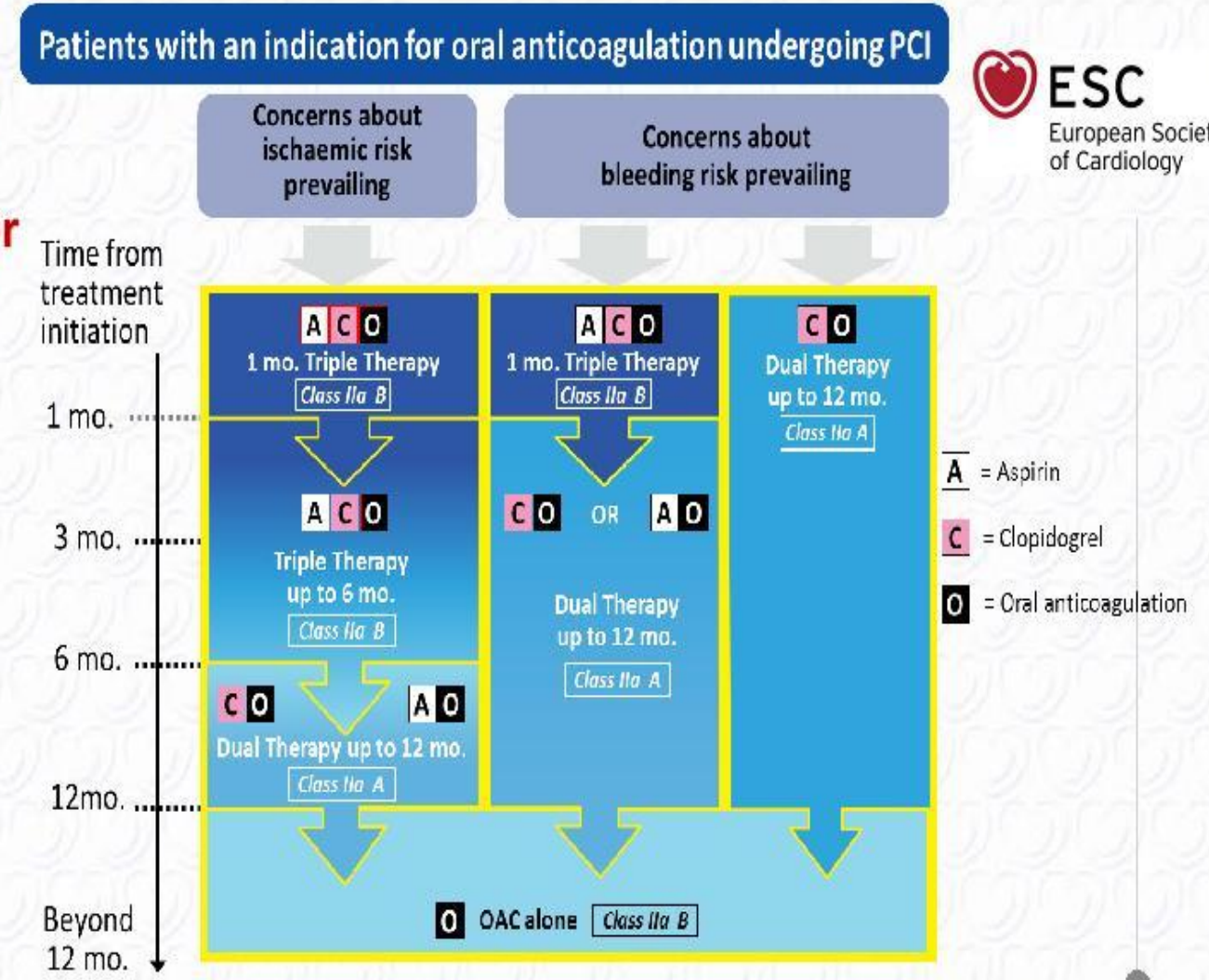
Evidence from RCTs suggests that patients undergoing implantation of safer, newer-generation DES may be treated with a minimum DAPT duration of 3 to 6 months to prevent early and largely stent-related thrombotic events, but extension of DAPT beyond 12 months entails a tradeoff. ***The declining risk of late stent thrombosis with newer-generation DES and the inability to predict life-threatening bleeding limit the appeal of 18 to 48 months of DAPT over 6 to 12 months of therapy***.

In contrast, ***patients with prior MI at high risk of atherothrombosis experience fewer ischemic events with prolonged DAPT at a cost of increased***

➢ Kdo má prospěch z prodloužené DAPT?

Algorithm for dual antiplatelet therapy (DAPT) in patients with an indication for oral anticoagulation undergoing percutaneous coronary intervention (PCI)

7-10%



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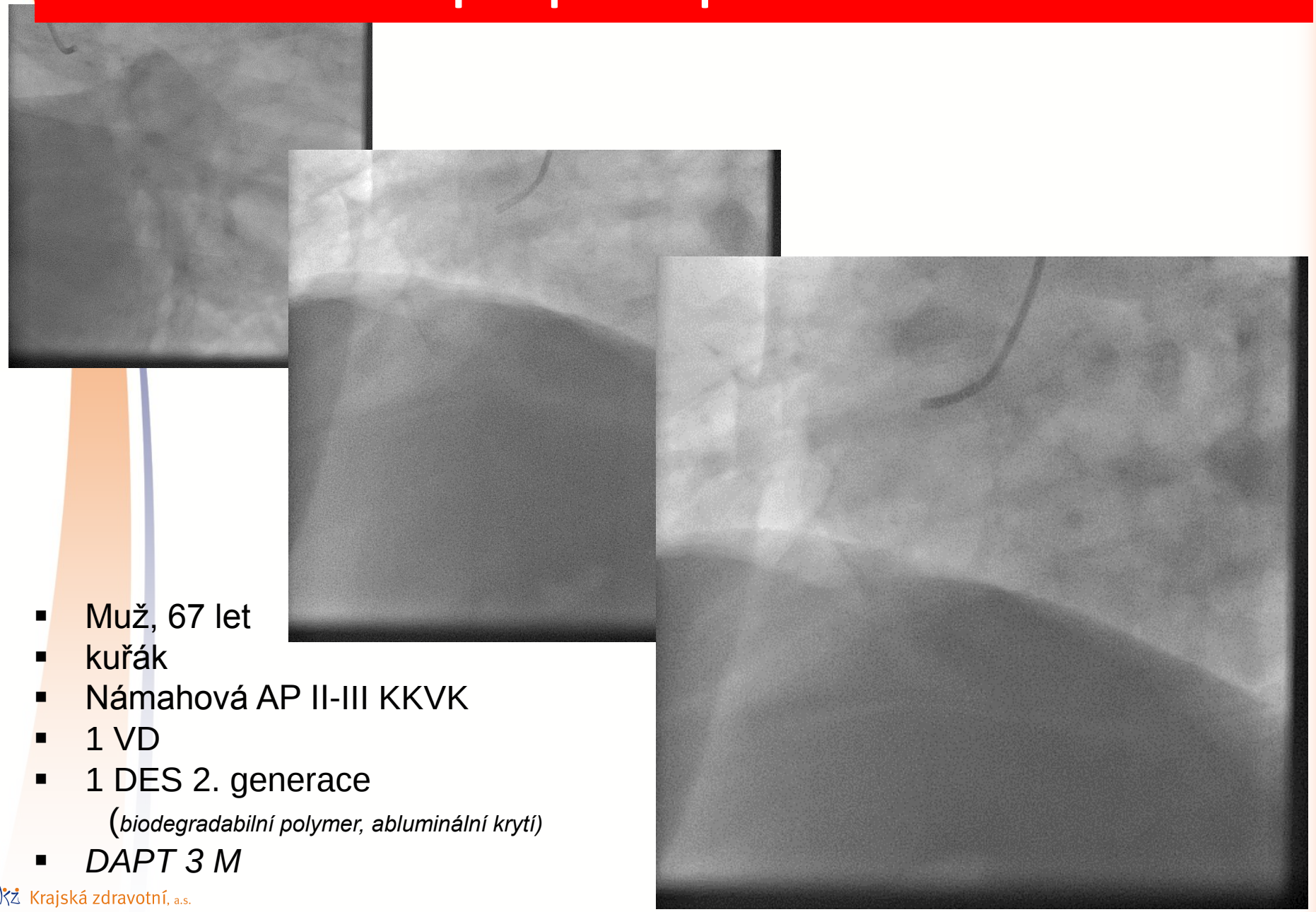
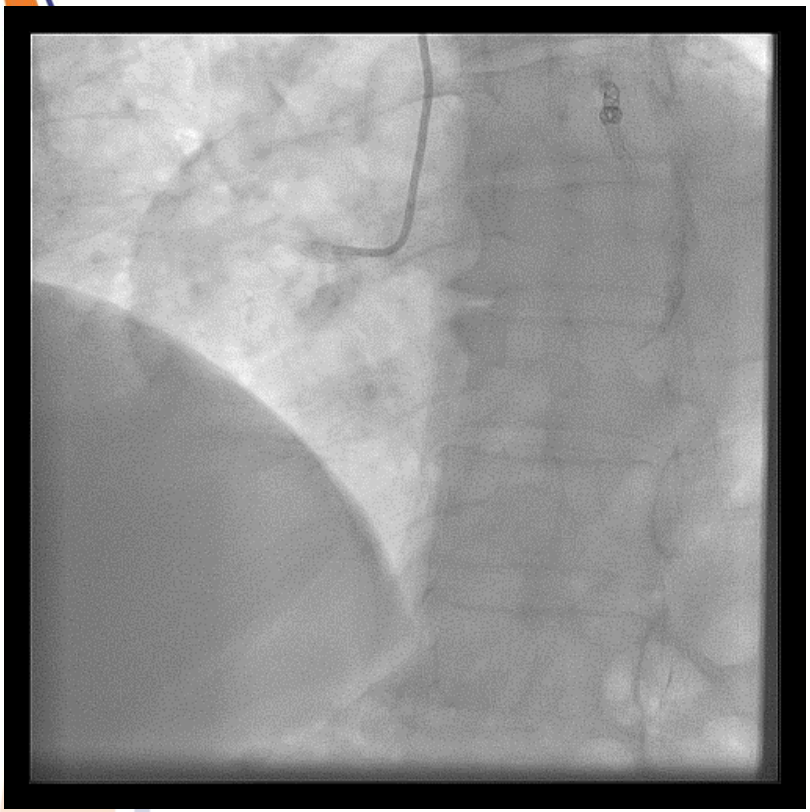
➢ Kdo má prospěch z prodloužené DAPT?



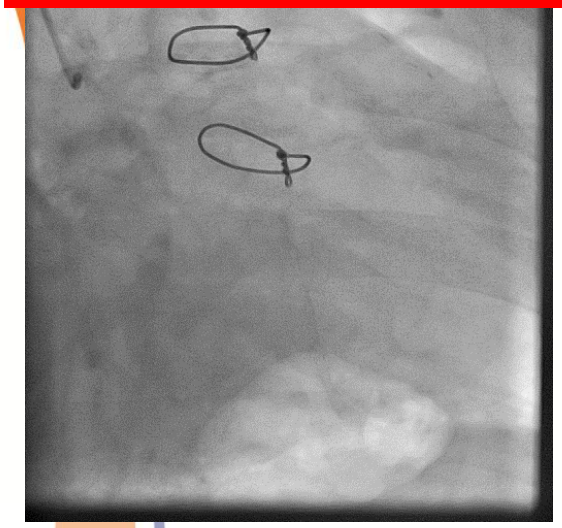
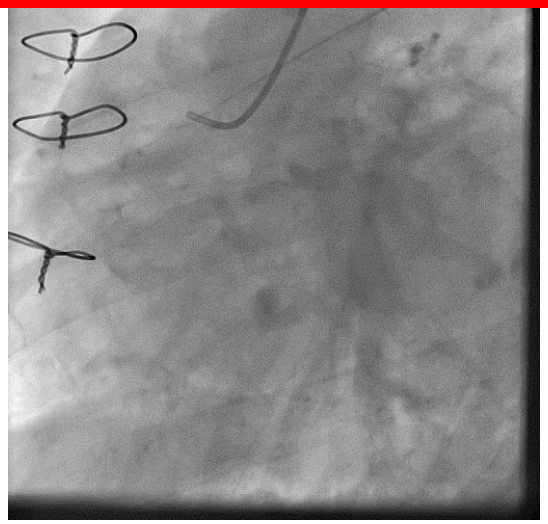
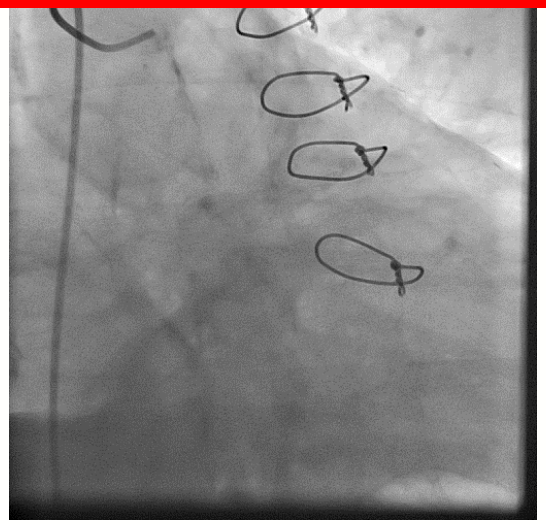
- Muž, 67 let
- kuřák
- Námahová AP II-III KKVK
- 1 VD
- 1 DES 2. generace
  (*biodegradabilní polymer, abluminální krytí)*
- *DAPT 3 M*

➢ Kdo má prospěch z prodloužené DAPT?

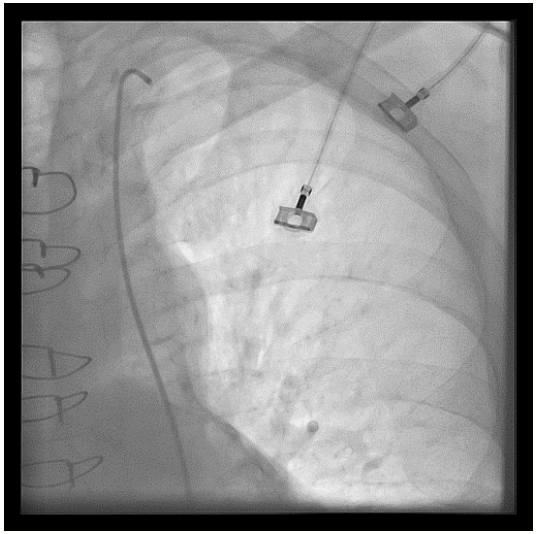
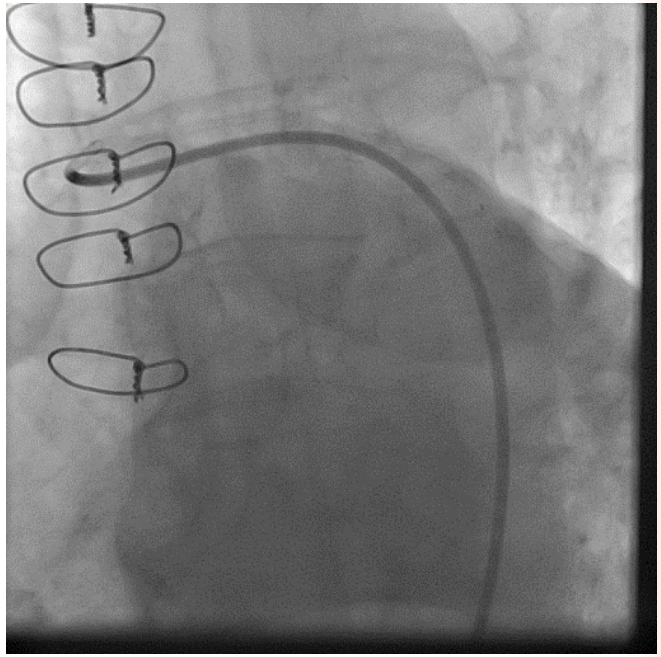


- žena, 77 let
- kuřačka, DM na PAD, art. hypertenze
- Stp.opakovaných STEMI (přední a spodní), stp. opak PCI
- 4/2017 MML: POBA RIA s DEB
- DAPT 12M (>12M?)

➢ Kdo má prospěch z prodloužené DAPT?

- muž, 74 let
- DM II. typu na inzulinu *(CHRI)*
- HLP, art. Hypertenze
- ICH tepen DK, PTA bil.
- 2002 LIMA RIA, AKB ad RD a RMS
- po recidiv. IM
-
- Nyní NSTEMI
- DES 2. generace (*biodegradabilní polymer, abluminální krytí*

  - ***DAPT >12 M***

➢ Kdo má prospěch z prodloužené DAPT?

❑ Závěry:

- *Individualizovaná DAPT na základě zhodnocení individuálního ischemického/krvácivého rizika a přání nemocného (zvážit dlouhodobou DAPT u nemocných s AKS/IM a dalšími RF zvyšující riziko opakování příhody)*

- *Kontinuální vývoj - nové studie, nové léky, nové stenty*

  - NOAK (dabigatran) + P2Y12 po PCI+Fis
  - Nové studie DAPT vs monoterapie P2Y12 ?
  (GLOBAL LEADERS, TWILIGHT study)
  - NOACs v dlouhodobé sekundární prevenci

➢ Kdo má prospěch z prodloužené DAPT?