Trombocythämning och OAK i initialskedet efter akut koronart syndrom respektive elektiv PCI

Förlängd behandling– vad säger riktlinjerna? Hur gör vi vid anemi och blödning? Nya strategier-framtid

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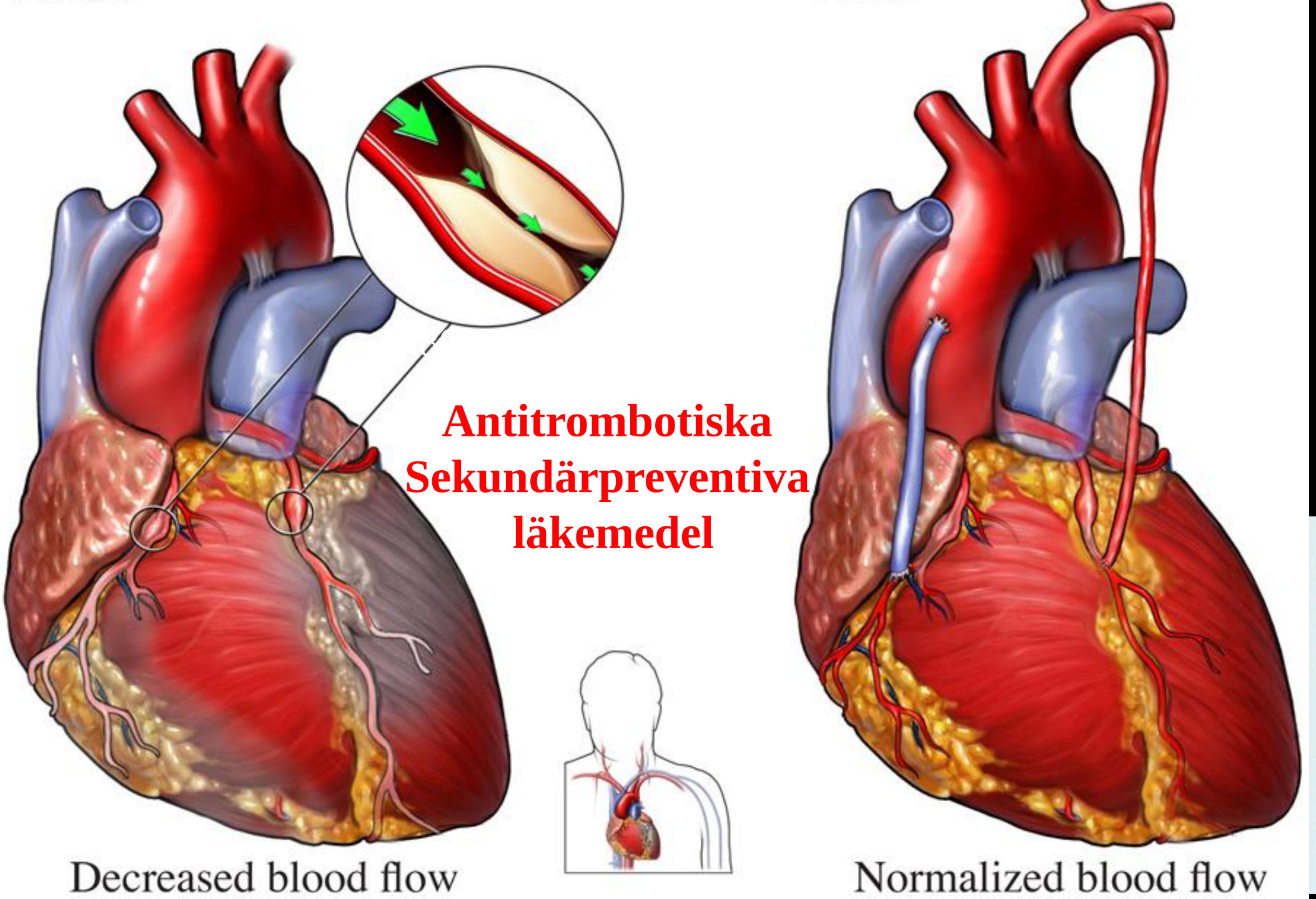
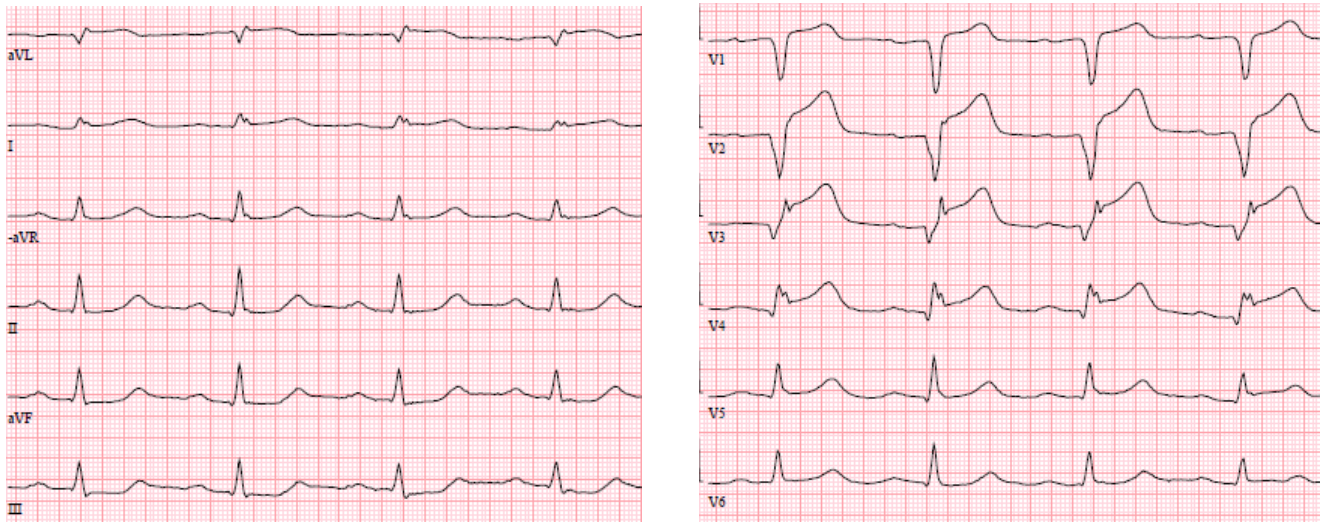
Inst för Medicinska Vetenskaper, Kardiologi
Akademiska Sjukhuset, Uppsala

Antitrombotiska Sekundärpreventiva läkemedel



60-årig kvinna, före detta rökare, överviktig med diabetes mellitus typ 2 och hypertoni.
Söker på akutmottagningen med bröstsmärta sedan 2 timmar.
Ingen tidigare hjärtinfarkt eller stroke.

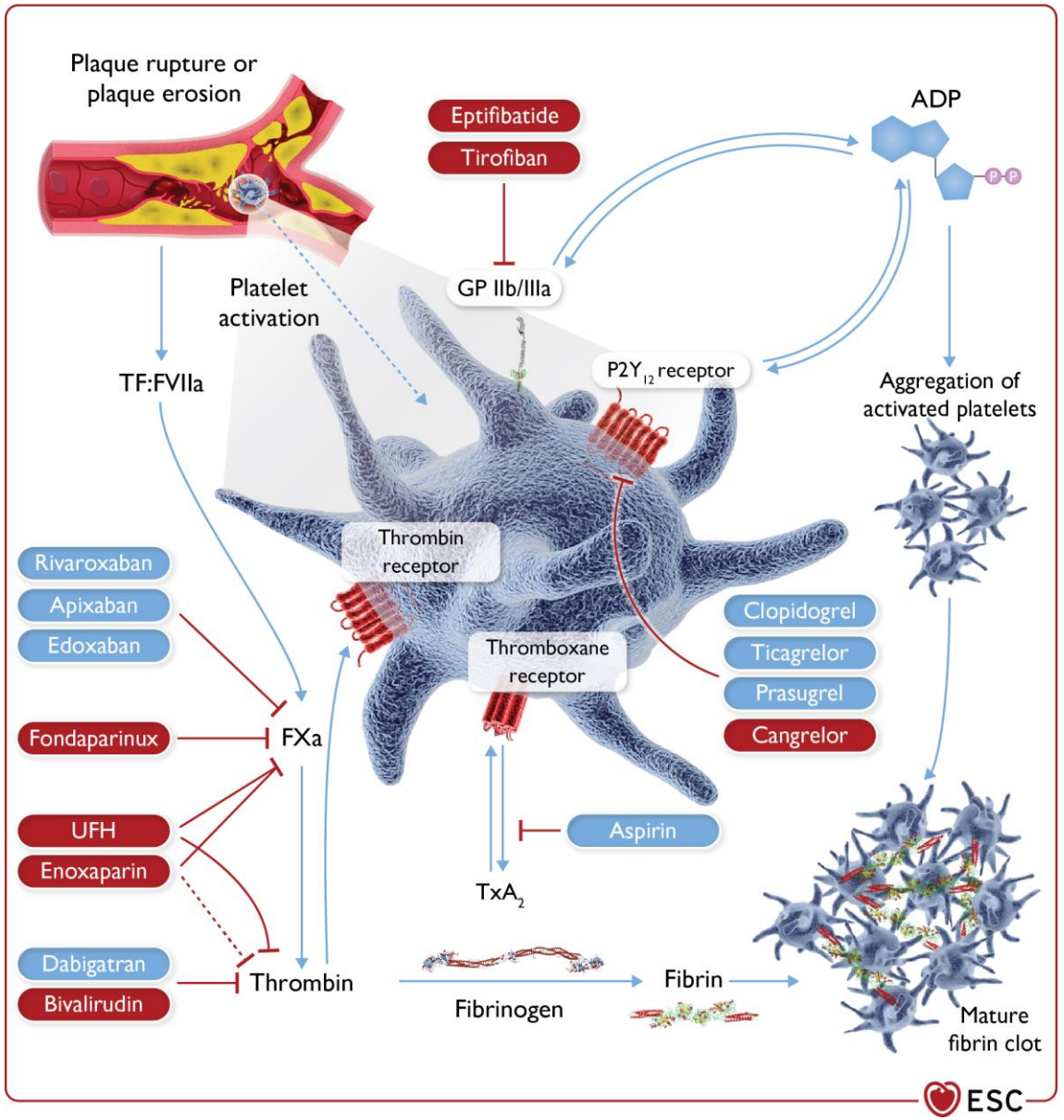


Vilken antitrombotisk behandling ordinerar Du?

1. Trombyl 75 mg x4 och heparin 5000 E
2. Trombyl 75 mg x4, Ticagrelor 180 mg och heparin 5000 E
3. Trombyl 75 mg x4, Prasugrel 60 mg och heparin 5000 E
4. Trombyl 75mg x4, Ticagrelor 180 mg och fondaparinux 2,5 mg x1

Figure 9

Antithrombotic treatments in acute coronary syndrome: pharmacological targets



2023 ESC Guidelines for the management of acute coronary syndromes
(European Heart Journal; 2023 – doi:10.1093/eurheartj/ehad191)

Trombocythämmare vid kranskärlssjukdom

Historik

Akut koronart syndrom:

1990 RISC-studien. **796 män** med akut kranskärlssjukdom.
Randomiserades till 75 mg ASA vs. Placebo

- **ASA gav 57% reduktion av ny hjärtinfarkt och död efter 5 dagar**
- **ASA gav 64% reduktion av ny hjärtinfarkt och död efter 3 månader**

Stabil angina:

1991 Physicians Health Study, **22,071 läkare (endast män!),** varav 333 hade stabil angina. Randomiserades till 325 mg ASA v.a.d vs. Placebo

- **ASA gav 70% minskning av hjärtinfarkt efter 60 månader**

Stabil angina:

1992 SAPAT-studien. 2035 patienter med stabil angina
Randomiserades till 75 mg ASA vs. Placebo

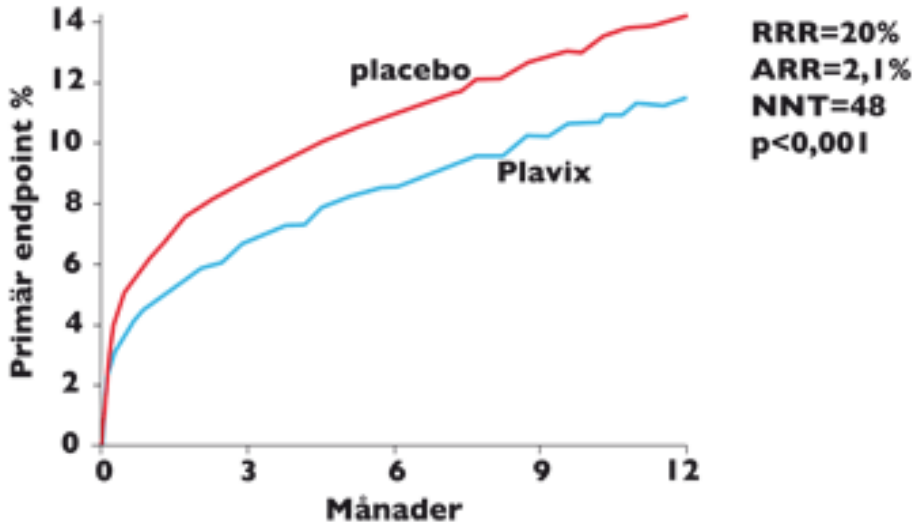
- **ASA gav en 34% minskning av hjärtinfarkt och död**

Trombocythämmande läkemedel

P2Y12- receptor hämmare – Hämmar receptorn för ADP och minskar trombocytaggregation

Clopidogrel, Prasugrel och Ticagrelor

Clopidogrel vid AKS

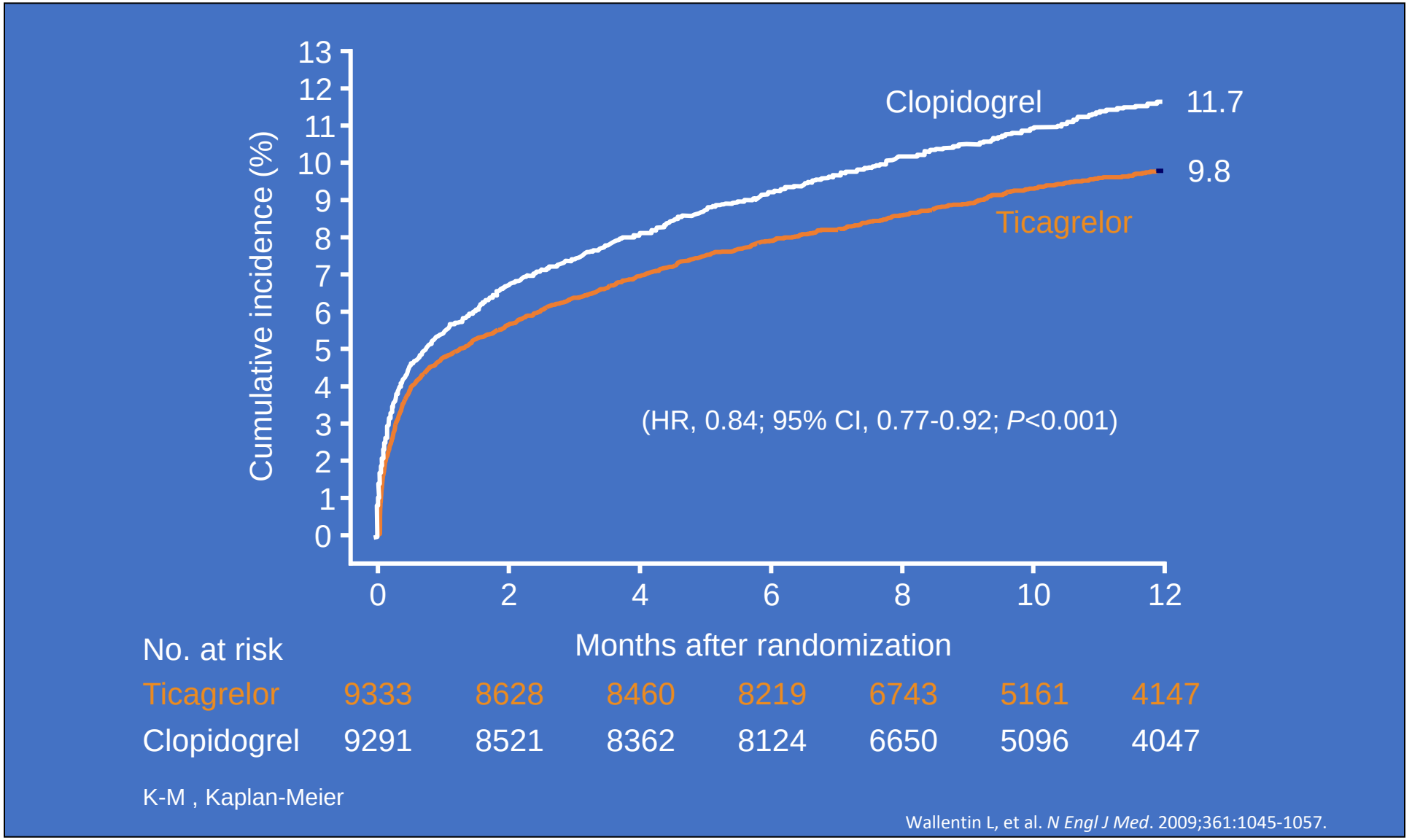


>12 000 patienter med akut koronart syndrom.

Randomiserades Clopidogrel +ASA vs ASA under 3-12 månader

NEJM 2001

PLATO: primärt effektmått



Wallentin L, et al. *N Engl J Med*. 2009;361:1045-1057.

Orala trombocythämmare

Namn	Mekanism	Tid till maxeffekt	Halveringstid	Tänk på:
Aspirin	Irreversibel hämning COX-1 och (COX-2)	30-40 min	15-30 min	Trombocythämning inom 1 timme. **Effekt kvarstår 4 d efter avslut**
Clopidogrel	Irreversibel hämning P2Y12	3-7 dagar för max trc-hämning	8 timmar	Laddningsdos snabbare effekt. **Effekt kvarstår upp till 10 d**
Prasugrel	Irreversibel hämning P2Y12	30 min	7 timmar	**Effekt kvarstår 5-7 d**
Ticagrelor	Reversibel hämning P2Y12	1.5 timmar	7 timmar	Påverkan på trombocyten **minskar till 30% efter 2.5 d**

Ortel et al Blood 2012

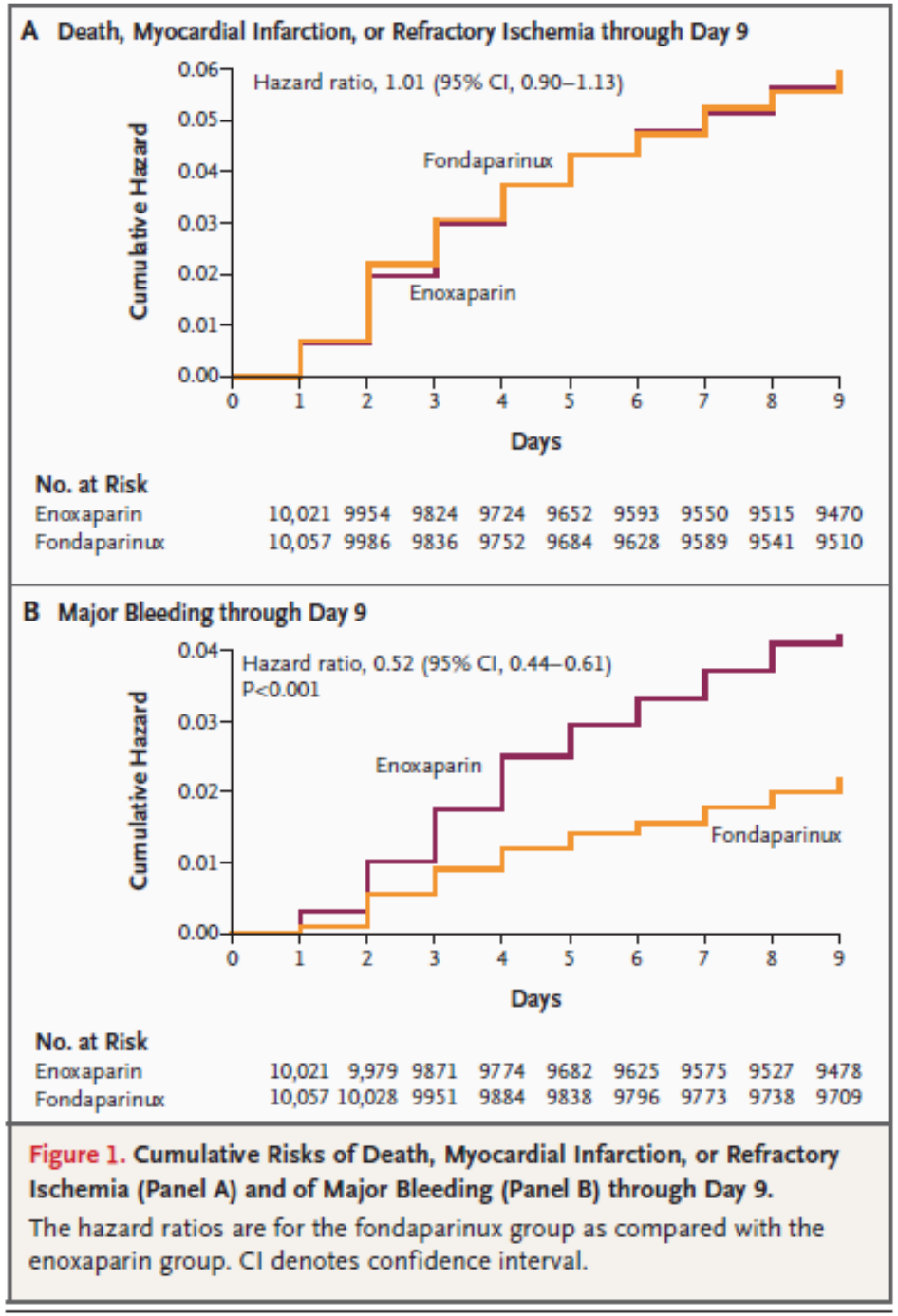


Figure 1. Cumulative Risks of Death, Myocardial Infarction, or Refractory Ischemia (Panel A) and of Major Bleeding (Panel B) through Day 9.

The hazard ratios are for the fondaparinux group as compared with the enoxaparin group. CI denotes confidence interval.

Fondaparinux färre blödningar än enoxaparin

NEJM 2006 354 1464-1476

Värdera blödningsrisk

Hur gör vi detta systematiskt?

Många riskmodeller: Crusade, PRECISE-DAPT score,
PARIS major bleeding score, ARC-HBR criteria

ARC-HBR (Academic Research Consortium High bleeding risk)

Definierat 20 kliniska faktorer som ökar blödningsrisk efter PCI

Major >4% allvarlig blödning på 1 år

Minor <4% allvarlig blödning på 1 år

Värdera blödningsrisk

ARC-HBR

Siverano A et al Int J Cardiol 2022 8-15

Table S12 Major and minor criteria for high bleeding risk according to the Academic Research Consortium for High Bleeding Risk at the time of percutaneous coronary intervention

Major criteria	Minor criteria
	Age >75 years
Anticipated use of long-term oral anticoagulation[a]	
Severe or end-stage CKD (eGFR <30 mL/min)	Moderate CKD (eGFR 30–59 mL/min)
Haemoglobin <11 g/dL	Haemoglobin 11–12.9 g/dL for men and 11–11.9 g/dL for women
Spontaneous bleeding requiring hospitalization or transfusion in the past 6 months or at any time, if recurrent	Spontaneous bleeding requiring hospitalization or transfusion within the past 12 months not meeting the major criterion
Moderate or severe baseline thrombocytopenia[b] (platelet count $<100 \times 10^9$/L)	
Chronic bleeding diathesis	
Liver cirrhosis with portal hypertension	
	Long-term use of oral non-steroidal anti-inflammatory drugs or steroids
Active malignancy[c] (excluding non-melanoma skin cancer) within the past 12 months	
Previous spontaneous ICH (at any time) Previous traumatic ICH within the past 12 months Presence of a brain arteriovenous malformation Moderate or severe ischaemic stroke[d] within the past 6 months	Any ischaemic stroke at any time not meeting the major criterion
Non-deferrable major surgery on dual antiplatelet therapy	
Recent major surgery or major trauma within 30 days before percutaneous coronary intervention	

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; ICH, intracranial haemorrhage.
Bleeding risk is high if at least one major criterion or two minor criteria are met.
[a]This excludes vascular protection doses.[143]
[b]Baseline thrombocytopenia is defined as thrombocytopenia before PCI.
[c]Active malignancy is defined as diagnosis within 12 months and/or ongoing requirement for treatment (including surgery, chemotherapy, or radiotherapy).
[d]National Institutes of Health Stroke Scale score >5.

Haemoglobin unit

13

g/dl

mmol/L

Age (years)

59

White blood cells unit

5

u/mcL

10^9/L

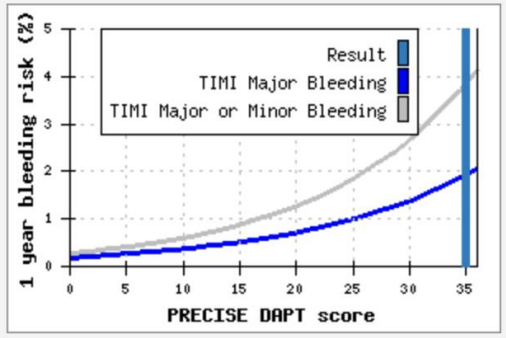
Creatinine Clearance (ml/min)

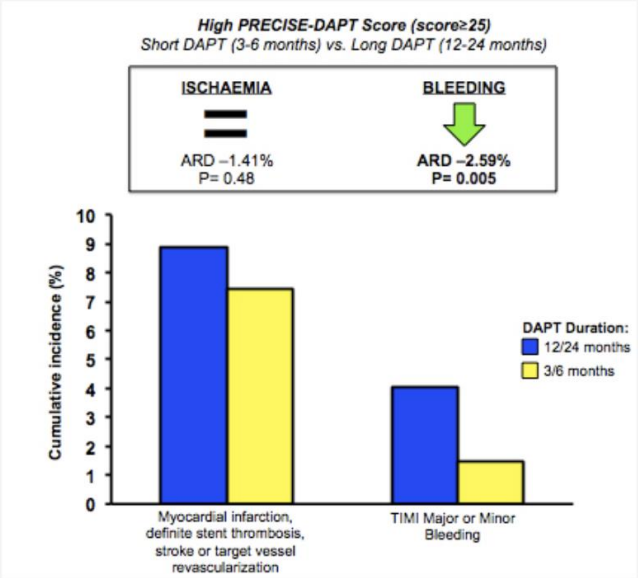
80

Prior Bleeding

CALCULATE

RESET





In patients with high PRECISE-DAPT score (Score>=25) a short DAPT (3-6 months) as compared with a long DAPT (12-24 months) was associated with lower TIMI major and minor bleeding and similar rate of the composite ischemic endpoint.

RESULT:

Cluster of risk:

High

Score Calculated

35

12 months risk of TIMI major or minor Bleeding

3.8%

12 months risk of TIMI Major Bleeding

1.9%

Copy to clipboard

60-årig kvinna, före detta rökare, överviktig med diabetes mellitus typ 2 och hypertoni.
Söker på akutmottagningen med bröstsmärta sedan 2 timmar.
Ingen tidigare hjärtinfarkt eller stroke.

PCI visar på proximal LAD ocklusion även stenos i LCX.
Erhåller 2 DES gott resultat

Utredningsresultat:

- GFR 45, Hb 120, TPK 210
- Ekokardiografi: måttligt nedsatt LV-EF
- Välreglerad i sin diabetes och blodtryck bra under vårdtid

Blödningsrisk ARC-HBR:

Inget major kriterium

Har minor kriterium

Antitrombotisk behandling?

ESC Guidelines AKS 2023

Table 4 **New recommendations**

Recommendations	Class[a]	Level[b]
Recommendations for antiplatelet and anticoagulant therapy in acute coronary syndrome		
If patients presenting with ACS stop DAPT to undergo coronary artery bypass grafting, it is recommended they resume DAPT after surgery for at least 12 months.	I	C
In older ACS patients, especially if HBR, clopidogrel as the $P2Y_{12}$ receptor inhibitor may be considered.	IIb	B
Recommendations for alternative antithrombotic therapy regimens		
In patients who are event-free after 3–6 months of DAPT and who are not high ischaemic risk, single antiplatelet therapy (preferably with a $P2Y_{12}$ receptor inhibitor) should be considered.	IIa	A
$P2Y_{12}$ inhibitor monotherapy may be considered as an alternative to aspirin monotherapy for long-term treatment.	IIb	A
In HBR patients, aspirin or $P2Y_{12}$ receptor inhibitor monotherapy after 1 month of DAPT may be considered.	IIb	B
In patients requiring OAC, withdrawing antiplatelet therapy at 6 months while continuing OAC may be considered.	IIb	B
De-escalation of antiplatelet therapy in the first 30 days after an ACS event is not recommended.	III	B

Recommendations for antiplatelet and anticoagulant therapy in acute coronary syndrome (1)

Recommendations	Class	Level
Antiplatelet therapy		
Aspirin is recommended for all patients without contraindications at an initial oral LD of 150–300 mg (or 75–250 mg i.v.) and an MD of 75–100 mg o.d. for long-term	I	A

2023 ESC Guidelines for the management of acute coronary syndromes
(European Heart Journal: 2023 – doi:10.1093/eurheartj/ehad191)

Recommendations for antiplatelet and anticoagulant therapy in acute coronary syndrome (1)

Recommendations	Class	Level
Antiplatelet therapy		
Aspirin is recommended for all patients without contraindications at an initial oral LD of 150–300 mg (or 75–250 mg i.v.) and an MD of 75–100 mg o.d. for long-term treatment.	I	A
In all ACS patients, a $P2Y_{12}$ receptor inhibitor is recommended in addition to aspirin, given as an initial oral LD followed by an MD for 12 months unless there is HBR.	I	A
A proton pump inhibitor in combination with DAPT is recommended in patients at high risk of gastrointestinal bleeding.	I	A
Prasugrel is recommended in $P2Y_{12}$ receptor inhibitor-naïve patients proceeding to PCI (60 mg LD, 10 mg o.d. MD, 5 mg o.d. MD for patients aged ≥75 years or with a body weight <60 kg).	I	B
Ticagrelor is recommended irrespective of the treatment strategy (invasive or conservative) (180 mg LD, 90 mg b.i.d. MD).	I	B

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Recommendations for antiplatelet and anticoagulant therapy in acute coronary syndrome (1)

Recommendations	Class	Level
Antiplatelet therapy		
Aspirin is recommended for all patients without contraindications at an initial oral LD of 150–300 mg (or 75–250 mg i.v.) and an MD of 75–100 mg o.d. for long-term treatment.	I	A
In all ACS patients, a $P2Y_{12}$ receptor inhibitor is recommended in addition to aspirin, given as an initial oral LD followed by an MD for 12 months unless there is HBR.	I	A
A proton pump inhibitor in combination with DAPT is recommended in patients at high risk of gastrointestinal bleeding.	I	A

2023 ESC Guidelines for the management of acute coronary syndromes
(European Heart Journal; 2023 – doi:10.1093/eurheartj/ehad191)

Recommendations for antiplatelet and anticoagulant therapy in acute coronary syndrome (2)

Recommendations	Class	Level
Antiplatelet therapy (continued)		
Clopidogrel (300–600 mg LD, 75 mg o.d. MD) is recommended when prasugrel or ticagrelor are not available, cannot be tolerated, or are contraindicated.	I	C
If patients presenting with ACS stop DAPT to undergo CABG, it is recommended they resume DAPT after surgery for at least 12 months.	I	C

2023 ESC Guidelines for the management of acute coronary syndromes
(European Heart Journal; 2023 – doi:10.1093/eurheartj/ehad191)

Recommendations for antiplatelet and anticoagulant therapy in acute coronary syndrome (2)

Recommendations	Class	Level
Antiplatelet therapy (continued)		
Clopidogrel (300–600 mg LD, 75 mg o.d. MD) is recommended when prasugrel or ticagrelor are not available, cannot be tolerated, or are contraindicated.	I	C
If patients presenting with ACS stop DAPT to undergo CABG, it is recommended they resume DAPT after surgery for at least 12 months.	I	C
Prasugrel should be considered in preference to ticagrelor for ACS patients who proceed to PCI.	IIa	B

See GL chapter 6.1.2

2023 ESC Guidelines for the management of acute coronary syndromes
(European Heart Journal; 2023 – doi:10.1093/eurheartj/ehad191)

Recommendations for antiplatelet and anticoagulant therapy in acute coronary syndrome (3)

Recommendations	Class	Level	
Antiplatelet therapy (continued)			
Pretreatment with a $P2Y_{12}$ receptor inhibitor may be considered in patients undergoing a primary PCI strategy.	IIb	B	
Pretreatment with a $P2Y_{12}$ receptor inhibitor may be considered in NSTE-ACS patients who are not expected to undergo an early invasive strategy (<24 h) and do not have HBR.	IIb	C	?
Pretreatment with a GP IIb/IIIa receptor antagonist is not recommended.	III	A	
Routine pretreatment with a $P2Y_{12}$ receptor inhibitor in NSTE-ACS patients in whom coronary anatomy is not known and early invasive management (<24 h) is planned is not recommended.	III	A	?

See GL chapter 6.1.2

2023 ESC Guidelines for the management of acute coronary syndromes
(European Heart Journal; 2023 – doi:10.1093/eurheartj/ehad191)

Recommendations for antiplatelet and anticoagulant therapy in acute coronary syndrome (5)

Recommendations	Class	Level
Patients with STEMI		
Enoxaparin should be considered as an alternative to UFH in patients with STEMI undergoing PPCI.	IIa	A
Bivalirudin with a full-dose post PCI infusion should be considered as an alternative to UFH in patients with STEMI undergoing PPCI.	IIa	A

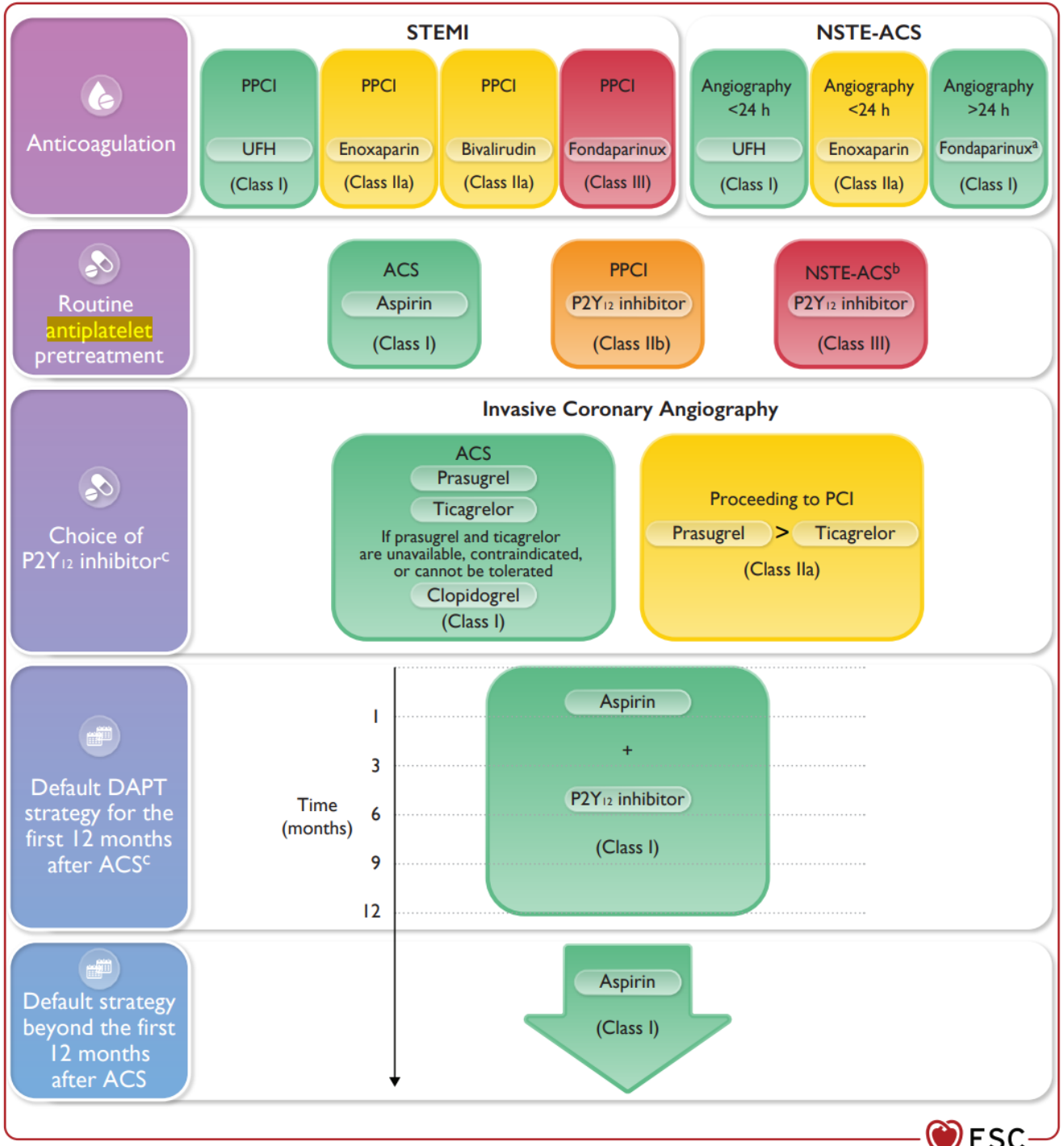
2023 ESC Guidelines for the management of acute coronary syndromes
(European Heart Journal; 2023 – doi:10.1093/eurheartj/ehad191)

Recommendations for antiplatelet and anticoagulant therapy in acute coronary syndrome (5)

Recommendations	Class	Level
Patients with STEMI		
Enoxaparin should be considered as an alternative to UFH in patients with STEMI undergoing PPCI.	IIa	A
Bivalirudin with a full-dose post PCI infusion should be considered as an alternative to UFH in patients with STEMI undergoing PPCI.	IIa	A
Fondaparinux is not recommended in patients with STEMI undergoing PPCI.	III	B
Patients with NSTE-ACS		
For patients with NSTE-ACS in whom early invasive angiography (i.e. within 24 h) is not anticipated, fondaparinux is recommended.	I	B
For patients with NSTE-ACS in whom early invasive angiography (i.e. within 24 h) is anticipated, enoxaparin should be considered as an alternative to UFH.	IIa	B

2023 ESC Guidelines for the management of acute coronary syndromes
(European Heart Journal; 2023 – doi:10.1093/eurheartj/ehad191)

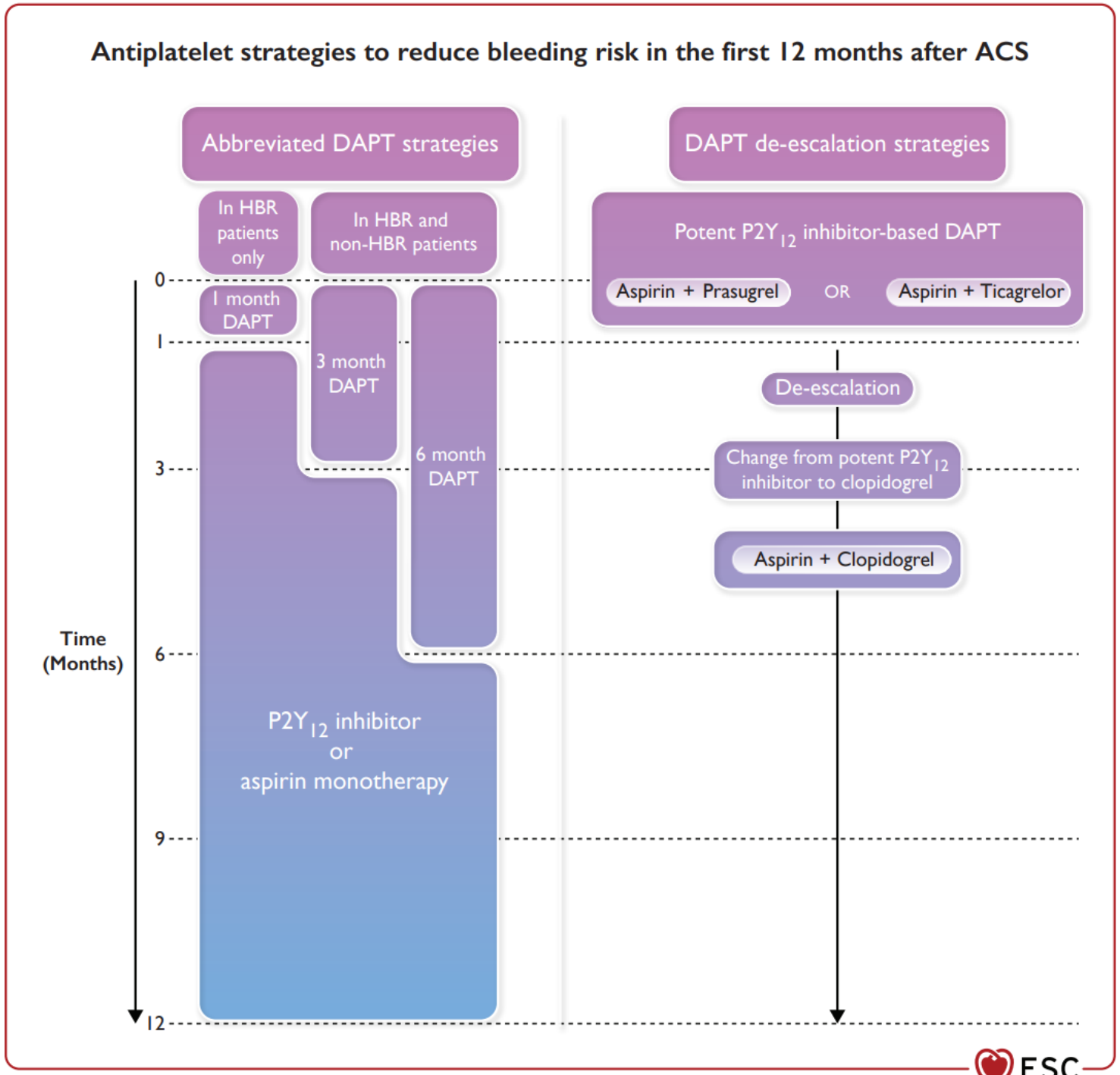
Antitrombotisk behandling vid AKS utan indikation för antikoagulantia



Förkortad antitrombotisk behandling för att minska risken för blödning?

Antitrombotisk behandling för att minska risken för blödning?

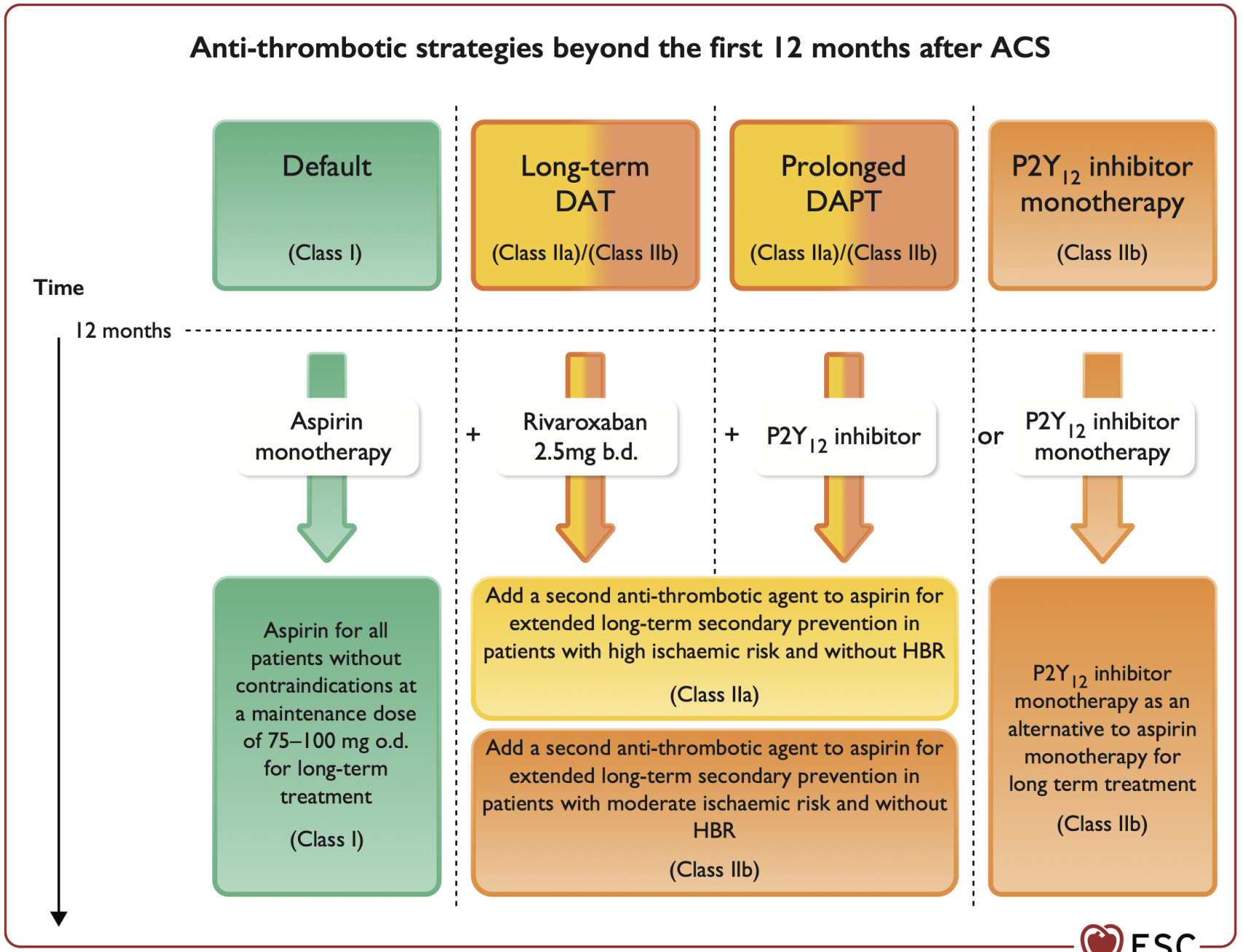
De-escalation från högpotent P2Y12 – hämmare till clopidogrel



Förlängd (>12 mån) antitrombotisk behandling utöver ASA?

Table S8 **Risk criteria for extended treatment with a second antithrombotic agent**

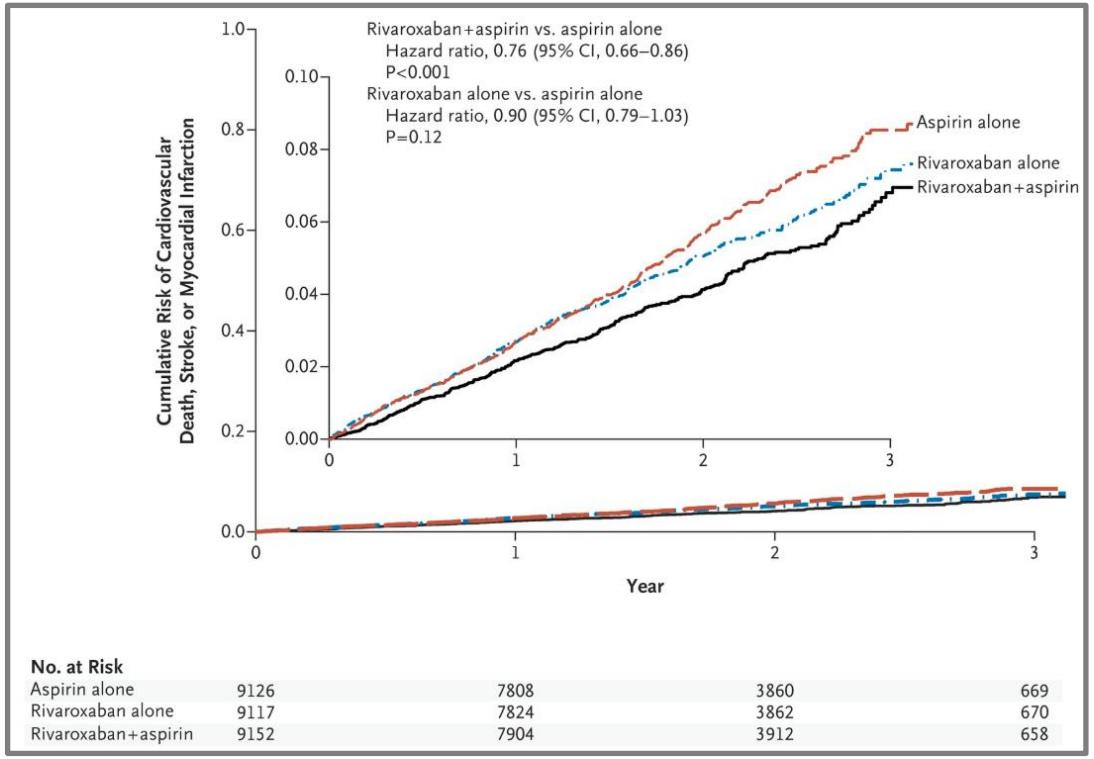
High thrombotic risk (Class IIa)	Moderate thrombotic risk (Class IIb)
Complex CAD and at least one criterion	Non-complex CAD and at least one criterion
Risk enhancers	
Diabetes mellitus requiring medication History of recurrent MI Any multivessel CAD Premature (<45 years) or accelerated (new lesion within a 2-year timeframe) CAD Concomitant systemic inflammatory disease (e.g. human immunodeficiency virus, systemic lupus erythematosus, chronic arthritis) Polyvascular disease (CAD plus PAD) CKD with eGFR 15–59 mL/min/1.73 m^2	Diabetes mellitus requiring medication History of recurrent MI Polyvascular disease (CAD plus PAD) CKD with eGFR 15–59 mL/min/1.73 m^2
Technical aspects	
At least three stents implanted At least three lesions treated Total stent length >60 mm History of complex revascularization (left main, bifurcation stenting with ≥2 stents implanted, chronic total occlusion, stenting of last patent vessel) History of stent thrombosis on antiplatelet treatment	


Anti-thrombotic strategies beyond the first 12 months after ACS
Default
(Class I)
Long-term DAT
(Class IIa)/(Class IIb)
Prolonged DAPT
(Class IIa)/(Class IIb)
P2Y12 inhibitor monotherapy
(Class IIb)
Time
12 months
Aspirin monotherapy
+
Rivaroxaban 2.5mg b.d.
+
P2Y12 inhibitor
or
P2Y12 inhibitor monotherapy
Aspirin for all patients without contraindications at a maintenance dose of 75–100 mg o.d. for long-term treatment
(Class I)
Add a second anti-thrombotic agent to aspirin for extended long-term secondary prevention in patients with high ischaemic risk and without HBR
(Class IIa)
Add a second anti-thrombotic agent to aspirin for extended long-term secondary prevention in patients with moderate ischaemic risk and without HBR
(Class IIb)
P2Y12 inhibitor monotherapy as an alternative to aspirin monotherapy for long term treatment
(Class IIb)
ESC

Låg dos oral antikoagulantia under lång tid – vilka patienter?

- 27000 patienter med stabil sjukdom ex. 1 år efter ACS
- Rivaroxaban 2,5 mg x2 + ASA bättre än Rivaroxaban 5 mg x2 eller ASA
- Färre kardiovaskulära händelser
- Färre blödningar

COMPASS



Eikelboom JW et al NEJM 2017

Antitrombotisk behandling vid AKS efter CABG

Recommendations for antiplatelet and anticoagulant therapy in acute coronary syndrome		
If patients presenting with ACS stop DAPT to undergo coronary artery bypass grafting, it is recommended they resume DAPT after surgery for at least 12 months.	I	C

Rekommendationer

Recommendation Table 6 — Recommendations for alternative antithrombotic therapy regimens

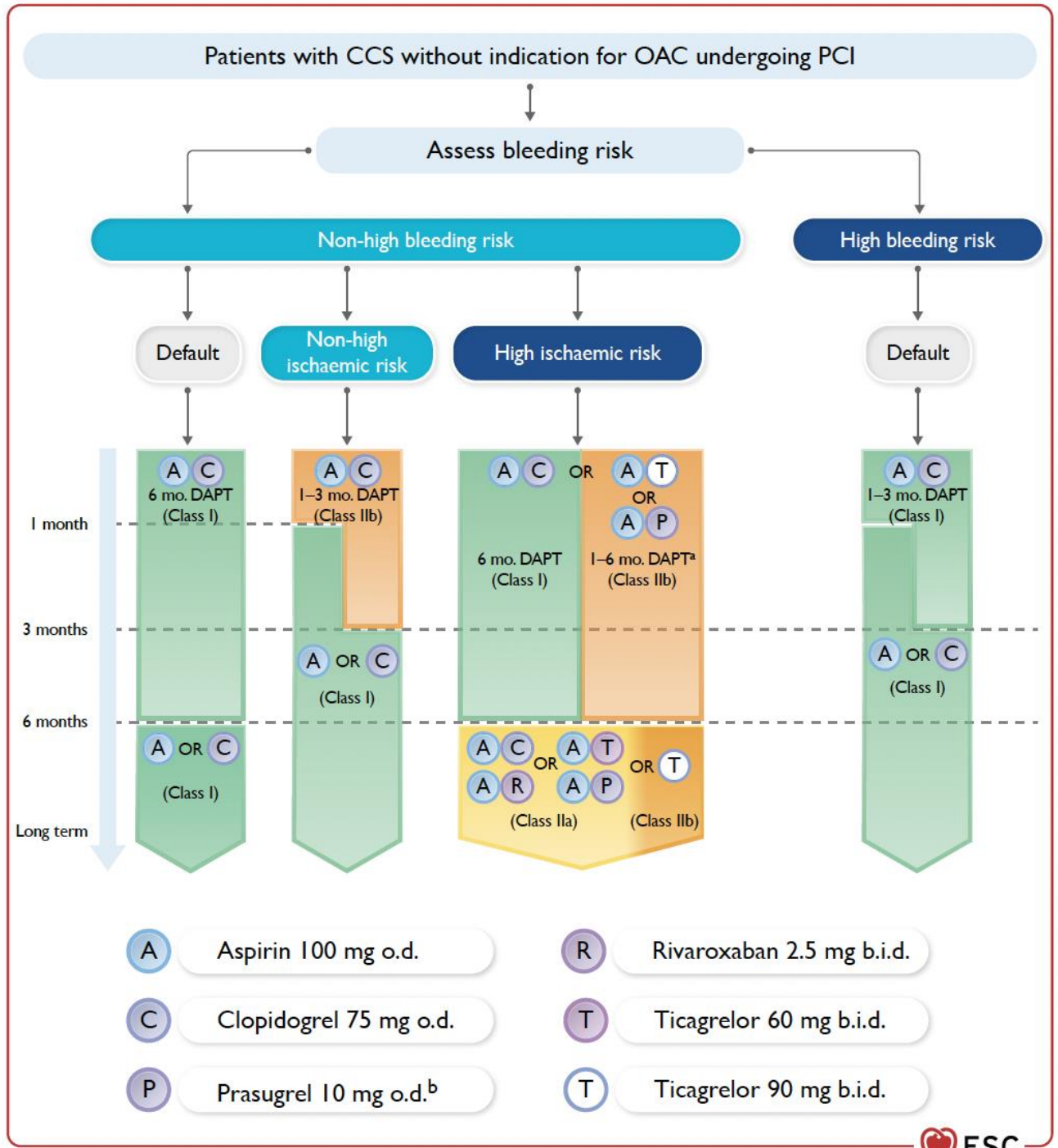
Recommendations	Class[a]	Level[b]
Shortening/de-escalation of antithrombotic therapy		
In patients who are event-free after 3–6 months of DAPT and who are not high ischaemic risk, single antiplatelet therapy (preferably with a $P2Y_{12}$ receptor inhibitor) should be considered.[264,268–271,273,274,276,313,320]	IIa	A
De-escalation of $P2Y_{12}$ receptor inhibitor treatment (e.g. with a switch from prasugrel/ticagrelor to clopidogrel) may be considered as an alternative DAPT strategy to reduce bleeding risk.[279–282,321,322]	IIb	A
In HBR patients, aspirin or $P2Y_{12}$ receptor inhibitor monotherapy after 1 month of DAPT may be considered.[276,313]	IIb	B
De-escalation of antiplatelet therapy in the first 30 days after an ACS event is not recommended.[238,323]	III	B
Prolonging antithrombotic therapy		
Discontinuation of antiplatelet treatment in patients treated with an OAC is recommended after 12 months.[324,325]	I	B
Adding a second antithrombotic agent to aspirin for extended long-term secondary prevention should be considered in patients with high ischaemic risk and without HBR[c].[314–318]	IIa	A
Adding a second antithrombotic agent to aspirin for extended long-term secondary prevention may be considered in patients with moderate ischaemic risk and without HBR[c].[314–318]	IIb	A
$P2Y_{12}$ inhibitor monotherapy may be considered as an alternative to aspirin monotherapy for long-term treatment.[326,327]	IIb	A

2024 ESC Guidelines for the management of chronic coronary syndromes

2024 ESC Guidelines for the management of chronic coronary syndromes
(European Heart Journal; 2024 – doi: 10.1093/eurheartj/ehae177)

New recommendations (12)

Recommendations	Class	Level
Antithrombotic therapy in patients with chronic coronary syndrome		
Long-term antithrombotic therapy in patients with chronic coronary syndrome and no clear indication for oral anticoagulation		
In CCS patients with a prior MI or PCI, clopidogrel 75 mg daily is recommended as a safe and effective alternative to aspirin monotherapy.	I	A
After CABG, aspirin 75–100 mg daily is recommended lifelong.	I	A
In CCS patients *without* prior MI or revascularization but with evidence of significant obstructive CAD, aspirin 75–100 mg daily is recommended lifelong.	I	B

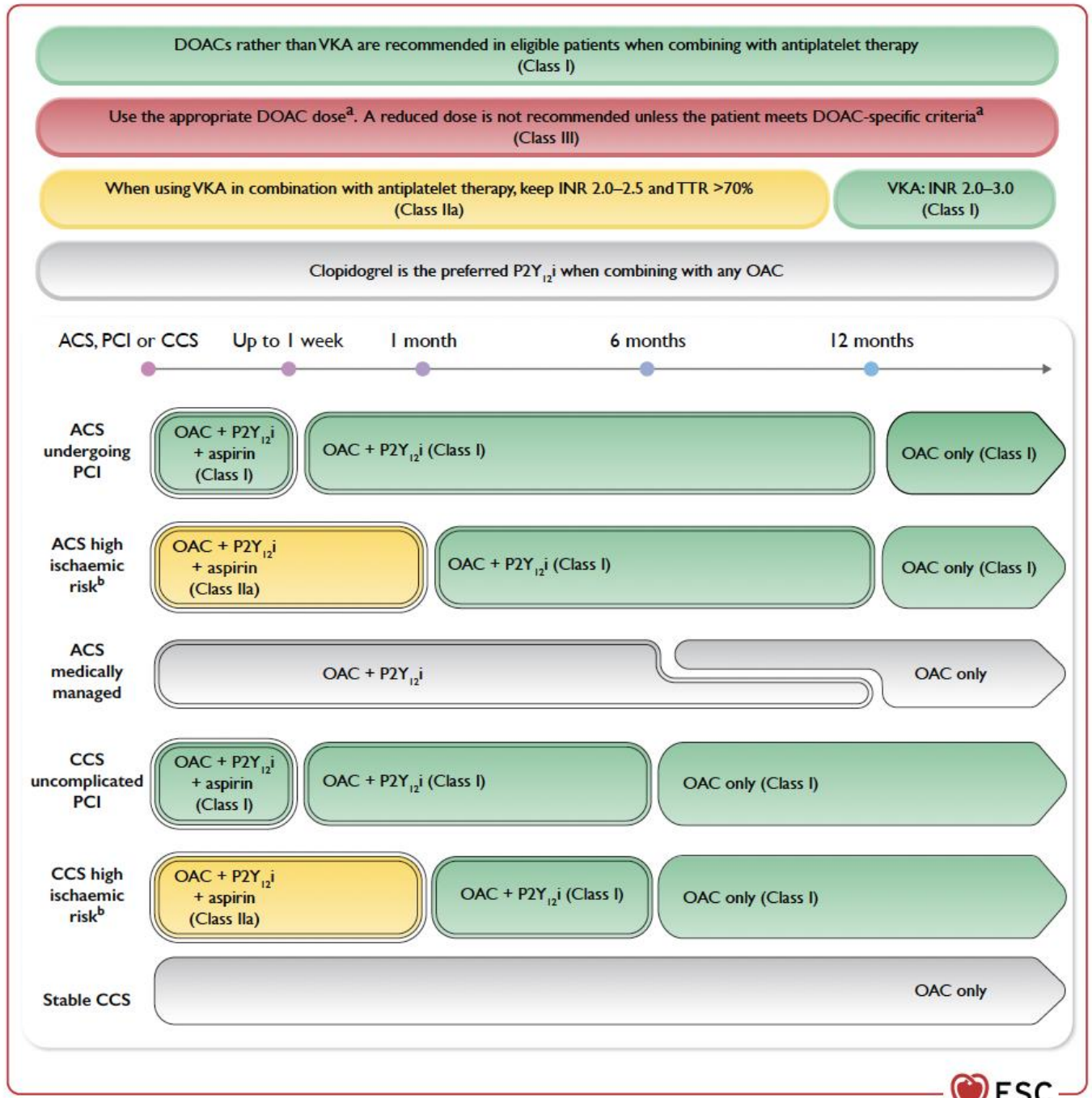

Patients with CCS without indication for OAC undergoing PCI
Assess bleeding risk
Non-high bleeding risk
High bleeding risk
Default
Non-high ischaemic risk
High ischaemic risk
Default
1 month
3 months
6 months
Long term
A C
6 mo. DAPT
(Class I)
A C
1–3 mo. DAPT
(Class IIb)
A OR C
(Class I)
A C OR A T
OR
A P
6 mo. DAPT
(Class I)
1–6 mo. DAPTa
(Class IIb)
A C
1–3 mo. DAPT
(Class I)
A OR C
(Class I)
A OR C
(Class I)
A C OR A T
A R A P
(Class IIa)
OR T
(Class IIb)
A Aspirin 100 mg o.d.
C Clopidogrel 75 mg o.d.
P Prasugrel 10 mg o.d.b
R Rivaroxaban 2.5 mg b.i.d.
T Ticagrelor 60 mg b.i.d.
T Ticagrelor 90 mg b.i.d.
ESC

Antithrombotic therapy after CABG

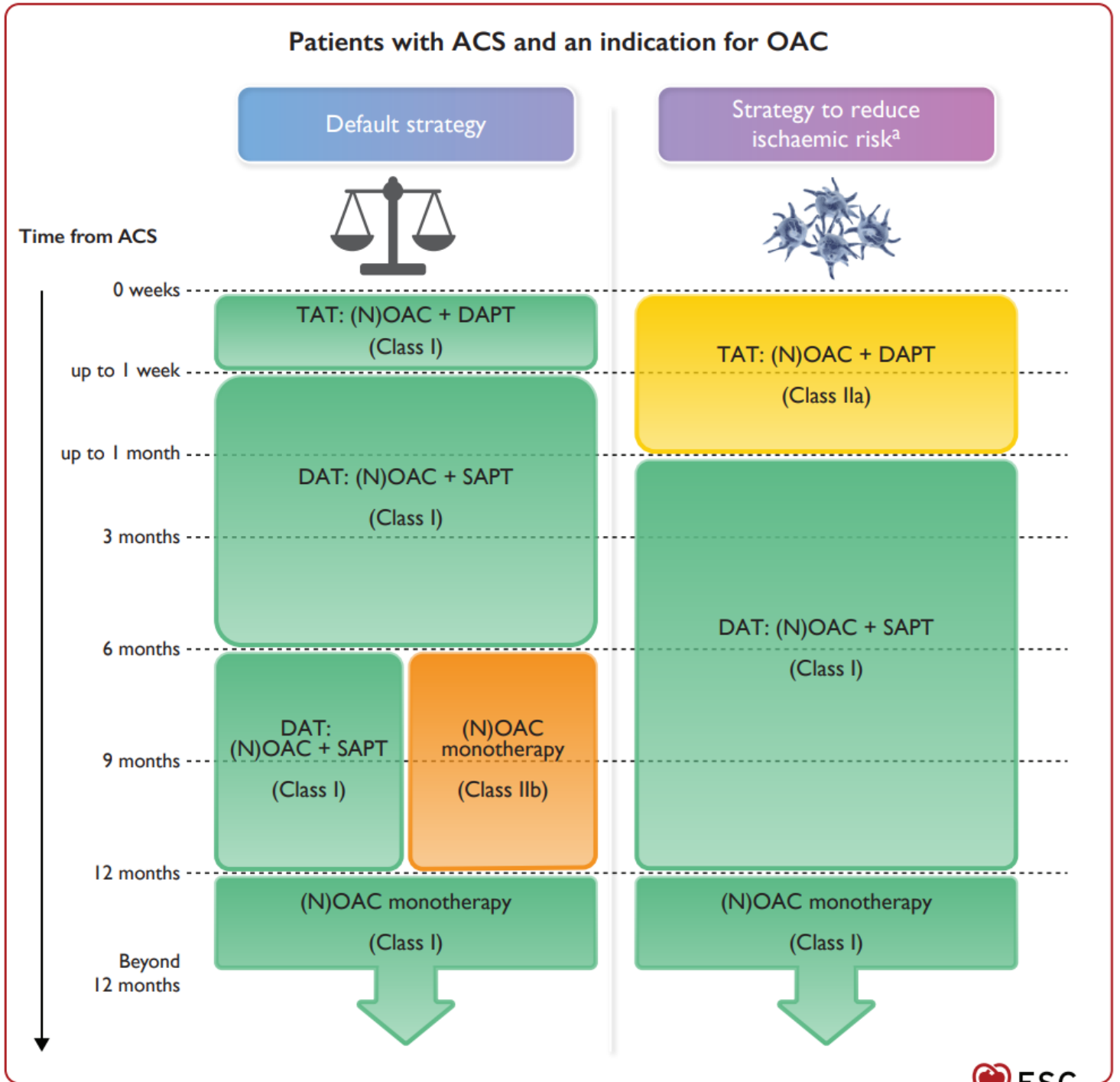
It is recommended to initiate aspirin post-operatively as soon as there is no concern over bleeding.[629,630]	I	B
DAPT may be considered after CABG in selected patients at greater risk of graft occlusion[f] and at low risk of bleeding.[635]	IIb	B

2024 ESC Guidelines for the management of atrial fibrillation

2024 ESC Guidelines for the management of atrial fibrillation
(European Heart Journal; 2024 – doi: 10.1093/eurheartj/ehae176)


DOACs rather than VKA are recommended in eligible patients when combining with antiplatelet therapy (Class I)
Use the appropriate DOAC dose[a]. A reduced dose is not recommended unless the patient meets DOAC-specific criteria[a] (Class III)
When using VKA in combination with antiplatelet therapy, keep INR 2.0–2.5 and TTR >70% (Class IIa)
VKA: INR 2.0–3.0 (Class I)
Clopidogrel is the preferred P2Y12i when combining with any OAC
ACS, PCI or CCS
Up to 1 week
1 month
6 months
12 months
ACS undergoing PCI
OAC + P2Y12i + aspirin (Class I)
OAC + P2Y12i (Class I)
OAC only (Class I)
ACS high ischaemic risk[b]
OAC + P2Y12i + aspirin (Class IIa)
OAC + P2Y12i (Class I)
OAC only (Class I)
ACS medically managed
OAC + P2Y12i
OAC only
CCS uncomplicated PCI
OAC + P2Y12i + aspirin (Class I)
OAC + P2Y12i (Class I)
OAC only (Class I)
CCS high ischaemic risk[b]
OAC + P2Y12i + aspirin (Class IIa)
OAC + P2Y12i (Class I)
OAC only (Class I)
Stable CCS
OAC only

AKS med indikation för OAC



Sammanfattning

- Nya ESC Guidelines för både AKS (2023) och KKS (2024)
- Viktigt väga in risken för blödning och ischemisk händelse i valet av antitrombotisk behandling
- Större flexibilitet i behandlingstid som kan bli både förlängd och förkortad
- Förbehandling vid NSTEMI nedtonad
- De-escalation kan övervägas men inte förrän tidigast > 30 dagar
- Pat med indikation för OAC – kort TAT max 1 vecka
- Pat med AKS som går till CABG bör återinsättas på DAPT postoperativt minst 12 mån


Tack för
uppmärksamheten!