In the name of God

2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

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Table 6 Dose regimen of antiplatelet and anticoagulant drugs in non-ST-segment elevation acute coronary syndrome patients[a] (1)

I. Antiplatelet drugs	
Aspirin	LD of 150–300 mg orally or 75–250 mg i.v. if oral ingestion is not possible, followed by oral MD of 75–100 mg o.d.
$P2Y_{12}$ receptor inhibitors (oral or i.v.)	
Clopidogrel	LD of 300–600 mg orally, followed by a MD of 75 mg o.d., no specific dose adjustment in CKD patients.
Prasugrel	LD of 60 mg orally, followed by a MD of 10 mg o.d. In patients with body weight <60 kg, a MD of 5 mg o.d. is recommended. In patients aged ≥75 years, prasugrel should be used with caution, but a dose of 5 mg o.d. should be used if treatment is deemed necessary. No specific dose adjustment in CKD patients. Prior stroke is a contraindication for prasugrel.

[a]All dosing regimens refer to doses given for the respective drugs for protection against thrombosis within the arterial system.

Table 6 Dose regimen of antiplatelet and anticoagulant drugs in non-ST-segment elevation acute coronary syndrome patients[a] (2)

I. Antiplatelet drugs	
$P2Y_{12}$ receptor inhibitors (oral or i.v.) (continued)	
Ticagrelor	LD of 180 mg orally, followed by a MD of 90 mg b.i.d., no specific dose adjustment in CKD patients.
Cangrelor	Bolus of 30 µg/kg i.v. followed by 4 µg/kg/min infusion for at least 2 h or the duration of the procedure (whichever is longer).
GP IIb/IIIa receptor inhibitors (i.v.)	
Abciximab	Bolus of 0.25 mg/kg i.v. and 0.125 µg/kg/min infusion (maximum 10 µg/min) for 12 h (drug is not supplied anymore).
Eptifibatide	Double bolus of 180 µg/kg i.v. (given at a 10-min interval) followed by an infusion of 2.0 µg/kg/min for up to18 h.

[a]All dosing regimens refer to doses given for the respective drugs for protection against thrombosis within the arterial system.

Table 6 Dose regimen of antiplatelet and anticoagulant drugs in non-ST-segment elevation acute coronary syndrome patients[a] (3)

I. Antiplatelet drugs	
GP IIb/IIIa receptor inhibitors (i.v.) (continued)	
Tirofiban	Bolus of 25 µg/kg i.v. over 3 min, followed by an infusion of 0.15 µg/kg/min for up to 18 h.
II. Anticoagulant drugs (for use before and during PCI)	
UFH	70–100 U/kg i.v. bolus when no GP IIb/IIIa inhibitor is planned followed up by an IV infusion until the invasive procedure. 50–70 U/kg i.v. bolus with GP IIb/IIIa inhibitors.
Enoxaparin	0.5 mg/kg i.v. bolus.
Bivalirudin	0.75 mg/kg i.v. bolus followed by i.v. infusion of 1.75 mg/kg/h for up to 4 h after the procedure as clinically warranted.

[a]All dosing regimens refer to doses given for the respective drugs for protection against thrombosis within the arterial system.

Table 6 Dose regimen of antiplatelet and anticoagulant drugs in non-ST-segment elevation acute coronary syndrome patients[a] (4)

II. Anticoagulant drugs (for use before and during PCI)	
Fondaparinux	2.5 mg/d subcutaneously (only before PCI).
III. Oral anticoagulant drugs[b]	
Rivaroxaban	Very low MD of 2.5 mg b.i.d. (in combination with aspirin) for long-term extended antithrombotic treatment in a secondary prevention setting of CAD patients.

[a]All dosing regimens refer to doses given for the respective drugs for protection against thrombosis within the arterial system.
[b]Section III lists the dosing for rivaroxaban in a secondary prevention setting in CAD patients. For a comprehensive summary on dosing of OACs (NOACs and VKAs) in a setting of full-dose anticoagulation please see: The 2018 European Heart Rhythm Association Practical Guide on the use of NOACs in patients with AF.

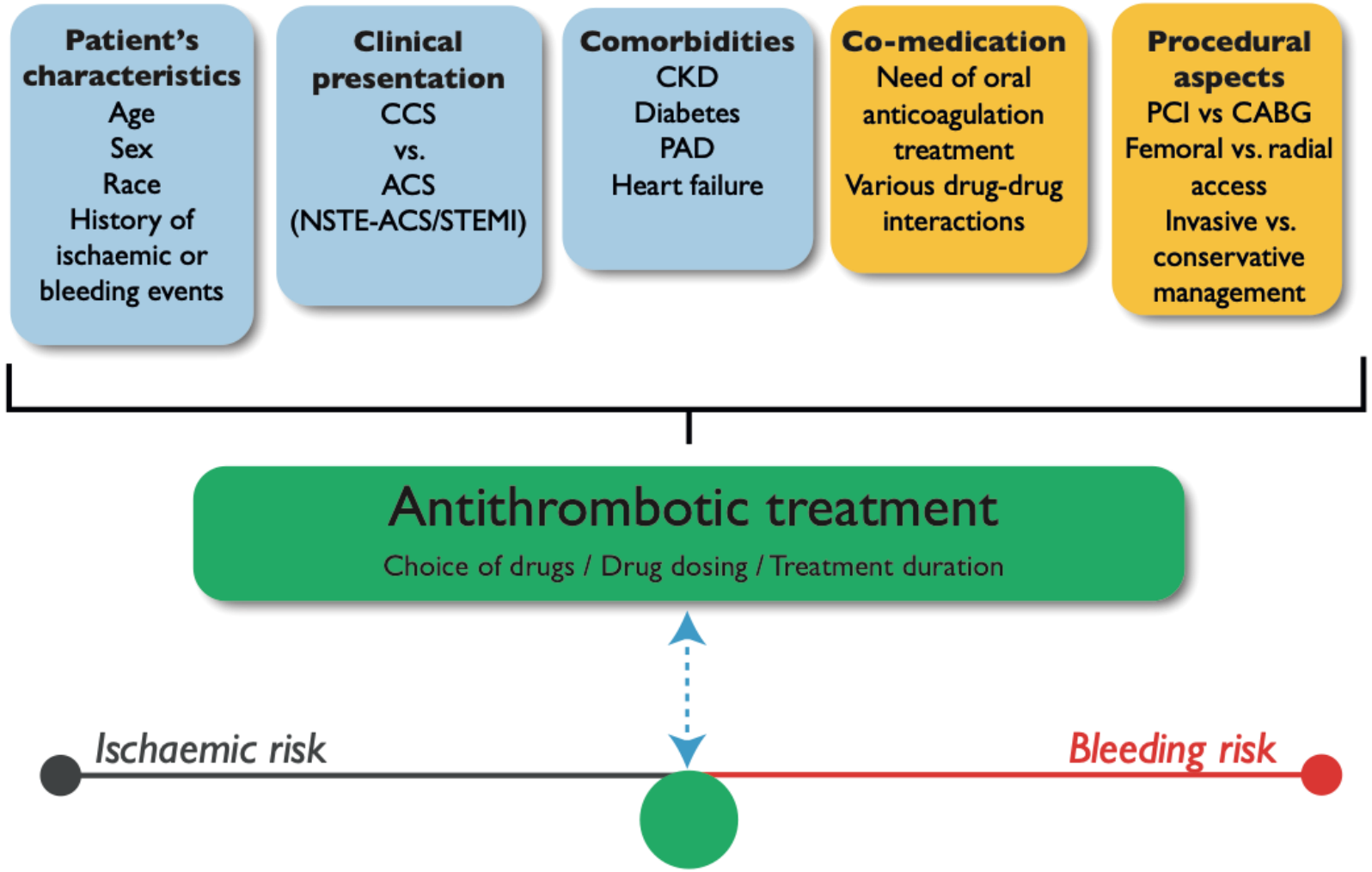

Figure 5

Determinants of antithrombotic treatment in coronary artery disease.

Intrinsic (in blue: patient's characteristics, clinical presentation & comorbidities) and extrinsic (in yellow: co-medication & procedural aspects) variables influencing the choice, dosing, and duration of antithrombotic treatment.

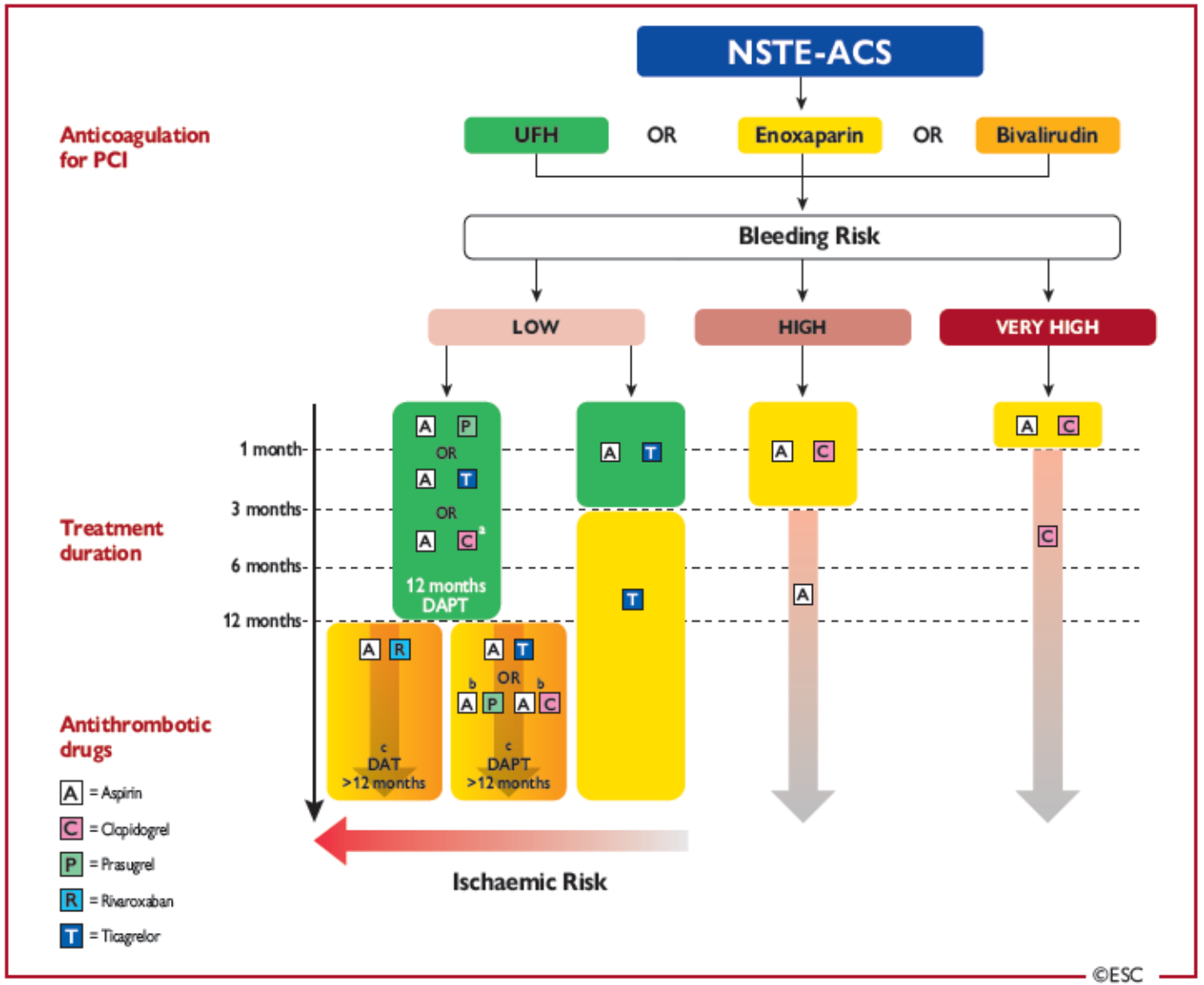

Figure 7 (1)

Algorithm for antithrombotic therapy in non-ST-segment elevation acute coronary syndrome patients without atrial fibrillation undergoing percutaneous coronary intervention.

= Class I = Class IIa = Class IIb

Very HBR is defined as recent bleeding in the past month and/or not deferrable planned surgery.

Recommendations for antithrombotic treatment in non-ST-segment elevation acute coronary syndrome patients undergoing percutaneous coronary intervention (1)

Recommendations	Class	Level
Antiplatelet treatment		
Aspirin is recommended for all patients without contraindications at an initial oral LD of 150–300 mg (or 75–250 mg i.v.), and at a MD of 75–100 mg o.d. for long-term treatment.	I	A
A $P2Y_{12}$ receptor inhibitor is recommended in addition to aspirin, and maintained over 12 months unless there are contraindications or an excessive risk of bleeding. Options are:	I	A
• Prasugrel in $P2Y_{12}$ receptor inhibitor-naïve patients proceeding to PCI (60 mg LD, 10 mg/d as standard dose, 5 mg/d for patients aged ≥75 years or with a body weight <60 kg).	I	B

Recommendations for antithrombotic treatment in non-ST-segment elevation acute coronary syndrome patients undergoing percutaneous coronary intervention (2)

Recommendations	Class	Level
Antiplatelet treatment (continued)		
• Ticagrelor irrespective of the planned treatment strategy (invasive or conservative) (180 mg LD, 90 mg b.i.d.).	I	B
• Clopidogrel (300–600 mg LD, 75 mg daily dose), only when prasugrel or ticagrelor are not available, cannot be tolerated, or are contraindicated.	I	C
Prasugrel should be considered in preference to ticagrelor for NSTE-ACS patients who proceed to PCI.	IIa	B
GP IIb/IIIa antagonists should be considered for bail-out if there is evidence of no-reflow or a thrombotic complication.	IIa	C

Recommendations for antithrombotic treatment in non-ST-segment elevation acute coronary syndrome patients undergoing percutaneous coronary intervention (3)

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Recommendations	Class	Level
Antiplatelet treatment (continued)		
Cangrelor may be considered in $P2Y_{12}$ receptor inhibitor-naïve patients undergoing PCI.	IIb	A
Pre-treatment with a $P2Y_{12}$ receptor inhibitor may be considered in patients with NSTE-ACS who are not planned to undergo an early invasive strategy and do not have an HBR.	IIb	C
Treatment with GP IIb/IIIa antagonists in patients in whom coronary anatomy is not known is not recommended.	III	A
It is not recommended to administer routine pre-treatment with a $P2Y_{12}$ receptor inhibitor in patients in whom coronary anatomy is not known and an early invasive management is planned.	III	A

Recommendations for post-interventional and maintenance treatment in patients with non-ST-segment elevation acute coronary syndrome (1)

Recommendations	Class	Level
In patients with NSTE-ACS treated with coronary stent implantation, DAPT with a $P2Y_{12}$ receptor inhibitor on top of aspirin is recommended for 12 months unless there are contraindications such as excessive risk of bleeding.	I	A
Prolonging antithrombotic treatment duration		
Adding a second antithrombotic agent to aspirin for extended long-term secondary prevention should be considered in patients with a high risk of ischaemic events and without increased risk of major or life-threatening bleeding (see *Tables 8* and *9* for options).	IIa	A

Recommendations for post-interventional and maintenance treatment in patients with non-ST-segment elevation acute coronary syndrome (2)

Recommendations	Class	Level
Prolonging antithrombotic treatment duration (continued)		
Adding a second antithrombotic agent to aspirin for extended long-term secondary prevention may be considered in patients with moderately increased risk of ischaemic events and without increased risk of major or life-threatening bleeding (see *Tables 8* and *9* for options).	IIb	A
In ACS patients with no prior stroke/transient ischaemic attack who are at high ischaemic risk and low bleeding risk and are receiving aspirin and clopidogrel, low-dose rivaroxaban (2.5 mg b.i.d. for approximately 1 year) may be considered after discontinuation of parenteral anticoagulation.	IIb	B

Recommendations for post-interventional and maintenance treatment in patients with non-ST-segment elevation acute coronary syndrome (3)

Recommendations	Class	Level
Shortening antithrombotic treatment duration		
After stent implantation with high risk of bleeding (e.g. PRECISE-DAPT ≥25 or ARC-HBR criteria met), discontinuation of $P2Y_{12}$ receptor inhibitor therapy after 3 months should be considered.	IIa	B
After stent implantation in patients undergoing a strategy of DAPT, stopping aspirin after 3–6 months should be considered, depending on the balance between the ischaemic and bleeding risk.	IIa	A

Recommendations for post-interventional and maintenance treatment in patients with non-ST-segment elevation acute coronary syndrome (4)

Recommendations	Class	Level
Shortening antithrombotic treatment duration (continued)		
De-escalation of $P2Y_{12}$ receptor inhibitor treatment (e.g. with a switch from prasugrel or ticagrelor to clopidogrel) may be considered as an alternative DAPT strategy, especially for ACS patients deemed unsuitable for potent platelet inhibition. De-escalation may be done unguided based on clinical judgment or guided by platelet function testing or CYP2C19 genotyping, depending on patient's risk profile and availability of respective assays.	IIb	A

Table 8 Treatment options for extended dual antithrombotic or antiplatelet therapies

Drug	Dose	Indication	NNT (ischaemic outcomes)	NNH (bleeding Outcomes)
DAT regimens for extended treatment (including aspirin 75–100 mg o.d.)				
Rivaroxaban (COMPASS trial)	2.5 mg b.i.d.	Patients with CAD or symptomatic PAD at high risk of ischaemic events	77	84
DAPT regimens for extended treatment (including aspirin 75–100 mg o.d.)				
Clopidogrel (DAPT trial)	75 mg/d	Post MI in patients who have tolerated DAPT for 1 year	63	105
Prasugrel (DAPT trial)	10 mg/d (5 mg/d if body weight <60 kg or age >75 years)	Post PCI for MI in patients who have tolerated DAPT for 1 year	63	105
Ticagrelor (PEGASUS-TIMI 54)	60/90 mg b.i.d.	Post MI in patients who have tolerated DAPT for 1 year	84	81

Drugs (in addition to aspirin 75–100 mg/d) for extended DAPT treatment options are in alphabetical order. For indications and definitions for high/moderately increased risk and bleeding risk see *Table 9* and *Figure 7*. NNT refers to the primary ischaemic endpoints of the respective trials and NNH refers to the key safety (bleeding) endpoints. NNT and NNH numbers from the DAPT trial are pooled numbers for clopidogrel and prasugrel.

Table 9 Risk criteria for extended treatment with a second antithrombotic agent (1)

High thrombotic risk (Class IIa)	Moderately increased thrombotic risk (Class IIb)
Complex CAD and at least 1 criterion	Non-complex CAD and at least 1 criterion
Risk enhancers	
Diabetes mellitus requiring medication	Diabetes mellitus requiring medication
History of recurrent MI	History of recurrent MI
Any multivessel CAD	Polyvascular disease (CAD plus PAD)
Polyvascular disease (CAD plus PAD)	CKD with eGFR 15–59 mL/min/1.73 m^2
Premature (<45 years) or accelerated (new lesion within a 2-year time frame) CAD	

In line with guideline recommendations, CAD patients are stratified into two different risk groups (high vs. moderately increased thrombotic or ischaemic risk). Stratification of patients towards complex vs. non-complex CAD is based on individual clinical judgement with knowledge of patients' cardiovascular history and/or coronary anatomy. Selection and composition of risk-enhancing factors are based on the combined evidence of clinical trials on extended antithrombotic treatment in CAD patients and on data from related registries.

Table 9 Risk criteria for extended treatment with a second antithrombotic agent (2)

High thrombotic risk (Class IIa)	Moderately increased thrombotic risk (Class IIb)
Complex CAD and at least 1 criterion	Non-complex CAD and at least 1 criterion
Risk enhancers (continued)	
Concomitant systemic inflammatory disease (e.g. human immunodeficiency virus, systemic lupus erythematosus, chronic arthritis)	
CKD with eGFR 15–59 mL/min/1.73 m^2	
Technical aspects	
At least 3 stents implanted	
At least 3 lesions treated	

In line with guideline recommendations, CAD patients are stratified into two different risk groups (high vs. moderately increased thrombotic or ischaemic risk). Stratification of patients towards complex vs. non-complex CAD is based on individual clinical judgement with knowledge of patients' cardiovascular history and/or coronary anatomy. Selection and composition of risk-enhancing factors are based on the combined evidence of clinical trials on extended antithrombotic treatment in CAD patients and on data from related registries

Table 9 Risk criteria for extended treatment with a second antithrombotic agent (3)

High thrombotic risk (Class IIa)	Moderately increased thrombotic risk (Class IIb)
Complex CAD and at least 1 criterion	Non-complex CAD and at least 1 criterion
Technical aspects (continued)	
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	

In line with guideline recommendations, CAD patients are stratified into two different risk groups (high vs. moderately increased thrombotic or ischaemic risk). Stratification of patients towards complex vs. non-complex CAD is based on individual clinical judgement with knowledge of patients' cardiovascular history and/or coronary anatomy. Selection and composition of risk-enhancing factors are based on the combined evidence of clinical trials on extended antithrombotic treatment in CAD patients and on data from related registries.

Recommendations for anti-ischaemic drugs in the acute phase of non-ST-segment elevation acute coronary syndrome

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Recommendations	Class	Level
Sublingual or i.v. nitrates and early initiation of beta-blocker treatment are recommended in patients with ongoing ischaemic symptoms and without contraindications.	I	C
It is recommended to continue chronic beta-blocker therapy, unless the patient is in overt heart failure.	I	C
i.v. nitrates are recommended in patients with uncontrolled hypertension or signs of heart failure.	I	C
In patients with suspected/confirmed vasospastic angina, calcium channel blockers and nitrates should be considered and beta-blockers avoided.	IIa	B

Recommendations for diabetes mellitus in non-ST-segment elevation acute coronary syndrome patients (1)

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Recommendations	Class	Level
It is recommended to screen all patients with NSTE-ACS for diabetes and to monitor blood glucose levels frequently in patients with known diabetes or admission hyperglycaemia.	I	C
Avoidance of hypoglycaemia is recommended.	I	B
Glucose-lowering therapy should be considered in ACS patients with blood glucose >10 mmol/L (>180 mg/dL), with the target adapted to comorbidities, while episodes of hypoglycaemia should be avoided.	IIa	B

Recommendations for patients with chronic kidney disease and non-ST-segment elevation acute coronary syndrome (1)

Recommendations	Class	Level
Risk stratification in CKD		
It is recommended to apply the same diagnostic and therapeutic strategies in patients with CKD (dose adjustment may be necessary) as for patients with normal renal function.	I	C
It is recommended to assess kidney function by eGFR in all patients.	I	C

Recommendations for patients with chronic kidney disease and non-ST-segment elevation acute coronary syndrome (2)

Recommendations	Class	Level
Myocardial revascularization in patients with CKD		
Use of low- or iso-osmolar contrast media (at lowest possible volume) are recommended in invasive strategies.	I	A
Pre- and post-hydration with isotonic saline should be considered if the expected contrast volume is >100 mL in invasive strategies.	IIa	C
As an alternative to the pre- and post-hydration regimen, tailored hydration regimens may be considered.	IIb	B
CABG should be considered over PCI in patients with multivessel CAD whose surgical risk profile is acceptable and life expectancy is >1 year.	IIa	B

Recommendations for older persons with non-ST-segment elevation acute coronary syndrome

Recommendations	Class	Level
It is recommended to apply the same diagnostic strategies in older patients as for younger patients.	I	B
It is recommended to apply the same interventional strategies in older patients as for younger patients.	I	B
The choice of antithrombotic agent and dosage, as well as secondary preventions, should be adapted to renal function, as well as specific contraindications.	I	B

Recommendations for pharmacological long-term management after non-ST-segment elevation acute coronary syndrome (excluding antithrombotic treatments) (1)

Recommendations	Class	Level
Lipid-lowering drugs		
Statins are recommended in all NSTE-ACS patients. The aim is to reduce LDL-C by ≥50% from baseline and to achieve LDL-C <1.4 mmol/L (<55 mg/dL) .	I	A
If the LDL-C goal[a] is not achieved after 4–6 weeks with the maximally tolerated statin dose, combination with ezetimibe is recommended.	I	B
If the LDL-C goal[c] is not achieved after 4–6 weeks despite maximally tolerated statin therapy and ezetimibe, the addition of a PCSK9 inhibitor is recommended.	I	B

[a]For patients at very high cardiovascular risk (such as patients with ACS), an LDL-C reduction of at least 50% from baseline and an LDL-C goal <1.4 mmol/L (<55 mg/dL) are recommended.

Recommendations for pharmacological long-term management after non-ST-segment elevation acute coronary syndrome (excluding antithrombotic treatments) (2)

Recommendations	Class	Level
Lipid-lowering drugs (continued)		
If the current NSTE-ACS episode is a recurrence within less than 2 years of a first ACS, while taking maximally tolerated statin-based therapy, an LDL-C goal of <1.0 mmol/L (<40 mg/dL) may be considered.	IIb	B
ACE inhibitors or ARBs		
ACE inhibitors (or ARBs in cases of intolerance to ACE inhibitors) are recommended in patients with heart failure with reduced LVEF (<40%), diabetes, or CKD unless contraindicated (e.g. severe renal impairment, hyperkalaemia, etc.) in order to reduce all-cause and cardiovascular mortality and cardiovascular morbidity.	I	A

Recommendations for pharmacological long-term management after non-ST-segment elevation acute coronary syndrome (excluding antithrombotic treatments) (3)

Recommendations	Class	Level
Beta-blockers		
Beta-blockers are recommended in patients with systolic LV dysfunction or heart failure with reduced LVEF (<40%).	I	A
In patients with prior MI, long-term oral treatment with a beta-blocker should be considered in order to reduce all-cause and cardiovascular mortality and cardiovascular morbidity.	IIa	B

Recommendations for pharmacological long-term management after non-ST-segment elevation acute coronary syndrome (excluding antithrombotic treatments) (4)

Recommendations	Class	Level
MRAs		
MRAs are recommended in patients with heart failure with reduced LVEF (<40%) in order to reduce all-cause and cardiovascular mortality and cardiovascular morbidity.	I	A
Proton pump inhibitors		
Concomitant use of a proton pump inhibitor is recommended in patients receiving aspirin monotherapy, DAPT, DAT, TAT, or OAC monotherapy who are at high risk of gastrointestinal bleeding in order to reduce the risk of gastric bleeds.	I	A

Figure 13 (1) Central illustration. Management strategy for non-ST-segment elevation acute coronary syndrome patients.

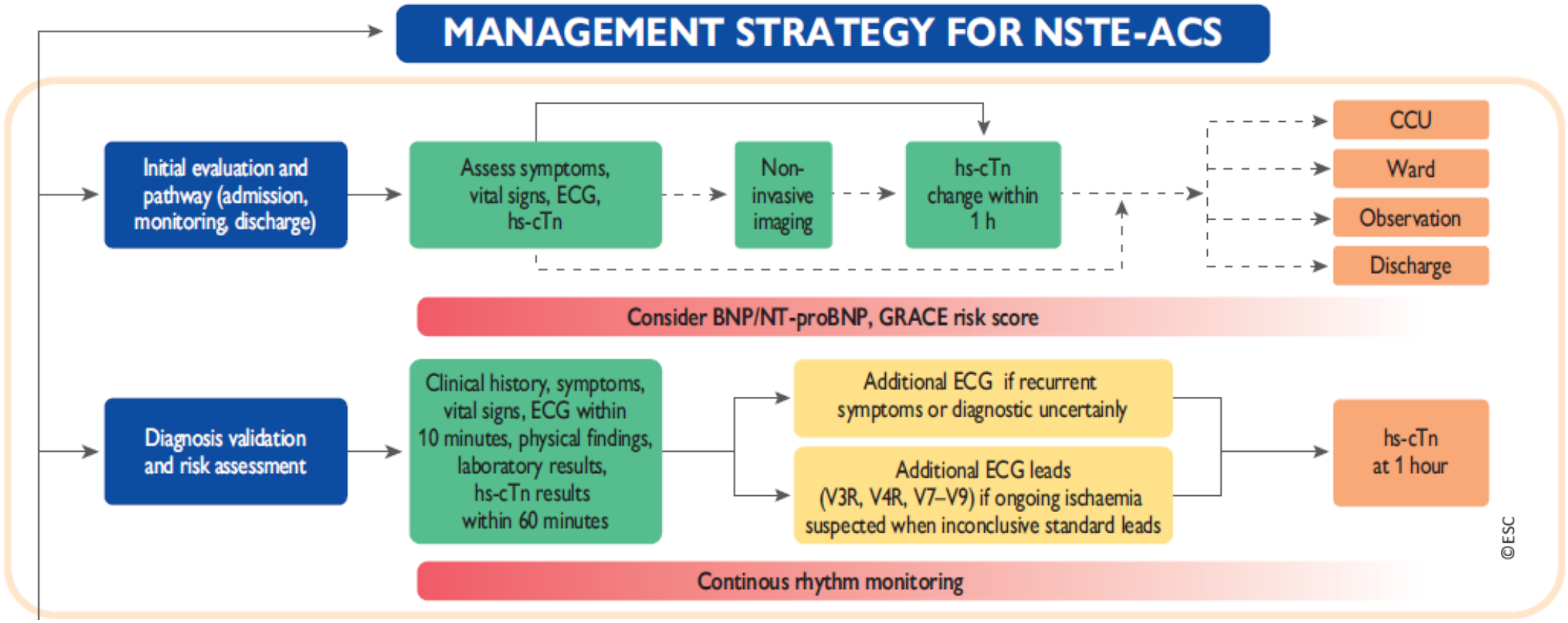


Figure 13 (2) Central illustration. Management strategy for non-ST-segment elevation acute coronary syndrome patients.

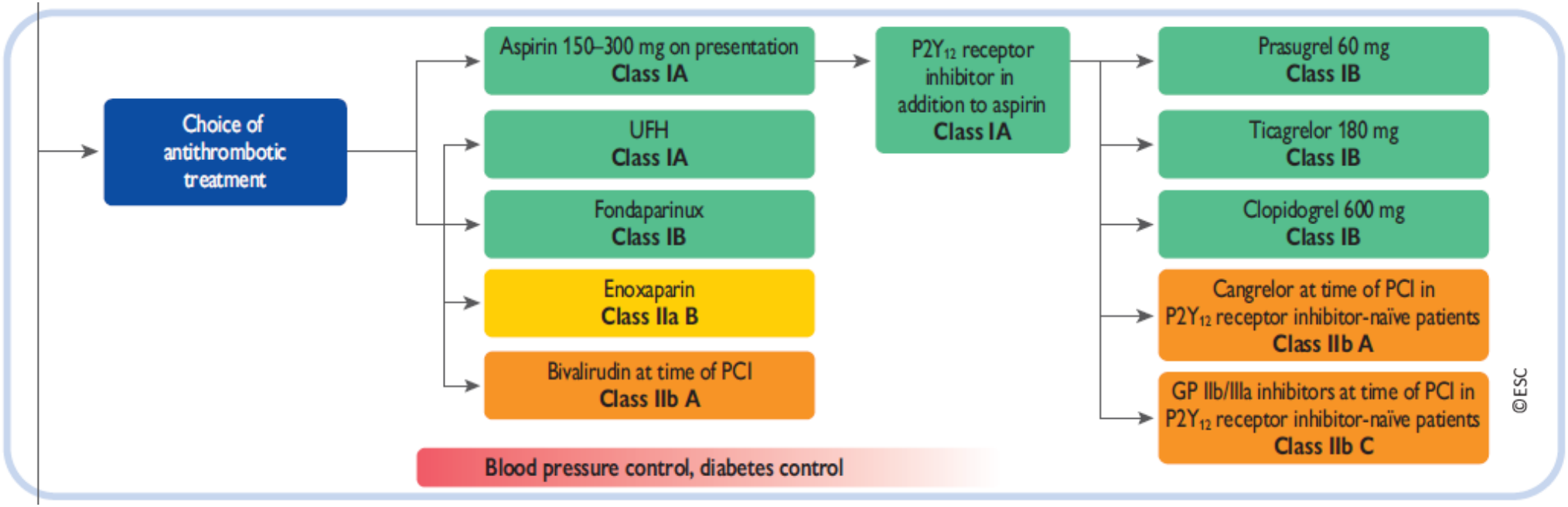


Figure 13 (3) Central illustration. Management strategy for non-ST-segment elevation acute coronary syndrome patients.

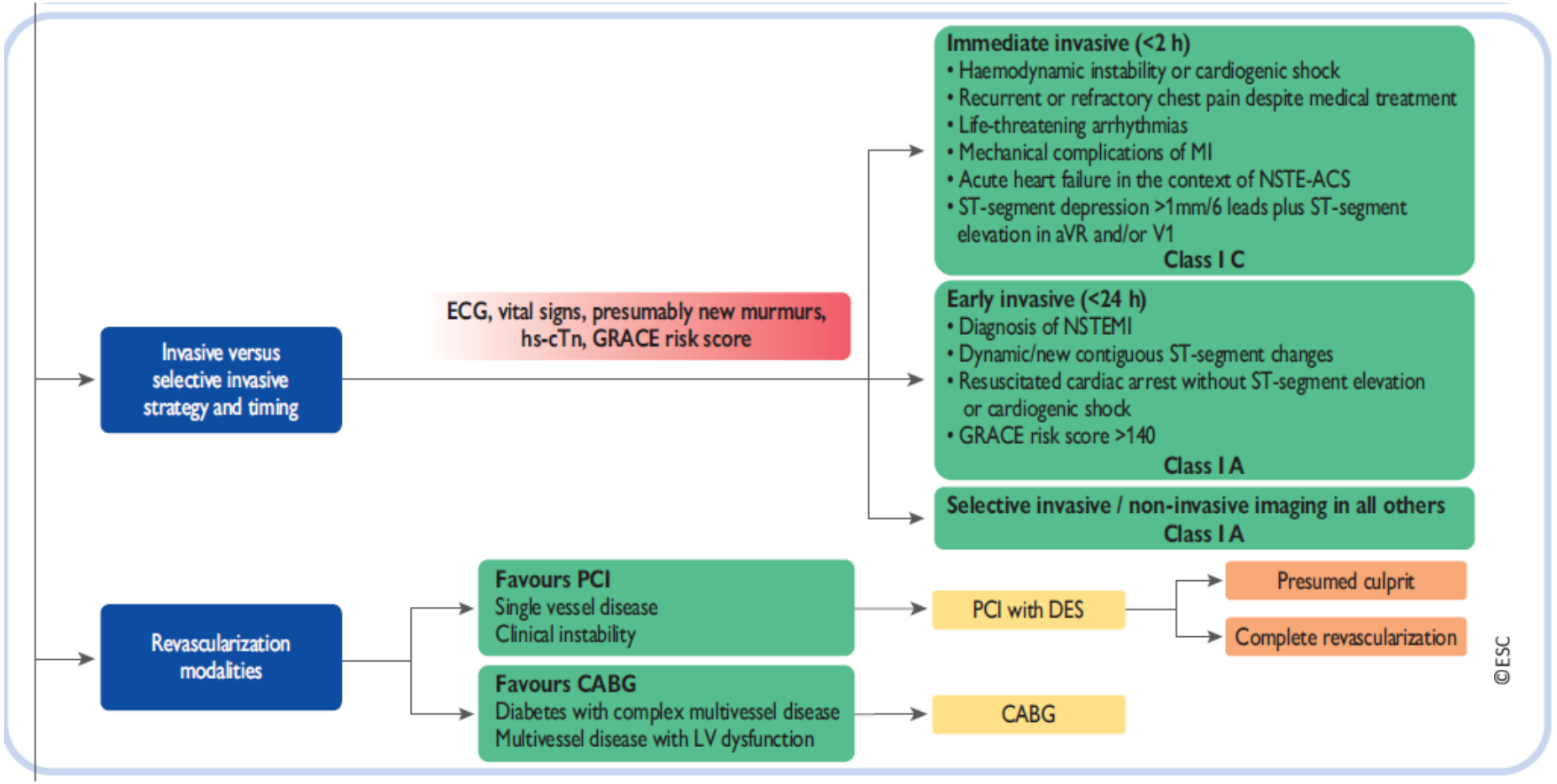
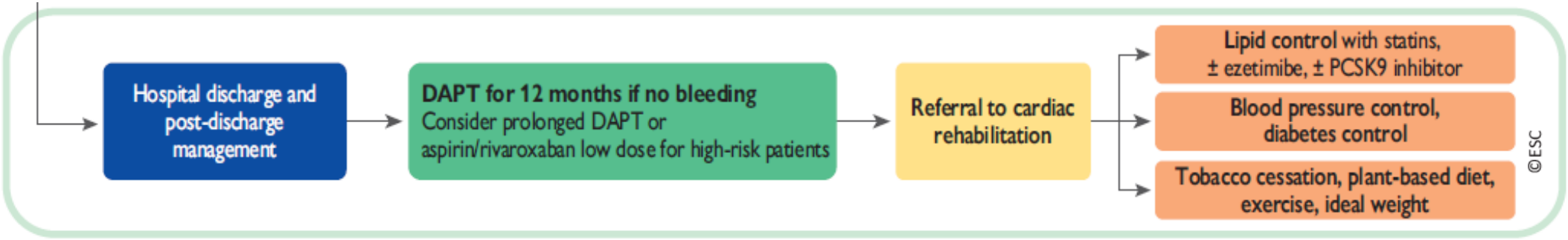


Figure 13 (4) Central illustration. Management strategy for non-ST-segment elevation acute coronary syndrome patients.



Supplementary Table 8 Lifestyle recommendations

Smoking cessation	Use pharmacological and behavioural strategies to help patients quit smoking. Avoid passive smoking.
Healthy diet	Diet high in vegetables, fruit, whole grains; limit saturated fat to <10% of total. Limit alcohol to <100 g/week or 15 g/day.
Physical activity	30–60 min moderate physical activity most days, but even irregular activity is beneficial.
Healthy weight	Obtain and maintain a healthy weight (BMI 18.5–25 kg/m^2) or reduce weight through recommended energy intake and increased physical activity.
Other	Take medication as prescribed. Sexual activity is low risk for stable patients who are not symptomatic at low-to-moderate activity levels.

Lifestyle recommendations are based on ESC CCS Guidelines

Supplementary Table 9 Healthy diet

Increase consumption of fruit and vegetables (≥200 g each per day)
35–45 g of fibre per day, preferably from whole grains
Moderate nut consumption (30 g unsalted)
1–2 servings of fish per week (one to be oily fish)
Limited lean meat, low-fat dairy products, and liquid vegetable oils
Saturated fats to account for <10% of total energy intake, replace with polyunsaturated fats
Trans unsaturated fats as low as possible, preferably no intake from processed food, and <1% of total energy intake
≤5–6 g of salt per day
If alcohol is consumed, limiting intake to ≤100 g/week or <15 g/day is recommended
Avoid energy-dense foods such as sugar-sweetened soft drinks

Results are based on the results of a systematic review by de Vries et al.