

ESC / ČKS guidelines 2015: Akutní koronární syndromy bez elevací ST

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Table 3 Clinical implications of high-sensitivity cardiac troponin assays

Compared with standard cardiac troponin assays, high-sensitivity assays:

- Have higher negative predictive value for acute MI.
- Reduce the “troponin-blind” interval leading to earlier detection of acute MI.
- Result in a ~4% absolute and ~20% relative increase in the detection of type I MI and a corresponding decrease in the diagnosis of unstable angina.
- Are associated with a 2-fold increase in the detection of type 2 MI.

Levels of high-sensitivity cardiac troponin should be interpreted as quantitative markers of cardiomyocyte damage (i.e. the higher the level, the greater the likelihood of MI):

- Elevations beyond 5-fold the upper reference limit have high (>90%) positive predictive value for acute type I MI.
- Elevations up to 3-fold the upper reference limit have only limited (50–60%) positive predictive value for acute MI and may be associated with a broad spectrum of conditions.
- It is common to detect circulating levels of cardiac troponin in healthy individuals.

Rising and/or falling cardiac troponin levels differentiate acute from chronic cardiomyocyte damage (the more pronounced the change, the higher the likelihood of acute MI).

Table 4 Conditions other than acute myocardial infarction type 1 associated with cardiac troponin elevation

Tachyarrhythmias
Heart failure
Hypertensive emergencies
Critical illness (e.g. shock/ sepsis/ burns)
Myocarditis ^a
Tako-Tsubo cardiomyopathy
Structural heart disease (e.g. aortic stenosis)
Aortic dissection
Pulmonary embolism, pulmonary hypertension
Renal dysfunction and associated cardiac disease
Coronary spasm
Acute neurological event (e.g. stroke or subarachnoid haemorrhage)
Cardiac contusion or cardiac procedures (CABG, PCI, ablation, pacing, cardioversion, or endomyocardial biopsy)
Hypo- and hyperthyroidism
Infiltrative diseases (e.g. amyloidosis, haemochromatosis, sarcoidosis, scleroderma)
Myocardial drug toxicity or poisoning (e.g. doxorubicin, 5-fluorouracil, herceptin, snake venoms)
Extreme endurance efforts
Rhabdomyolysis

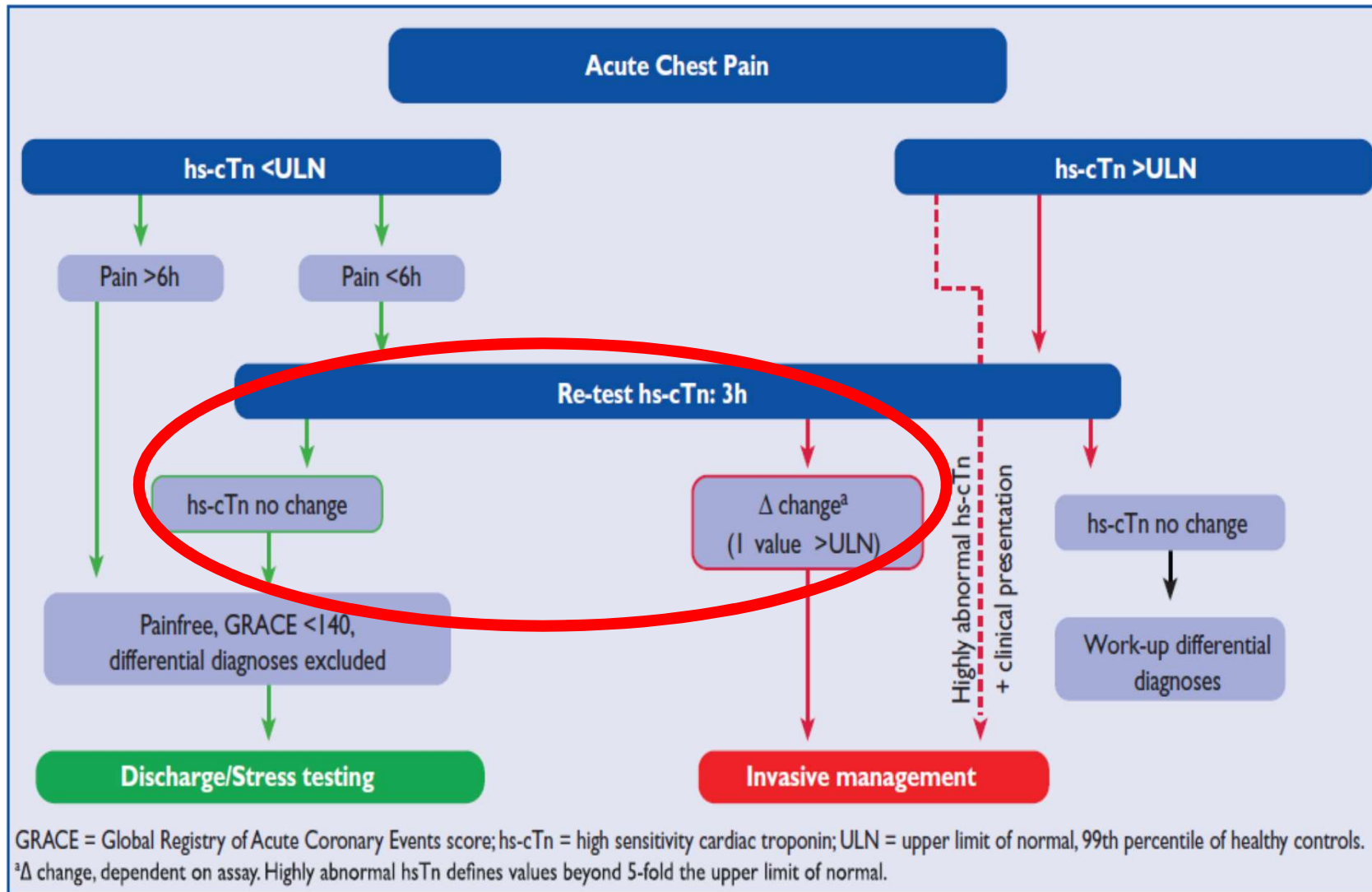


Figure 2 0 h/3 h rule-out algorithm of non-ST-elevation acute coronary syndromes using high-sensitivity cardiac troponin assays.

Table 6 Differential diagnoses of acute coronary syndromes in the setting of acute chest pain

Cardiac	Pulmonary	Vascular	Gastro-intestinal	Orthopaedic	Other
Myopericarditis Cardiomyopathies ^a	Pulmonary embolism	Aortic dissection	Oesophagitis, reflux or spasm	Musculoskeletal disorders	Anxiety disorders
Tachyarrhythmias	(Tension)-Pneumothorax	Symptomatic aortic aneurysm	Peptic ulcer, gastritis	Chest trauma	Herpes zoster
Acute heart failure	Bronchitis, pneumonia	Stroke	Pancreatitis	Muscle injury/ inflammation	Anaemia
Hypertensive emergencies	Pleuritis		Cholecystitis	Costochondritis	
Aortic valve stenosis				Cervical spine pathologies	
Tako-Tsubo cardiomyopathy					
Coronary spasm					
Cardiac trauma					

Bold = common and/or important differential diagnoses.

^aDilated, hypertrophic and restrictive cardiomyopathies may cause angina or chest discomfort.

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

Recommendations	Class ^a	Level ^b	Ref. ^c
Early initiation of <u>beta-blocker</u> treatment is recommended in patients with ongoing ischaemic symptoms and without contraindications.	I	B	119
It is recommended to continue chronic beta-blocker therapy, unless the patient is in Killip class III or higher.	I	B	126
Sublingual or i.v. <u>nitrates</u> are recommended to relieve angina; ^d i.v. treatment is recommended in patients with recurrent angina, 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	127

Recommendations for platelet inhibition in non-ST-elevation acute coronary syndromes

Recommendations	Class ^a	Level ^b	Ref. ^c
Oral antiplatelet therapy			
Aspirin is recommended for all patients without contraindications at an initial oral loading dose ^d of 150–300 mg (in aspirin-naive patients) and a maintenance dose of 75–100 mg/day long-term regardless of treatment strategy.	I	A	129–132
A P2Y ₁₂ inhibitor is recommended, in addition to aspirin, for 12 months unless there are contraindications such as excessive risk of bleeds.	I	A	137, 148, 153
<ul style="list-style-type: none"> Ticagrelor (180 mg loading dose, 90 mg twice daily) is recommended, in the absence of contraindications,^e for all patients at moderate-to-high risk of ischaemic events (e.g. elevated cardiac troponins), regardless of initial treatment strategy and including those pretreated with clopidogrel (which should be discontinued when ticagrelor is started). 	I	B	153
<ul style="list-style-type: none"> Prasugrel (60 mg loading dose, 10 mg daily dose) is recommended in patients who are proceeding to PCI if no contraindication.^e 	I	B	148, 164
<ul style="list-style-type: none"> Clopidogrel (300–600 mg loading dose, 75 mg daily dose) is recommended for patients who cannot receive ticagrelor or prasugrel or who require oral anticoagulation. 	I	B	137
P2Y ₁₂ inhibitor administration for a shorter duration of 3–6 months after DES implantation may be considered in patients deemed at high bleeding risk.	IIb	A	187–189, 192

It is not recommended to administer prasugrel in patients in whom coronary anatomy is not known.	III	B	164
Intravenous antiplatelet therapy			
GPIIb/IIIa inhibitors during PCI should be considered for bailout situations or thrombotic complications.	IIa	C	
Cangrelor may be considered in P2Y ₁₂ inhibitor-naive patients undergoing PCI.	IIb	A	158–161
It is not recommended to administer GPIIb/IIIa inhibitors in patients in whom coronary anatomy is not known.	III	A	198, 199
Long-term P2Y₁₂ inhibition			
P2Y ₁₂ inhibitor administration in addition to aspirin beyond 1 year may be considered after careful assessment of the ischaemic and bleeding risks of the patient.	IIb	A	184, 186
General recommendations			
A proton pump inhibitor in combination with DAPT is recommended in patients at higher than average risk of gastrointestinal bleeds (i.e. history of gastrointestinal ulcer/haemorrhage, anticoagulant therapy, chronic NSAID/corticosteroid use or two or more of the following: age ≥ 65 years, dyspepsia, gastro-oesophageal reflux disease, <i>Helicobacter pylori</i> infection, chronic alcohol use).	I	B	208, 209
In patients on P2Y ₁₂ inhibitors who need to undergo non-emergency major non-cardiac surgery, ^f postponing surgery for at least 5 days after cessation of ticagrelor or clopidogrel, and for 7 days for prasugrel, should be considered if clinically feasible and unless the patient is at high risk of ischaemic events.	IIa	C	
In case of a non-cardiac surgical procedure that cannot be postponed or of a bleeding complication, discontinuation of the P2Y ₁₂ inhibitor may be considered after a minimum of 1 and 3 months from PCI with BMS and new-generation DES, respectively.	IIb	C	

Table 11 Dosing of anticoagulants in patients with normal and impaired renal function

Drug	Recommendations		
	Normal renal function or stage 1–3 CKD (eGFR ≥ 30 mL/min/1.73m ²)	Stage 4 CKD (eGFR 15–29 mL/min/1.73m ²)	Stage 5 CKD (eGFR < 15 mL/min/1.73m ²)
Unfractionated heparin	<ul style="list-style-type: none"> • Prior to coronary angiography: <u>60–70 IU/kg i.v.</u> (max 5000 IU) and infusion (12–15 IU/kg/h) (max 1000 IU/h), target aPTT 1.5–2.5x control • <u>During PCI: 70–100 IU/kg i.v.</u> (50–70 IU/kg if concomitant with GPIIb/IIIa inhibitors) 	<p>bud' 60-70 j. anebo 70-10 j. NESČÍTAT dohromady !!</p> <p>No dose adjustment</p>	No dose adjustment
Enoxaparin	1 mg/kg s.c. twice a day	1 mg/kg s.c. once a day	Not recommended
Fondaparinux	2.5 mg s.c. once a day	Not recommended if eGFR < 20 mL/min/1.73m ²	Not recommended
Bivalirudin	Bolus 0.75 mg/kg i.v., infusion 1.75 mg/kg/h	No adjustment of bolus, reduce infusion rate to 1 mg/kg/h	On dialysis, no adjustment of bolus, reduce infusion rate to 0.25 mg/kg/h

Recommendations for anticoagulation in non-ST-elevation acute coronary syndromes

Recommendations	Class ^a	Level ^b	Ref. ^c
Parenteral anticoagulation is recommended at the time of diagnosis according to both ischaemic and bleeding risks.	I	B	227
Fondaparinux (2.5 mg s.c. daily) is recommended as having the most favourable efficacy–safety profile regardless of the management strategy.	I	B	218, 228, 229
Bivalirudin (0.75 mg/kg i.v. bolus, followed by 1.75 mg/kg/h for up to 4 h after the procedure) is recommended as an alternative to UFH plus GPIIb/IIIa inhibitors during PCI.	I	A	205, 222, 223
<u>UFH 70–100 IU/kg i.v.</u> (50–70 IU/kg if concomitant with GPIIb/IIIa inhibitors) is recommended in patients undergoing PCI who did not receive any anticoagulant.	I	B	219, 229
In patients on fondaparinux (2.5 mg s.c. daily) undergoing PCI, a single i.v. bolus of UFH (70–85 IU/kg, or 50–60 IU/kg in the case of concomitant use of GPIIb/IIIa inhibitors) is recommended during the procedure.	I	B	219

Enoxaparin (1 mg/kg s.c. twice daily) or UFH are recommended when fondaparinux is not available.	I	B	218, 230
Enoxaparin should be considered as an anticoagulant for PCI in patients pretreated with s.c. enoxaparin.	IIa	B	211
Additional ACT-guided i.v. boluses of UFH during PCI may be considered following initial UFH treatment.	IIb	B	231
<u>Discontinuation of anticoagulation</u> should be considered <u>after PCI</u> , unless otherwise indicated.	IIa	C	
Crossover between UFH and LMWH is not recommended.	III	B	216
In NSTEMI patients with no prior stroke/TIA and at high ischaemic risk as well as low bleeding risk receiving aspirin and clopidogrel, <u>low-dose rivaroxaban (2.5 mg twice daily for approximately 1 year)</u> may be considered after discontinuation of parenteral anticoagulation.	IIb	B	226

Table 12 Suggested strategies to reduce bleeding risk related to PCI

- Anticoagulant doses adjusted to bodyweight and renal function, especially in women and elderly patients.
- Radial approach preferred.
- Proton pump inhibitors in patients on DAPT at higher than average risk of gastrointestinal bleeds (i.e. history of gastrointestinal ulcer/haemorrhage, anticoagulant therapy, chronic NSAIDs/corticosteroid use, or two or more among age ≥ 65 years, dyspepsia, gastrooesophageal reflux disease, *Helicobacter pylori* infection, and chronic alcohol use).
- In patients on OAC
 - o PCI performed without interruption of VKAs or NOACs.
 - o In patients on VKAs, do not administer UFH if INR value >2.5 .
 - o In patients on NOACs, regardless of the timing of the last administration of NOACs, add additional low-dose parenteral anticoagulation (e.g. enoxaparin 0.5 mg/kg i.v. or UFH 60 IU/kg).
 - o Aspirin indicated but avoid pretreatment with P2Y₁₂ inhibitors.
 - o GPIIb/IIIa inhibitors only for bailout of periprocedural complications.

Recommendations for combining antiplatelet agents and anticoagulants in non-ST-elevation acute coronary syndrome patients requiring chronic oral anticoagulation

Recommendations	Class ^a	Level ^b	Ref. ^c
In patients with a firm indication for OAC (e.g. atrial fibrillation with a CHA ₂ DS ₂ -VASc score ≥ 2 , recent venous thromboembolism, LV thrombus or mechanical valve prosthesis), OAC is recommended in addition to antiplatelet therapy.	I	C	
An early invasive coronary angiography (within 24 h) should be considered in moderate- to high-risk patients, ^d irrespective of OAC exposure, to expedite treatment allocation (medical vs. PCI vs. CABG) and to determine the optimal antithrombotic regimen.	IIa	C	
Initial dual antiplatelet therapy with aspirin plus a P2Y ₁₂ inhibitor in addition to OAC before coronary angiography is not recommended.	III	C	
Patients undergoing coronary stenting			
Anticoagulation			
During PCI, additional parenteral anticoagulation is recommended, irrespective of the timing of the last dose of all NOACs and if INR is < 2.5 in VKA-treated patients.	I	C	
Uninterrupted therapeutic anticoagulation with VKA or NOACs should be considered during the periprocedural phase.	IIa	C	

Antiplatelet treatment

Following coronary stenting, DAPT including new P2Y ₁₂ inhibitors should be considered as an alternative to triple therapy for patients with NSTEMI-ACS and atrial fibrillation with a CHA ₂ DS ₂ -VASc score of 1 (in males) or 2 (in females).	IIa	C	
If at low bleeding risk (HAS-BLED ≤ 2), triple therapy with OAC, aspirin (75–100 mg/day) and clopidogrel 75 mg/day should be considered for 6 months, followed by OAC and aspirin 75–100 mg/day or clopidogrel (75 mg/day) continued up to 12 months.	IIa	C	
If at high bleeding risk (HAS-BLED ≥ 3), triple therapy with OAC, aspirin (75–100 mg/day) and clopidogrel 75 mg/day should be considered for a duration of 1 month, followed by OAC and aspirin 75–100 mg/day or clopidogrel (75 mg/day) continued up to 12 months irrespective of the stent type (BMS or new-generation DES).	IIa	C	
Dual therapy with OAC and clopidogrel 75 mg/day may be considered as an alternative to triple antithrombotic therapy in selected patients (HAS-BLED ≥ 3 and low risk of stent thrombosis).	IIb	B	246, 248
The use of ticagrelor or prasugrel as part of triple therapy is not recommended.	III	C	
Vascular access and stent type			
Radial over femoral access is recommended for coronary angiography and PCI.	I	A	251
The use of new-generation DES over BMS should be considered among patients requiring OAC.	IIa	B	245, 252
Medically managed patients			
One antiplatelet agent in addition to OAC should be considered for up to 1 year.	IIa	C	

NSTE-ACS patients with non-valvular atrial fibrillation

Management strategy

PCI

Medically managed / CABG

Bleeding risk

Low to intermediate
(e.g. HAS-BLED = 0-2)

High
(e.g. HAS-BLED ≥ 3)

Time from PCI/ACS

0

4 weeks

6 months

12 months

Lifelong

Triple therapy

O **A** **C**

Triple or dual therapy^a

O **A** **C**

Dual therapy^b

O **C** or **A**

Dual therapy^b

O **C** or **A**

Dual therapy^b

O **C** or **A**

O Monotherapy^c

O Oral anticoagulation
(VKA or NOACs)

A Aspirin 75-100 mg daily

C Clopidogrel 75 mg daily

Table 13 Risk criteria mandating invasive strategy in NSTE-ACS

Very-high-risk criteria

- Haemodynamic instability or cardiogenic shock
- Recurrent or ongoing chest pain refractory to medical treatment
- Life-threatening arrhythmias or cardiac arrest
- Mechanical complications of MI
- Acute heart failure
- Recurrent dynamic ST-T wave changes, particularly with intermittent ST-elevation

High-risk criteria

- Rise or fall in cardiac troponin compatible with MI
- Dynamic ST- or T-wave changes (symptomatic or silent)
- GRACE score > 140

Intermediate-risk criteria

- Diabetes mellitus
- Renal insufficiency (eGFR <60 mL/min/1.73 m²)
- LVEF <40% or congestive heart failure
- Early post-infarction angina
- Prior PCI
- Prior CABG
- GRACE risk score > 109 and < 140

Low-risk criteria

- Any characteristics not mentioned above

Postup jako u STEMI

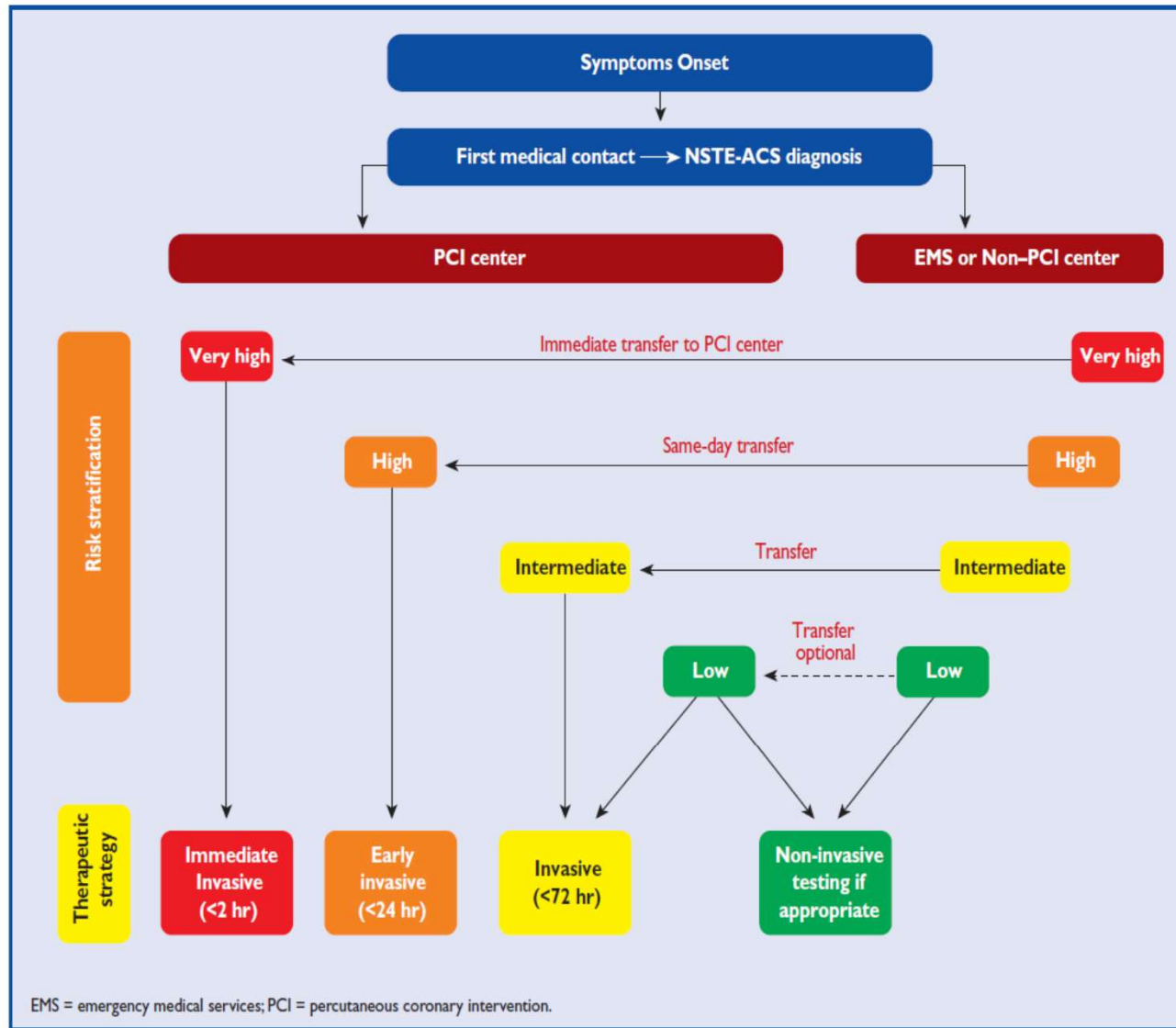


Figure 6 Selection of non-ST-elevation acute coronary syndrome (NSTEMI-ACS) treatment strategy and timing according to initial risk stratification.

Recommendations for long-term management after non-ST-elevation acute coronary syndromes

Recommendations (for the recommendations on antithrombotic treatment, see sections 5.2.9 and 5.3.3)	Class ^a	Level ^b	Ref. ^c
It is recommended to advise all patients on lifestyle changes (including smoking cessation, regular physical activity and a healthy diet).	I	A	536, 537
It is recommended to start high-intensity <u>statin therapy</u> as early as possible, unless contraindicated, and maintain it long term.	I	A	522, 527, 528
An <u>ACE inhibitor</u> is recommended in patients with LVEF $\leq 40\%$ or heart failure, hypertension or diabetes, unless contraindicated. An ARB provides an alternative, particularly if ACE inhibitors are not tolerated.	I	A	478–481, 530, 531, 538

<u>Beta-blocker therapy</u> is recommended in patients with LVEF $\leq 40\%$, unless contraindicated.	I	A	482–486
<u>Mineralocorticoid receptor antagonists</u> , preferably eplerenone, are recommended in patients with LVEF $\leq 35\%$ and either heart failure or diabetes after NSTEMI-ACS but no significant renal dysfunction or hyperkalaemia. ^d	I	A	487, 488, 525
A <u>diastolic blood pressure goal of < 90 mmHg</u> is recommended (< 85 mmHg in diabetic patients).	I	A	539, 540
Participation in a well-structured cardiac rehabilitation programme to modify lifestyle habits and increase adherence to treatment should be considered.	IIa	A	535, 541–546
In patients with LDL cholesterol ≥ 70 mg/dL (≥ 1.8 mmol/L) despite a maximally tolerated statin dose, further reduction in LDL cholesterol with a non-statin agent ^e should be considered.	IIa	B	529
A systolic blood pressure goal of < 140 mmHg should be considered.	IIa	B	547–549

Nejdůležitější doporučení

Diagnoza a farmakoterapie:

- Rychlý protokol k vyloučení / potvrzení AKS s užitím 2x hs-Tn (dynamika !)
- Echokardiografie (EF, dif.dg.)
- Ticagrelor nebo prasugrel na 1 rok
- Clopidogrel pro pac. užívající OAC
- Prasugrel se má podávat až po koronarografii (tica/clopi možno i před SKG)
- Vysoké dávky statinů od začátku hospitalizace

Invazivní postup:

- SKG do 120 minut od stanovení diagnózy při vysokém riziku (selhání či šok, recid.stenokardie, závažné arytmie, ST \uparrow či ST \downarrow)
- SKG do 24 hodin při středním riziku (dynamice Tn, změnách ST-T nebo GRACE >140).
- Radiální přístup preferován
- Při MVD indikace přes Heart-team