New NSTEMI Guidelines

Leonardo Bolognese, MD, FESC, FACC
Cardiovascular Department, Arezzo, Italy

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ISO 9001

New 2015 ESC guidelines for the management of NSTEMI

What's new?

- New diagnostic algorithm using high-sensitivity cardiac troponin
- Guidance on cardiac rhythm monitoring
- Revascularization
- Antithrombotic therapy
- Secondary prevention

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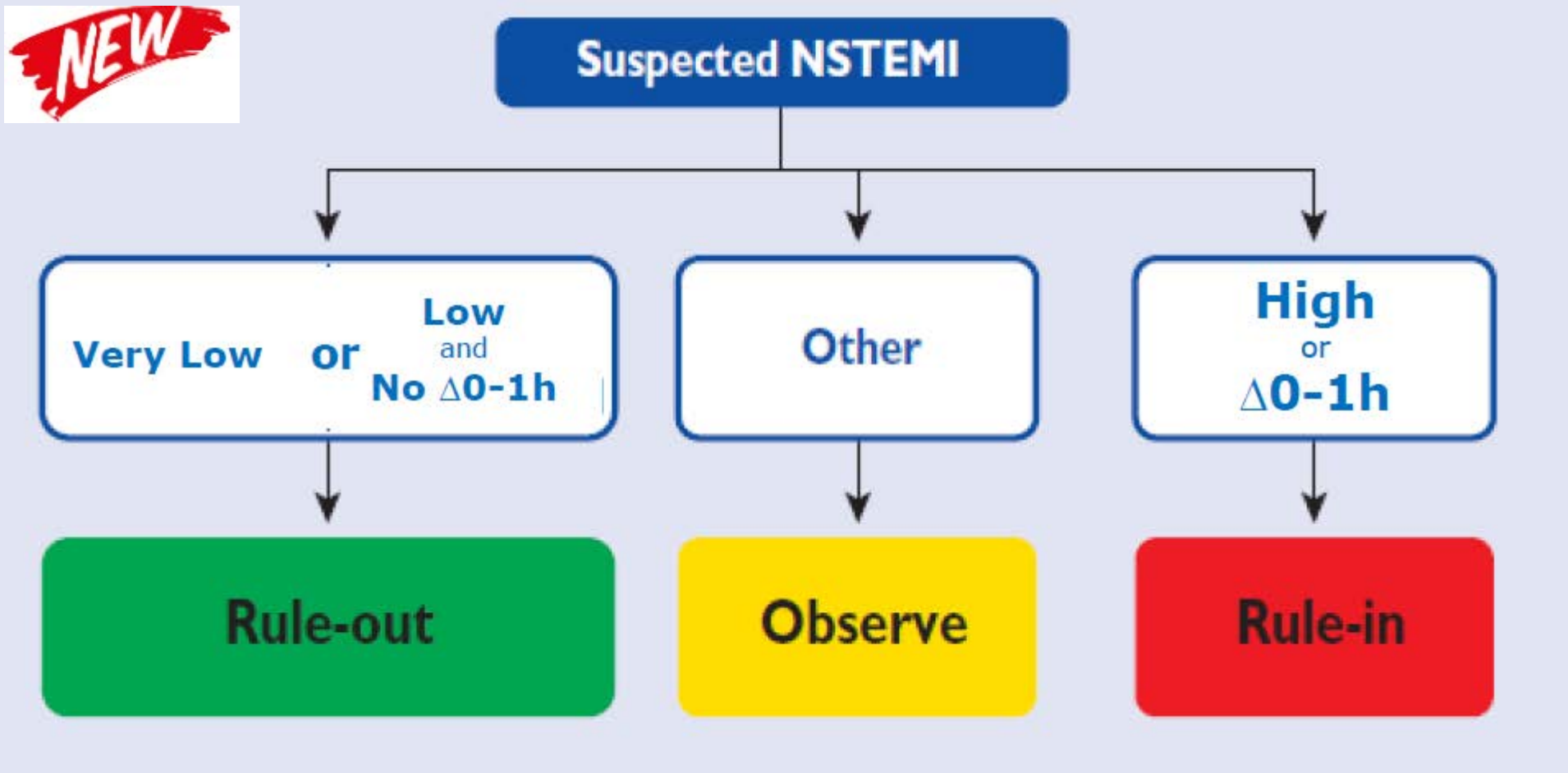
0 h/1 h Rule-in and rule-out algorithms using hs-cTn assays in patients presenting with suspected NSTEMI



- Negative predictive value >98% for acute MI
- Positive predictive value 75-80% for acute MI
- Cut-offs for « rule-in » and « rule-out » assay specific

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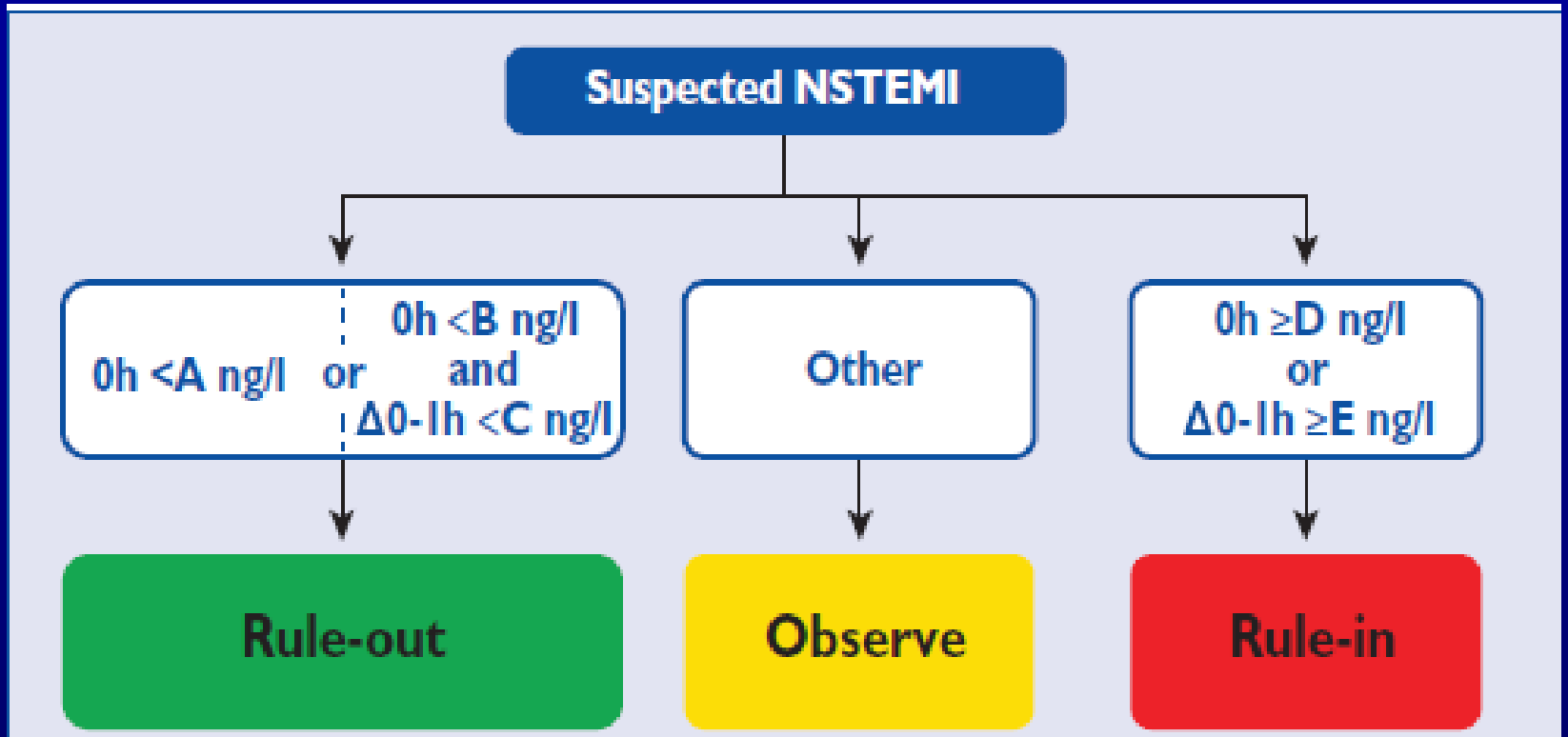

	A	B	C	D	E
hs-cTnT (Elecsys)	5	12	3	52	5
hs-cTnI (Architect)	2	5	2	52	6
hs-cTnI (Dimension Vista)	0.5	5	2	107	19

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'Rule-in' and 'rule-out' algorithms

Recommendations	Class[a]	Level[b]
It is recommended to measure cardiac troponins with sensitive or high-sensitivity assays and obtain the results within 60 min.	I	A
A rapid rule-out protocol at 0 h and 3 h is recommended if high-sensitivity cardiac troponin tests are available.	I	B
A rapid rule-out and rule-in protocol at 0 h and 1 h is recommended if a high-sensitivity cardiac troponin test with a validated 0 h/1 h algorithm is available. Additional testing after 3–6 h is indicated if the first two troponin measurements are not conclusive and the clinical condition is still suggestive of ACS.	I	B

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Recommended unit and duration of *monitoring* according to clinical presentation after established NSTE-ACS diagnosis

Clinical Presentation	Unit	Rhythm monitoring
Unstable angina	Regular ward or discharge	None
NSTEMI at low risk for cardiac arrhythmias[a]	Intermediate care unit or coronary care unit	≤24 h
NSTEMI at intermediate to high risk for cardiac arrhythmias[b]	Intensive/coronary care units or intermediate care unit	>24 h

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Selection of NSTE-ACS treatment strategy and timing according to initial risk stratification

From Primary or Secondary High Risk Criteria in 2011 GL

- Very High Risk Criteria
- High Risk Criteria
- Intermediate Risk Criteria

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

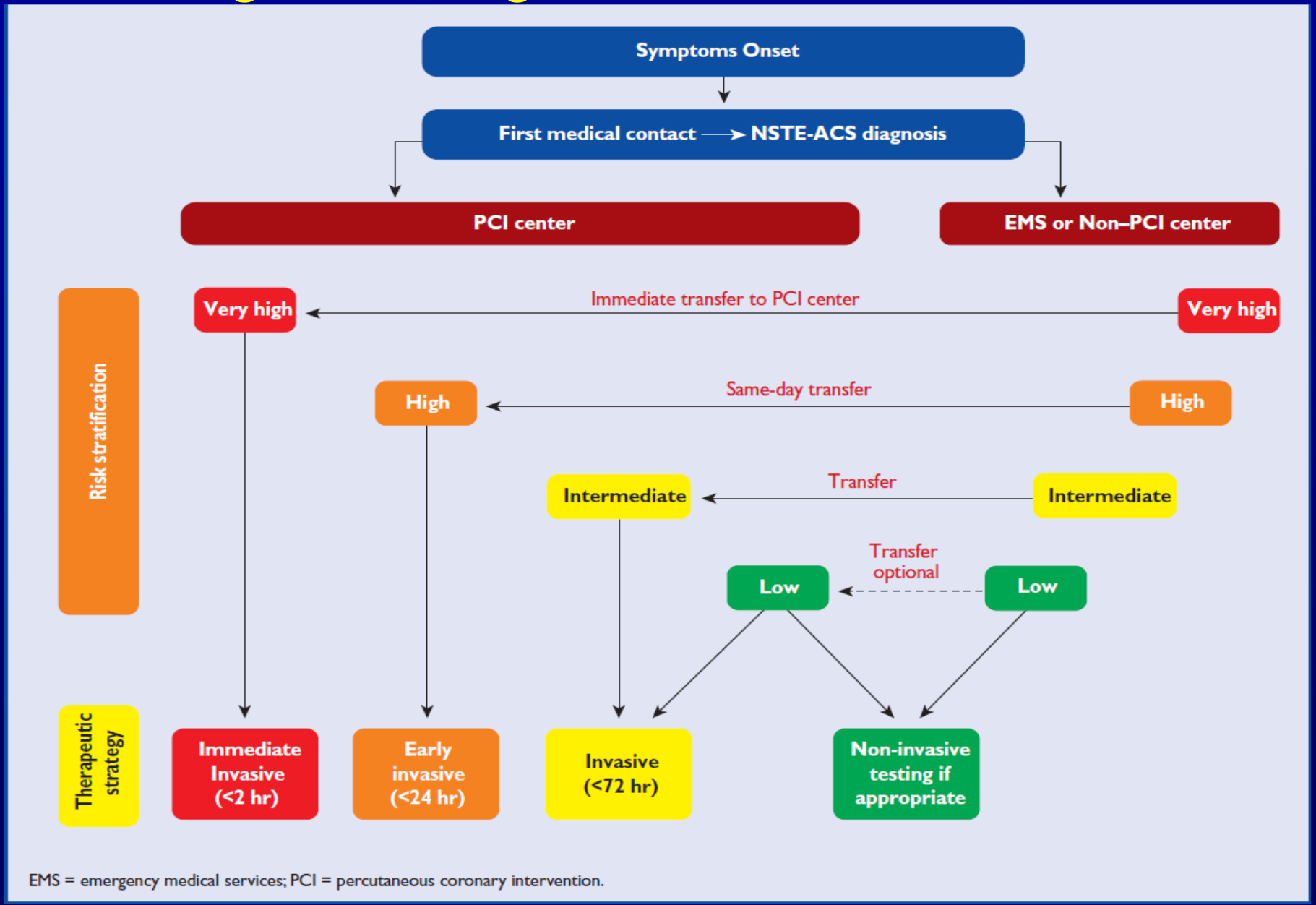
Recommendations for invasive coronary angiography and revascularization in NSTE-ACS

Recommendations	Class	Level	Ref.
An immediate invasive strategy (<2 h) is recommended in patients with at least one 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 with refractory angina or ST deviation – recurrent dynamic ST- or T-wave changes, particularly with intermittent ST-elevation.	I	C	
An early invasive strategy (<24 h) is recommended in patients with at least one high-risk criteria: – rise or fall in troponin compatible with MI – dynamic ST- or T-wave changes (symptomatic or silent) – GRACE score >140.	I	A	TIMACS Katrisis et al. Navarese et al.

Recommendations for invasive coronary angiography and revascularization in NSTE-ACS

Recommendations	Class	Level	Ref.
An invasive strategy (<72 h) is recommended in patients with at least one intermediate risk criteria: - diabetes mellitus - renal insufficiency(eGFR <60 mL/min/1.73 m2) - LVEF <40% or congestive heart failure - early post-infarction angina - recent PCI - prior CABG - GRACE risk score >109 and <140, or recurrent symptoms or ischaemia on non-invasive testing	I	A	Bavry et al. Fox et al.
In patients with none of the above mentioned risk criteria and no recurrent symptoms, non-invasive testing for ischaemia (preferably with imaging) is recommended before deciding on invasive evaluation.	I	A	Nyman et al. Amsterdam et al.

Selection of NSTE-ACS treatment strategy and timing according to initial risk stratification



EMS = emergency medical services; PCI = percutaneous coronary intervention.

Recommendations for invasive coronary angiography and revascularization in NSTE-ACS

2011 NSTEACS GL → No formal reco for access site selection

The choice of vascular access site depends on operator expertise and local preference, but, due to the large impact of bleeding complications on clinical outcome in patients with elevated bleeding risk, the choice may become important. Since the radial approach has been shown to reduce the risk of bleeding when compared with the femoral approach, this access site should be preferred in patients at high risk of bleeding provided the operator has sufficient experience with this technique

page 3007

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Recommendations	Class	Level	Ref.
In centres experienced with radial access, a radial approach is recommended for coronary angiography and PCI.	I	A	MATRIX Meta-analysis

- **It is recommended that centres treating ACS pts implement a transition from transfemoral to transradial access.**
- **Proficiency in the femoral approach should be maintained (e.g. for IABP insertion and structural as well as peripheral procedures)**

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Recommendations for invasive coronary angiography and revascularization in NSTE-ACS

Recommendations	Class	Level	Ref.
In patients with multivessel CAD, it is recommended to base the revascularization strategy (e.g. ad hoc culprit-lesion PCI, multivessel PCI, CABG) on the clinical status and co-morbidities as well as the disease severity (including distribution, angiographic lesion characteristics, SYNTAX score), according to the local Heart Team protocol	I	C	
In patients undergoing PCI, new-generation DESs are recommended.	I	A	Bangalore et al. Kirtane et al.
In patients in whom a short DAPT duration (30 days) is planned because of an increased bleeding risk, a new-generation DES may be considered over a BMS	IIb	B	ZEUS NEW

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Antithrombotic therapy
What's new?

- Anticoagulants
- Timing of P2Y12 (pretreatment)
- Duration of dual antiplatelet therapy
- Switching
- New agents: cangrelor and vorapaxar
- Patients requiring long-term OAC
- Special populations
- Antiplatelet agents and CABG

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Emphasis on Fondaparinux

Anticoagulation for NSTE-ACS

Recommendations for anticoagulation in NSTE-ACS		
Recommendations	**Class[a]**	**Level[b]**
Parenteral anticoagulation is recommended at the time of diagnosis according to both ischaemic and bleeding risks.	I	B
Bivalirudin (0.75 mg/kg i.v. bolus, followed by 1.75 mg/kg/hour for up to 4 hours after the procedure) is recommended as alternative to UFH plus GPIIb/IIIa inhibitors during PCI.	I	A
Fondaparinux (2.5 mg s.c. daily) is recommended as having the most favourable efficacy–safety profile regardless of the management strategy.	I	B
UFH 70–100 IU/kg i.v. (50–70 IU/kg if concomitant with GPIIb/IIIa inhibitors) is recommended in patients undergoing PCI who did not receive any anticoagulant.	I	B
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 PCI.	I	B

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Anticoagulation for NSTE-ACS

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

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Antiplatelet therapy

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
It is not recommended to administer prasugrel in patients in whom coronary anatomy is not known.	III	B	164

NEW

NEW

ACCOAST

A $P2Y_{12}$ inhibitor should be added to aspirin ~~as soon as possible~~ and maintained over 12 months, unless there are contraindications such as excessive risk of bleeding. **2011** | I | A

Personalized approach for Pretreatment!

- As the optimal timing of ticagrelor or clopidogrel in NSTE-ACS pts scheduled for an invasive strategy has not been adequately investigated, *no recommendation for or against pretreatment with these agents can be formulated*. Prasugrel is recommended only after coronary angiography prior to PCI

- In conservative strategy without high bleeding risk, ticagrelor (preferred over clopidogrel) is recommended once the NSTEMI is established

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The need for dual antiplatelet therapy

"mandatory"* **"possibly beneficial*"**

< 12 months

> 12 months

***** ***Premature discontinuation of DAPT would lead to an unacceptably high rate of ST***

***** ***Mitigating the risk of recurrent ischemic events unrelated to previous PCI***

EXCELLENT
RESET
SECURITY
ISAR SAFE
OPTIMIZE

PRODIGY
ITALIC

ARCTIC INTERRUPTION
DES-LATE
REAL/ZEST
DAPT
PEGASUS
TRA 2° P-TIMI 50

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DAPT Duration

Evidence to support the extension of DAPT after DES beyond 1 year in NSTE-ACS patients is limited (Page 20; 5.2.6)

Recommendations	Class[a]	Level[b]	
Oral antiplatelet therapy			
$P2Y_{12}$ inhibitor adm… DES implantation … risk.		A	NEW
Long-term $P2Y_{12}$ in…			
$P2Y_{12}$ 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	NEW

Personalized options for DAPT duration

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Antiplatelet therapy

NEW

Recommendations	Class[a]	Level[b]	Ref.[c]
Oral antiplatelet therapy			
• 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

Prasugrel (60-mg loading dose, 10-mg daily dose) is recommended ~~for $P2Y_{12}$ inhibitor naïve patients~~ (especially diabetics) in whom coronary anatomy is known and who are proceeding to PCI unless there is a high risk of life-threatening bleeding or other contraindications.[d]

2011

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New 2015 ESC guidelines for the management of NSTEMI

I.V. Antiplatelet Therapy

Intravenous antiplatelet therapy	NEW	
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
It is not recommended to administer GPIIb/IIIa inhibitors in patients in whom coronary anatomy is not known.	III	A

- More limited role for GPIIb/IIIa inhibitors
- Cangrelor is a new option for i.v. therapy

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Vorapaxar

Web Addenda

(TRACER; TRA 2P-TIMI 50)

While approved by the FDA and EMA for reducing ischaemic events in patients with a history of MI, the benefit of vorapaxar in addition to aspirin and clopidogrel is modest and must be carefully weighed against the increase in bleeding events, including intracranial haemorrhage. Its use is contraindicated in patients with a history of cerebrovascular disease.

European Heart Journal doi:10.1093/eurheartj/ehv320

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General Recommendations

Recommendations for combining antiplatelet agents and anticoagulants in NSTE-ACS patients requiring chronic oral anticoagulation		
Recommendations	**Class[a]**	**Level[b]**
In patients with a firm indication for OAC (e.g. atrial fibrillation with CHA_2DS_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 hours) should be considered in moderate to high risk patients[c] 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

Anticoagulation during Stenting on OAC

Patients undergoing coronary stenting		
Anticoagulation		
During PCI, use of additional parenteral anticoagulation is recommended, irrespective of the timing of the last dose of all NOACs and if INR<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 Therapy after Stenting on OAC

Antiplatelet treatment		
Following coronary stenting, DAPT including new $P2Y_{12}$ inhibitors should be considered as alternative to triple therapy for patients with NSTE-ACS and atrial fibrillation with a CHA_2DS_2-VASc score = 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 irrespective of stent type 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) 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**
The use of ticagrelor or prasugrel as part of triple therapy is not recommended.	**III**	**C**

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WOEST

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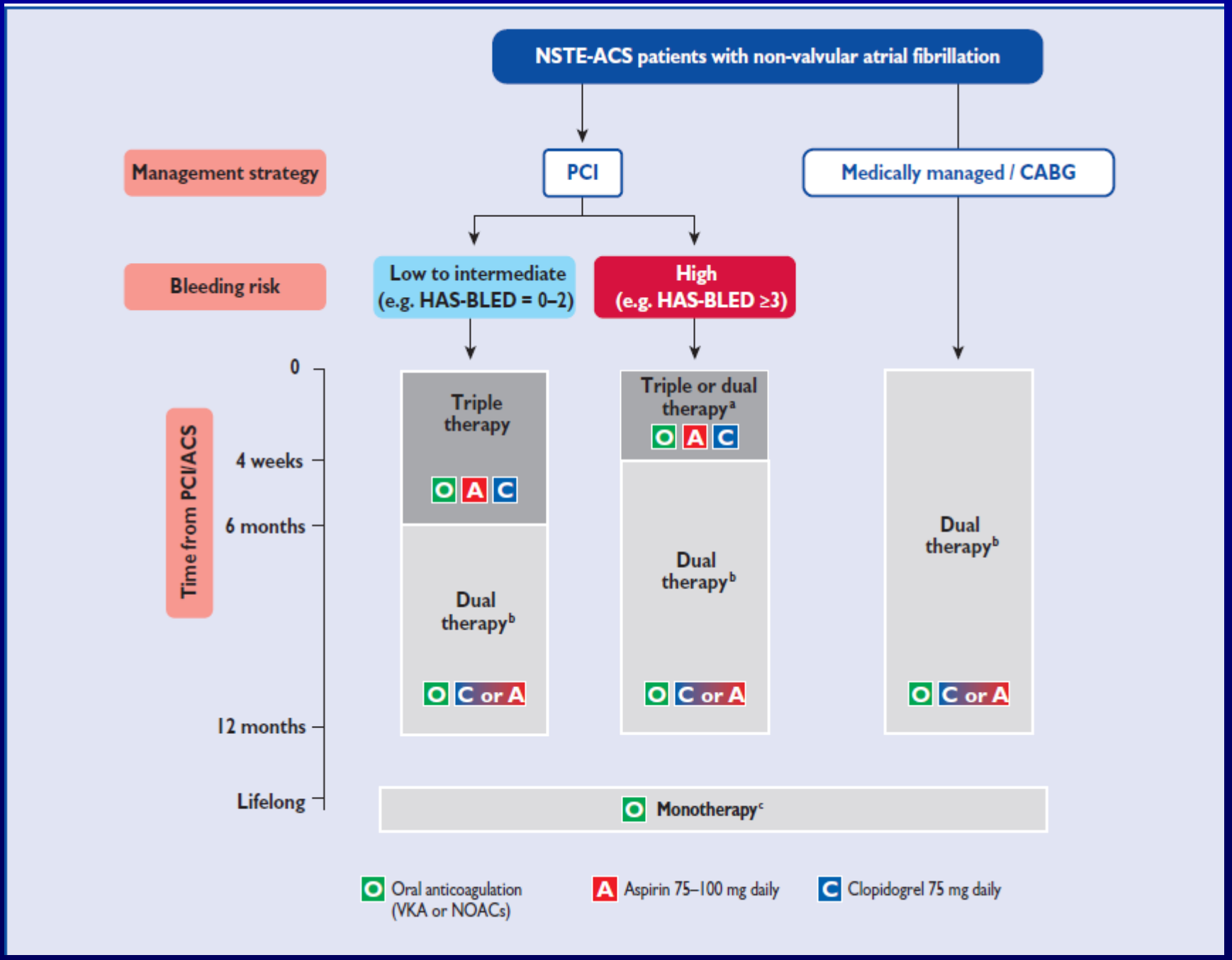

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Elderly

Recommendations	Class[a]	Level[b]	Ref.[c]
It is recommended to tailor antithrombotic treatment according to bodyweight and renal function.	I	C	
Elderly patients should be considered for an invasive strategy and, if appropriate, revascularization after careful evaluation of potential risks and benefits, estimated life expectancy, comorbidities, quality of life, frailty and patient values and preferences.	IIa	A	408, 418
Adjusted dosing regimens of beta-blockers, ACE inhibitors, ARBs and statins should be considered to prevent side effects.	IIa	C	

was B

Italian Elderly ACS

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Diabetes mellitus

Recommendations on antithrombotic treatment (ie, as in non-diabetic) *unchanged*

Recommendations	Class[a]	Level[b]	Ref.[c]
Antithrombotic treatment and invasive strategy			
It is recommended to administer the same antithrombotic treatment in diabetic and non-diabetic patients.	I	C	
An invasive strategy is recommended over non-invasive management.	I	A	352, 441, 442

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Chronic Kidney Disease

Unchanged

Recommendations	Class[a]	Level[b]	Ref.[c]
It is recommended to administer the same first-line antithrombotic treatment as in patients with normal kidney function, with appropriate dose adjustment if indicated.	I	B	453, 454

New (Web Addenda)

The choice and dose of antithrombotic drugs need to be carefully considered in CKD. While most anticoagulants may need dose adjustment in renal insufficiency, this is not the case for oral antiplatelet agents.[449] Safety and efficacy data for the use of $P2Y_{12}$ inhibitors in stage 5 CKD patients (i.e. eGFR <15 mL/min/1.73m^2) are insufficient. Therefore in this setting, $P2Y_{12}$ inhibitors should be reserved for selected high-risk indications (i.e. coronary stent thrombosis prevention), with bleeding risk carefully weighed. In this context there is more safety experience with clopidogrel than ticagrelor or prasugrel.

2011

Clopidogrel	No information in patients with renal dysfunction.
Prasugrel	No dose adjustment necessary, including in patients with end-stage disease.
Ticagrelor	No dose reduction required; no information in dialysis patients.

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Recommendations for perioperative management of antiplatelet therapy in NSTEMI patients requiring CABG

Recommendations	Class	Level	Ref.
Irrespective of the revascularization strategy, a P2Y12 inhibitor is recommended in addition to aspirin and maintained over 12 months unless there are contraindications such as excessive risk of bleeding events.	I	A	CURE TRITON PLATO NEW
It is recommended that the Heart Team should estimate the individual bleeding and ischaemic risks and guide the timing of CABG as well as management of DAPT.	I	C	NEW
It is recommended to perform CABG without delay in patients with haemodynamic instability, ongoing myocardial ischaemia or very-high-risk coronary anatomy, regardless of antiplatelet treatment.	I	C	NEW
Aspirin is recommended 6–24 h post-CABG in the absence of ongoing bleeding events.	I	A	Lim et al. Gavaghan et al.

Recommendations for perioperative management of antiplatelet therapy in NSTEMI patients requiring CABG

Recommendations	Class	Level	Ref.
It is recommended to continue low-dose aspirin until CABG.	I	B	Biondi-Zoccai et al. Sun et al. Deja et al.
In stabilised patients requiring CABG who are on DAPT, discontinuation of ticagrelor and clopidogrel 5 days before and prasugrel 7 days prior to surgery should be considered.	IIa	B	PLATO Biancari et al. Nijjer et al.
After CABG, resuming P2Y12 inhibitor therapy should be considered as soon as deemed safe.	IIa	C	
Platelet function testing may be considered in shortening the time window to CABG following P2Y12 inhibitor discontinuation.	IIb	B	TARGET-CABG 

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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]
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

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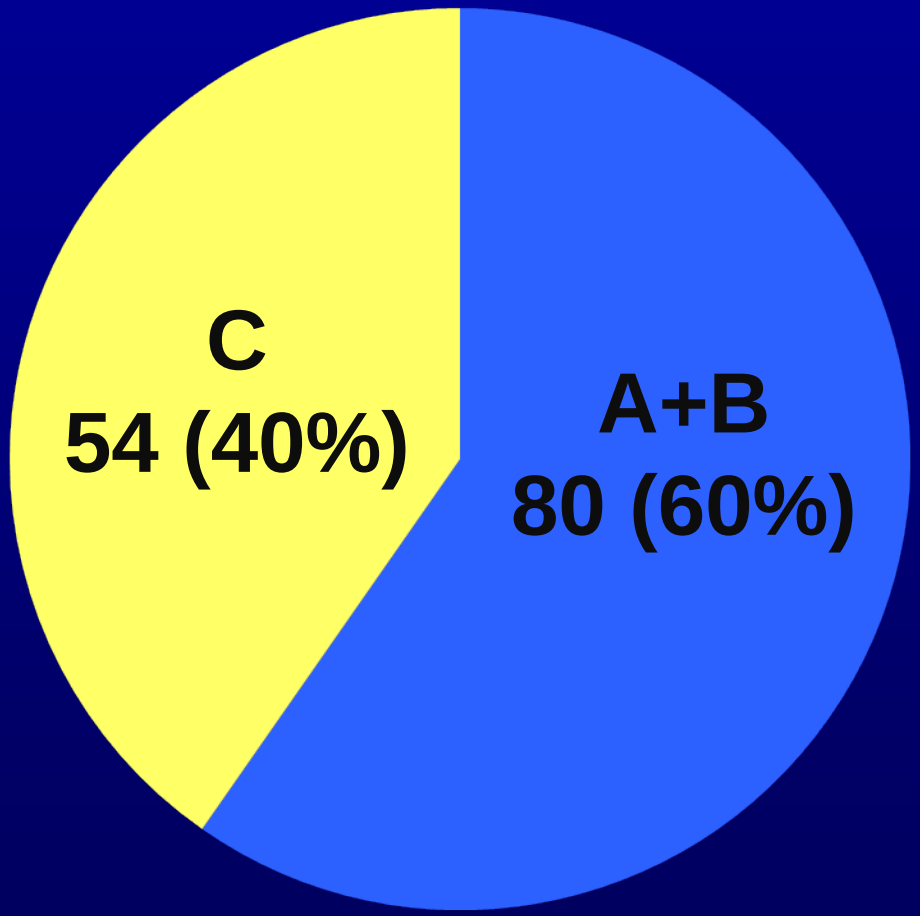
Level of Reco



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NSTEMI ACS- Gaps in evidence

- The role of genetic testing to individualize treatment
- The clinical advantage of hs-cTn assays over sensitive assays
- The performance of the 1 h algorithm has not been tested within an RCT
- The role of beta-blockers in patients with normal or mildly depressed LV function
- The development of a single risk score that assesses ischaemic/bleeding risks
- The optimal timing of ticagrelor in pts intended for an invasive strategy

NSTEMI ACS- Gaps in evidence

- Optimal duration of DAPT
- The development of antidotes in pts with ongoing major bleeding events while on P2Y12 inhibitors or NOACs
- The safety, effectiveness and optimal duration of combined OAC and antiplatelet therapy
- The role of CABG vs PCI
- The role of a profound LDL cholesterol–lowering (e.g. PCSK-9 inhibition)
- The burden of late CV events calls for reappraisal of the pathophysiology of these adverse outcomes and innovative preventive strategies