2015 ESC Guidelines for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-segment Elevation*

The Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-segment Elevation of the European Society of Cardiology (ESC)

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European Heart Journal 2015
doi: 10.1093/eurheartj/ehv320

Clinical implications of high-sensivity troponin assays

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 1 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 1 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).

MI = myocardial infarction.

European Heart Journal 2015
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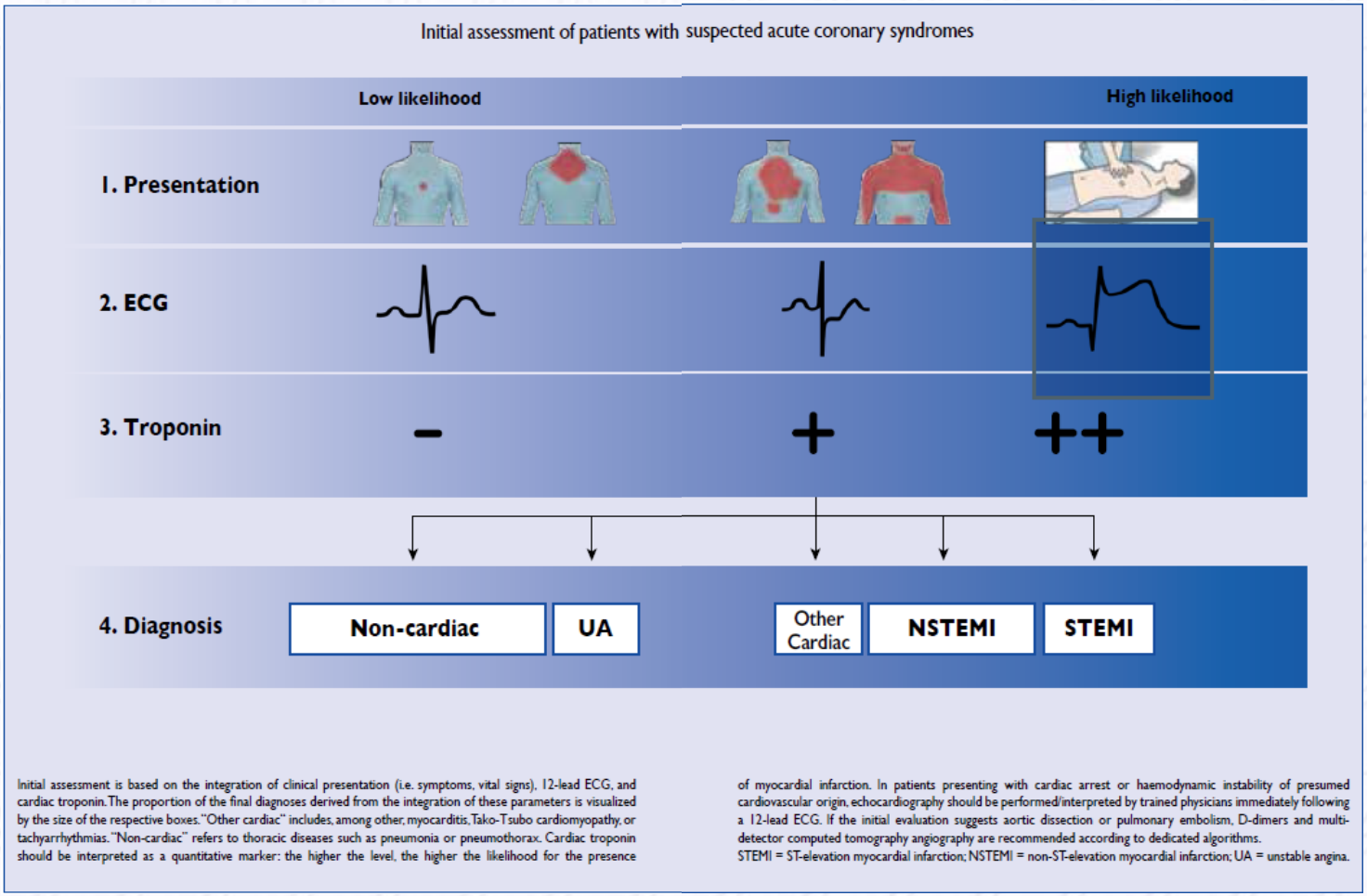
Conditions other than Type I acute myocardial infarction associated with cardiac troponin elevation
Tachyarrhythmias
Heart failure
Hypertensive emergencies
Critical illness (e.g. shock/ sepsis/ burns)
Myocarditis[a]
Tako-Tsubo cardiomyopathy
Structural heart disease (e.g. aortic stenosis)
Aortic dissection
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

CABG = coronary artery bypass surgery; PCI = percutaneous coronary intervention.
[a]Includes myocardial extension of endocarditis or pericarditis.
Bold and italic: the most frequent conditions.

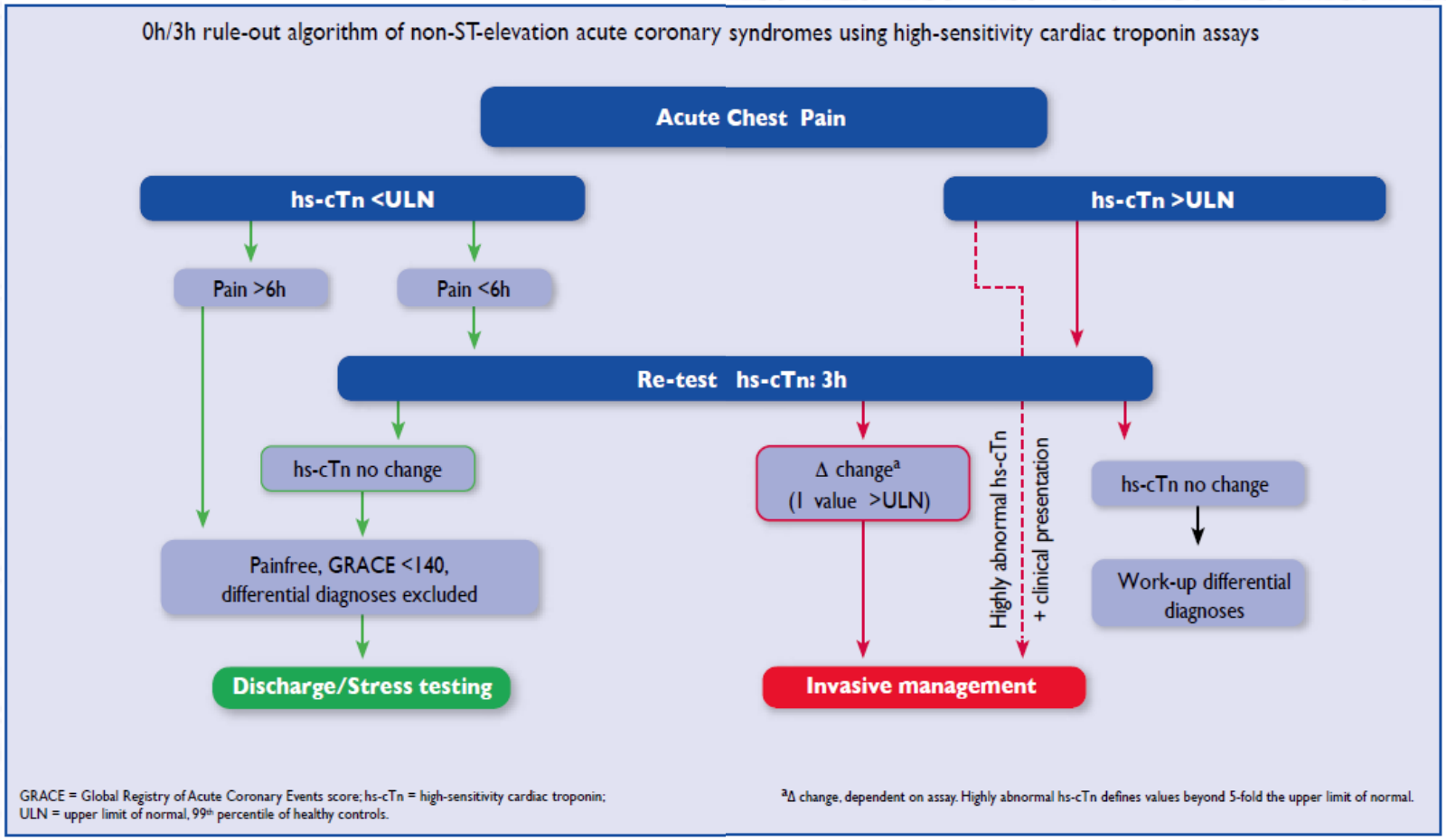
Conditions other than Type I acute myocardial infraction associated with cardiac troponin elevation

Initial assessment of patients with suspected acute coronary syndromes



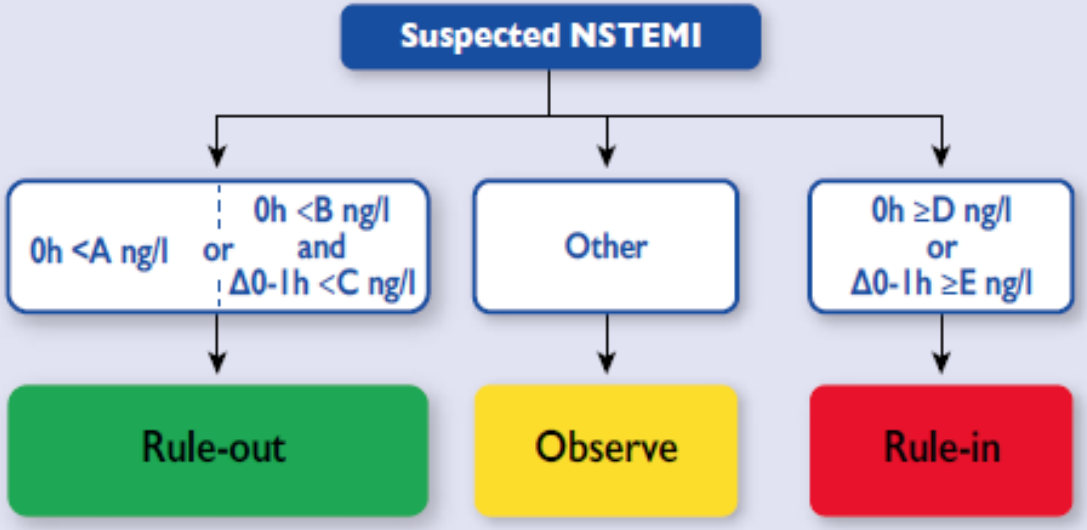
Initial assessment is based on the integration of clinical presentation (i.e. symptoms, vital signs), 12-lead ECG, and cardiac troponin. The proportion of the final diagnoses derived from the integration of these parameters is visualized by the size of the respective boxes. "Other cardiac" includes, among other, myocarditis, Tako-Tsubo cardiomyopathy, or tachyarrhythmias. "Non-cardiac" refers to thoracic diseases such as pneumonia or pneumothorax. Cardiac troponin should be interpreted as a quantitative marker: the higher the level, the higher the likelihood for the presence of myocardial infarction. In patients presenting with cardiac arrest or haemodynamic instability of presumed cardiovascular origin, echocardiography should be performed/interpreted by trained physicians immediately following a 12-lead ECG. If the initial evaluation suggests aortic dissection or pulmonary embolism, D-dimers and multi-detector computed tomography angiography are recommended according to dedicated algorithms.
STEMI = ST-elevation myocardial infarction; NSTEMI = non-ST-elevation myocardial infarction; UA = unstable angina.

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



0h/1h rule-in and rule-out algorithms using high-sensitivity cardiac troponin assays

0h/1h rule-in and rule-out algorithms using high-sensitivity cardiac troponins assays.



	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

0h/1h rule-in and rule-out algorithms using high-sensitivity cardiac troponins (hs-cTn) in patients presenting with suspected non-ST-elevation myocardial infarction (NSTEMI) to the emergency department. 0h and 1h refer to the time from first blood test. NSTEMI can be ruled-out already at presentation, if the hs-cTn concentration is very low. NSTEMI can also be ruled-out by the combination of low baseline levels and the lack of a relevant increase within 1h. Patients have a high likelihood for NSTEMI if the hs-cTn concentration at presentation is at least moderately elevated or hs-cTn concentrations show a clear rise within the first hour. Cut-off levels are assay-specific. Cut-off levels for other hs-cTn assays are in development.

Recommendations for diagnosis, risk stratification, imaging, and rhythm monitoring in patients with suspected NSTE-ACS		
Recommendations	**Class[a]**	**Level[b]**
Diagnosis and risk stratification		
It is recommended to base diagnosis and initial short-term ischaemic and bleeding risk stratification on a combination of clinical history, symptoms, vital signs, other physical findings, ECG and laboratory results.	I	A
It is recommended to obtain a 12-lead ECG within 10 min after first medical contact and to have it immediately interpreted by an experienced physician. It is recommended to obtain an additional 12-lead ECG in case of recurrent symptoms or diagnostic uncertainty.	I	B
Additional ECG leads (V_{3R}, V_{4R}, V_7–V_9) are recommended if ongoing ischaemia is suspected when standard leads are inconclusive.	I	C
It is recommended to measure cardiac troponins with sensitive or high-sensitivity assays and obtain the results within 60 minutes.	I	A
A rapid rule-out protocol at 0h and 3h is recommended if high-sensitivity cardiac troponin tests are available.	I	B
A rapid rule-out and rule-in protocol at 0h and 1h is recommended if a high-sensitivity cardiac troponin test with a validated 0h/1h algorithm is available. Additional testing after 3–6h is indicated if the first two troponin measurements are not conclusive and the clinical condition is still suggestive of ACS.	I	B
It is recommended to use established risk scores for prognosis estimation.	I	B
The use of the CRUSADE score may be considered in patients undergoing coronary angiography to quantify bleeding risk.	IIb	B
Imaging		
In patients with no recurrence of chest pain, normal ECG findings, and normal levels of cardiac troponin (preferably high-sensitivity), but suspected ACS, a non-invasive stress test (preferably with imaging) for inducible ischaemia is recommended before deciding on an invasive strategy.	I	A
Echocardiography is recommended to evaluate regional and global LV function and to rule in or rule out differential diagnoses.[c]	I	C
MDCT coronary angiography should be considered as an alternative to invasive angiography to exclude ACS when there is a low to intermediate likelihood of CAD and when cardiac troponin and/or ECG are inconclusive.	IIa	A

Recommendations for diagnosis, risk stratification, imaging, and rhythm monitoring in patients with suspected NSTE-ACS

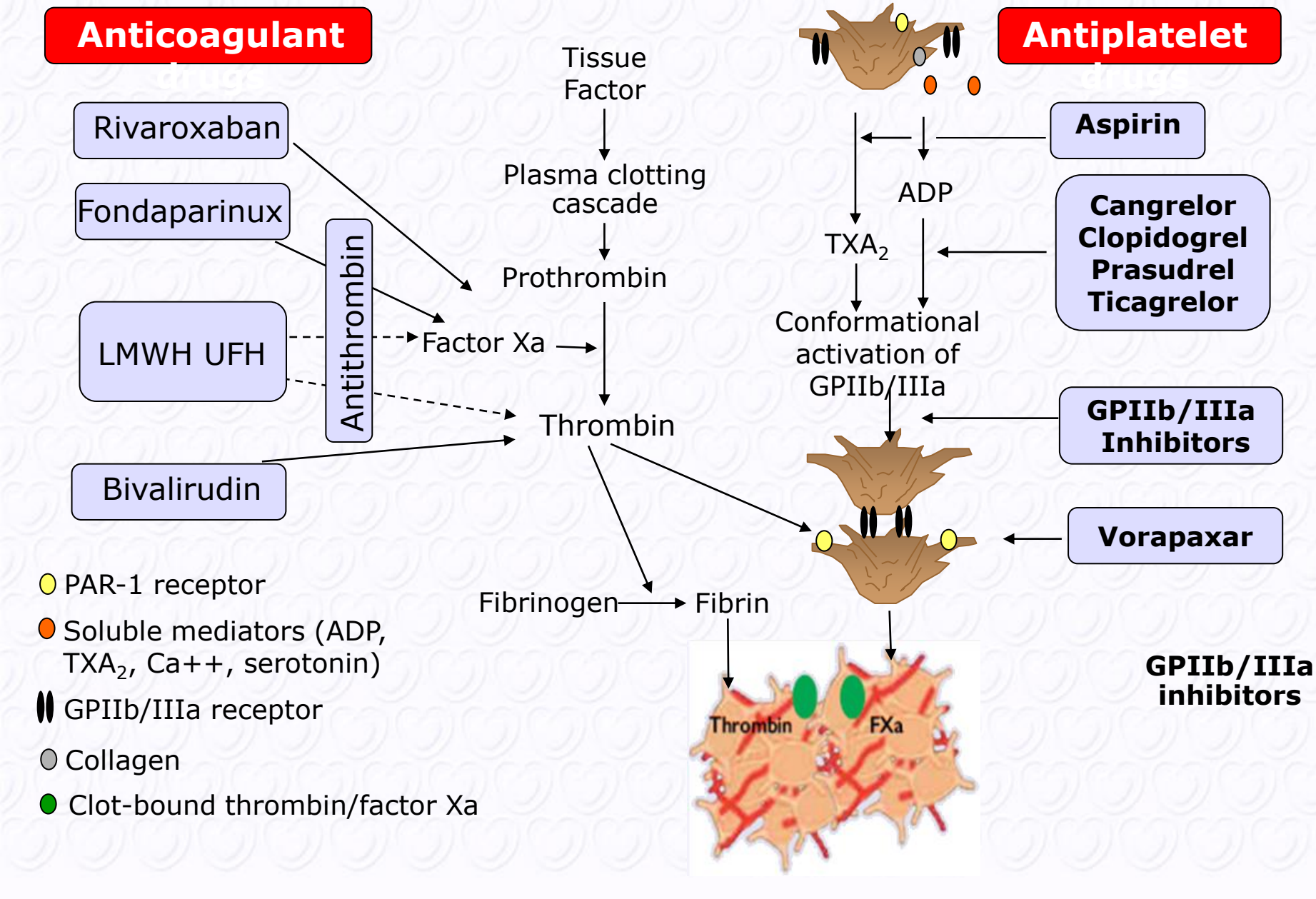
Recommendations for anti-ischaemic drugs in the acute phase of NSTE-ACS

Recommendations for anti-ischaemic drugs in the acute phase of NSTE-ACS		
Recommendations	**Class[a]**	**Level[b]**
Early initiation of beta-blocker treatment is recommended in patients with ongoing ischaemic symptoms and without contraindications.	I	B
It is recommended to continue chronic beta-blocker therapy, unless the patient is in Killip Class III or higher.	I	B
Sublingual or i.v. nitrates are recommended to relieve angina[c]; 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

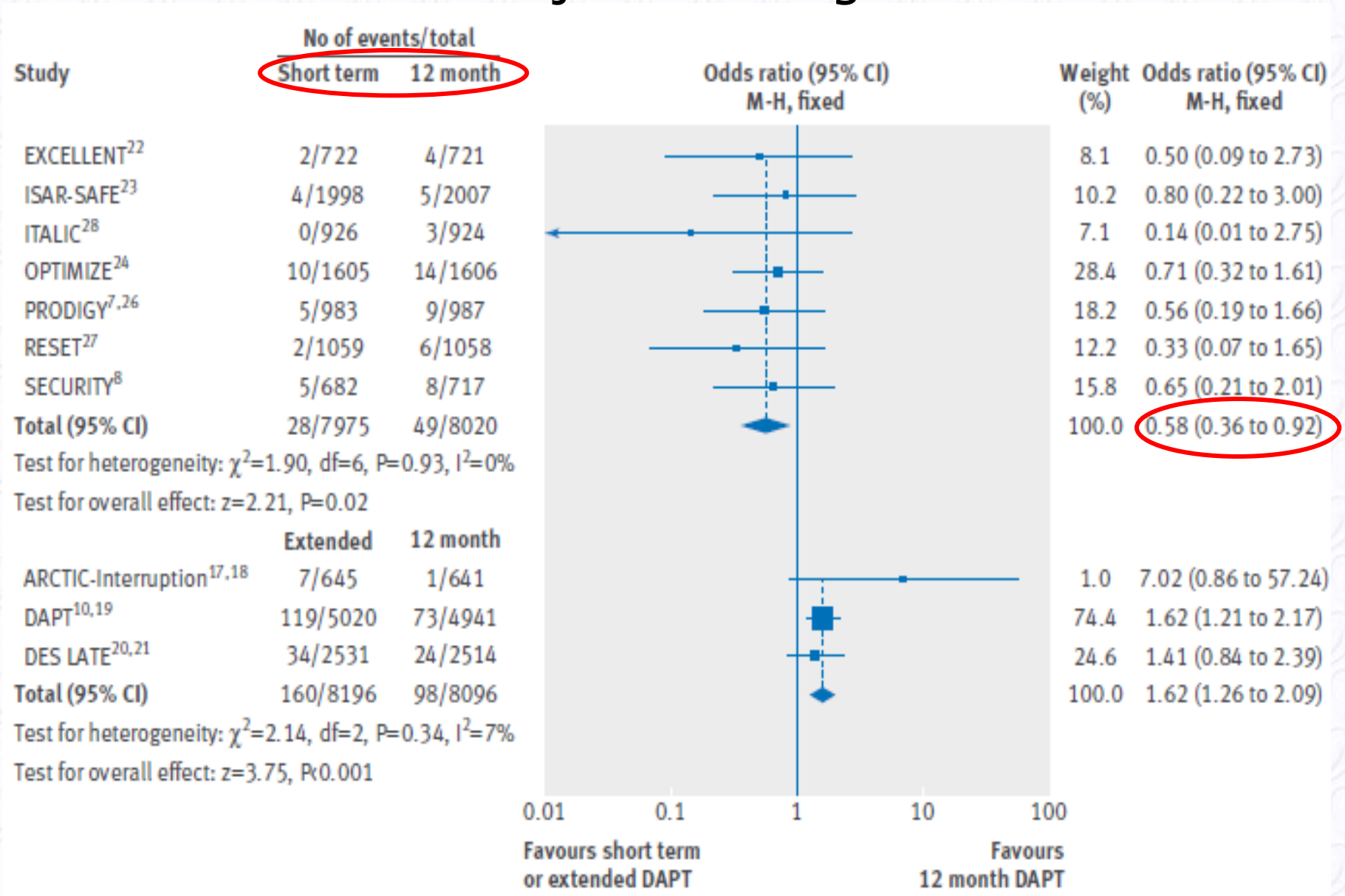
i.v.=intravenous. - [a]Class of recommendation. [b]Level of evidence. [c]Should not be administered in patients with recent intake of sildenafil or vardenafil (<24 h) or of tadalafil (<48 h).

Recommendations for platelet inhibition in NSTE-ACS		
Recommendations	**Class[a]**	**Level[b]**
Oral antiplatelet therapy		
Aspirin is recommended for all patients without contra-indications at an initial oral loading dose[c] of 150–300 mg (in aspirin-naïve patients) and a maintenance dose of 75–100 mg daily long-term regardless of treatment strategy.	I	A
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
• Ticagrelor (180 mg loading dose, 90 mg twice daily) is recommended, in the absence of contraindications[d], 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
• Prasugrel (60 mg loading dose, 10 mg daily dose) is recommended in patients who are proceeding to PCI if no contraindication.[d]	I	B
• 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
$P2Y_{12}$ 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
It is not recommended to administer prasugrel in patients in whom coronary anatomy is not known.	III	B
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-naïve 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

Targets for antithrombotic drugs



Major Bleeding

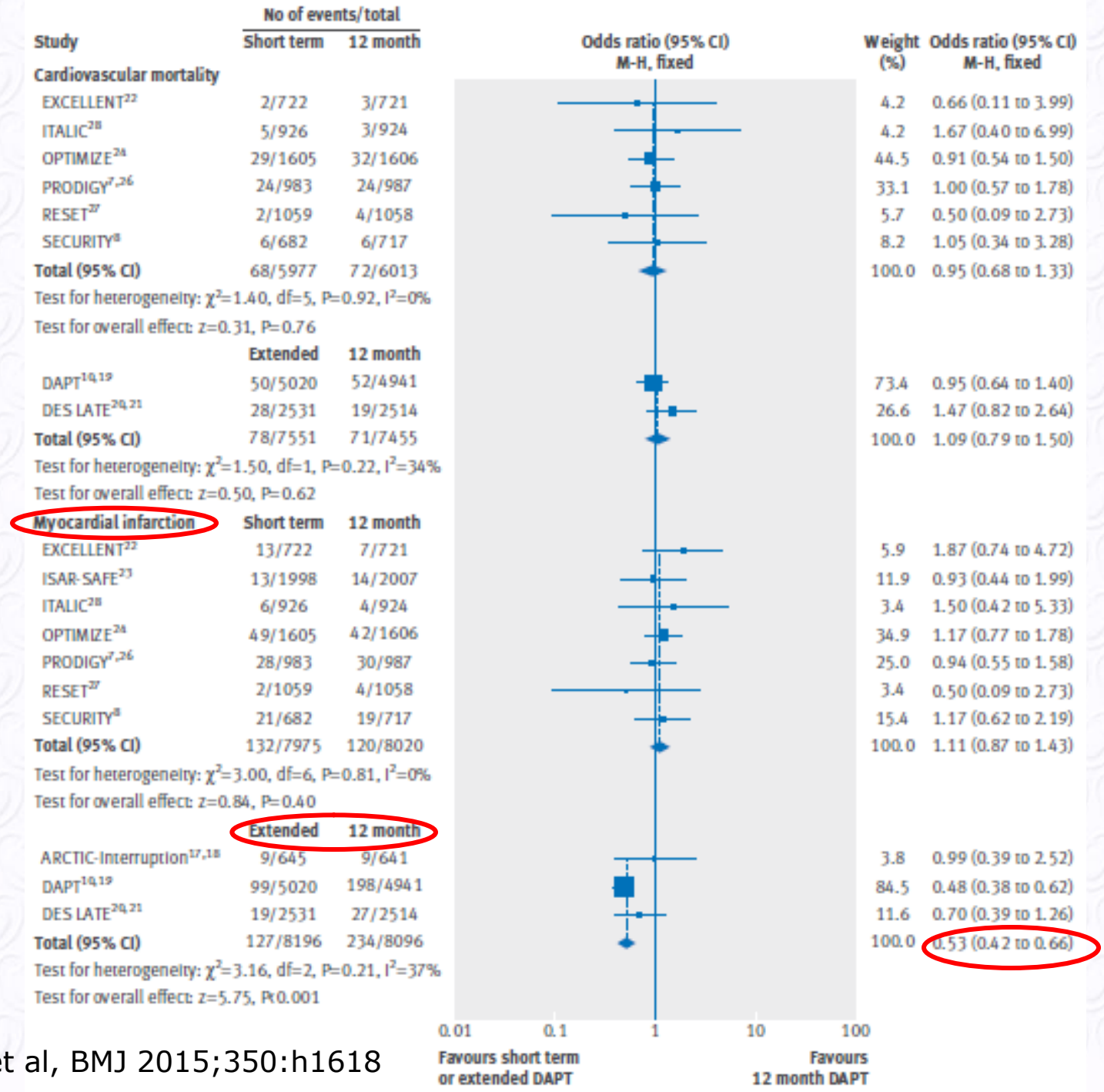


Navarese et al, BMJ 2015;350:h1618

Timing of $P2Y_{12}$ Inhibitor Initiation

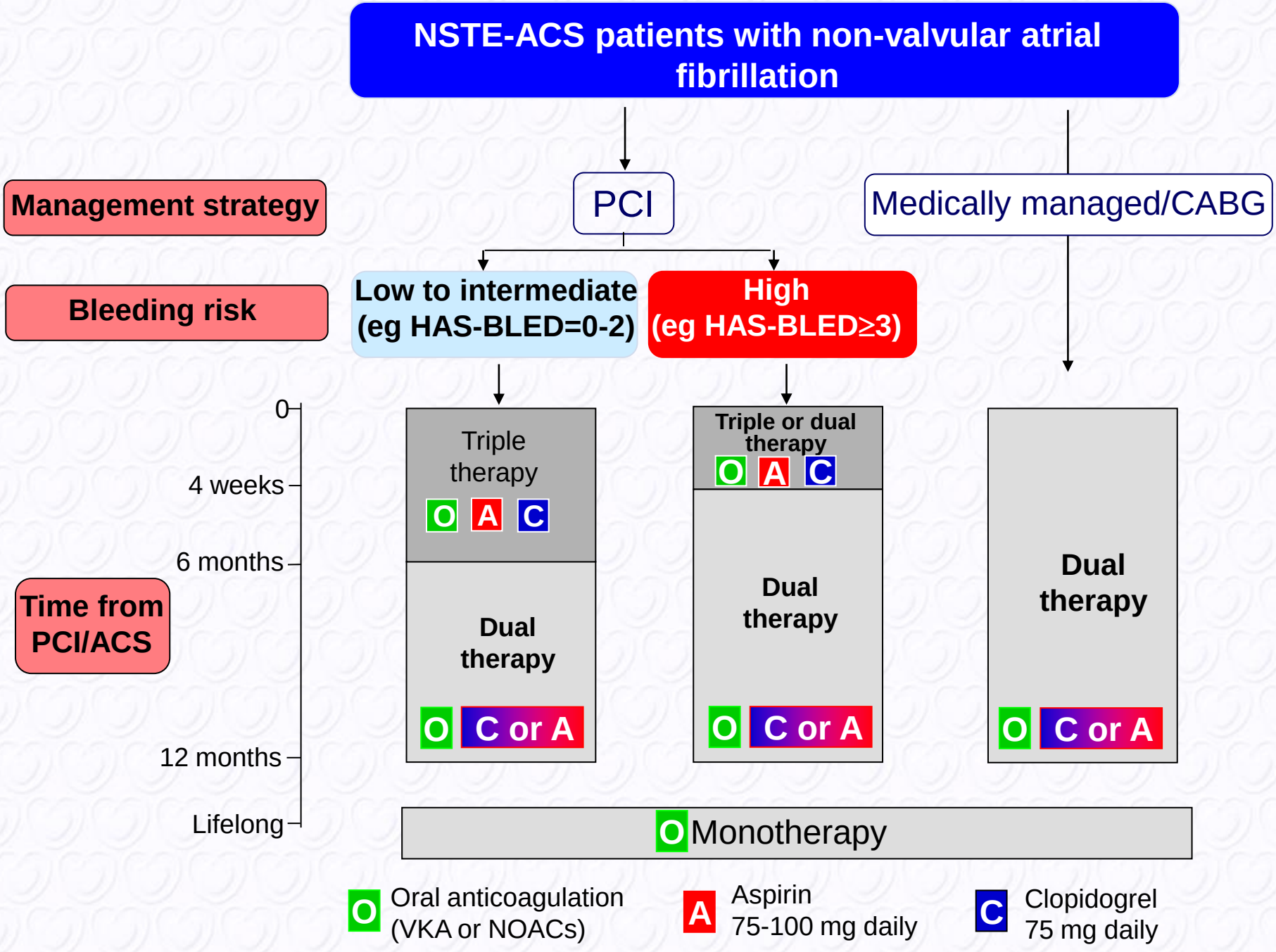
- As the optimal timing of ticagrelor or clopidogrel administration in NSTE-ACS patients scheduled for an invasive strategy has not been adequately investigated, no recommendation for or against pretreatment with these agents can be formulated. Based on the ACCOAST results, pretreatment with prasugrel is not recommended.

Recommendations for platelet inhibition in NSTE-ACS (continued)		
Recommendations	**Class[a]**	**Level[b]**
Long-term $P2Y_{12}$ 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**
General recommendations		
A proton pump inhibitor in combination with DAPT is recommended in patients at higher than average risk of gastrointestinal bleeds (i.e. with a history of gastrointestinal ulcer/haemorrhage, anticoagulant therapy, chronic NSAID/corticosteroid use or two or more among age ≥65 years, dyspepsia, gastro-oesophageal reflux disease, *Helicobacter pylori* infection, and chronic alcohol use).	**I**	**B**
In patients on $P2Y_{12}$ inhibitors who need to undergo non-emergency major non-cardiac surgery[e], 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 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**

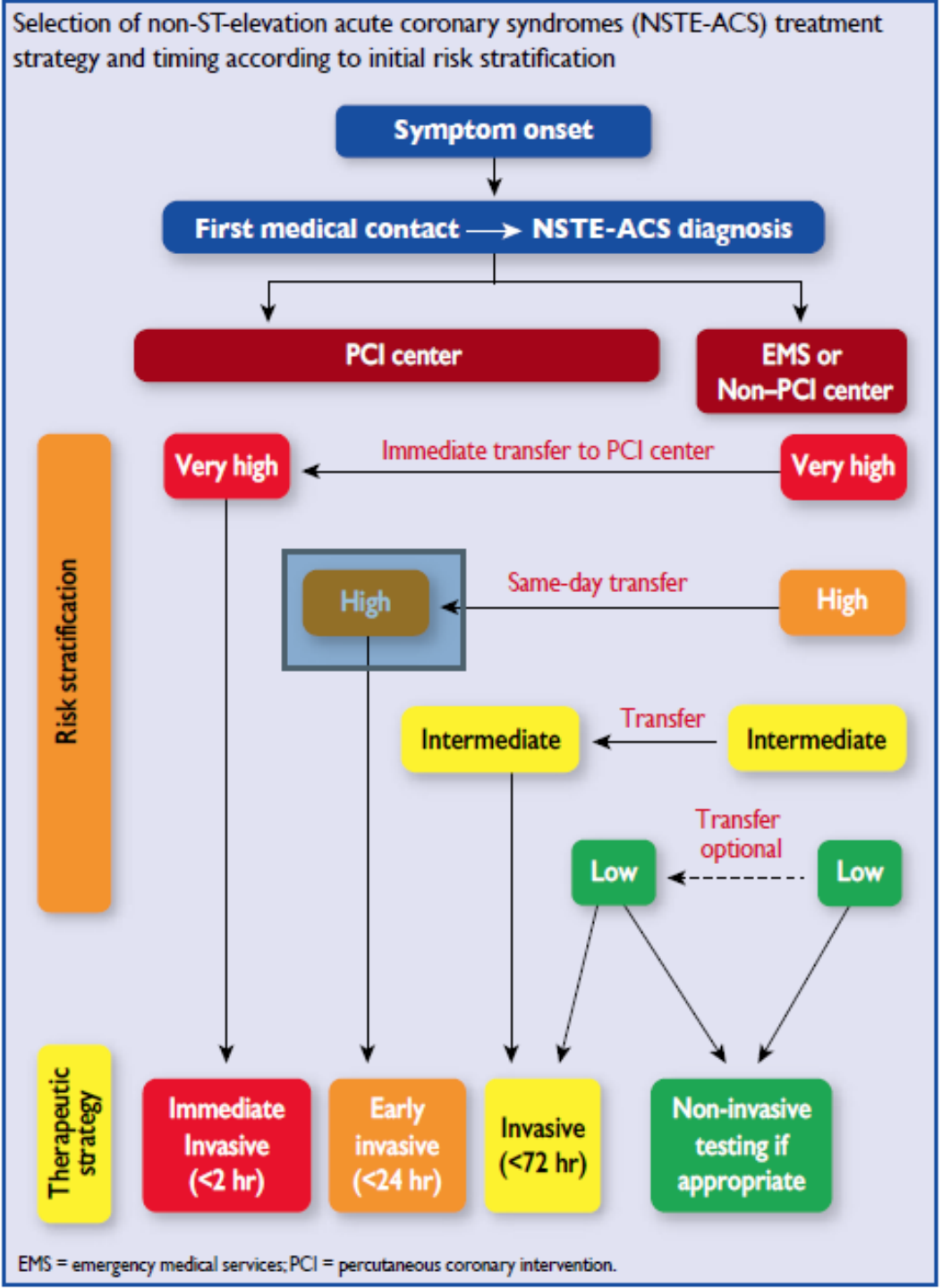


Navarese et al, BMJ 2015;350:h1618

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**
Fondaparinux (2.5 mg s.c. daily) is recommended as having the most favourable efficacy–safety profile regardless of the management strategy.	**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**
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 the procedure.	**I**	**B**
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**


NSTE-ACS patients with non-valvular atrial fibrillation
Management strategy
PCI
Medically managed/CABG
Bleeding risk
Low to intermediate (eg HAS-BLED=0-2)
High (eg HAS-BLED≥3)
Time from PCI/ACS
0
4 weeks
6 months
12 months
Lifelong
Triple therapy
O A C
Dual therapy
O C or A
Triple or dual therapy
O A C
Dual therapy
O C or A
Dual therapy
O C or A
O Monotherapy
O Oral anticoagulation (VKA or NOACs)
A Aspirin 75-100 mg daily
C Clopidogrel 75 mg daily

Recommendations for long-term management post NSTE-ACS		
Recommendations (for the recommendations on antithrombotic treatment see sections 5.2.9 and 5.3.3).[d]	**Class[a]**	**Level[b]**
It is recommended to advise all patients on life style changes (including smoking cessation, regular physical activity and a healthy diet).	I	A
It is recommended to start high-intensity statin therapy as early as possible, unless contraindicated, and maintain it long-term.	I	A
An ACE inhibitor is recommended in patients with LVEF ≤40%, or heart failure, hypertension or diabetes, unless contraindicated. An ARB provides an alternative, particularly if ACE inhibitors are not tolerated.	I	A
Beta-blocker therapy is recommended in patients with LVEF ≤40%, unless contra-indicated.	I	A



Selection of non-ST-elevation acute coronary syndromes (NSTE-ACS) treatment strategy and timing according to initial risk stratification

Recommendations for invasive coronary angiography and revascularization in NSTE-ACS		
Recommendations	**Class[a]**	**Level[b]**
An **immediate invasive strategy (<2h)** is recommended in patients with at least one of the following 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 (<24h)** is recommended in patients with at least one of the following high-risk criteria: • rise or fall in cardiac troponin compatible with MI • dynamic ST- or T-wave changes (symptomatic or silent) • GRACE score >140.	I	A
An **invasive strategy (<72h)** is recommended in patients with: • at least one of the following intermediate-risk criteria: o diabetes mellitus o renal insufficiency (eGFR <60 mL/min/1.73 m²) o LVEF <40% or congestive heart failure o early post-infarction angina o recent PCI o prior CABG o GRACE risk score >109 and <140 or • recurrent symptoms or ischaemia on non-invasive testing.	I	A
In patients with none of the mentioned risk criteria and no recurrent symptoms, non-invasive testing for ischaemia (preferably with imaging) is recommended before deciding on invasive evaluation.	I	A
In centres experienced with radial access, a radial approach is recommended for coronary angiography and PCI.	I	A
In patients undergoing PCI, new-generation DESs are recommended.	I	A

Recommendations for invasive coronary angiography and revascularization in NSTE-ACS

Recommendations for diabetic patients presenting with NSTE-ACS		
Recommendations	**Class[a]**	**Level[b]**
Blood glucose control		
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
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	C
Less stringent glucose control should be considered both in the acute phase and at follow-up in patients with more advanced cardiovascular disease, older age, longer diabetes duration, and more comorbidities.	IIa	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
It is recommended to monitor renal function for 2–3 days after coronary angiography or PCI in patients with baseline renal impairment or on metformin.	I	C
In patients undergoing PCI, new-generation DESs are recommended over BMSs.	I	A
In patients with stabilized multivessel CAD and an acceptable surgical risk, CABG is recommended over PCI.	I	A
In patients with stabilized multivessel CAD and a SYNTAX score ≤22, PCI should be considered as alternative to CABG.	IIa	B

ACS = acute coronary syndromes; BMS = bare-metal stent; CABG = coronary artery bypass grafting; CAD = coronary artery disease; DES = drug-eluting stent; NSTE-ACS, non-ST-elevation acute coronary syndromes; PCI = percutaneous coronary intervention; SYNTAX = SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery.

[a]Class of recommendation.

[b]Level of evidence.

Recommendations for diabetic patients presenting with NSTE-ACS

Options for Revascularisation

Acute coronary syndromes:

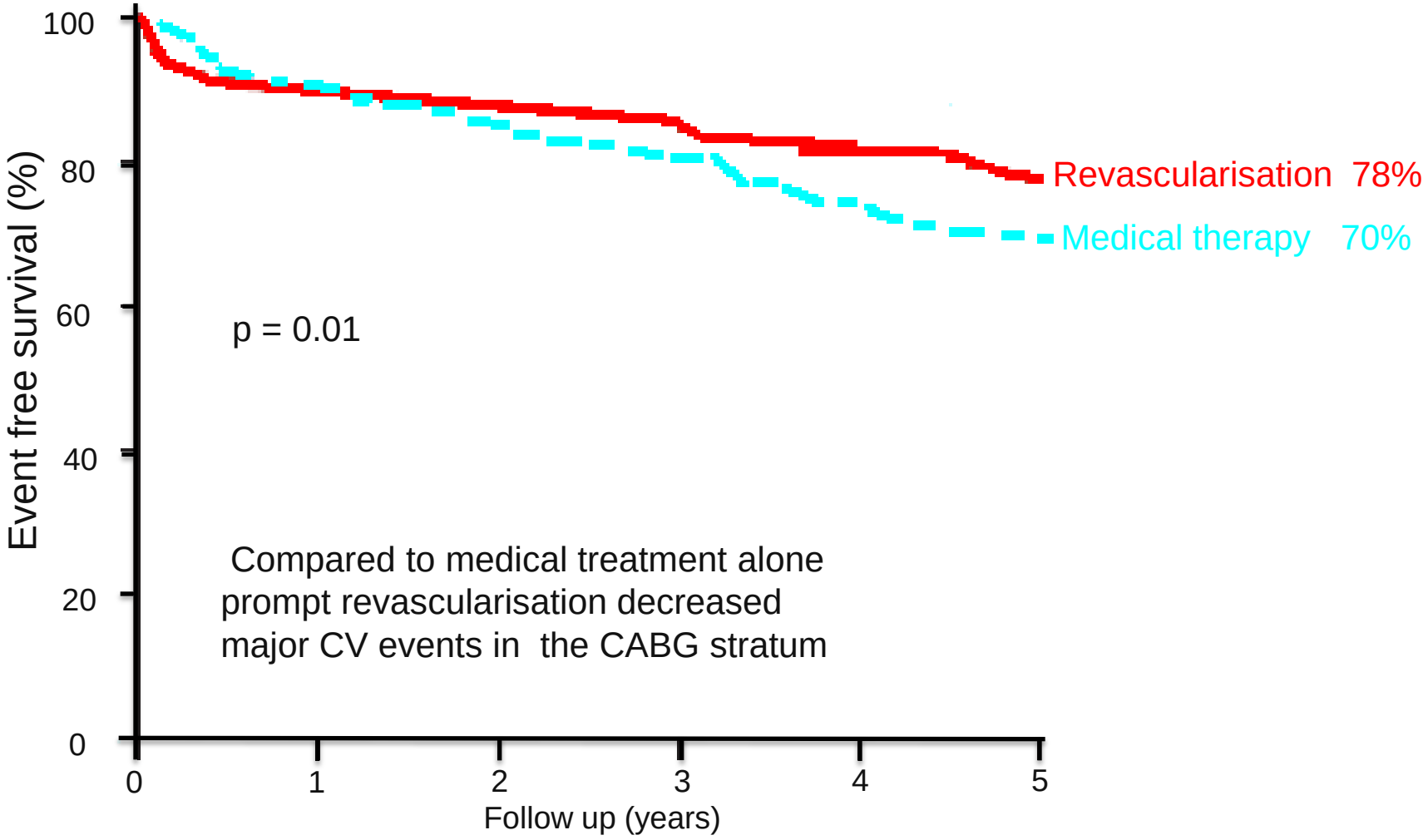
- Early revascularization (as in non DM).

Stable coronary artery disease :

- CABG preferred option if myocardial area at risk is large.
- PCI with DES may be performed for symptom control in single and two-vessel disease.

Myocardial revascularisation vs. medical therapy in people with diabetes

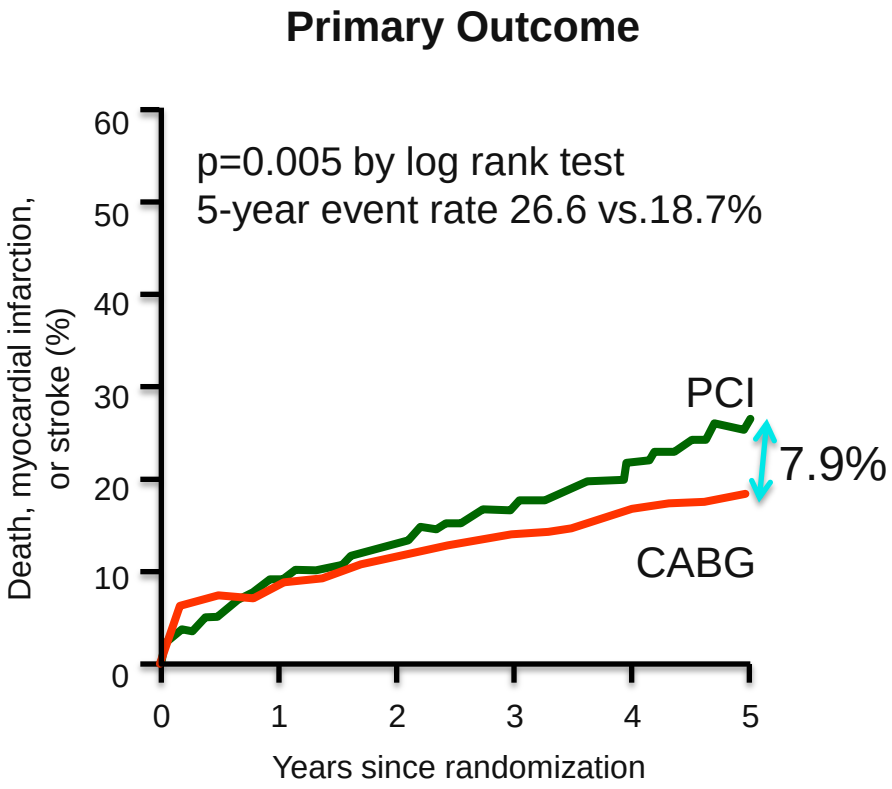
Event free survival in the BARI 2 D study – CABG stratum

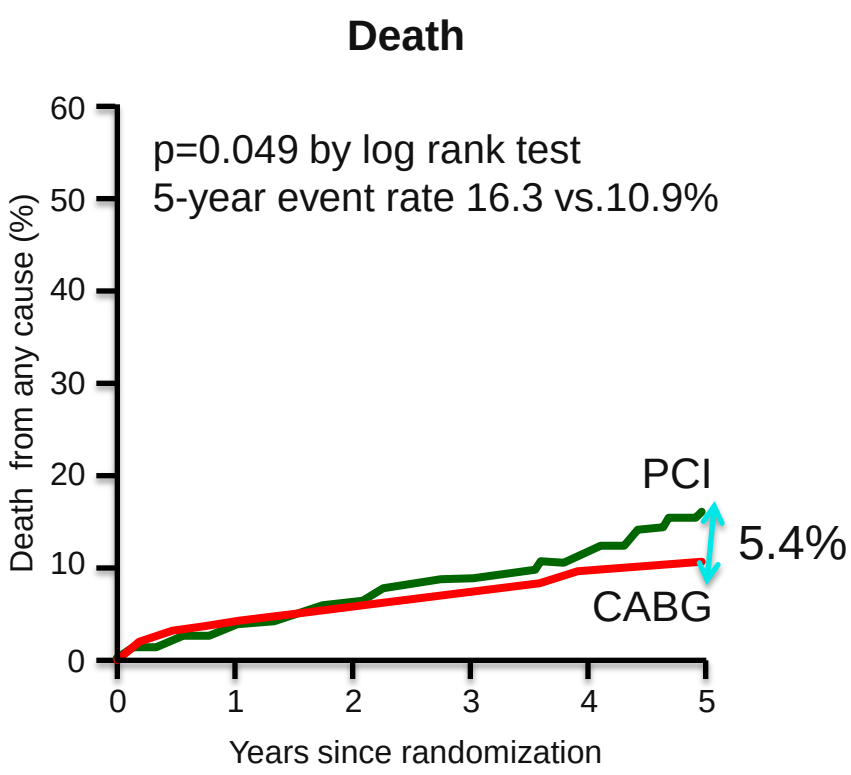


BARI 2D Study group New Engl J Med 2009; 360: 2503

CABG vs. PCI in people with diabetes

The FREEDOM trial



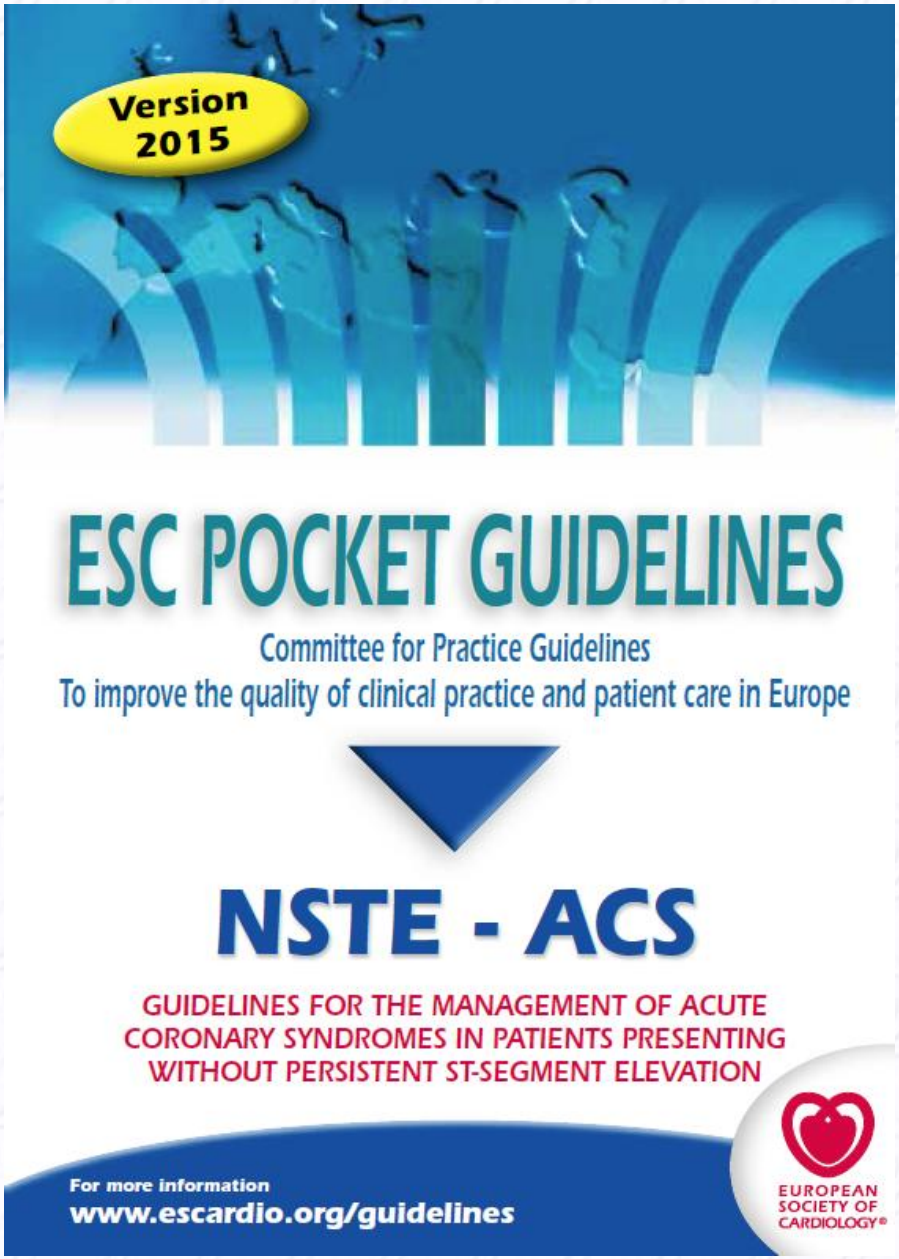


Farkouh et al New Engl J Med 2012; 367: 2375

Revascularisation in people with diabetes

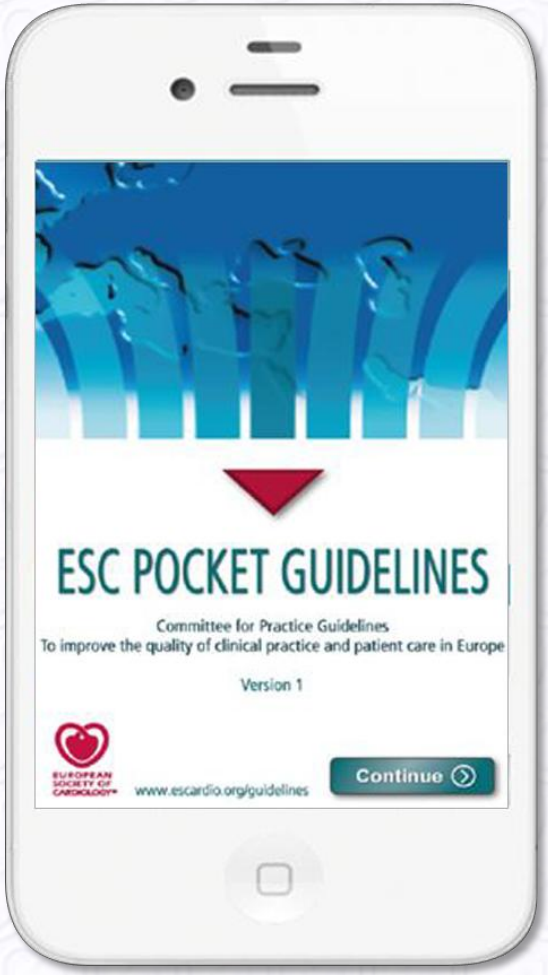
Recommendations	Class	Level
Optimal medical treatment should be considered as preferred treatment in patients with stable CAD and DM unless there are large areas of ischaemia or significant left main or proximal LAD lesion.	IIa	B
CABG is recommended in patients with DM and multivessel or complex (SYNTAX Score >22) CAD to improve survival free from major cardiovascular events.	I	A
PCI for symptom control may be considered as an alternative to CABG in patients with DM and less complex multivessel CAD (SYNTAX score ≤22) in need of revascularization.	IIb	B
Primary PCI is recommended over fibrinolysis in DM patients presenting with STEMI if performed within recommended time limits.	I	B
In DM patients subjected to PCI, DES rather than BMS are recommended to reduce risk of target vessel revascularization.	I	A
Renal function should be carefully monitored after coronary angiography/PCI in all patients on metformin.	I	C
If renal function deteriorates in patients on metformin undergoing coronary angiography/PCI it is recommended to withhold treatment for 48 h or until renal function has returned to its initial level.	I	C

Recommendations for long-term management post NSTE-ACS (continued)		
Recommendations (for the recommendations on antithrombotic treatment see sections 5.2.9 and 5.3.3).[d]	**Class[a]**	**Level[b]**
Mineralocorticoid receptor antagonists, preferably eplerenone, are recommended in patients with LVEF ≤35% and either heart failure or diabetes after NSTE-ACS but no significant renal dysfunction or hyperkalaemia.[c]	**I**	**A**
A diastolic blood pressure goal of <90 mmHg is recommended (<85 mmHg in diabetic patients).	**I**	**A**
Participation in a well-structured cardiac rehabilitation program to modify lifestyle habits and increase adherence to treatment should be considered.	**IIa**	**A**
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**
A systolic blood pressure goal of <140 mmHg should be considered.	**IIa**	**B**



European Heart Journal 2015
doi: 10.1093/eurheartj/ehv320

ESC Pocket Guidelines application available!



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European Heart Journal (2015) doi:10.1093/eurheartj/ehv319