2014 AHA/ACC Guideline for the Management of Patients With Non–ST-Elevation Acute Coronary Syndromes

Developed in Collaboration with the Society of Thoracic Surgeons and Society for Cardiovascular Angiography and Interventions

Endorsed by the American Association for Clinical Chemistry

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Citation

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The full-text guidelines are also available on the following Web sites: ACC (www.cardiosource.org) and AHA (my.americanheart.org)

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Applying Classification of Recommendations and Levels of Evidence

SIZE OF TREATMENT EFFECT

ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT

	CLASS I *Benefit >>> Risk* Procedure/Treatment **SHOULD** be performed/ administered	CLASS IIa *Benefit >> Risk* *Additional studies with focused objectives needed* **IT IS REASONABLE** to perform procedure/administer treatment	CLASS IIb *Benefit ≥ Risk* *Additional studies with broad objectives needed; additional registry data would be helpful* Procedure/Treatment **MAY BE CONSIDERED**	CLASS III *No Benefit* or CLASS III *Harm* Procedure/Test / Treatment COR III: No benefit — Not Helpful / No Proven Benefit COR III: Harm — Excess Cost w/o Benefit or Harmful / Harmful to Patients
LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	■ Recommendation that procedure or treatment is useful/effective ■ Sufficient evidence from multiple randomized trials or meta-analyses	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Sufficient evidence from multiple randomized trials or meta-analyses
LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is useful/effective ■ Evidence from single randomized trial or nonrandomized studies	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Evidence from single randomized trial or nonrandomized studies
LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	■ Recommendation that procedure or treatment is useful/effective ■ Only expert opinion, case studies, or standard of care	■ Recommendation in favor of treatment or procedure being useful/effective ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation's usefulness/efficacy less well established ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Only expert opinion, case studies, or standard of care
Suggested phrases for writing recommendations	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown/unclear/uncertain or not well established	COR III: No Benefit — is not recommended; is not indicated; should not be performed/ administered/ other; is not useful/ beneficial/ effective COR III: Harm — potentially harmful; causes harm; associated with excess morbidity/mortality; should not be performed/ administered/ other
Comparative effectiveness phrases†	treatment/strategy A is recommended/indicated in preference to treatment B treatment A should be chosen over treatment B	treatment/strategy A is probably recommended/indicated in preference to treatment B it is reasonable to choose treatment A over treatment B		

A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Although randomized trials are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

*Data available from clinical trials or registries about the usefulness/ efficacy in different subpopulations, such as sex, age, history of diabetes, history of prior myocardial infarction, history of heart failure, and prior aspirin use.

†For comparative effectiveness recommendations (Class I and IIa; Level of Evidence A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

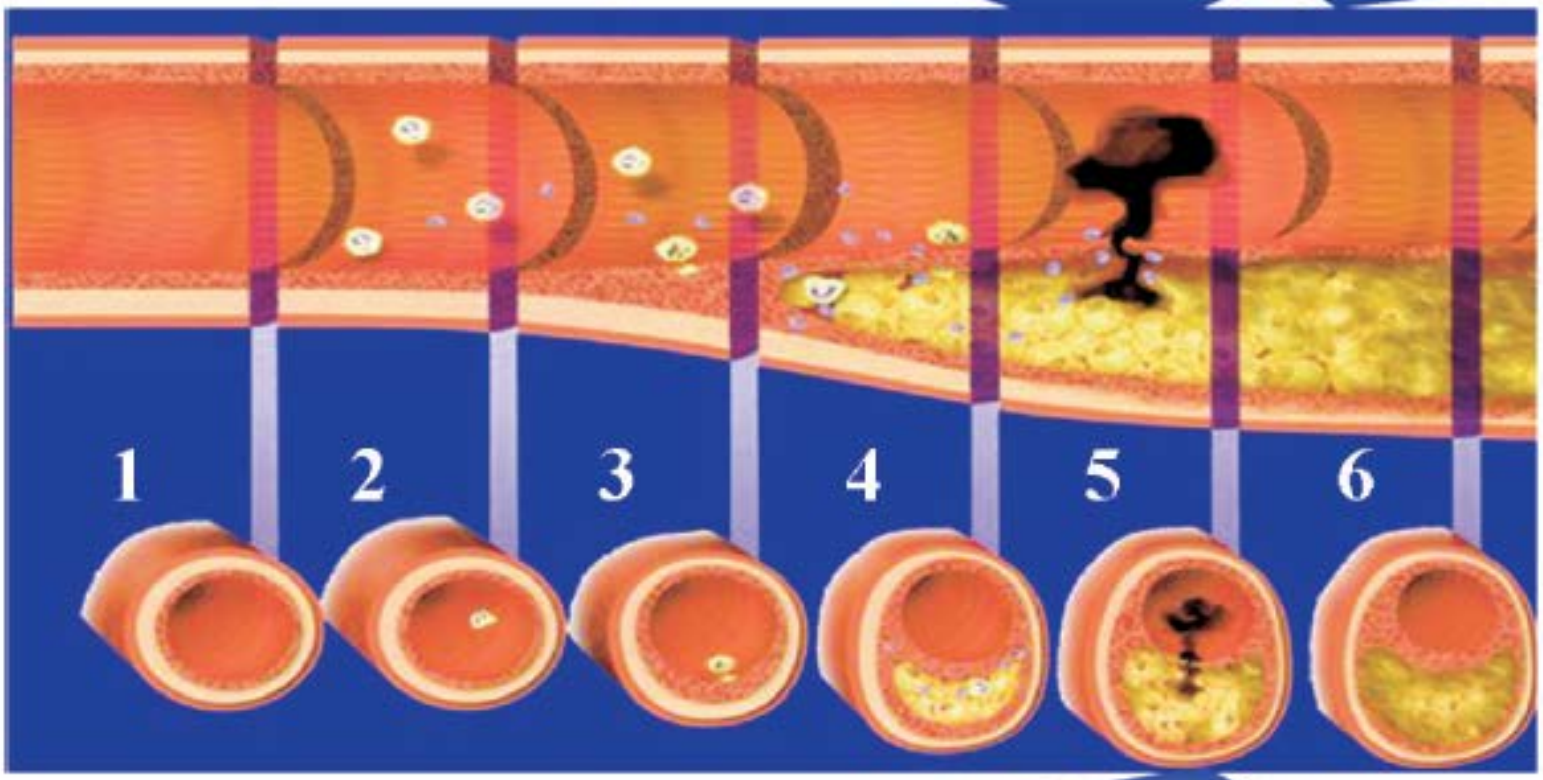
Acute Coronary Syndromes (top half)

Onset of NSTE-ACS
-Initial recognition and management in the ED by first responders or ED personnel
-Risk stratification
-Immediate management

Hospital Management
-Medication
-Conservative versus invasive strategy
-Special groups
-Preparation for discharge

Secondary Prevention/
Long-Term Management

Management Prior to
NSTE-ACS



Acute Coronary Syndromes (top half cont'd)

The top half of the figure illustrates the progression of plaque formation and onset and complications of NSTE-ACS, with management at each stage. The numbered section of an artery depicts the process of atherogenesis from 1) normal artery to 2) extracellular lipid in the subintima to 3) fibrofatty stage to 4) procoagulant expression and weakening of the fibrous cap. ACS develops with 5) disruption of the fibrous cap, which is the stimulus for thrombogenesis. 6) Thrombus resorption may be followed by collagen accumulation and smooth muscle cell growth. Thrombus formation and possible coronary vasospasm reduce blood flow in the affected coronary artery and cause ischemic chest pain.

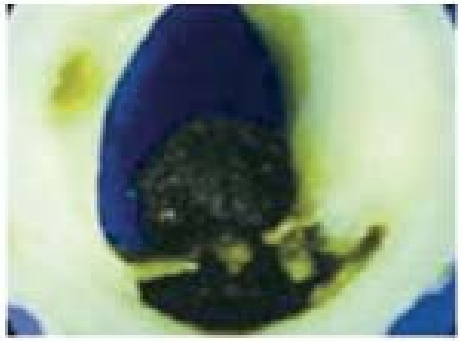
Acute Coronary Syndromes (bottom half)

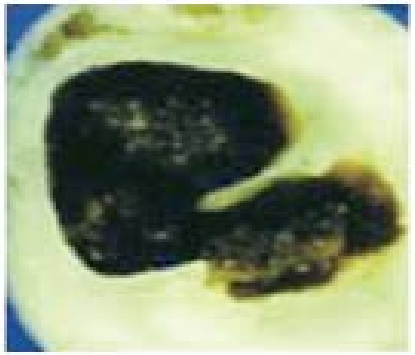
Presentation

Ischemic Discomfort

ACS

Working Dx





ECG

← No ST Elevation →

ST Elevation

← NSTE-ACS →

Cardiac Biomarker

UA

NSTEMI*

STEMI*

Unstable Angina

Myocardial Infarction

NQMI

QwMI

Noncardiac Etiologies

Final Dx

Acute Coronary Syndromes (bottom half cont'd)

The bottom half of the figure illustrates the clinical, pathological, electrocardiographic, and biomarker correlates in ACS and the general approach to management. Flow reduction may be related to a completely occlusive thrombus (bottom half, right side) or subtotally occlusive thrombus (bottom half, left side). Most patients with ST elevation (thick white arrow in bottom panel) develop QwMI, and a few (thin white arrow) develop NQMI. Those without ST elevation have either UA or NSTEMI (thick red arrows), a distinction based on cardiac biomarkers. Most patients presenting with NSTEMI develop NQMI; a few may develop QwMI. The spectrum of clinical presentations including UA, NSTEMI, and STEMI is referred to as ACS. This NSTE-ACS CPG includes sections on initial management before NSTE-ACS, at the onset of NSTE-ACS, and during the hospital phase. Secondary prevention and plans for long-term management begin early during the hospital phase. Patients with noncardiac etiologies make up the largest group presenting to the ED with chest pain (dashed arrow).

Initial Evaluation and Management

Clinical Assessment and Initial Evaluation

Recommendations	COR	LOE
Patients with suspected ACS should be risk stratified based on the likelihood of ACS and adverse outcome(s) to decide on the need for hospitalization and assist in the selection of treatment options.	I	B
Patients with suspected ACS and high-risk features such as continuing chest pain, severe dyspnea, syncope/presyncope, or palpitations should be referred immediately to the ED and transported by emergency medical services when available.	I	C
Patients with less severe symptoms may be considered for referral to the ED, a chest pain unit, or a facility capable of performing adequate evaluation depending on clinical circumstances.	IIb	C

Prognosis: Early Risk Stratification

Recommendations	COR	LOE
In patients with chest pain or other symptoms suggestive of ACS, a 12-lead ECG should be performed and evaluated for ischemic changes within 10 minutes of the patient's arrival at an emergency facility.	I	C
If the initial ECG is not diagnostic but the patient remains symptomatic and there is a high clinical suspicion for ACS, serial ECGs (e.g., 15- to 30-minute intervals during the first hour) should be performed to detect ischemic changes.	I	C
Serial cardiac troponin I or T levels (when a contemporary assay is used) should be obtained at presentation and 3 to 6 hours after symptom onset (see Section 3.4, Class I, #3 recommendation if time of symptom onset is unclear) in all patients who present with symptoms consistent with ACS to identify a rising and/or falling pattern of values.	I	A

Prognosis: Early Risk Stratification (cont'd)

Recommendations	COR	LOE
Additional troponin levels should be obtained beyond 6 hours after symptom onset (see Section 3.4, Class I, #3 recommendation if time of symptom onset is unclear) in patients with normal troponin levels on serial examination when changes on ECG and/or clinical presentation confer an intermediate or high index of suspicion for ACS.	I	A
Risk scores should be used to assess prognosis in patients with NSTE-ACS.	I	A
Risk-stratification models can be useful in management.	IIa	B

Prognosis: Early Risk Stratification (cont'd)

Recommendations	COR	LOE
It is reasonable to obtain supplemental electrocardiographic leads V_7 to V_9 in patients whose initial ECG is nondiagnostic and who are at intermediate/high risk of ACS.	IIa	B
Continuous monitoring with 12-lead ECG may be a reasonable alternative in patients whose initial ECG is nondiagnostic and who are at intermediate/high risk of ACS.	IIb	B
Measurement of B-type natriuretic peptide or N-terminal pro–B-type natriuretic peptide may be considered to assess risk in patients with suspected ACS.	IIb	B

TIMI Risk Score* for NSTE-ACS

TIMI Risk Score	All-Cause Mortality, New or Recurrent MI, or Severe Recurrent Ischemia Requiring Urgent Revascularization Through 14 d After Randomization, %
0–1	4.7
2	8.3
3	13.2
4	19.9
5	26.2
6–7	40.9

*The TIMI risk score is determined by the sum of the presence of 7 variables at admission; 1 point is given for each of the following variables: ≥65 y of age; ≥3 risk factors for CAD; prior coronary stenosis ≥50%; ST deviation on ECG; ≥2 anginal events in prior 24 h; use of aspirin in prior 7 d; and elevated cardiac biomarkers.

GRACE Risk Model Nomogram

1. Find Points for Each Predictive Factor:

Killip Class	Points	SBP, mm Hg	Points	Heart Rate, Beats/min	Points	Age, y	Points	Creatinine Level, mg/dL	Points
I	0	≤80	58	≤50	0	≤30	0	0-0.39	1
II	20	80-99	53	50-69	3	30-39	8	0.40-0.79	4
III	39	100-119	43	70-89	9	40-49	25	0.80-1.19	7
IV	59	120-139	34	90-109	15	50-59	41	1.20-1.59	10
		140-159	24	110-149	24	60-69	58	1.60-1.99	13
		160-199	10	150-199	38	70-79	75	2.00-3.99	21
		≥200	0	≥200	46	80-89	91	>4.0	28
						≥90	100		

Other Risk Factors	Points
Cardiac Arrest at Admission	39
ST-Segment Deviation	28
Elevated Cardiac Enzyme Levels	14

2. Sum Points for All Predictive Factors:

Killip Class	+	SBP	+	Heart Rate	+	Age	+	Creatinine Level	+	Cardiac Arrest at Admission	+	ST-Segment Deviation	+	Elevated Cardiac Enzyme Levels	=	Total Points				

3. Look Up Risk Corresponding to Total Points:

Total Points	≤60	70	80	90	100	110	120	130	140	150	160	170	180	190	200	210	220	230	240	≥250
Probability of In-Hospital Death, %	≤0.2	0.3	0.4	0.6	0.8	1.1	1.6	2.1	2.9	3.9	5.4	7.3	9.8	13	18	23	29	36	44	≥52

For example, a patient has Killip class II, SBP of 100 mm Hg, heart rate of 100 beats/min, is 65 years of age, has serum creatinine level of 1 mg/dL, did not have a cardiac arrest at admission but did have ST-segment deviation and elevated enzyme levels.

His score would be: 20 + 53 + 15 + 58 + 7 + 0 + 28 + 14 = 196

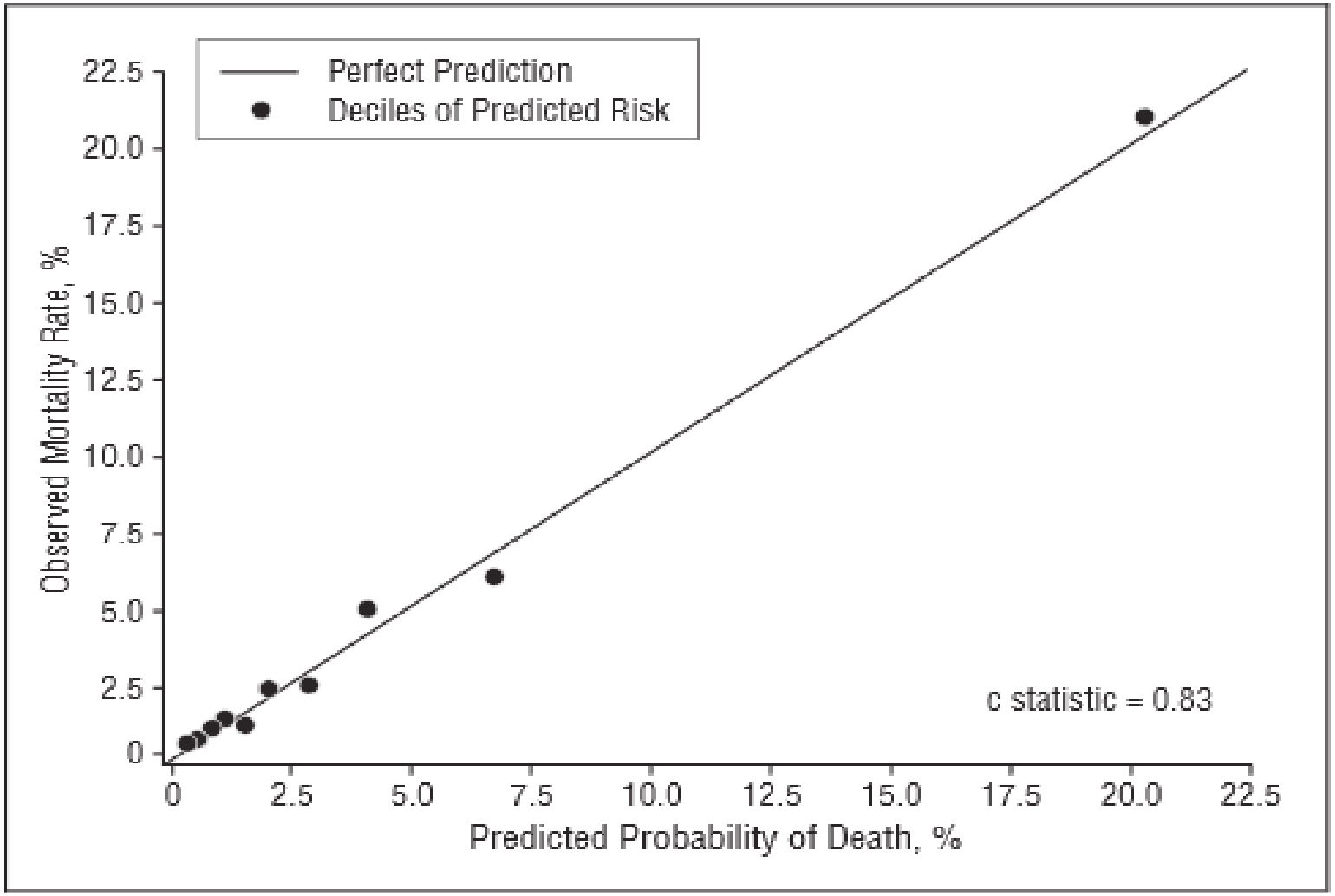
This person would have about a 16% risk of having an in-hospital death.

Similarly, a patient with Killip class I, SBP of 80 mm Hg, heart rate of 60 beats/min, is 55 years of age, has serum creatinine level of 0.4, and no risk factors would have the following score:

0 + 58 + 3 + 41 + 1 = 103, which gives approximately a 0.9% risk of having an in-hospital death.

To convert serum creatinine level to micromoles per liter, multiply by 88.4.

Calibration of Simplified Global Registry of ACS Mortality Model



Cardiac Biomarkers and the Universal Definition of MI

Biomarkers: Diagnosis

Recommendations	COR	LOE
Cardiac-specific troponin (troponin I or T when a contemporary assay is used) levels should be measured at presentation and 3 to 6 hours after symptom onset in all patients who present with symptoms consistent with ACS to identify a rising and/or falling pattern.	I	A
Additional troponin levels should be obtained beyond 6 hours after symptom onset in patients with normal troponins on serial examination when electrocardiographic changes and/or clinical presentation confer an intermediate or high index of suspicion for ACS.	I	A
If the time of symptom onset is ambiguous, the time of presentation should be considered the time of onset for assessing troponin values.	I	A
With contemporary troponin assays, creatine kinase myocardial isoenzyme (CK-MB) and myoglobin are not useful for diagnosis of ACS.	III: No Benefit	A

Biomarkers: Prognosis

Recommendations	COR	LOE
The presence and magnitude of troponin elevations are useful for short- and long-term prognosis.	I	B
It may be reasonable to remeasure troponin once on day 3 or day 4 in patients with MI as an index of infarct size and dynamics of necrosis.	IIb	B
Use of selected newer biomarkers, especially B-type natriuretic peptide, may be reasonable to provide additional prognostic information.	IIb	B

Immediate Management

Immediate Management

Recommendations	COR	LOE
It is reasonable to observe patients with symptoms consistent with ACS without objective evidence of myocardial ischemia (nonischemic initial ECG and normal cardiac troponin) in a chest pain unit or telemetry unit with serial ECGs and cardiac troponin at 3- to 6-hour intervals.	IIa	B
It is reasonable for patients with possible ACS who have normal serial ECGs and cardiac troponins to have a treadmill ECG (*Level of Evidence: A)*, stress myocardial perfusion imaging, or stress echocardiography before discharge or within 72 hours after discharge. *(Level of Evidence: B)*	IIa	A B

Immediate Management (cont'd)

Recommendations	COR	LOE
In patients with possible ACS and a normal ECG, normal cardiac troponins, and no history of CAD, it is reasonable to initially perform (without serial ECGs and troponins) coronary CT angiography to assess coronary artery anatomy *(Level of Evidence: A)* or rest myocardial perfusion imaging with a technetium-99m radiopharmaceutical to exclude myocardial ischemia. (*Level of Evidence: B*)	IIa	A B
It is reasonable to give low-risk patients who are referred for outpatient testing daily aspirin, short-acting nitroglycerin, and other medication if appropriate (e.g., beta blockers), with instructions about activity level and clinician follow-up.	IIa	C

Early Hospital Care

Standard Medical Therapies

Oxygen

Recommendation	COR	LOE
Supplemental oxygen should be administered to patients with NSTE-ACS with arterial oxygen saturation less than 90%, respiratory distress, or other high-risk features of hypoxemia.	I	C

Anti-Ischemic and Analgesic Medications: Nitrates

Recommendations	COR	LOE
Patients with NSTE-ACS with continuing ischemic pain should receive sublingual nitroglycerin (0.3 mg to 0.4 mg) every 5 minutes for up to 3 doses, after which an assessment should be made about the need for intravenous nitroglycerin if not contraindicated.	I	C
Intravenous nitroglycerin is indicated for patients with NSTE-ACS for the treatment of persistent ischemia, HF, or hypertension.	I	B
Nitrates should not be administered to patients with NSTE-ACS who recently received a phosphodiesterase inhibitor, especially within 24 hours of sildenafil or vardenafil, or within 48 hours of tadalafil.	III: Harm	B

Anti-Ischemic and Analgesic Medications: Analgesic Therapy

Recommendations	COR	LOE
In the absence of contraindications, it may be reasonable to administer morphine sulfate intravenously to patients with NSTE-ACS if there is continued ischemic chest pain despite treatment with maximally tolerated anti-ischemic medications.	IIb	B
Nonsteroidal anti-inflammatory drugs (NSAIDs) (except aspirin) should not be initiated and should be discontinued during hospitalization for NSTE-ACS because of the increased risk of MACE associated with their use.	III: Harm	B

Anti-Ischemic and Analgesic Medications: Beta-Adrenergic Blockers

Recommendations	COR	LOE
Oral beta-blocker therapy should be initiated within the first 24 hours in patients who do not have any of the following: 1) signs of HF, 2) evidence of low-output state, 3) increased risk for cardiogenic shock, or 4) other contraindications to beta blockade (e.g., PR interval >0.24 second, second- or third-degree heart block without a cardiac pacemaker, active asthma, or reactive airway disease).	I	A
In patients with concomitant NSTE-ACS, *stabilized* HF, and reduced systolic function, it is recommended to continue beta-blocker therapy with 1 of the 3 drugs proven to reduce mortality in patients with HF: sustained-release metoprolol succinate, carvedilol, or bisoprolol.	I	C

Anti-Ischemic and Analgesic Medications: Beta-Adrenergic Blockers (cont'd)

Recommendations	COR	LOE
Patients with documented contraindications to beta blockers in the first 24 hours of NSTE-ACS should be re-evaluated to determine their subsequent eligibility.	I	C
It is reasonable to continue beta-blocker therapy in patients with normal LV function with NSTE-ACS.	IIa	C
Administration of intravenous beta blockers is potentially harmful in patients with NSTE-ACS who have risk factors for shock.	III: Harm	B

Anti-Ischemic and Analgesic Medications: Calcium Channel Blockers

Recommendations	COR	LOE
In patients with NSTE-ACS, continuing or frequently recurring ischemia, and a contraindication to beta blockers, a nondihydropyridine calcium channel blocker (CCB) (e.g., verapamil or diltiazem) should be given as initial therapy in the absence of clinically significant LV dysfunction, increased risk for cardiogenic shock, PR interval greater than 0.24 second, or second- or third-degree atrioventricular block without a cardiac pacemaker.	I	B
Oral nondihydropyridine calcium antagonists are recommended in patients with NSTE-ACS who have recurrent ischemia in the absence of contraindications, after appropriate use of beta blockers and nitrates.	I	C

Anti-Ischemic and Analgesic Medications: Calcium Channel Blockers (cont'd)

Recommendations	COR	LOE
CCBs† are recommended for ischemic symptoms when beta blockers are not successful, are contraindicated, or cause unacceptable side effects.	I	C
Long-acting CCBs and nitrates are recommended in patients with coronary artery spasm.	I	C
Immediate-release nifedipine should not be administered to patients with NSTE-ACS in the absence of beta-blocker therapy.	III: Harm	B

†Short-acting dihydropyridine calcium channel antagonists should be avoided.

Anti-Ischemic and Analgesic Medications: Cholesterol Management

Recommendations	COR	LOE
High-intensity statin therapy should be initiated or continued in all patients with NSTE-ACS and no contraindications to its use.	I	A
It is reasonable to obtain a fasting lipid profile in patients with NSTE-ACS, preferably within 24 hours of presentation.	IIa	C

Inhibitors of Renin-Angiotensin-Aldosterone System

Inhibitors of Renin-Angiotensin-Aldosterone System

Recommendations	COR	LOE
ACE inhibitors should be started and continued indefinitely in all patients with LVEF less than 0.40 and in those with hypertension, diabetes mellitus, or stable CKD (Section 7.6), unless contraindicated.	I	A
ARBs are recommended in patients with HF or MI with LVEF less than 0.40 who are ACE inhibitor intolerant.	I	A
Aldosterone blockade is recommended in patients post–MI without significant renal dysfunction (creatinine >2.5 mg/dL in men or >2.0 mg/dL in women) or hyperkalemia (K >5.0 mEq/L) who are receiving therapeutic doses of ACE inhibitor and beta blocker and have a LVEF 0.40 or less, diabetes mellitus, or HF.	I	A

Inhibitors of Renin-Angiotensin-Aldosterone System (cont'd)

Recommendations	COR	LOE
ARBs are reasonable in other patients with cardiac or other vascular disease who are ACE inhibitor intolerant.	IIa	B
ACE inhibitors may be reasonable in all other patients with cardiac or other vascular disease.	IIb	B

Initial Antiplatelet/Anticoagulant Therapy in Patients With Definite or Likely NSTE-ACS

Treated With an Initial Invasive or Ischemia-Guided Strategy

Recommendations	COR	LOE
Non–enteric-coated, chewable aspirin (162 mg to 325 mg) should be given to *all* patients with NSTE-ACS without contraindications as soon as possible after presentation, and a maintenance dose of aspirin (81 mg/d to 162 mg/d) should be continued indefinitely.	I	A
In patients with NSTE-ACS who are unable to take aspirin because of hypersensitivity or major gastrointestinal intolerance, a loading dose of clopidogrel followed by a daily maintenance dose should be administered.	I	B

Treated With an Initial Invasive or Ischemia-Guided Strategy (cont'd)

Recommendations	COR	LOE
A $P2Y_{12}$ inhibitor (either clopidogrel or ticagrelor) in addition to aspirin should be administered for up to 12 months to all patients with NSTE-ACS without contraindications who are treated with either an early invasive or ischemia-guided strategy. Options include: • Clopidogrel: 300-mg or 600-mg loading dose, then 75 mg daily • Ticagrelor‖: 180-mg loading dose, then 90 mg twice daily	I	B B

‖The recommended maintenance dose of aspirin to be used with ticagrelor is 81 mg daily.

Treated With an Initial Invasive or Ischemia-Guided Strategy (cont'd)

Recommendations	COR	LOE
It is reasonable to use ticagrelor in preference to clopidogrel for $P2Y_{12}$ treatment in patients with NSTE-ACS who undergo an early invasive or ischemia-guided strategy.	IIa	B
In patients with NSTE-ACS treated with an early invasive strategy and dual antiplatelet therapy (DAPT) with intermediate/high-risk features (e.g., positive troponin), a GP IIb/IIIa inhibitor may be considered as part of initial antiplatelet therapy. Preferred options are eptifibatide or tirofiban.	IIb	B

Initial Parenteral Anticoagulant Therapy in Patients With Definite NSTE-ACS

Recommendations	COR	LOE
In patients with NSTE-ACS, anticoagulation, in addition to antiplatelet therapy, is recommended for all patients irrespective of initial treatment strategy. Treatment options include: • Enoxaparin: 1 mg/kg subcutaneous (SC) every 12 hours (reduce dose to 1 mg/kg SC once daily in patients with creatinine clearance [CrCl] <30 mL/min), continued for the duration of hospitalization or until PCI is performed. An initial intravenous loading dose is 30 mg.	I	A

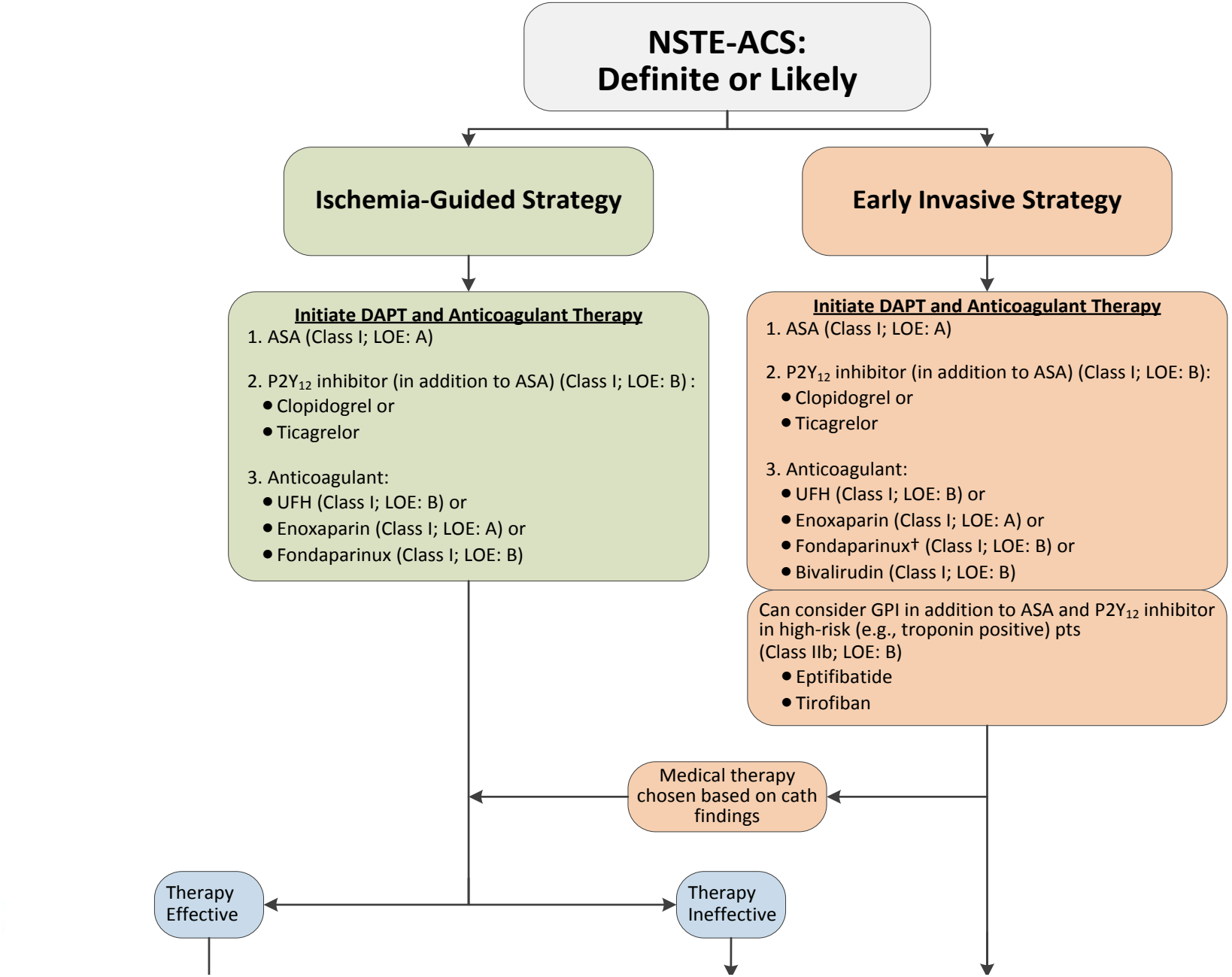
Initial Parenteral Anticoagulant Therapy in Patients With Definite NSTE-ACS (cont'd)

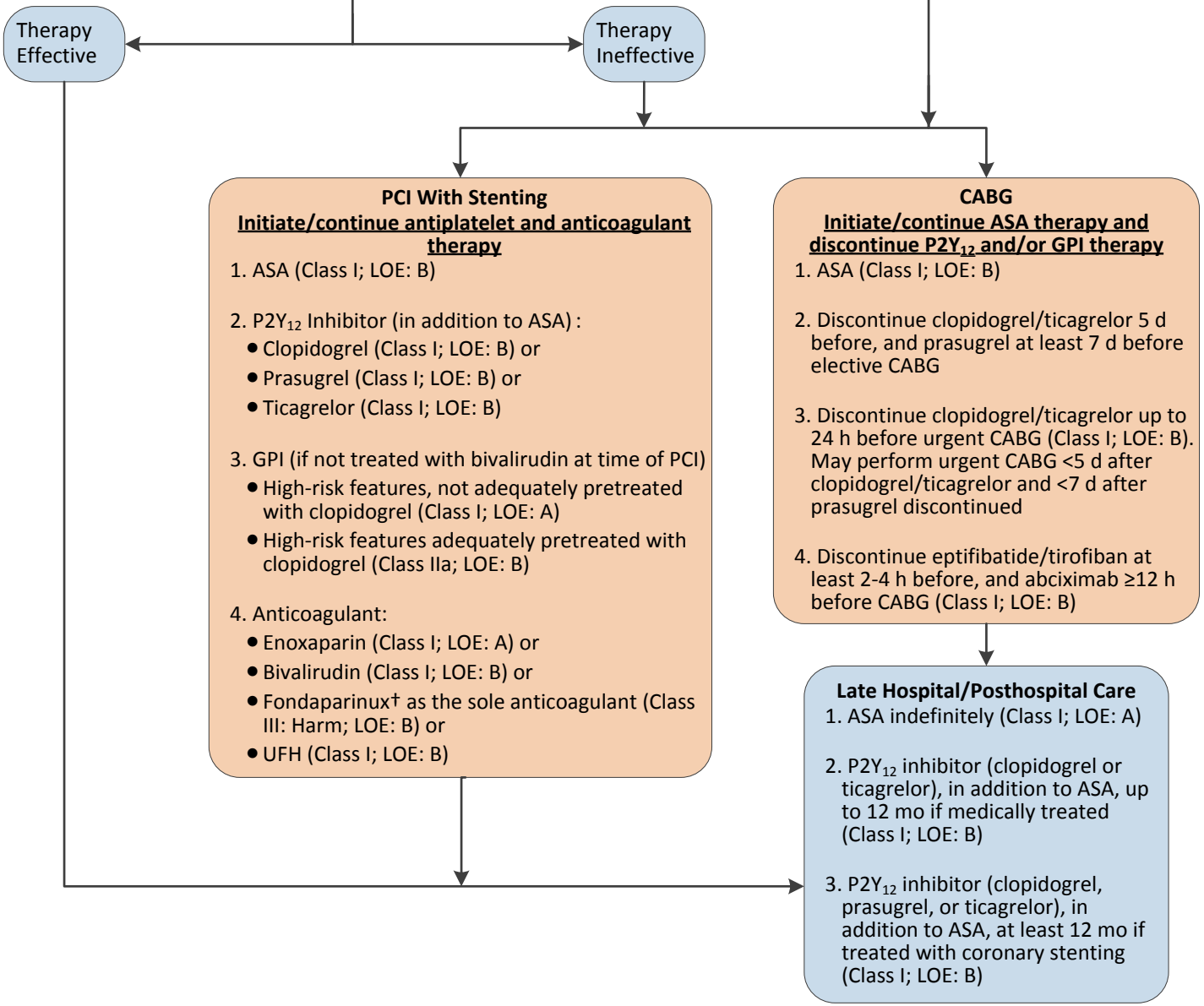
Recommendations	COR	LOE
(cont'd) • Bivalirudin: 0.10 mg/kg loading dose followed by 0.25 mg/kg per hour (only in patients managed with an early invasive strategy), continued until diagnostic angiography or PCI, with only provisional use of GP IIb/IIIa inhibitor, provided the patient is also treated with DAPT. • Fondaparinux: 2.5 mg SC daily, continued for the duration of hospitalization or until PCI is performed.	I	B B

Initial Parenteral Anticoagulant Therapy in Patients With Definite NSTE-ACS (cont'd)

Recommendations	COR	LOE
(cont'd) • If PCI is performed while the patient is on fondaparinux, an additional anticoagulant with anti-IIa activity (either UFH or bivalirudin) should be administered because of the risk of catheter thrombosis. • UFH IV: initial loading dose of 60 IU/kg (maximum 4,000 IU) with initial infusion of 12 IU/kg per hour (maximum 1,000 IU/h) adjusted per activated partial thromboplastin time to maintain therapeutic anticoagulation according to the specific hospital protocol, continued for 48 hours or until PCI is performed.	I	B B
In patients with NSTE-ACS (i.e., without ST elevation, true posterior MI, or left bundle-branch block not known to be old), intravenous fibrinolytic therapy should not be used.	III: Harm	A

Algorithm for Management of Patients With Definite or Likely NSTE-ACS





†In patients who have been treated with fondaparinux (as upfront therapy) who are undergoing PCI, an additional anticoagulant with anti-IIa activity should be administered at the time of PCI because of the risk of catheter thrombosis.

Ischemia-Guided Strategy Versus Early Invasive Strategies

Early Invasive and Ischemia: Guided Strategies

Recommendations	COR	LOE
An urgent/immediate invasive strategy (diagnostic angiography with intent to perform revascularization if appropriate based on coronary anatomy) is indicated in patients (men and women) with NSTE-ACS who have refractory angina or hemodynamic or electrical instability (without serious comorbidities or contraindications to such procedures).	I	A
An early invasive strategy (diagnostic angiography with intent to perform revascularization if appropriate based on coronary anatomy) is indicated in initially stabilized patients with NSTE-ACS (without serious comorbidities or contraindications to such procedures) who have an elevated risk for clinical events.	I	B

Early Invasive and Ischemia: Guided Strategies (cont'd)

Recommendations	COR	LOE
It is reasonable to choose an early invasive strategy (within 24 hours of admission) over a delayed invasive strategy (within 25 to 72 hours) for initially stabilized high-risk patients with NSTE-ACS. For those not at high/intermediate risk, a delayed invasive approach is reasonable.	IIa	B
In initially stabilized patients, an ischemia-guided strategy may be considered for patients with NSTE-ACS (without serious comorbidities or contraindications to this approach) who have an elevated risk for clinical events.	IIb	B
The decision to implement an ischemia-guided strategy in initially stabilized patients (without serious comorbidities or contraindications to this approach) may be reasonable after considering clinician and patient preference.	IIb	C

Early Invasive and Ischemia: Guided Strategies (cont'd)

Recommendations	COR	LOE
An early invasive strategy (i.e., diagnostic angiography with intent to perform revascularization) is not recommended in patients with: a. Extensive comorbidities (e.g., hepatic, renal, pulmonary failure, cancer), in whom the risks of revascularization and comorbid conditions are likely to outweigh the benefits of revascularization. *(Level of Evidence: C)* b. Acute chest pain and a low likelihood of ACS *(Level of Evidence: C)* who are troponin-negative, especially women. (*Level of Evidence: B)*	III: No Benefit	C C B

Factors Associated With Appropriate Selection of Early Invasive Strategy or Ischemia-Guided Strategy in Patients With NSTE-ACS

Immediate invasive (within 2 h)	Refractory angina
	Signs or symptoms of HF or new or worsening mitral regurgitation
	Hemodynamic instability
	Recurrent angina or ischemia at rest or with low-level activities despite intensive medical therapy
	Sustained VT or VF
Ischemia-guided strategy	Low-risk score (e.g., TIMI [0 or 1], GRACE [<109])
	Low-risk Tn-negative female patients
	Patient or clinician preference in the absence of high-risk features
Early invasive (within 24 h)	None of the above, but GRACE risk score >140
	Temporal change in Tn (Section 3.4)
	New or presumably new ST depression
Delayed invasive (within 25–72 h)	None of the above but diabetes mellitus
	Renal insufficiency (GFR <60 mL/min/1.73 m^2)
	Reduced LV systolic function (EF <0.40)
	Early postinfarction angina
	PCI within 6 mo
	Prior CABG
	GRACE risk score 109–140; TIMI score ≥2

Risk Stratification Before Discharge for Patients With an Ischemia-Guided Strategy of NSTE-ACS

Risk Stratification Before Discharge for Patients With an Ischemia-Guided Strategy of NSTE-ACS

Recommendations	COR	LOE
Noninvasive stress testing is recommended in low- and intermediate-risk patients who have been free of ischemia at rest or with low-level activity for a minimum of 12 to 24 hours.	I	B
Treadmill exercise testing is useful in patients able to exercise in whom the ECG is free of resting ST changes that may interfere with interpretation.	I	C
Stress testing with an imaging modality should be used in patients who are able to exercise but have ST changes on resting ECG that may interfere with interpretation. In patients undergoing a low-level exercise test, an imaging modality can add prognostic information.	I	B

Risk Stratification Before Discharge for Patients With an Ischemia-Guided Strategy of NSTE-ACS (cont'd)

Recommendations	COR	LOE
Pharmacological stress testing with imaging is recommended when physical limitations preclude adequate exercise stress.	I	C
A noninvasive imaging test is recommended to evaluate LV function in patients with definite ACS.	I	C

Myocardial Revascularization

Myocardial Revascularization

Percutaneous Coronary Intervention

General Considerations

Recommendation	COR	LOE
A strategy of multivessel PCI, in contrast to culprit lesion–only PCI, may be reasonable in patients undergoing coronary revascularization as part of treatment for NSTE-ACS.	IIb	B

Antiplatelet and Anticoagulant Therapy: Oral and Antiplatelet Agents

Recommendations	COR	LOE
Patients already taking daily aspirin before PCI should take 81 mg to 325 mg non–enteric-coated aspirin before PCI.	I	B
Patients not on aspirin therapy should be given non–enteric-coated aspirin 325 mg as soon as possible before PCI.	I	B
After PCI, aspirin should be continued indefinitely at a dose of 81 mg to 325 mg daily.	I	B

Antiplatelet and Anticoagulant Therapy: Oral and Antiplatelet Agents (cont'd)

Recommendations	COR	LOE
A loading dose of a $P2Y_{12}$ receptor inhibitor should be given before the procedure in patients undergoing PCI with stenting. *(Level of Evidence: A)* Options include:	I	A
a. Clopidogrel: 600 mg *(Level of Evidence: B)* or		B
b. Prasugrel[#]: 60 mg *(Level of Evidence: B)* or		B
c. Ticagrelor[‖]: 180 mg *(Level of Evidence: B)*		B

[#]Patients should receive a loading dose of prasugrel, provided that they were not pretreated with another P2Y12 receptor inhibitor.

[‖]The recommended maintenance dose of aspirin to be used with ticagrelor is 81 mg daily.

Antiplatelet and Anticoagulant Therapy: Oral and Antiplatelet Agents (cont'd)

Recommendations	COR	LOE
In patients with NSTE-ACS and high-risk features (e.g., elevated troponin) not adequately pretreated with clopidogrel or ticagrelor, it is useful to administer a GP IIb/IIIa inhibitor (abciximab, double-bolus eptifibatide, or high-dose bolus tirofiban) at the time of PCI.	I	A

Antiplatelet and Anticoagulant Therapy: Oral and Antiplatelet Agents (cont'd)

Recommendations	COR	LOE
In patients receiving a stent (bare-metal stent or drug-eluting stent [DES]) during PCI for NSTE-ACS, $P2Y_{12}$ inhibitor therapy should be given for at least 12 months. Options include:	I	
a. Clopidogrel: 75 mg daily *(Level of Evidence: B)* or		B
b. Prasugrel[#]: 10 mg daily *(Level of Evidence: B)* or		B
c. Ticagrelor[‖]: 90 mg twice daily *(Level of Evidence: B)*		B

[#]Patients should receive a loading dose of prasugrel, provided that they were not pretreated with another $P2Y_{12}$ receptor inhibitor.

[‖]The recommended maintenance dose of aspirin to be used with ticagrelor is 81 mg daily.

Antiplatelet and Anticoagulant Therapy: Oral and Antiplatelet Agents (cont'd)

Recommendations	COR	LOE
It is reasonable to choose ticagrelor over clopidogrel for $P2Y_{12}$ inhibition treatment in patients with NSTE-ACS treated with an early invasive strategy and/or coronary stenting.	IIa	B
It is reasonable to choose prasugrel over clopidogrel for $P2Y_{12}$ treatment in patients with NSTE-ACS who undergo PCI who are not at high risk of bleeding complications.	IIa	B
In patients with NSTE-ACS and high-risk features (e.g., elevated troponin) treated with UFH and adequately pretreated with clopidogrel, it is reasonable to administer a GP IIb/IIIa inhibitor (abciximab, double-bolus eptifibatide, or high-bolus dose tirofiban) at the time of PCI.	IIa	B

Antiplatelet and Anticoagulant Therapy: Oral and Antiplatelet Agents (cont'd)

Recommendations	COR	LOE
After PCI, it is reasonable to use 81 mg per day of aspirin in preference to higher maintenance doses.	IIa	B
If the risk of morbidity from bleeding outweighs the anticipated benefit of a recommended duration of $P2Y_{12}$ inhibitor therapy after stent implantation, earlier discontinuation (e.g., <12 months) of $P2Y_{12}$ inhibitor therapy is reasonable.	IIa	C
Continuation of DAPT beyond 12 months may be considered in patients undergoing stent implantation.	IIb	C
Prasugrel should not be administered to patients with a prior history of stroke or transient ischemic attack.	III: Harm	B

Antiplatelet and Anticoagulant Therapy: GP IIb/IIIa Inhibitors

Recommendations	COR	LOE
In patients with NSTE-ACS and high-risk features (e.g., elevated troponin) and not adequately pretreated with clopidogrel or ticagrelor, it is useful to administer a GP IIb/IIIa inhibitor (abciximab, double-bolus eptifibatide, or high-dose bolus tirofiban) at the time of PCI.	I	A
In patients with NSTE-ACS and high-risk features (e.g., elevated troponin) treated with UFH and adequately pretreated with clopidogrel, it is reasonable to administer a GP IIb/IIIa inhibitor (abciximab, double-bolus eptifibatide, or high-dose bolus tirofiban) at the time of PCI.	IIa	B

Antiplatelet and Anticoagulant Therapy: Anticoagulant Therapy in Patients Undergoing PCI

Recommendations	COR	LOE
An anticoagulant should be administered to patients with NSTE-ACS undergoing PCI to reduce the risk of intracoronary and catheter thrombus formation.	I	C
Intravenous UFH is useful in patients with NSTE-ACS undergoing PCI.	I	C
Bivalirudin is useful as an anticoagulant with or without prior treatment with UFH in patients with NSTE-ACS undergoing PCI.	I	B

Antiplatelet and Anticoagulant Therapy: Anticoagulant Therapy in Patients Undergoing PCI (cont'd)

Recommendations	COR	LOE
An additional dose of 0.3 mg/kg IV enoxaparin should be administered at the time of PCI to patients with NSTE-ACS who have received fewer than 2 therapeutic subcutaneous doses (e.g., 1 mg/kg SC) or received the last subcutaneous enoxaparin dose 8 to 12 hours before PCI.	I	B
If PCI is performed while the patient is on fondaparinux, an additional 85 IU/kg of UFH should be given intravenously immediately before PCI because of the risk of catheter thrombosis (60 IU/kg IV if a GP IIb/IIIa inhibitor used with UFH dosing based on the target-activated clotting time).	I	B
In patients with NSTE-ACS, anticoagulant therapy should be discontinued after PCI unless there is a compelling reason to continue such therapy.	I	C

Antiplatelet and Anticoagulant Therapy: Anticoagulant Therapy in Patients Undergoing PCI (cont'd)

Recommendations	COR	LOE
In patients with NSTE-ACS undergoing PCI who are at high risk of bleeding, it is reasonable to use bivalirudin monotherapy in preference to the combination of UFH and a GP IIb/IIIa receptor antagonist.	IIa	B
Performance of PCI with enoxaparin may be reasonable in patients treated with upstream subcutaneous enoxaparin for NSTE-ACS.	IIb	B
Fondaparinux should not be used as the sole anticoagulant to support PCI in patients with NSTE-ACS due to an increased risk of catheter thrombosis.	III: Harm	B

Dosing of Parenteral Anticoagulants During PCI

Drug*	In Patients Who Have Received Prior Anticoagulant Therapy	In Patients Who Have Not Received Prior Anticoagulant Therapy
Enoxaparin	• For prior treatment with enoxaparin, if last SC dose was administered 8–12 h earlier or if <2 therapeutic SC doses of enoxaparin have been administered, an IV dose of enoxaparin 0.3 mg/kg should be given • If the last SC dose was administered within prior 8 h, no additional enoxaparin should be given	• 0.5 mg/kg–0.75 mg/kg IV loading dose
Bivalirudin	• For patients who have received UFH, wait 30 min, then give 0.75 mg/kg IV loading dose, then 1.75 mg/kg/h IV infusion • For patients already receiving bivalirudin infusion, give additional loading dose 0.5 mg/kg and increase infusion to 1.75 mg/kg/h during PCI	• 0.75 mg/kg loading dose, 1.75 mg/kg/h IV infusion

Dosing of Parenteral Anticoagulants During PCI

Drug*	In Patients Who Have Received Prior Anticoagulant Therapy	In Patients Who Have Not Received Prior Anticoagulant Therapy
Fondaparinux	• For prior treatment with fondaparinux, administer additional IV treatment with anticoagulant possessing anti-IIa activity, considering whether GPI receptor antagonists have been administered	N/A
UFH	• IV GPI planned: additional UFH as needed (e.g., 2,000–5,000 U) to achieve ACT of 200–250 s • No IV GPI planned: additional UFH as needed (e.g., 2,000–5,000 U) to achieve ACT of 250–300 s for HemoTec, 300–350 s for Hemochron	• IV GPI planned: 50–70 U/kg loading dose to achieve ACT of 200–250 s • No IV GPI planned: 70–100 U/kg loading dose to achieve target ACT of 250–300 s for HemoTec, 300–350 s for Hemochron

*Drugs are presented in order by the COR then the LOE. When more than 1 drug exists within the same LOE and there are no comparative data, then the drugs are listed alphabetically.

Timing of Urgent CABG in Patients With NSTE-ACS in Relation to Use of Antiplatelet Agents

Timing of Urgent CABG in Patients With NSTE-ACS in Relation to Use of Antiplatelet Agents

Recommendations	COR	LOE
Non–enteric-coated aspirin (81 mg to 325 mg daily) should be administered preoperatively to patients undergoing CABG.	I	B
In patients referred for elective CABG, clopidogrel and ticagrelor should be discontinued for at least 5 days before surgery *(Level of Evidence: B*) and prasugrel for at least 7 days before surgery. *(Level of Evidence: C)*	I	B C
In patients referred for urgent CABG, clopidogrel and ticagrelor should be discontinued for at least 24 hours to reduce major bleeding.	I	B

Timing of Urgent CABG in Patients With NSTE-ACS in Relation to Use of Antiplatelet Agents (cont'd)

Recommendations	COR	LOE
In patients referred for CABG, short-acting intravenous GP IIb/IIIa inhibitors (eptifibatide or tirofiban) should be discontinued for at least 2 to 4 hours before surgery (418, 419) and abciximab for at least 12 hours before to limit blood loss and transfusion.	I	B
In patients referred for urgent CABG, it may be reasonable to perform surgery less than 5 days after clopidogrel or ticagrelor has been discontinued and less than 7 days after prasugrel has been discontinued.	IIb	C

Late Hospital Care, Hospital Discharge, and Posthospital Discharge Care

Medical Regimen and Use of Medications at Discharge

Medical Regimen and Use of Medications at Discharge

Recommendations	COR	LOE
Medications required in the hospital to control ischemia should be continued after hospital discharge in patients with NSTE-ACS who do not undergo coronary revascularization, patients with incomplete or unsuccessful revascularization, and patients with recurrent symptoms after revascularization. Titration of the doses may be required.	I	C
All patients who are post–NSTE-ACS should be given sublingual or spray nitroglycerin with verbal and written instructions for its use.	I	C
Before hospital discharge, patients with NSTE-ACS should be informed about symptoms of worsening myocardial ischemia and MI and should be given verbal and written instructions about how and when to seek emergency care for such symptoms.	I	C

Medical Regimen and Use of Medications at Discharge (cont'd)

Recommendations	COR	LOE
Before hospital discharge, patients who are post–NSTE-ACS and/or designated responsible caregivers should be provided with easily understood and culturally sensitive verbal and written instructions about medication type, purpose, dose, frequency, side effects, and duration of use.	I	C
For patients who are post–NSTE-ACS and have initial angina lasting more than 1 minute, nitroglycerin (1 dose sublingual or spray) is recommended if angina does not subside within 3 to 5 minutes; call 9-1-1 immediately to access emergency medical services.	I	C

Medical Regimen and Use of Medications at Discharge (cont'd)

Recommendations	COR	LOE
If the pattern or severity of angina changes, suggesting worsening myocardial ischemia (e.g., pain is more frequent or severe or is precipitated by less effort or occurs at rest), patients should contact their clinician without delay to assess the need for additional treatment or testing.	I	C
Before discharge, patients should be educated about modification of cardiovascular risk factors.	I	C

Late Hospital and Posthospital Oral Antiplatelet Therapy

Late Hospital and Posthospital Oral Antiplatelet Therapy

Recommendations	COR	LOE
Aspirin should be continued indefinitely. The maintenance dose should be 81 mg daily in patients treated with ticagrelor and 81 mg to 325 mg daily in all other patients.	I	A
In addition to aspirin, a $P2Y_{12}$ inhibitor (either clopidogrel or ticagrelor) should be continued for up to 12 months in all patients with NSTE-ACS without contraindications who are treated with an ischemia-guided strategy. Options include: a. Clopidogrel: 75 mg daily or b. Ticagrelor‖: 90 mg twice daily	I	B B

‖The recommended maintenance dose of aspirin to be used with ticagrelor is 81 mg daily.

Medical Regimen and Use of Medications at Discharge

Recommendations	COR	LOE
In patients receiving a stent (bare-metal stent or DES) during PCI for NSTE-ACS, $P2Y_{12}$ inhibitor therapy should be given for at least 12 months. Options include: a. Clopidogrel: 75 mg daily or b. Prasugrel[#]: 10 mg daily or c. Ticagrelor[‖]: 90 mg twice daily	I	B B B
It is reasonable to use an aspirin maintenance dose of 81 mg per day in preference to higher maintenance doses in patients with NSTE-ACS treated either invasively or with coronary stent implantation.	IIa	B

[#]Patients should receive a loading dose of prasugrel, provided that they were not pretreated with another $P2Y_{12}$ receptor inhibitor.

[‖]The recommended maintenance dose of aspirin to be used with ticagrelor is 81 mg daily.

Medical Regimen and Use of Medications at Discharge (cont'd)

Recommendations	COR	LOE
It is reasonable to choose ticagrelor over clopidogrel for maintenance $P2Y_{12}$ treatment in patients with NSTE-ACS treated with an early invasive strategy and/or PCI.	IIa	B
It is reasonable to choose prasugrel over clopidogrel for maintenance $P2Y_{12}$ treatment in patients with NSTE-ACS who undergo PCI who are not at high risk for bleeding complications.	IIa	B
If the risk of morbidity from bleeding outweighs the anticipated benefit of a recommended duration of $P2Y_{12}$ inhibitor therapy after stent implantation, earlier discontinuation (e.g., <12 months) of $P2Y_{12}$ inhibitor therapy is reasonable.	IIa	C
Continuation of DAPT beyond 12 months may be considered in patients undergoing stent implantation.	IIb	C

Combined Oral Anticoagulant Therapy and Antiplatelet Therapy in Patients With NSTE-ACS

Combined Oral Anticoagulant Therapy and Antiplatelet Therapy in Patients With NSTE-ACS

Recommendations	COR	LOE
The duration of triple antithrombotic therapy with a vitamin K antagonist, aspirin, and a $P2Y_{12}$ receptor inhibitor in patients with NSTE-ACS should be minimized to the extent possible to limit the risk of bleeding.	I	C
Proton pump inhibitors should be prescribed in patients with NSTE-ACS with a history of gastrointestinal bleeding who require triple antithrombotic therapy with a vitamin K antagonist, aspirin, and a $P2Y_{12}$ receptor inhibitor.	I	C

Combined Oral Anticoagulant Therapy and Antiplatelet Therapy in Patients With NSTE-ACS (cont'd)

Recommendations	COR	LOE
Proton pump inhibitor use is reasonable in patients with NSTE-ACS *without* a known history of gastrointestinal bleeding who require triple antithrombotic therapy with a vitamin K antagonist, aspirin, and a $P2Y_{12}$ receptor inhibitor.	IIa	C
Targeting oral anticoagulant therapy to a lower international normalized ratio (e.g., 2.0 to 2.5) may be reasonable in patients with NSTE-ACS managed with aspirin and a $P2Y_{12}$ inhibitor.	IIb	C

Risk Reduction Strategies for Secondary Prevention

Risk Reduction Strategies for Secondary Prevention

Recommendations	COR	LOE
All eligible patients with NSTE-ACS should be referred to a comprehensive cardiovascular rehabilitation program either before hospital discharge or during the first outpatient visit.	I	B
The pneumococcal vaccine is recommended for patients 65 years of age and older and in high-risk patients with cardiovascular disease.	I	B
Patients should be educated about appropriate cholesterol management, blood pressure (BP), smoking cessation, and lifestyle management.	I	C

Risk Reduction Strategies for Secondary Prevention (cont'd)

Recommendations	COR	LOE
Patients who have undergone PCI or CABG derive benefit from risk factor modification and should receive counseling that revascularization does not obviate the need for lifestyle changes.	I	C
Before hospital discharge, the patient's need for treatment of chronic musculoskeletal discomfort should be assessed, and a stepped-care approach should be used for selection of treatments. Pain treatment before consideration of NSAIDs should begin with acetaminophen, nonacetylated salicylates, tramadol, or small doses of narcotics if these medications are not adequate.	I	C
It is reasonable to use nonselective NSAIDs, such as naproxen, if initial therapy with acetaminophen, nonacetylated salicylates, tramadol, or small doses of narcotics is insufficient.	IIa	C

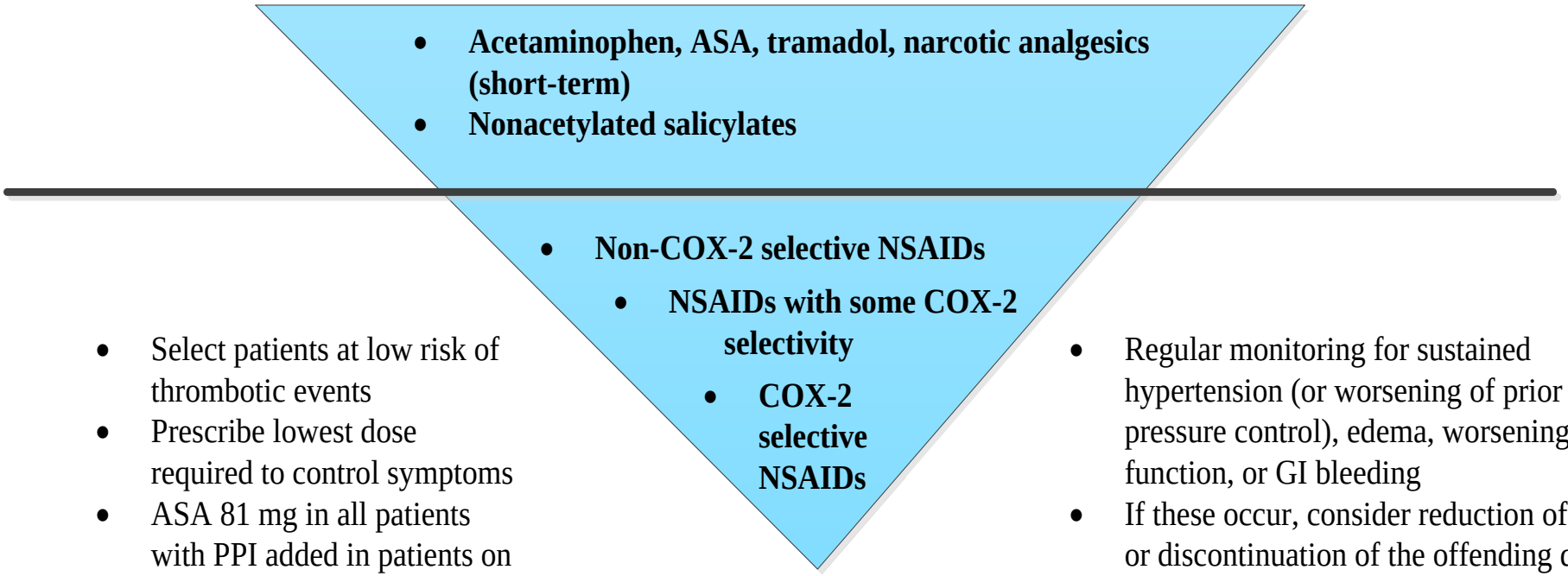
Risk Reduction Strategies for Secondary Prevention (cont'd)

Recommendations	COR	LOE
NSAIDs with increasing degrees of relative cyclooxygenase-2 selectivity may be considered for pain relief only for situations in which intolerable discomfort persists despite attempts at stepped-care therapy with acetaminophen, nonacetylated salicylates, tramadol, small doses of narcotics, or nonselective NSAIDs. In all cases, use of the lowest effective doses for the shortest possible time is encouraged.	IIb	C
Antioxidant vitamin supplements (e.g., vitamins E, C, or beta carotene) should not be used for secondary prevention in patients with NSTE-ACS.	III: No Benefit	A
Folic acid, with or without vitamins B_6 and B_{12}, should not be used for secondary prevention in patients with NSTE-ACS.	III: No Benefit	A

Risk Reduction Strategies for Secondary Prevention (cont'd)

Recommendations	COR	LOE
Hormone therapy with estrogen plus progestin, or estrogen alone, should not be given as new drugs for secondary prevention of coronary events to postmenopausal women after NSTE-ACS and should not be continued in previous users unless the benefits outweigh the estimated risks.	III: Harm	A
NSAIDs with increasing degrees of relative cyclooxygenase-2 selectivity should not be administered to patients with NSTE-ACS and chronic musculoskeletal discomfort when therapy with acetaminophen, nonacetylated salicylates, tramadol, small doses of narcotics, or nonselective NSAIDs provide acceptable pain relief.	III: Harm	B

Stepped-Care Approach to Pharmacological Therapy for Musculoskeletal Symptoms in Patients With Known Cardiovascular Disease or Risk Factors for Ischemic Heart Disease



- Select patients at low risk of thrombotic events
- Prescribe lowest dose required to control symptoms
- ASA 81 mg in all patients with PPI added in patients on ASA and NSAIDs to decrease risk of upper GI bleeding

- Regular monitoring for sustained hypertension (or worsening of prior blood pressure control), edema, worsening renal function, or GI bleeding
- If these occur, consider reduction of dose or discontinuation of the offending drug, a different drug, or alternative therapeutic modalities, as dictated by clinical circumstances

Plan of Care for Patients With NSTE-ACS

Plan of Care for Patients With NSTE-ACS

Recommendations	COR	LOE
Posthospital systems of care designed to prevent hospital readmissions should be used to facilitate the transition to effective, coordinated outpatient care for all patients with NSTE-ACS.	I	B
An evidence-based plan of care (e.g., GDMT) that promotes medication adherence, timely follow-up with the healthcare team, appropriate dietary and physical activities, and compliance with interventions for secondary prevention should be provided to patients with NSTE-ACS.	I	C

Plan of Care for Patients With NSTE-ACS (cont'd)

Recommendations	COR	LOE
In addition to detailed instructions for daily exercise, patients should be given specific instruction on activities (e.g., lifting, climbing stairs, yard work, and household activities) that are permissible and those to avoid. Specific mention should be made of resumption of driving, return to work, and sexual activity.	I	B
An annual influenza vaccination is recommended for patients with cardiovascular disease.	I	C

Special Patient Groups

NSTE-ACS in Older Patients

Recommendations	COR	LOE
Older patients** with NSTE-ACS should be treated with GDMT, an early invasive strategy, and revascularization as appropriate.	I	A
Pharmacotherapy in older patients with NSTE-ACS should be individualized and dose adjusted by weight and/or CrCl to reduce adverse events caused by age-related changes in pharmacokinetics/dynamics, volume of distribution, comorbidities, drug interactions, and increased drug sensitivity.	I	A
Management decisions for older patients with NSTE-ACS should be patient centered, considering patient preferences/goals, comorbidities, functional and cognitive status, and life expectancy.	I	B

**Those ≥75 years of age.

NSTE-ACS in Older Patients (cont'd)

Recommendations	COR	LOE
Bivalirudin, rather than a GP IIb/IIIa inhibitor plus UFH, is reasonable in older patients with NSTE-ACS, both initially and at PCI, given similar efficacy but less bleeding risk.	IIa	B
It is reasonable to choose CABG over PCI in older patients** with NSTE-ACS who are appropriate candidates, particularly those with diabetes mellitus or complex 3-vessel CAD (e.g., SYNTAX score >22), with or without involvement of the proximal left anterior descending artery, to reduce cardiovascular disease events and readmission and to improve survival.	IIa	B

Heart Failure and Cardiogenic Shock

Recommendations	COR	LOE
Patients with a history of HF and NSTE-ACS should be treated according to the same risk stratification guidelines and recommendations for patients without HF.	I	B
Selection of a specific revascularization strategy should be based on the degree, severity, and extent of CAD; associated cardiac lesions; the extent of LV dysfunction; and the history of prior revascularization procedures.	I	B
Early revascularization is recommended in suitable patients with cardiogenic shock due to cardiac pump failure after NSTE-ACS.	I	B

Diabetes Mellitus

Recommendation	COR	LOE
Medical treatment in the acute phase of NSTE-ACS and decisions to perform stress testing, angiography, and revascularization should be similar in patients with and without diabetes mellitus.	I	A

Post-CABG

Recommendation	COR	LOE
Patients with prior CABG and NSTE-ACS should receive antiplatelet and anticoagulant therapy according to GDMT and should be strongly considered for early invasive strategy because of their increased risk.	I	B

Perioperative NSTE-ACS Related to Noncardiac Surgery

Recommendations	COR	LOE
Patients who develop NSTE-ACS following noncardiac surgery should receive GDMT as recommended for patients in the general population but with the modifications imposed by the specific noncardiac surgical procedure and the severity of NSTE-ACS.	I	C
In patients who develop NSTE-ACS after noncardiac surgery, management should be directed at the underlying cause.	I	C

Chronic Kidney Disease

Recommendations	COR	LOE
CrCl should be estimated in patients with NSTE-ACS, and doses of renally cleared medications should be adjusted according to the pharmacokinetic data for specific medications.	I	B
Patients undergoing coronary and LV angiography should receive adequate hydration.	I	C
An invasive strategy is reasonable in patients with mild (stage 2) and moderate (stage 3) CKD.	IIa	B

Women

Recommendations	COR	LOE
Women with NSTE-ACS should be managed with the same pharmacological therapy as that for men for acute care and for secondary prevention, with attention to weight and/or renally-calculated doses of antiplatelet and anticoagulant agents to reduce bleeding risk.	I	B
Women with NSTE-ACS and high-risk features (e.g., troponin positive) should undergo an early invasive strategy.	I	A
Myocardial revascularization is reasonable in pregnant women with NSTE-ACS if an ischemia-guided strategy is ineffective for management of life-threatening complications.	IIa	C
Women with NSTE-ACS and low-risk features (see Section 3.3.1 in the full-text CPG) should not undergo early invasive treatment because of the lack of benefit and the possibility of harm.	III: No Benefit	B

Anemia, Bleeding, and Transfusion

Recommendations	COR	LOE
All patients with NSTE-ACS should be evaluated for the risk of bleeding.	I	C
Anticoagulant and antiplatelet therapy should be weight-based where appropriate and should be adjusted when necessary for CKD to decrease the risk of bleeding in patients with NSTE-ACS.	I	B
A strategy of routine blood transfusion in hemodynamically stable patients with NSTE-ACS and hemoglobin levels greater than 8 g/dL is not recommended.	III: No Benefit	B

Cocaine and Methamphetamine Users

Recommendations	COR	LOE
Patients with NSTE-ACS and a recent history of cocaine or methamphetamine use should be treated in the same manner as patients without cocaine- or methamphetamine-related NSTE-ACS. The only exception is in patients with signs of acute intoxication (e.g., euphoria, tachycardia, and/or hypertension) and beta-blocker use, unless patients are receiving coronary vasodilator therapy.	I	C
Benzodiazepines alone or in combination with nitroglycerin are reasonable for management of hypertension and tachycardia in patients with NSTE-ACS and signs of acute cocaine or methamphetamine intoxication.	IIa	C
Beta blockers should not be administered to patients with ACS with a recent history of cocaine or methamphetamine use who demonstrate signs of acute intoxication due to the risk of potentiating coronary spasm.	III: Harm	C

Vasospastic (Prinzmetal) Angina

Recommendations	COR	LOE
CCBs alone or in combination with long-acting nitrates are useful to treat and reduce the frequency of vasospastic angina.	I	B
Treatment with HMG-CoA reductase inhibitor, cessation of tobacco use, and additional atherosclerosis risk factor modification are useful in patients with vasospastic angina.	I	B
Coronary angiography (invasive or noninvasive) is recommended in patients with episodic chest pain accompanied by transient ST elevation to rule out severe obstructive CAD.	I	C

Vasospastic (Prinzmetal) Angina (cont'd)

Recommendations	COR	LOE
Provocative testing during invasive coronary angiography†† may be considered in patients with suspected vasospastic angina when clinical criteria and noninvasive testing fail to establish the diagnosis.	IIb	B

††Provocative testing during invasive coronary angiography (e.g., using ergonovine, acetylcholine, methylergonovine) is relatively safe, especially when performed in a controlled manner by experienced operators. However, sustained spasm, serious arrhythmias, and even death can also occur very infrequently. Therefore, provocative testing should be avoided in patients with significant left main disease, advanced 3-vessel disease, presence of high-grade obstructive lesions, significant valvular stenosis, significant LV systolic dysfunction, and advanced HF.

ACS With Angiographically Normal Coronary Arteries

Recommendation	COR	LOE
If coronary angiography reveals normal coronary arteries and endothelial dysfunction is suspected, invasive physiological assessment such as coronary flow reserve measurement may be considered.	IIb	B

Stress (Takotsubo) Cardiomyopathy

Recommendations	COR	LOE
Stress (Takotsubo) cardiomyopathy should be considered in patients who present with apparent ACS and nonobstructive CAD at angiography.	I	C
Imaging with ventriculography, echocardiography, or magnetic resonance imaging should be performed to confirm or exclude the diagnosis of stress (Takotsubo) cardiomyopathy.	I	B
Patients should be treated with conventional agents (ACE inhibitors, beta blockers, aspirin, and diuretics) as otherwise indicated if hemodynamically stable.	I	C
Anticoagulation should be administered in patients who develop LV thrombi.	I	C

Stress (Takotsubo) Cardiomyopathy (cont'd)

Recommendations	COR	LOE
It is reasonable to use catecholamines for patients with symptomatic hypotension if outflow tract obstruction is not present.	IIa	C
The use of an intra-aortic balloon pump is reasonable for patients with refractory shock.	IIa	C
It is reasonable to use beta blockers and alpha-adrenergic agents in patients with outflow tract obstruction.	IIa	C
Prophylactic anticoagulation may be considered to inhibit the development of LV thrombi.	IIb	C

Quality of Care and Outcomes for ACS-Use of Performance Measures and Registries

Quality of Care and Outcomes for ACS-Use of Performance Measures and Registries

Recommendation	COR	LOE
Participation in a standardized quality-of-care data registry designed to track and measure outcomes, complications, and performance measures can be beneficial in improving the quality of NSTE-ACS care.	IIa	B