individualized according to the patient's risks for thrombotic and bleeding complications.

In patients undergoing CABG for stable CAD, DAPT for 12 months may be reasonable to improve the patency of vein grafts.

KEY POINTS

- Percutaneous coronary intervention may alleviate angina symptoms but does not decrease mortality or risk for myocardial infarction in patients with stable angina.
- Coronary artery bypass graft revascularization is associated with improved survival in patients with multivessel coronary artery disease, diabetes mellitus, or severe left ventricular dysfunction.
- In patients with stable angina who undergo percutaneous coronary intervention, dual antiplatelet therapy should be continued for at least 1 month after bare metal stent implantation and at least 6 months after drug-eluting stent implantation.

Acute Coronary Syndromes

General Considerations

An acute coronary syndrome (ACS) results from acute or subacute disruption in coronary blood flow. Patients present with acute-onset chest pain or an angina equivalent that occurs without a clear precipitant. Unlike stable angina, which involves a gradual narrowing in the coronary artery, an ACS is caused by acute plaque rupture or erosion, often in sections of the coronary artery with mild or moderate stenosis. The presentation depends on the degree of coronary flow impairment.

ACS is classified as ST-elevation myocardial infarction (STEMI) or non-ST-elevation acute coronary syndrome (NSTE-ACS) based on findings on ECG (**Figure 6**). The hallmark ECG features of STEMI are ST-segment elevation of 1 mm or more in two or more contiguous limb or chest leads, excepting leads V_2 and V_3. STEMI is defined as ST-segment elevation of 2 mm or greater in men and 1.5 mm or greater in women in leads V_2 and V_3. Posterior MI typically manifests as ST-segment depression greater than 2 mm in the anterior leads (V_1 through V_4), often with ST-segment elevation in the inferior or lateral leads. New left bundle branch block is considered a STEMI equivalent and potentially reflects an acute left anterior descending artery occlusion.

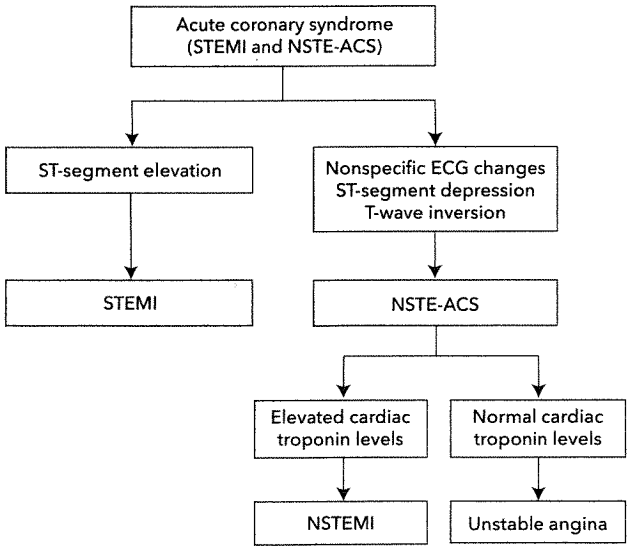

FIGURE 6. Diagnosis of acute coronary syndromes. ECG = electrocardiographic; NSTE-ACS = non-ST-elevation acute coronary syndrome; NSTEMI = non-ST-elevation myocardial infarction; STEMI = ST-elevation myocardial infarction.

NSTE-ACS is further categorized according to the presence of biomarkers of cardiac injury (troponin T or I) in the serum. Non-ST-elevation myocardial infarction (NSTEMI) is defined as a biomarker-positive presentation that does not meet criteria for STEMI. Unstable angina is characterized by new or worsening angina, with or without ECG changes, and without detectable levels of cardiac injury markers. The use of troponin assays has resulted in increased diagnosis of NSTEMI. New high-sensitivity troponin assays can detect cardiac injury with even greater sensitivity and earlier in the setting of ACS than previous tests. Their clinical use may expedite risk stratification in patients with chest pain but may increase detection of non-ACS events and consequent downstream testing.

ST-Elevation Myocardial Infarction

Recognition

The pathogenesis of STEMI typically involves plaque rupture within a coronary artery. The rupture causes platelet adhesion, activation, and aggregation, resulting in a thrombosed coronary artery and acute vessel occlusion. The sudden loss of coronary blood flow leads to transmural ischemia of the myocardium and the ECG manifestation of ST-segment elevation. Because oxygen delivery to the affected artery is acutely and completely obstructed, prompt recognition and initiation of reperfusion therapy are vital (**Figure 7**).

Although the presentation of STEMI is often dramatic and clear, several diagnoses can mimic STEMI. These disease entities need to be distinguished from STEMI to minimize patient harm. Acute pericarditis presents with acute chest pain, albeit pain with a pleuritic and positional nature, and ST-segment elevation. The ST-segment elevation of pericarditis tends to be diffuse and concave; however, it can be easily misinterpreted for STEMI on ECG (**Figure 8**). Pericarditis can also be localized and present with regional ST-segment elevation, such as in the inferior leads. Myopericarditis resulting from viral infections or autoimmune conditions can cause cardiac enzyme release, further confusing the clinical picture. A thorough history and physical examination combined with review of the ECG findings may help differentiate the conditions.

Left ventricular hypertrophy–induced ECG changes may also look similar to ST-segment elevation injury currents; however, these changes are typically concave in appearance. Comparison with previous ECG results is helpful in assessing for acute changes.

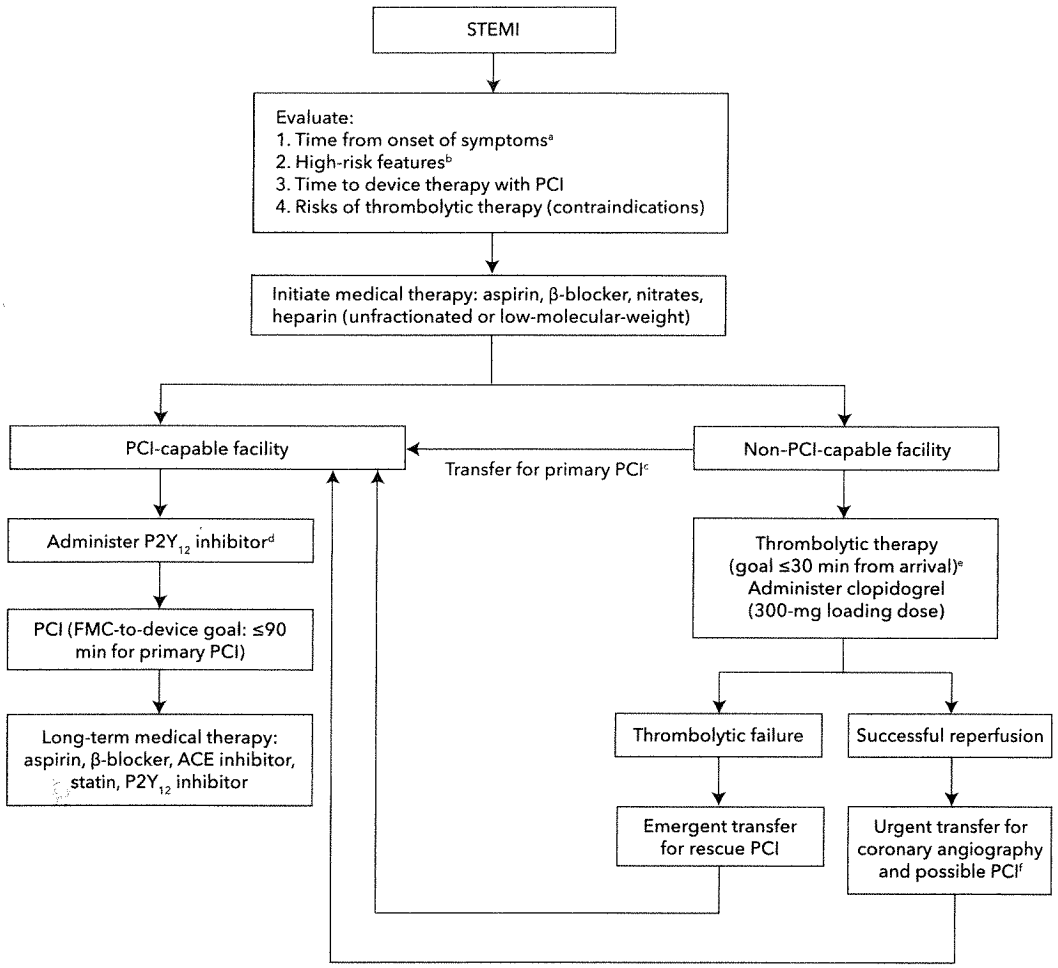

FIGURE 7. Management of ST-elevation myocardial infarction. FMC = first medical contact; PCI = percutaneous coronary intervention; STEMI = ST-elevation myocardial infarction.

[a]If 4 or more hours have elapsed since symptom onset, PCI is preferred.

[b]High-risk features, such as cardiogenic shock and heart failure, favor PCI.

[c]FMC-to-device ("door-to-balloon") goal for patients being transferred for primary PCI is as soon as possible and ≤120 minutes.

[d]$P2Y_{12}$ inhibitors: clopidogrel, prasugrel, ticagrelor.

[e]Patients with STEMI presenting to a hospital without PCI capabilities and who cannot be transferred to a PCI-capable center and undergo PCI within 120 minutes of FMC ("door-to-balloon time") should be treated with thrombolytic therapy within 30 minutes of hospital presentation ("door-to-needle time") as a systems goal unless thrombolytic therapy is contraindicated.

[f]In patients with successful reperfusion after thrombolytic therapy, it is reasonable to transfer these patients to a PCI-capable center for subsequent coronary angiography. Angiography should not be performed within 2 to 3 hours after thrombolytic administration but is ideally performed within 24 hours.

Recommendations based on O'Gara PT, Kushner FG, Ascheim DD, Casey DE Jr, Chung MK, de Lemos JA, et al; American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2013;127:e362-425. [PMID: 23247304] doi:10.1161/CIR.0b013e3182742cf6

CONT.

Aortic dissection can cause ST-segment elevation if the dissection involves the left or right coronary artery. In these cases, the ST-segment elevation is due to transmural myocardial ischemia. Aortic dissection is a surgical emergency and must be recognized early because treatment paradigms are drastically different. Diagnostic clues that help differentiate the two conditions include differential blood pressures in the upper extremities and mediastinal widening on chest radiograph with aortic dissection.

Severe hypercalcemia may result in ST-segment elevation that mimics ACS; however, other findings include a short QT interval and flattened T waves.

Reperfusion

Upon STEMI recognition, reperfusion with thrombolytic agents or primary PCI (PPCI) is necessary. PPCI is the preferred method of reperfusion in most cases.

Thrombolytic Therapy

Thrombolytic therapy is recommended for patients with STEMI when symptom onset is within 12 hours and PPCI is not available within 120 minutes of first medical contact. If symptoms began 12 to 24 hours before presentation and there is evidence of hemodynamic instability or significant myocardium at risk

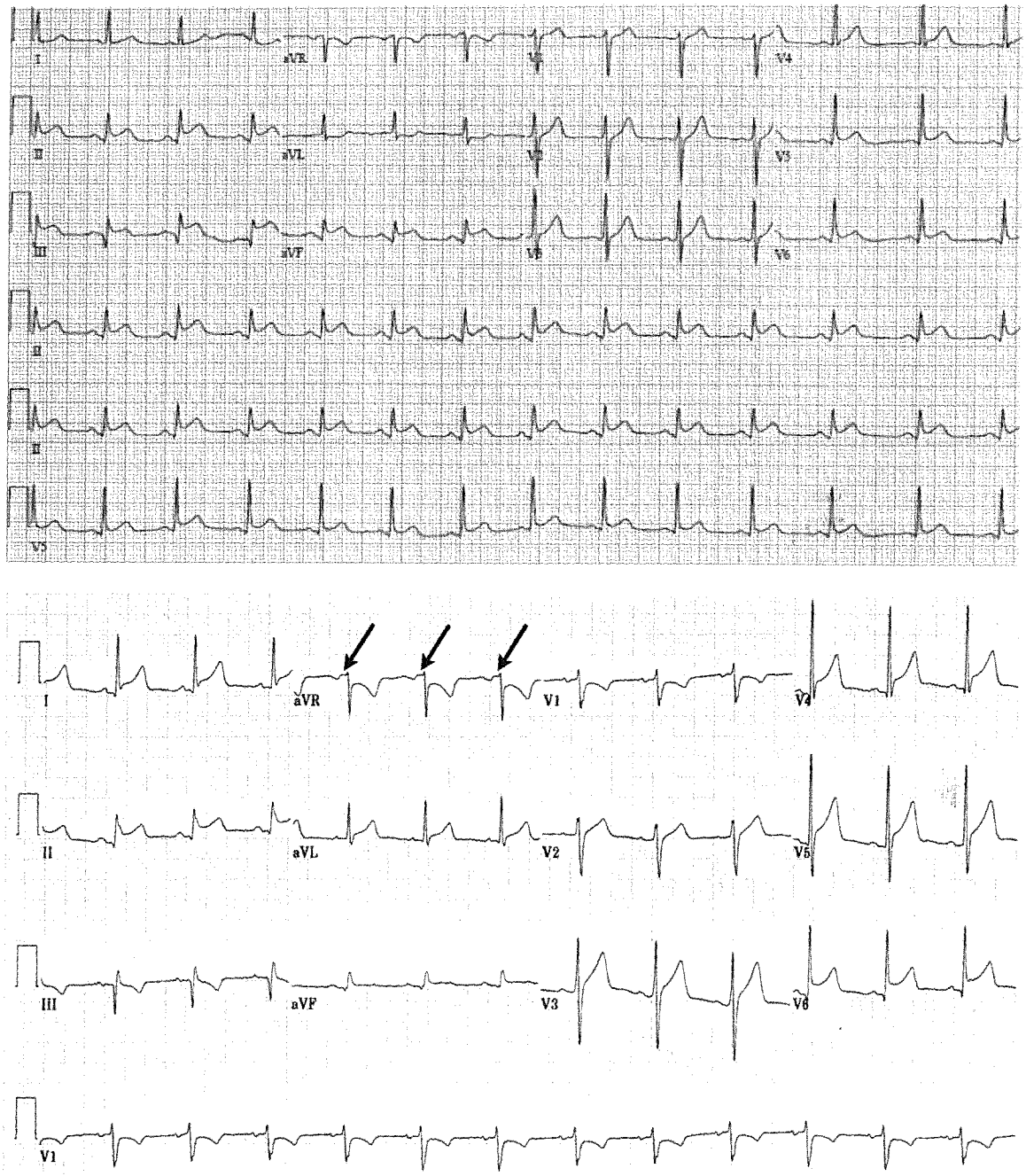

FIGURE 8. *Top panel:* Electrocardiogram showing findings consistent with an acute inferior ST-elevation myocardial infarction. Note the ST-segment elevation isolated to the inferior and lateral precordial leads, which is consistent with a single coronary vascular distribution (that is, the right coronary artery in this case). *Bottom panel:* Electrocardiogram demonstrating acute pericarditis with diffuse ST-segment elevation and slight PR-segment depression (see lead I) and reciprocal PR-segment elevation ("knuckle sign") in lead aVR (*arrows*).

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(such as with anterior MI), thrombolytic therapy should be considered. Characteristics of the various thrombolytic agents are presented in **Table 7**.

In addition to thrombolytic therapy, all patients without a specific contraindication should receive a loading dose of aspirin (162-325 mg) as well as intravenous heparin, enoxaparin, or fondaparinux. Clopidogrel loading has been demonstrated to increase rates of vessel patency and is also recommended in this setting.

After thrombolytic therapy is administered, the ECG should be monitored at 60 minutes and 90 minutes to confirm at least 50% improvement in maximal ST-segment

TABLE 7. Characteristics of Thrombolytic Agents Commonly Used in the Treatment of ST-Elevation Myocardial Infarction

Characteristic	Streptokinase	Alteplase	Reteplase	Tenecteplase
Dose	1.5 megaunits over 30-60 min	Up to 100 mg in 90 min (based on weight)[a]	10 units × 2 (30 min apart), each over 2 min	30-50 mg based on weight[b]
Bolus administration	No	No	Yes	Yes
Antigenic	Yes	No	No	No
Allergic reactions (hypotension most common)	Yes	No	No	No
Systemic fibrinogen depletion	Marked	Mild	Moderate	Minimal
TIMI flow grade 3	~30%	~50%	~60%	~60%
TIMI flow grade 2/3	~55%	~75%	~83%	~83%
Rate of intracerebral hemorrhage	~0.4%	~0.4%-0.7% (100-mg dose)	~0.8%	~0.9%
Fibrin specificity	None	++	+	+++
Fibrin affinity	None	+++	+	++++
Cost per recommended MI dose (U.S.)[c]	$562.50	$3404.78	$2872.50	$2917.48 for 50 mg

[a]Bolus 15 mg, infusion 0.75 mg/kg × 30 min (maximum 50 mg), then 0.5 mg/kg not to exceed 35 mg over the next 60 min to an overall maximum of 100 mg.

[b]30 mg for weight <60 kg (132 lb), 35 mg for 60-69 kg (132-152 lb), 40 mg for 70-79 kg (154-174 lb), 45 mg for 80-89 kg (176-196 lb), and 50 mg for 90 kg (198 lb) or more.

[c]Department of Health and Human Services, Office of Inspector General. Red Book, 2005. Available at https://oig.hhs.gov/publications/docs/redbook/Red%20Book%202005.pdf.

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elevation. One quarter to one third of patients do not achieve reperfusion, particularly if time from symptom onset to receipt of thrombolytic therapy is delayed. Owing to the potential for thrombolytic failure, patients with STEMI treated with thrombolytic therapy should be subsequently transferred to a PCI-capable hospital. Rescue PCI is associated with improved outcomes compared with conservative management in the event of failed reperfusion. Coronary angiography is generally recommended in all patients before discharge, even after successful thrombolysis. Patients with STEMI who present with heart failure or cardiogenic shock, or who develop these complications after thrombolytic therapy, are a particularly high-risk group (mortality rate >50%) and should be immediately transferred to a PCI-capable center.

Although thrombolytic therapy is potentially life-saving, it carries significant risks, primarily related to bleeding. Intracerebral hemorrhage is the most catastrophic complication of thrombolytic therapy and occurs in approximately 1% of patients. Relative and absolute contraindications to thrombolytic therapy are listed in **Table 8**.

Primary Percutaneous Coronary Intervention

PPCI refers to the process by which an emergency medical provider activates a team of providers to initiate emergent coronary angiography and PCI in patients with STEMI. Ideally, the time from first medical contact until PCI is less than 90 minutes. The amount of myocardial salvage is directly related to ischemic time; therefore, the quicker the artery can be opened, the better the final outcome. Because the rates of achieving vessel patency are higher and more reliable with

TABLE 8. Contraindications to Thrombolytic Therapy for ST-Elevation Myocardial Infarction

Absolute Contraindications
Any previous intracerebral hemorrhage
Known cerebrovascular lesion (e.g., arteriovenous malformation)
Ischemic stroke within 3 mo
Suspected aortic dissection
Active bleeding or bleeding diathesis (excluding menses)
Significant closed head or facial trauma within 3 mo
Relative Contraindications
History of chronic, severe, poorly controlled hypertension
Severe uncontrolled hypertension on presentation (SBP >180 mm Hg or DBP >110 mm Hg)[a]
History of ischemic stroke (>3 mo), dementia, or known intracranial abnormality
Traumatic or prolonged (>10 min) CPR or major surgery (<3 wk)
Recent (within 2-4 wk) internal bleeding
Noncompressible vascular puncture site
For streptokinase/anistreplase: previous exposure (>5 d) or previous allergic reaction to these agents
Pregnancy
Active peptic ulcer disease
Current use of anticoagulants: the higher the INR, the higher the bleeding risk

CPR = cardiopulmonary resuscitation; DBP = diastolic blood pressure; SBP = systolic blood pressure.

[a]Thrombolytic therapy can be considered if SBP can be reduced to <140 mm Hg and DBP to <90 mm Hg with initial medical therapy.

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PPCI than with thrombolysis, PPCI is the preferred method of treating STEMI when the patient presents to a hospital capable of performing PCI or can be transferred from an index hospital to a PCI-capable center quickly (time from first medical contact to PPCI of ≤120 minutes). Once the patient is in the catheterization suite, the initial focus is on quickly restoring flow to the acutely occluded artery. There is ongoing debate as to the timing and potential benefit of PCI of nonculprit vessels.

Patients undergoing PPCI should receive aspirin and heparin before thrombolytic therapy. During the procedure, patients generally receive intravenous heparin (with or without glycoprotein IIb/IIIa blockade) or bivalirudin. Most patients undergo stenting and receive loading doses of additional antiplatelet drugs ($P2Y_{12}$ inhibitors) (**Table 9**). Clopidogrel has historically been the most commonly prescribed $P2Y_{12}$ inhibitor. Compared with clopidogrel, prasugrel is more potent, has a quicker onset of action, and has a lower risk for thrombotic complications; however, prasugrel is also associated with an increased risk for bleeding. Prasugrel should not be used in patients with a history of stroke and those aged 75 years and older, and dosing must be adjusted for those weighing less than 60 kg (132 lb). Ticagrelor, a nonthienopyridine $P2Y_{12}$ inhibitor, also has greater potency and faster onset of platelet inhibition than clopidogrel. In the PLATO trial of patients with ACS, ticagrelor treatment resulted in significantly lower mortality rates compared with clopidogrel. Ticagrelor causes subjective dyspnea in some patients; this symptom is usually self-limited but occasionally causes drug discontinuation.

Medical Therapy

Medical therapies for the treatment of patients with ACS are summarized in **Table 10**.

All patients presenting with STEMI should receive aspirin and anticoagulation therapy. Regardless of the selected reperfusion strategy, patients should also be treated with a $P2Y_{12}$ inhibitor. Clopidogrel is indicated in patients receiving thrombolytic therapy, whereas clopidogrel, prasugrel, and ticagrelor are options for those undergoing PPCI (see Table 9).

β-Blockers decrease myocardial oxygen demand, reduce the incidence of ventricular arrhythmias, and improve long-term survival in patients with STEMI. Current guidelines suggest initiating these drugs within 24 hours of presentation. The COMMIT/CCS-2 trial demonstrated that intravenous metoprolol reduced the early risk for reinfarction and ventricular fibrillation in patients with acute MI but also resulted in a higher rate of cardiogenic shock. β-Blockers should not be given if there is evidence of hypotension, cardiogenic shock, pulmonary congestion, or atrioventricular block. In these cases, β-blockers may be withheld initially and introduced once the patient is stabilized.

ACE inhibitors are indicated in most patients with STEMI and particularly in patients with impaired left ventricular function, heart failure, or anterior wall infarction. ARBs may be used if the patient is intolerant of ACE inhibitors. These agents have shown significant early benefit and should be administered within the first 24 hours of presentation, assuming there are no contraindications.

Eplerenone, an aldosterone antagonist, has proved beneficial in patients with STEMI who have an ejection fraction less than or equal to 40% and either heart failure or diabetes; however, the treatment effects were demonstrated only when eplerenone was initiated within 1 week of presentation. Potassium levels must be carefully monitored, particularly in patients with pre-existing kidney dysfunction and those receiving ACE inhibitors or ARBs.

High-intensity statin therapy is indicated in patients with STEMI. Cholesterol levels may be transiently lower around the time of MI, and a low LDL cholesterol level should not dissuade clinicians from prescribing statins.

TABLE 9. $P2Y_{12}$ Inhibitors Used in the Treatment of Patients with Coronary Artery Disease

Drug	Indications	Loading Dose	Maintenance Dose	Adverse Effects	Contraindications
Clopidogrel	Stable CAD treated with PCI ACS	300-600 mg	75 mg/d	Increased bleeding risk	Known allergy to the drug
Ticagrelor	ACS	180 mg	90 mg twice daily[a]	Increased bleeding risk, dyspnea	Known allergy to the drug
Prasugrel	ACS treated with PCI[b]	60 mg	10 mg/d[c]	Increased bleeding risk	Known allergy to the drug, prior transient ischemic attack/ stroke, age ≥75 y

ACS = acute coronary syndrome; CAD = coronary artery disease; PCI = percutaneous coronary intervention.

[a]Ticagrelor should be used with aspirin, 81 mg/d.

[b]Prasugrel should not be loaded "upstream" (before catheterization).

[c]Prasugrel, 5 mg/d, should be considered for those weighing less than 60 kg (132 lb) or at moderate to high risk for bleeding (e.g., patients with significant kidney function impairment).

TABLE 10. Medical Therapy for Acute Coronary Syndromes

Medication	Drugs in Class	Dosage	Indications	Comments
Antiplatelet Medications				
Aspirin	N/A	81-162 mg/d	All patients with ACS, unless intolerant or allergic	
Clopidogrel	N/A	75 mg/d	$P2Y_{12}$ inhibitor in combination with aspirin is indicated in all patients after ACS for at least 1 y	Clopidogrel is recommended as an alternative for patients with intolerance or allergy to aspirin
Prasugrel	N/A	5-10 mg/d	$P2Y_{12}$ inhibitor in combination with aspirin is indicated only in patients in whom PCI is performed for at least 1 y	Contraindicated with age >75 y or history of stroke/TIA Dosage adjustment to 5 mg/d should be considered for patients weighing <60 kg (132 lb)
Ticagrelor	N/A	90 mg twice daily	$P2Y_{12}$ inhibitor in combination with aspirin is indicated in all patients after ACS for at least 1 y	More rapid onset of action; does not require first-pass hepatic metabolism; no known genetic polymorphisms Decreased effectiveness with aspirin doses ≥100 mg
Cardioprotective Medications				
β-Blockers	Atenolol, metoprolol, carvedilol, nebivolol	Variable	All patients with prior MI or LV systolic dysfunction	Avoid in patients with cardiogenic shock, hypotension, or conduction disturbances
ACE inhibitors	Benazepril, captopril, enalapril, fosinopril, perindopril, trandolapril, lisinopril, ramipril, quinapril	Variable	All patients with LV systolic dysfunction, hypertension, diabetes mellitus, or kidney disease	Particularly beneficial in patients with anterior MI
Angiotensin receptor blockers	Losartan, valsartan, olmesartan, candesartan, irbesartan, telmisartan	Variable	All patients with LV systolic dysfunction, hypertension, diabetes, or kidney disease who are intolerant of ACE inhibitors	Should not be used in patients already taking an ACE inhibitor
Aldosterone inhibitor	Eplerenone	25-50 mg/d	STEMI patients with LVEF ≤40% and either clinical heart failure or diabetes	Caution is advised in patients with chronic kidney disease or hyperkalemia
High-intensity statin therapy	Atorvastatin	40-80 mg/d	For all patients with evidence of coronary artery disease and age ≤75 y	
	Rosuvastatin	20-40 mg/d		
Moderate-intensity statin therapy	Atorvastatin	10-20 mg/d	For all patients with evidence of coronary artery disease and age >75 y or otherwise intolerant of high-intensity statin therapy	
	Rosuvastatin	5-10 mg/d		
	Simvastatin	20-40 mg/d		
	Pravastatin	40-80 mg/d		
	Lovastatin	40 mg/d		
	Fluvastatin	40 mg twice daily		
Antianginal Medications				
Nitroglycerin	Nitrostat (SL)	0.4 mg every 5 min for a total of three doses	As part of multimodality treatment for ongoing chest pain	Avoid with SBP <90 mm Hg or ≥30 mm Hg below baseline, bradycardia, tachycardia, RV infarction, PDE-5 inhibitor use within the last 24-48 h, HCM, or severe AS
	Nitronal (IV)	Initial IV infusion rate of 5-10 µg/min	For persistent chest pain following three SL doses and as part of multimodality treatment for heart failure, hypertension	

(Continued on the next page)

TABLE 10. Medical Therapy for Acute Coronary Syndromes *(Continued)*

Medication	Drugs in Class	Dosage	Indications	Comments
Nondihydropyridine calcium channel blockers	Diltiazem, verapamil	Variable	Patients with NSTE-ACS who are intolerant of β-blockers or with angina refractory to nitrates and β-blockers	No benefit in STEMI patients May worsen clinical status with coincidental heart failure or LV dysfunction Avoid with evidence of heart failure, cardiogenic shock, or conduction abnormalities

ACS = acute coronary syndrome; AS = aortic stenosis; HCM = hypertrophic cardiomyopathy; IV = intravenous; LV = left ventricular; LVEF = left ventricular ejection fraction; MI = myocardial infarction; N/A = not applicable; NSTE-ACS = non-ST-elevation acute coronary syndrome; PCI = percutaneous coronary intervention; PDE = phosphodiesterase; RV = right ventricular; SBP = systolic blood pressure; SL = sublingual; STEMI = ST-elevation myocardial infarction; TIA = transient ischemic attack.

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Intravenous nitroglycerin can be used to treat patients with STEMI and hypertension or heart failure; however, there is no role for the routine use of oral nitrates in the convalescent phase of STEMI. Calcium channel blockers and ranolazine also have no role in treating patients with STEMI.

Complications of STEMI

Arrhythmias commonly occur in the peri-infarct setting. Atrial fibrillation, which affects up to 10% to 20% of patients with STEMI, complicates management and may cause hemodynamic instability. Ventricular tachycardia and fibrillation may also occur during MI or after reperfusion. Repetitive and sustained bouts of postinfarct ventricular arrhythmias may warrant consultation with an electrophysiologist, as predischarge implantable cardioverter-defibrillator therapy has a role in treating late arrhythmias complicating STEMI. Routine suppression of ventricular ectopy with antiarrhythmic agents is generally not recommended and is associated with increased risk for ventricular arrhythmias. In particular, accelerated idioventricular rhythm, which commonly arises after reperfusion, is generally benign and transient, requiring no treatment. Atrioventricular blocks, including Wenckebach and complete heart block, may occur after inferior MIs. Temporary transvenous pacemakers are sometimes necessary, but permanent pacing is rarely required. Benign forms of vagally mediated heart block must be differentiated from Mobitz type 2 second-degree atrioventricular block, which is more frequently observed with anterior infarction and damage to the conduction system. Mobitz type 2 block may progress to complete heart block and necessitates permanent pacing.

Cardiogenic shock is a common complication of STEMI. It typically results from a large anterior MI due to severely reduced left ventricular systolic function and carries a mortality rate of 50% to 80%. Patients with cardiogenic shock, particularly those younger than 75 years, have a higher rate of survival if they receive emergent revascularization. In these cases, an intra-aortic balloon pump (IABP) or left ventricular assist device may be implanted temporarily, although limited data support their benefits in cardiogenic shock. Once the patient is stabilized, weening the patient from mechanical and inotropic support and gentle uptitration of afterload-reducing agents, such as captopril, can be attempted. β-Blockers should be avoided initially and can be introduced once the patient is stabilized. Diuretics should be used to treat pulmonary vascular congestion.

Approximately 10% to 20% of cases of anterior STEMI are complicated by left ventricular apical thrombus. Although not supported by rigorous studies, anticoagulation with warfarin is generally recommended for at least 3 months to reduce the risk for systemic embolization.

Rates of mechanical complications after STEMI, including left ventricular free wall rupture, right ventricular infarction, ventricular septal defect (VSD), and acute mitral regurgitation, are low; however, clinicians must be able to recognize these complications, given their highly morbid nature. Free wall rupture produces sudden-onset chest pain or syncope with rapid progression to pulseless electrical activity. It is more common in older adults, women, patients with anterior MI, those receiving anti-inflammatory agents, and patients with a significant delay in receiving reperfusion therapy (>12 hours). Surgery should be considered, but mortality rates, even among those who survive to the operating room, are very high.

Right ventricular infarction, typically indicated by ST-segment elevation in right-sided ECG leads (V_1 and V_4R), can complicate right coronary artery occlusion. It presents with hypotension, elevated jugular venous pressure, and an absence of findings on lung auscultation. Right ventricle pump dysfunction causes inadequate filling of the left ventricle, resulting in shock. Treatments include volume resuscitation and positive inotropes (dobutamine or dopamine) to bridge the right ventricle to recovery, which generally takes 2 to 3 days. Nitrates are contraindicated because they may worsen hypotension by reducing preload.

Acquired VSD from septal wall rupture may complicate inferior or anterior STEMI. With inferior STEMI, the VSD tends to be located in the inferior basal septum, whereas

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anterior STEMI generally leads to an apical VSD. VSDs typically occur within 3 to 5 days of STEMI presentation. Patients present with worsening heart failure and shock, and a harsh holosystolic murmur may be heard at the left lower sternal border. The diagnosis is confirmed with echocardiography. Although initial management may include afterload reduction with medical therapy and IABP support, the mortality rate in patients with medically treated postinfarct VSDs approaches 100%. Surgical closure should be considered; however, the mortality rate in surgical series is still high (approximately 50%). Patch closure can be very difficult owing to the necrotic tissue and inability to find viable myocardium to suture and patch. Percutaneous closure with a VSD occluder device is possible but often unsuccessful because of the nature of the defect, and residual shunting around the device is common.

Acute severe mitral regurgitation may occur as a result of papillary muscle rupture. Most often, the posteromedial papillary muscle ruptures with right coronary artery occlusion. This complication tends to occur several days after STEMI. Afterload reduction and IABP placement may be tried, but urgent surgical intervention is usually necessary. Acute severe mitral regurgitation may also result from left ventricular dysfunction and is often related to an inferior MI with restriction of the posterior mitral leaflet, termed functional ischemic mitral regurgitation. Ischemic mitral regurgitation is treated with revascularization and medical therapy.

KEY POINTS

- Primary percutaneous coronary intervention is preferred to thrombolytic therapy for the treatment of ST-elevation myocardial infarction.
- If primary percutaneous coronary intervention (PPCI) is not available within 120 minutes of first medical contact, patients with ST-elevation myocardial infarction should receive thrombolytic therapy and be urgently transferred to a PPCI-capable center.
- β-Blockers reduce the incidence of ventricular arrhythmias and improve long-term survival in patients with ST-elevation myocardial infarction; however, these agents are contraindicated when signs or symptoms of cardiogenic shock are present.
- All patients presenting with an ST-elevation myocardial infarction should be treated with aspirin, anticoagulation therapy, and a $P2Y_{12}$ inhibitor.

Non-ST-Elevation Acute Coronary Syndromes

NSTE-ACS is a common presentation of CAD. The chest pain associated with an NSTE-ACS is generally acute, is new in onset, and often occurs with rest or minimal exertion. The pathogenesis is plaque rupture within a coronary artery and transient or incomplete occlusion of the vessel. NSTEMI is differentiated from unstable angina by the presence of elevated serum cardiac biomarkers at the time of evaluation.

Risk Stratification

Many treatment options are available for patients with NSTE-ACS, and risk stratification tools can be used to aid in diagnostic and therapeutic decision making. The two most commonly used risk scores are the TIMI and GRACE risk models. The simpler of the two models, the TIMI risk score, predicts 14-day death, recurrent MI, and urgent revascularization rates (**Table 11**). The GRACE risk score (available at www.gracescore.org) is more complex, requiring a nomogram to calculate. It incorporates physical examination findings (heart rate, blood pressure, Killip class), clinical features (age, cardiac arrest at admission), electrocardiographic findings (ST-segment deviation), and biomarker variables (creatinine levels, elevated cardiac enzymes) to predict in-house and postdischarge death and MI risk. These scoring systems are useful in determining which patients may benefit most from more aggressive strategies, such as anticoagulation or an early invasive approach (**Figure 9**). An elevated troponin level is itself a powerful predictor of outcomes and identifies patients who will benefit from aggressive medical and invasive strategies (coronary angiography).

Medical Therapy

Medical therapies for patients with NSTE-ACS are similar to those for other ACS presentations; however, some unique features in this patient population are highly relevant to the

TABLE 11. TIMI Risk Score for Non-ST-Elevation Acute Coronary Syndromes

Prognostic Variables (1 Point Each)	
Age ≥65 y	
≥3 Traditional CAD risk factors[a]	
Documented CAD with ≥50% diameter stenosis	
ST-segment deviation	
≥2 Anginal episodes in the past 24 h	
Aspirin use in the past wk	
Elevated cardiac biomarkers (creatine kinase MB or troponin)	
TIMI Risk Score (Sum of Prognostic Variables)	
0-2	Low risk
3-4	Intermediate risk
5-7	High risk

CAD = coronary artery disease; TIMI = thrombolysis in myocardial infarction.

[a]Hypertension, hypercholesterolemia, diabetes mellitus, being a current smoker, family history of CAD.

Information from Antman EM, Cohen M, Bernink PJ, McCabe CH, Horacek T, Papuchis G, et al. The TIMI risk score for unstable angina/non-ST elevation MI: a method for prognostication and therapeutic decision making. JAMA. 2000;284:835-42. [PMID: 10938172]

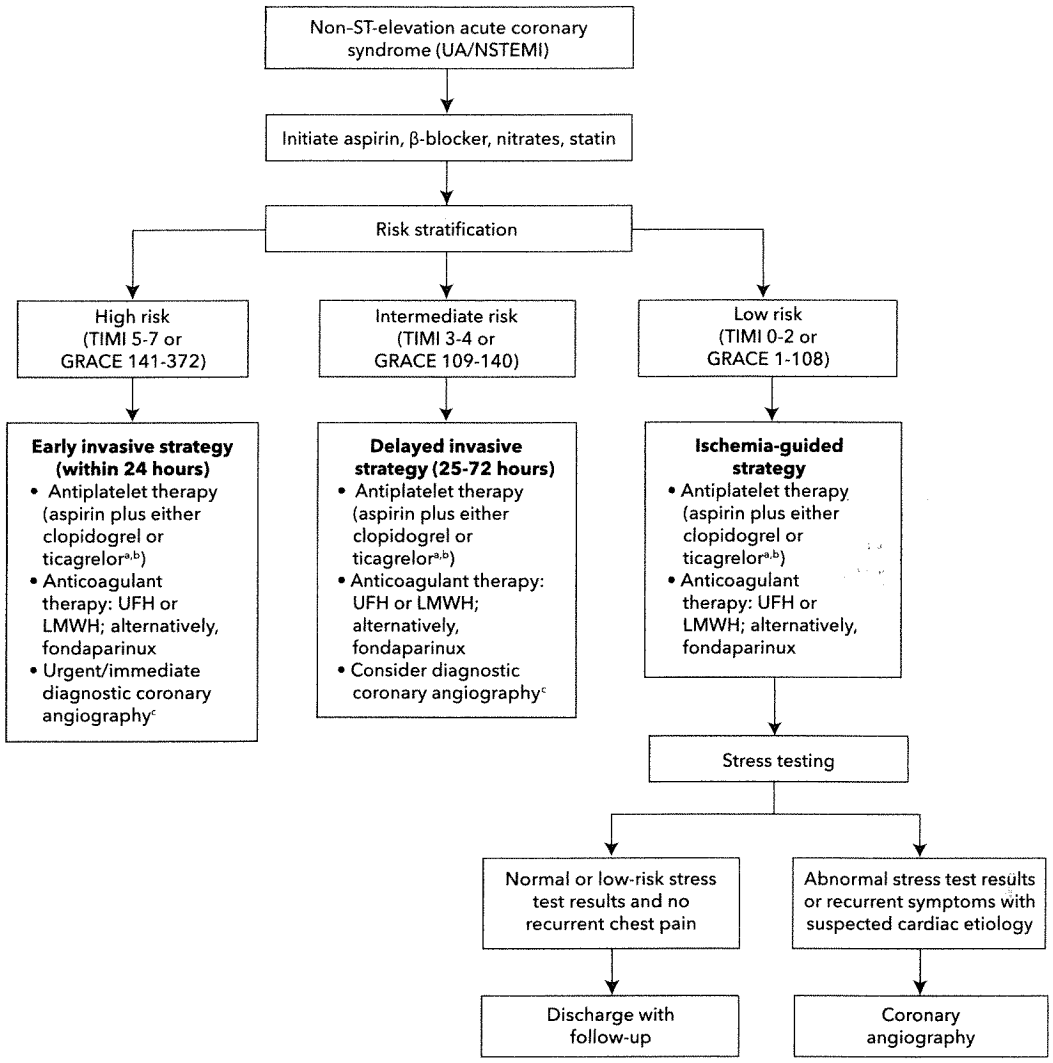

FIGURE 9. Initial management of non-ST-elevation acute coronary syndromes. LMWH = low-molecular-weight heparin; NSTEMI = non-ST-elevation myocardial infarction; UA = unstable angina; UFH = unfractionated heparin.

[a]Clopidogrel or ticagrelor may be dosed at the time of hospital admission and diagnosis of acute coronary syndrome.

[b]If coronary artery bypass grafting is required, clopidogrel or ticagrelor should be stopped, and surgery should be delayed for at least 5 days.

[c]If the decision is made to withhold a $P2Y_{12}$ inhibitor until the time of angiography and a $P2Y_{12}$ inhibitor is desired, clopidogrel, ticagrelor, or prasugrel can be initiated.

Recommendations based on Amsterdam EA, Wenger NK, Brindis RG, Casey DE Jr, Ganiats TG, Holmes DR Jr, et al; ACC/AHA Task Force Members. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014;130:2354-94. [PMID: 25249586] doi:10.1161/CIR.0000000000000133

CONT. treatment of this condition. Notably, thrombolytic therapy is not beneficial in patients with NSTE-ACS and is not recommended. Medical therapies for the treatment of NSTE-ACS are summarized in Table 10.

Antiplatelet Medications

Aspirin (162-325 mg) should be administered at presentation to all patients with definite or likely NSTE-ACS, followed by a daily dose of 81 to 162 mg. Early clopidogrel loading has been recommended in patients with NSTEMI; however, the optimal timing for loading of other oral antiplatelet agents is unclear. Prasugrel loading before coronary angiography is not beneficial. Clopidogrel or ticagrelor therapy is recommended for 1 year after NSTE-ACS presentation, regardless of the treatment strategy. Prasugrel is indicated only in patients treated with PCI. Evidence supports continuing DAPT beyond 1 year in patients at high risk for recurrent vascular events (such as those with depressed left ventricular function, saphenous vein graft stenting, or diabetes) in whom the benefit exceeds the bleeding risk.

The use of intravenous glycoprotein IIb/IIIa inhibitors (eptifibatide, tirofiban) has decreased over the past decade. Although these drugs had been shown to improve outcomes in patients with NSTE-ACS (particularly higher-risk and troponin-positive patients), subsequent study demonstrated

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no benefit of upstream glycoprotein IIb/IIIa blockade and an increased risk for bleeding. These agents are generally reserved for use during PCI; however, given the advent of quicker-acting and more potent oral antiplatelet agents, administration of glycoprotein IIb/IIIa inhibitors in the setting of PCI has also significantly declined.

Anticoagulant Medications

Patients with definite NSTE-ACS should undergo anticoagulation. Intravenous unfractionated heparin and subcutaneous enoxaparin are most commonly used. Intravenous heparin is preferred in patients with kidney dysfunction because enoxaparin and similar agents are partially cleared by the kidneys. For patients proceeding to the catheterization laboratory, anticoagulant therapy should be provided until revascularization with PCI or CABG. In medically treated patients, anticoagulation is recommended for at least 48 hours and is generally continued until discharge.

Antianginal Medications

β-Blockers should be administered within 24 hours of NSTE-ACS because these agents reduce ventricular arrhythmias and long-term mortality. β-Blockers are not appropriate for patients with evidence of heart failure or shock at presentation. Likewise, these agents should not be given to patients with bradycardia, heart block, or a PR interval greater than 240 ms on ECG.

Calcium channel blockers are recommended for patients with NSTE-ACS intolerant of β-blocker therapy or in patients with angina symptoms despite therapy with nitrates and β-blockers. The nondihydropyridine calcium channel blockers reduce heart rate, blood pressure, and cardiac contractility, thereby reducing myocardial oxygen demand. However, because of these hemodynamic effects, use of these agents is also contraindicated in the setting of shock, pulmonary edema, or significant conduction disease. Importantly, short-acting dihydropyridine calcium channel blockers are contraindicated, owing to their ability to acutely lower the blood pressure and raise the heart rate.

Nitrates are primarily used to manage angina symptoms in patients with NSTE-ACS. Sublingual nitrates should be administered at presentation to relieve chest pain. For patients with persistent chest pain despite β-blockade, intravenous nitroglycerin can alleviate symptoms, particularly in those with hypertension. Patients receiving nitroglycerin infusions for a prolonged time will often require increased doses due to the development of nitrate tolerance. Nitrates should be avoided in patients who have had recent exposure (within 24-48 hours) to phosphodiesterase type 5 inhibitors such as sildenafil.

Patients with chest pain refractory to antianginal medications should be evaluated for noncardiac causes of chest pain and biomarker elevation, as well as for the possibility of severe underlying CAD or electrocardiographically silent coronary thrombosis.

Lipid-Lowering Medications

Statin therapy reduces mortality and adverse clinical event rates after ACS. High-intensity statin therapy is recommended because it improves outcomes compared with lower-intensity treatment. Initiating statins in the inpatient setting is associated with greater medication adherence. Furthermore, statin preloading before PCI has been associated with lower rates of periprocedural MI.

Invasive Versus Ischemia-Guided Treatment

Immediate invasive treatment (within 2 hours) is recommended for patients with NSTE-ACS who have hemodynamic instability, refractory chest pain, heart failure, or ventricular arrhythmias. In patients with an elevated clinical risk score, significant ST-segment deviation, or elevated cardiac biomarkers, cardiac catheterization is usually performed within 24 hours of presentation. The type of revascularization procedure (PCI or CABG) depends on the results of angiography.

An invasive strategy improves the composite clinical endpoint of death, recurrent MI, and repeat hospitalization compared with an ischemia-guided approach in high-risk and troponin-positive patients with NSTE-ACS. An invasive strategy is the favored approach, with the exception of patients with extensive noncardiac comorbid conditions (such as cancer), in whom the clinical benefits of revascularization may be lower, and patients with acute chest pain unlikely to be related to CAD.

With an ischemia-guided treatment strategy, patients undergo noninvasive stress testing before hospital discharge; cardiac catheterization is reserved for patients with active or intermittent ischemia, including those with angina despite medical therapy or evidence of ischemia on stress testing, and patients at very high clinical risk based on risk score. The ischemia-guided approach is appropriate for low-risk patients (TIMI score <2 or GRACE score <109). H

KEY POINTS

- In patients with a non–ST-elevation acute coronary syndrome, initial risk stratification with the TIMI or GRACE risk scores aids in diagnostic and therapeutic decision making.
- Thrombolytic therapy is not indicated in patients with non–ST-elevation acute coronary syndromes. HVC
- The decision to pursue an invasive approach versus an ischemia-guided approach in patients with a non–ST-elevation acute coronary syndrome depends on the patient's risk for clinical events.
- Dual antiplatelet therapy is indicated for at least 1 year after a non–ST-elevation acute coronary syndrome (NSTE-ACS); clopidogrel and ticagrelor may be used in all patients with NSTE-ACS, whereas prasugrel may be used only in patients treated with percutaneous coronary intervention.

Acute Coronary Syndromes Not Associated with Obstructive Coronary Disease

Elevations in cardiac enzymes, particularly cardiac troponins, coupled with ECG changes provide excellent diagnostic discrimination for ACS. However, conditions not caused by acute coronary plaque rupture can present with similar findings, and treatment of these conditions with antithrombotic agents and revascularization is not beneficial or recommended.

Patients with accelerated hypertension, significant left ventricular hypertrophy, and cardiomyopathies may present with chest pain and elevated cardiac troponin levels caused by elevated left ventricular filling pressures or wall tension rather than plaque rupture. The ECG findings are often abnormal in these patients. Patients with supraventricular tachycardias, which may also dramatically increase the rate-pressure product, often present with chest pain, ST-segment depressions, and elevated cardiac enzyme levels, even if no CAD is present.

Coronary vasospasm is sudden constriction of a coronary artery. It may occur spontaneously or follow use of illicit substances (methamphetamines, cocaine) or prescription drugs (5-fluorouracil, bromocriptine). ECG abnormalities may be nonspecific or mimic STEMI patterns. Coronary vasospasm is a diagnosis of exclusion. Unless the patient has a history of vasospasm, patients often undergo coronary angiography, which may reveal normal findings or slowed coronary flow resulting from microvascular dysfunction. Provocative testing can be performed but is not usually indicated. Patients suspected of having vasospasm (or the related microvascular dysfunction) are usually treated empirically with nitrates and/or calcium channel blockers.

Takotsubo cardiomyopathy, alternatively termed stress cardiomyopathy or apical ballooning syndrome, is a relatively uncommon form of ACS (see Heart Failure). Patients present with acute chest pain, ECG changes (often ST-segment elevations), and elevated cardiac enzyme levels. Takotsubo cardiomyopathy most commonly occurs in women, and there is often, but not always, an antecedent psychological or physical stressor. Patients may initially be diagnosed with STEMI but found to have no significant coronary stenosis at the time of cardiac catheterization. Systolic apical ballooning and notable sparing of the base of the heart on echocardiography or ventriculography are characteristic of this syndrome.

Cardiac syndrome X is a poorly defined condition characterized by anginal chest pain in the presence of angiographically normal coronary arteries or insignificant CAD (<50% stenosis). Cardiac syndrome X is a frequent cause of chest pain syndromes in women, and patients often present without traditional risk factors for CAD. Several hypotheses have been proposed to explain the pathogenesis of this syndrome. One of the most accepted centers on microvascular dysfunction as the cause. Patients may be treated with β-blockers, calcium channel blockers, and nitrates.

Patients with chronic inflammatory muscle diseases or neuromuscular diseases may have elevated levels of cardiac troponin T due to expression of this enzyme in skeletal muscle. The cardiac troponin I level is normal in these cases, which can be helpful in differentiating ACS from these other entities.

Care After an Acute Coronary Syndrome

All patients with ACS should continue aspirin, preferably 81 mg/d, indefinitely. DAPT is recommended for at least 1 year (see Table 10). There is some evidence for extending DAPT beyond 1 year in stented and medically treated patients; however, the decision to prolong therapy should be individualized, with the risk for bleeding weighed against the risk for thrombosis. Statin therapy should continue indefinitely. β-Blockade and ACE inhibitor therapy should also be continued indefinitely in patients with left ventricular dysfunction; continuation of these medications is reasonable in patients with normal left ventricular function. Guidelines recommend avoiding NSAIDs if possible, owing to the increased cardiovascular risk associated with these drugs. Patients should be referred for cardiac rehabilitation, a medically observed exercise program, to improve functional capacity and risk factor profiles.

Management of Coronary Artery Disease in Special Populations

Women

Clinical Presentation

Women usually develop ischemic heart disease at an older age than men and more commonly present with stable CAD than an ACS. In women with typical angina symptoms, nonobstructive coronary stenoses are present on coronary angiography in more than 50% of cases, and microvascular dysfunction (endothelium-dependent or endothelium-independent) is thought to be a predominant cause of symptoms in these patients. In women with acute MI, the predominant symptom is chest pain or pressure; however, women can often have atypical symptoms, such as fatigue, dyspnea, nausea, or abdominal symptoms.

Several unique manifestations of cardiovascular disease, including spontaneous coronary artery dissection, takotsubo cardiomyopathy, and coronary vasospasm, occur primarily in women. Spontaneous coronary artery dissection is a common cause of chest pain among younger women who present with ACS. In many cases, spontaneous coronary artery dissection occurs in the peripartum period and is thought to be caused by hormonal changes, although the true cause is unknown. Given the preponderance of young women with this condition, minimizing radiation exposure and avoiding invasive angiography are recommended. This can typically be achieved with the use of supportive care with or without CT angiography. In severe cases, vessel occlusion causes STEMI and necessitates emergent revascularization.

Evaluation and Treatment

Noninvasive stress testing for the evaluation of CAD symptoms has a lower sensitivity and specificity in women than in men,