Testing in Cardiology), reducing both unnecessary stenting and the need for urgent revascularization.

Percutaneous Coronary Intervention

Percutaneous coronary intervention (PCI) comprises several different catheter-based techniques to improve coronary blood flow by relieving coronary obstruction. Following early experience with balloon angioplasty and bare metal stenting, most PCI procedures currently involve second-generation drug-eluting stent placement, which reduces the risk for in-stent restenosis compared with bare metal stenting.

PCI is indicated to relieve symptoms in patients with medically refractory angina, those unable to tolerate optimal medical therapy, and those with high-risk features on noninvasive testing. PCI has not been shown to be superior to guideline-directed medical therapy in reducing the risk for death or MI in patients with stable angina with or without diabetes.

Coronary Artery Bypass Graft Surgery

Coronary artery bypass grafting (CABG) with optimal medical therapy is generally recommended for patients with multivessel CAD because it results in decreased recurrence of angina, lower rates of MI, and fewer repeat revascularization procedures compared with PCI or medical therapy alone, especially when arterial (internal mammary artery) conduits are utilized. CABG is associated with improved survival in patients with left main or three-vessel CAD and is indicated in those with multivessel disease and diabetes. CABG also improves 10-year survival compared with medical therapy alone in patients with severe LV dysfunction. Although myocardial viability is associated with improved survival and ventricular recovery following revascularization in patients with LV dysfunction, the role of viability testing before revascularization has not been established as a predictor of outcome.

After Revascularization

Aspirin is recommended indefinitely after revascularization. The addition of a $P2Y_{12}$ inhibitor to aspirin (dual antiplatelet therapy [DAPT]) is indicated to reduce risk for stent thrombosis and remote ischemic events. DAPT duration depends on clinical considerations, including patient presentation and bleeding and ischemic risks.

In patients treated with bare metal stent placement, a minimum of 1 month of DAPT is recommended. Current guidelines recommend treating patients with stable angina with DAPT for at least 6 months without interruption after drug-eluting stent placement, with the option to continue therapy for a longer duration in those with a high risk for thrombosis-related complications (e.g., depressed LV function, saphenous vein graft stenting, and diabetes) and a favorable bleeding profile. In patients at high risk for bleeding, current evidence supports 3 months of DAPT followed by lifelong antiplatelet monotherapy as a reasonable strategy. Although guidelines define minimum DAPT duration, the optimal duration should be individualized according to the patient's risks for thrombotic and bleeding complications.

In patients requiring oral anticoagulation for atrial fibrillation, warfarin or a direct oral anticoagulant (preferred) plus clopidogrel can be considered without aspirin, often after 2 to 4 weeks of triple therapy. In patients with a mechanical valve prosthesis, warfarin plus clopidogrel therapy is reasonable; direct oral anticoagulants are contraindicated in these patients.

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

KEY POINTS

- The primary goals of revascularization in stable ischemic syndromes are to lessen angina and improve quality of life.
- Percutaneous coronary intervention may alleviate angina symptoms but does not decrease mortality or risk for myocardial infarction in patients with stable angina.
- In patients with stable angina who require revascularization, coronary artery bypass graft revascularization is generally preferred to percutaneous coronary intervention in those with left main or three-vessel coronary artery disease or multivessel coronary artery disease plus diabetes mellitus.
- Ten-year survival is improved in patients with coronary artery disease and severe left ventricular dysfunction who undergo coronary artery bypass grafting compared with those who receive medical therapy.
- 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 placement and at least 6 months after drug-eluting stent placement.

Acute Coronary Syndromes

General Considerations

An acute coronary syndrome (ACS) results from acute or subacute plaque rupture or erosion and coronary blood flow impairment, manifesting as acute-onset chest pain or an angina equivalent, often without a clear precipitant. The spectrum of ACS is further characterized by the presence of serum biomarkers of myocardial injury (elevated troponin T or I). Myocardial injury or MI may be related to an atherothrombotic event (type 1) or demand/supply mismatch (type 2) (**Figure 7**).

ST-elevation MI (STEMI) is differentiated from non–ST-elevation acute coronary syndrome (NSTE-ACS) by findings on ECG (**Figure 8**). The hallmark ECG features of STEMI are ST-segment elevation of at least 1 mm in two or more contiguous limb or chest leads, although ST-segment elevation in leads V_2 and V_3 must be at least 2 mm in men and at least

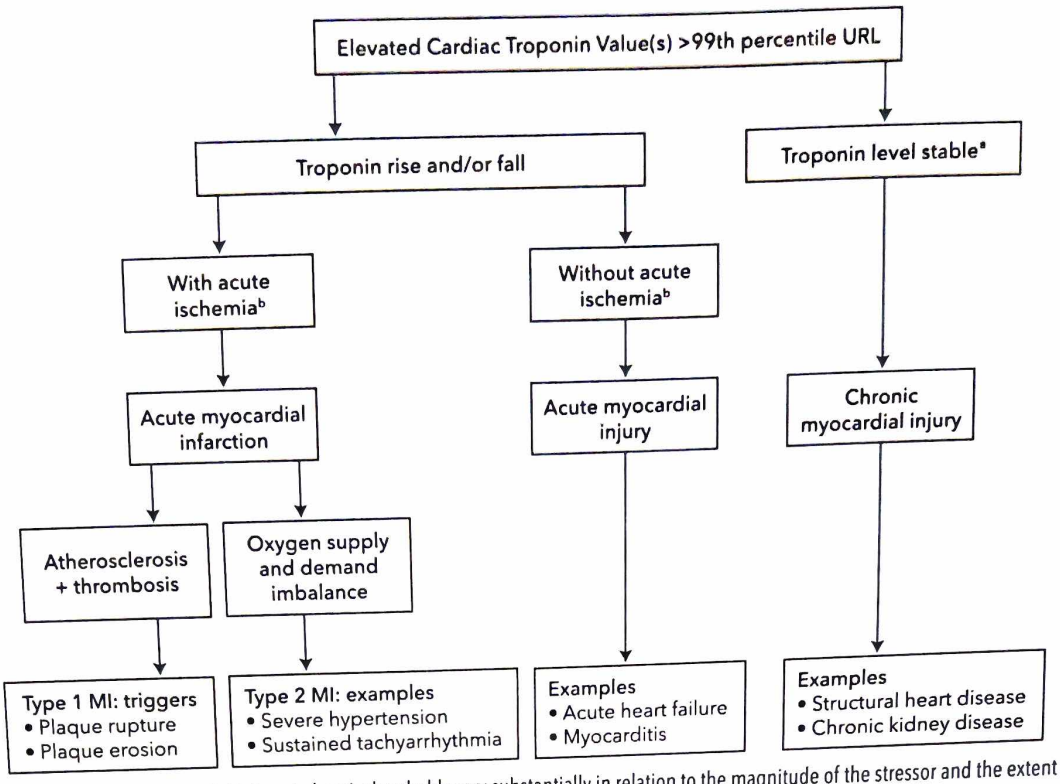

FIGURE 7. A model for interpreting myocardial injury. Ischemic thresholds vary substantially in relation to the magnitude of the stressor and the extent of underlying cardiac disease. MI = myocardial infarction; URL = upper reference limit.

[a]Stable denotes ≤20% variation of troponin values in the appropriate clinical context.

[b]Ischemia denotes signs and/or symptoms of clinical myocardial ischemia.

1.5 mm in women for diagnosis. Posterior MI typically manifests as ST-segment depression greater than 2 mm in the anterior leads (V_1 through V_4) with tall R waves, often with ST-segment elevation in the inferior or lateral leads and ST-segment elevation in posterior leads V_7 through V_9. New bundle branch block may be considered a STEMI equivalent and potentially reflects an acute left anterior descending artery occlusion or extensive injury.

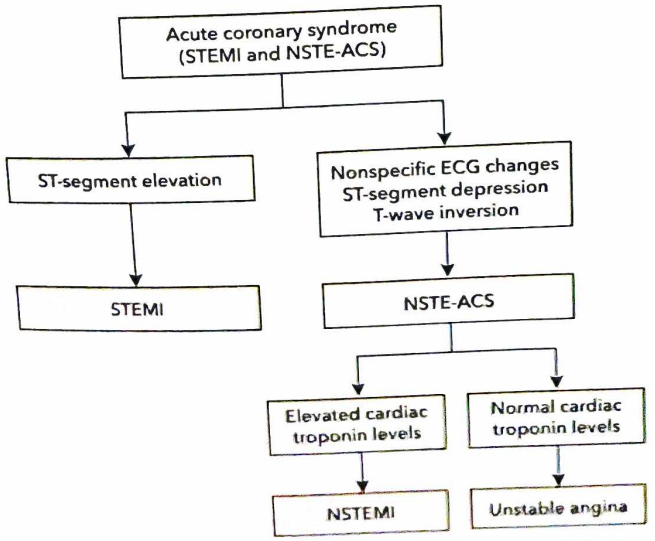

FIGURE 8. Diagnosis of acute coronary syndromes. NSTE-ACS = non–ST-elevation acute coronary syndrome; NSTEMI = non–ST-elevation myocardial infarction; STEMI = ST-elevation myocardial infarction.

NSTE-ACS is categorized according to the presence of biomarkers of cardiac injury (troponin T or I) in the serum. Non–ST-elevation MI 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.

ST-Elevation Myocardial Infarction

Recognition

STEMI typically involves coronary plaque rupture causing platelet adhesion, activation, and aggregation and acute thrombotic occlusion. The sudden transmural myocardial ischemia manifests as ST-segment elevation and signifies the need for rapid initiation of reperfusion therapy (**Figure 9**).

Although the presentation of STEMI is often dramatic and clear, several diagnoses can mimic STEMI. Acute pericarditis presents with acute chest pain and ST-segment elevation suggestive of STEMI. Distinguishing features may include pleuritic or positional pain and diffuse or localized concave ST-segment elevation with corresponding PR segment depression (**Figure 10**). Pericarditis and myopericarditis resulting from viral infections or autoimmune conditions can cause cardiac enzyme release, further confusing the clinical picture and necessitating a

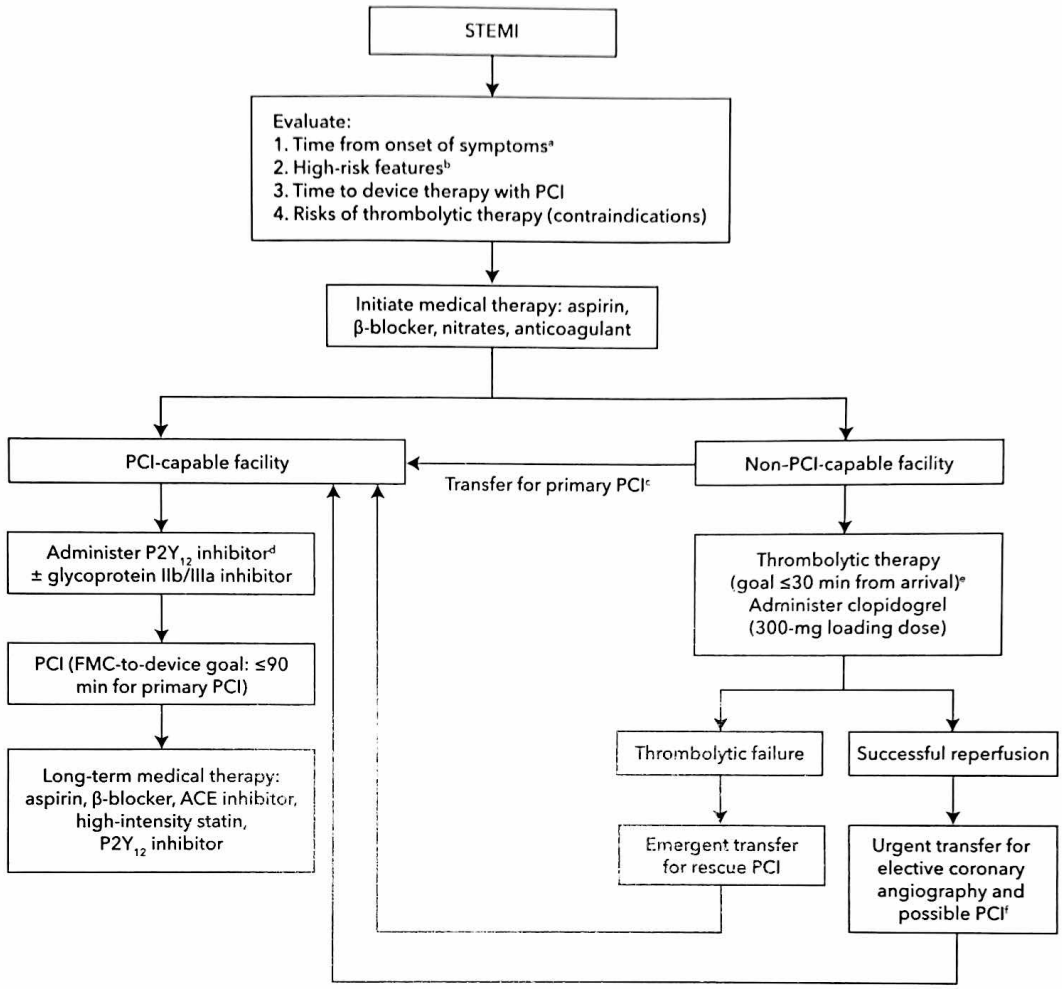

FIGURE 9. Management of ST-elevation myocardial infarction (STEMI). FMC = first medical contact; PCI = percutaneous coronary intervention.

[a]If ≥4 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 therapy administration but is ideally performed within 24 hours.

Recommendations based on O'Gara PT, Kushner FG, Ascheim DD, 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

thorough history, physical examination, and careful study of the ECG and biomarker release patterns.

Acute aortic syndromes can cause ST-segment elevation if the dissection involves the left or right coronary artery and is due to transmural myocardial ischemia. Early recognition is essential for this surgical emergency. Diagnostic clues to aortic dissection include differential blood pressures in the upper extremities, tearing quality of pain with radiation to the back, and mediastinal widening on chest radiograph.

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

Patients with accelerated hypertension, significant LV hypertrophy, and cardiomyopathies may present with chest pain and elevated cardiac troponin levels caused by elevated LV filling pressures or wall tension with associated subendocardial ischemia. The ECG findings are often abnormal in these patients. LV hypertrophy–induced ECG changes may look similar to ST-segment elevation injury currents; however, these changes are typically concave in appearance. Comparison with previous ECG findings is helpful in identifying acute changes.

Patients with supraventricular tachycardias, which may dramatically increase the rate-pressure product, often present

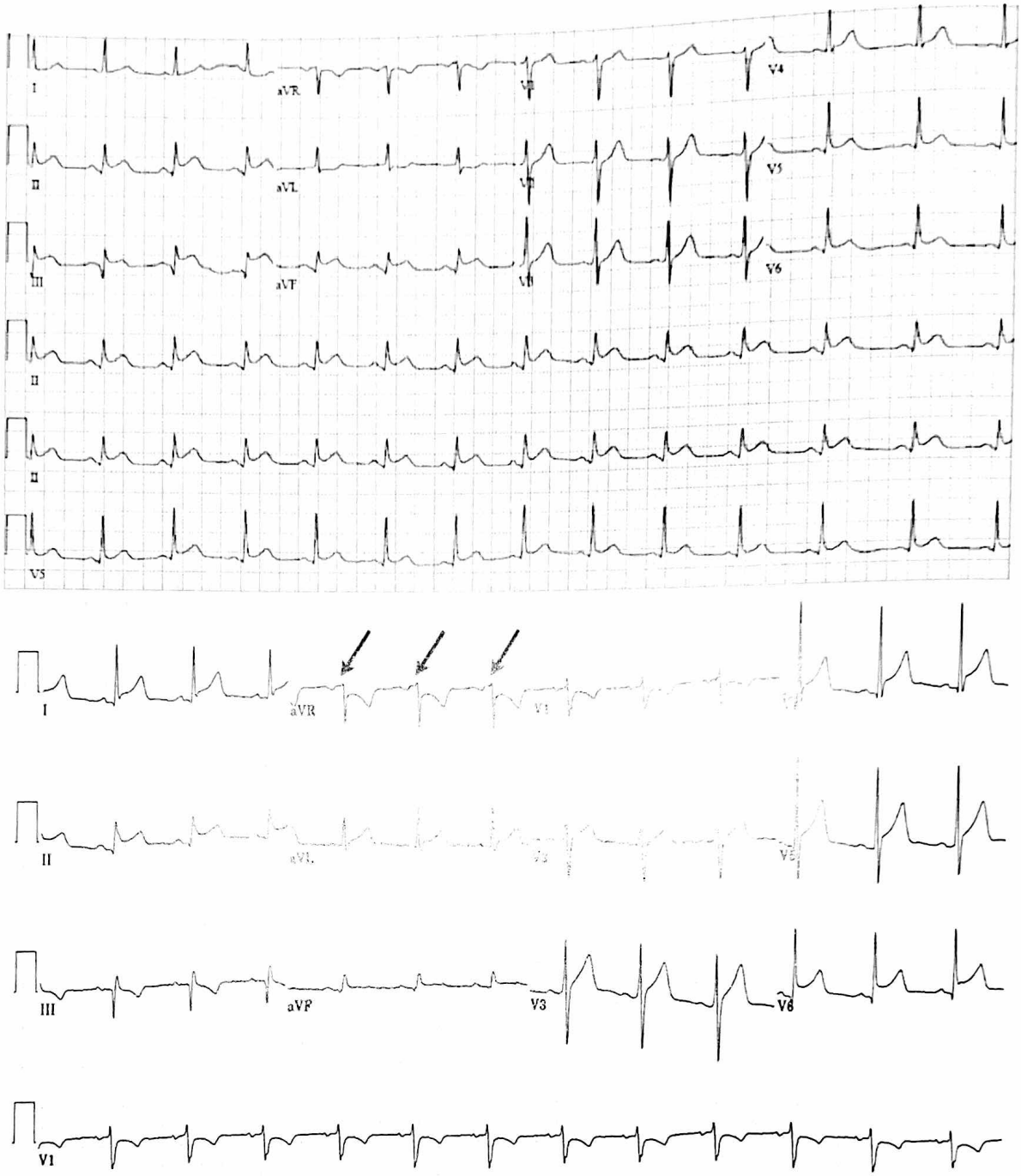

FIGURE 10. *Top panel:* ECG showing findings consistent with an acute inferior ST-elevation myocardial infarction. Note the ST-segment elevation isolated to the inferior and lateral precordial leads, which is consistent with a single coronary vascular distribution (i.e., the right coronary artery). *Bottom panel:* ECG demonstrating acute pericarditis with diffuse ST-segment elevation and slight PR-segment depression (lead I) and reciprocal PR-segment elevation ("knuckle sign") in lead aVR (*arrows*).

with chest pain, ST-segment depression, and elevated cardiac enzyme levels, even if no CAD is present.

Reperfusion

Prompt reperfusion with primary PCI (PPCI) or thrombolytic therapy is indicated in all patients with STEMI who do not have limited life expectancy from other nonreversible disease (see Figure 9). Short times to reperfusion are correlated with improved outcome regardless of reperfusion strategy.

Primary Percutaneous Coronary Intervention

PPCI refers to the process by which an emergency medical provider activates a team of clinicians to initiate emergent coronary angiography and PCI in patients with STEMI. The goal time from first medical contact until PPCI is 90 minutes or less. Because rates of achieving vessel patency are higher and more reliable with PPCI than with thrombolysis, PPCI is the preferred method of treating STEMI when the patient presents to a PCI-capable hospital or can be transferred from an

TABLE 7.* $P2Y_{12}$ Inhibitors Used in the Treatment of Patients With CAD Undergoing PCI

Drug	Indications	Loading Dose	Maintenance Dose	Adverse Effects	Contraindications
Clopidogrel	Stable CAD treated with PCI	300-600 mg	75 mg/d	Increased bleeding risk	Known allergy to the drug
	ACS				
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, previous transient ischemic attack/stroke[d], 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).

[d]Prasugrel carries a black box warning for significant, sometimes fatal, bleeding and is contraindicated in patients with active pathologic bleeding or a history of transient ischemic attack or stroke.

index hospital to a PCI-capable center quickly (time from first medical contact to PPCI of ≤120 minutes). Although the initial focus of PPCI is on quickly restoring flow to the acutely occluded artery, there is a demonstrable reduction in cardiovascular death and MI end points associated with complete revascularization compared with culprit-only PCI in patients with multivessel disease. The relative benefit associated with timing of PCI of nonculprit vessels during the same procedure or within a short interval after PCI of the infarct-related vessel is not established.

Patients undergoing PPCI should receive aspirin (162-325 mg), intravenous unfractionated heparin (with or without glycoprotein IIb/IIIa blockade) or bivalirudin, and loading doses of additional antiplatelet drugs ($P2Y_{12}$ inhibitors) prior to or upon arrival in the catheterization laboratory (**Table 7**).

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 (such as with anterior MI), thrombolytic therapy should be considered if timely transfer for PPCI (the preferred strategy) is not available. Thrombolytic therapy is most effective within the first 3 to 6 hours from symptom onset, after which time fibrin cross-linking renders the clot relatively resistant to lysis. When compared with streptokinase, newer fibrin-specific thrombolytic agents (alteplase, reteplase, tenecteplase) are associated with improved infarct artery patency and fewer allergic reactions, although they are more costly and have not lowered the risk for intracerebral hemorrhage (0.5%-0.9%).

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

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 unfractionated heparin, enoxaparin, or fondaparinux. Clopidogrel loading (300 mg orally) has been demonstrated to increase rates of vessel patency and is also recommended in this setting.

Prompt transfer to a PCI-capable center following thrombolytic therapy (for possible rescue PCI) is reasonable when this option is available. The ECG should be monitored at 60 to 90 minutes to confirm reperfusion, reflected by at least 50% improvement in maximal ST-segment elevation. One quarter to one third of patients do not achieve reperfusion, particularly with delayed presentation. Rescue PCI is associated with improved outcomes compared with conservative management in cases of failed reperfusion. Coronary angiography is recommended in all patients before discharge, even after successful thrombolysis.

KEY POINTS

- When available in a timely manner, primary percutaneous coronary intervention is preferred to thrombolytic therapy for the treatment of ST-elevation myocardial infarction.
- If primary percutaneous coronary intervention (PCI) is not available within 120 minutes of first medical contact, patients with ST-elevation myocardial infarction should receive thrombolytic therapy and be transferred urgently to a PCI-capable center.

Complications of STEMI

Arrhythmias are common in the peri-infarct setting. Atrial fibrillation, which affects up to 20% of patients with STEMI,

TABLE 8.3 Contraindications and Cautions for Thrombolytic Therapy in ST-Elevation Myocardial Infarction[a]

Absolute Contraindications
Any previous intracranial hemorrhage
Known structural cerebrovascular lesion (e.g., arteriovenous malformation)
Known malignant intracranial neoplasm (primary or metastatic)
Ischemic stroke within 3 mo (except acute ischemic stroke within 4.5 h)
Suspected aortic dissection
Active bleeding or bleeding diathesis (excluding menses)
Significant closed head or facial trauma within 3 mo
Intracranial or intraspinal surgery within 2 mo
Severe uncontrolled hypertension (unresponsive to emergency therapy)
For streptokinase: treatment within the previous 6 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 previously)
Dementia
Known intracranial abnormality not covered in absolute contraindications
Traumatic or prolonged (>10 min) CPR
Major surgery within 3 wk
Recent (within 2-4 wk) internal bleeding
Noncompressible vascular puncture site
Pregnancy
Active peptic ulcer disease
Oral anticoagulant therapy

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

[a]Viewed as advisory for clinical decision making and may not be all-inclusive or definitive.

complicates management and may cause hemodynamic instability. Ventricular tachycardia or fibrillation may occur during MI or after reperfusion. Repetitive and sustained bouts of postinfarction ventricular arrhythmias, especially beyond 48 hours, may warrant a longer period of inpatient telemetry and predischarge implantable cardioverter-defibrillator therapy. Routine suppression of ventricular ectopy with antiarrhythmic agents is not recommended and is associated with increased arrhythmias and adverse outcomes. In particular, accelerated idioventricular rhythm, which commonly arises after reperfusion, is generally benign and transient, requiring no treatment. Atrioventricular block, including Wenckebach and complete heart block, may occur after inferior infarction, requiring temporary transvenous pacing; however, 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 requires permanent pacing.

Cardiogenic shock, a common complication of STEMI, typically results from a large anterior MI due to severely reduced LV systolic function. Cardiogenic shock carries a mortality rate of 50% to 80% and must be recognized early. Shock is suggested by hypotension, sinus tachycardia, oliguria, cool extremities, and altered mentation. Untreated cardiogenic shock can progress rapidly to end-organ failure, such as acute kidney or liver failure or mesenteric infarction. Patients, particularly those younger than 75 years, have a higher rate of survival if they receive emergent revascularization. An intra-aortic balloon pump (IABP), an LV assist device, or extracorporeal membrane oxygenation may be used temporarily, although limited data support their benefit in cardiogenic shock. Once the patient is stabilized, weaning the patient from mechanical and inotropic support and slow 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 hemodynamically stable. Diuretics should be used to treat pulmonary vascular congestion.

Approximately 10% to 20% of cases of anterior STEMI are complicated by LV apical thrombus. Anticoagulation is generally recommended for at least 3 months to reduce the risk for systemic embolization, although LV aneurysm without associated thrombus generally is not treated with anticoagulation unless other indications, such as atrial fibrillation, are present.

Right ventricular (RV) infarction, typically identified by ST-segment elevation on right-sided ECG leads (V_1 and V_4R), can complicate right coronary artery occlusion. Patients present with hypotension, elevated central venous pressure, and clear lungs. RV dysfunction causes inadequate filling of the LV, resulting in shock. Transthoracic echocardiography reveals RV dilatation and dysfunction and may be useful in establishing the diagnosis. Volume resuscitation, inotropes (dobutamine or dopamine), and RV mechanical support may be necessary to bridge to RV recovery, which generally takes 2 to 3 days. Nitrates are contraindicated because they may worsen hypotension by reducing preload.

LV free wall rupture produces sudden-onset chest pain or syncope with rapid progression to pulseless electrical activity. LV free wall rupture is more common in older adults, women, patients with anterior MI, those receiving anti-inflammatory agents, and patients with delayed reperfusion. Surgical, or sometimes percutaneous, repair is indicated, but mortality rates are very high.

Acquired ventricular septal defect (VSD) from septal wall rupture may complicate inferior or anterior STEMI, usually in patients with multivessel CAD. VSDs typically occur within 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 because of 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.

When the posteromedial papillary muscle blood supply from the posterior descending artery is interrupted during MI, rupture may occur, resulting in severe acute mitral regurgitation several days after STEMI. Afterload reduction and IABP placement may be temporizing, although urgent surgical intervention usually is indicated. Acute severe mitral regurgitation also may result from LV 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.

Non–ST-Elevation Acute Coronary Syndromes

NSTE-ACS, like STEMI, is on the spectrum of acute ischemic disorders attributable to plaque erosion or rupture and thrombotic occlusion, manifesting as acute chest pain at rest or with minimal exertion. Unlike the complete coronary obstruction resulting in STEMI, NSTE-ACS involves incomplete or transient obstruction without ST-segment elevation, although ST-segment depression is often present.

Risk Stratification

Initial assessment of suspected NSTE-ACS involves a careful history, physical examination, ECG, and serial biomarker measurement to determine the likelihood of a cardiac process. In patients with low likelihood of a coronary event, alternative causes should be investigated. In patients with an intermediate or a high likelihood of ACS, prognostic assessment with risk scores, such as TIMI and GRACE risk models, is indicated. The simpler of the two models, the TIMI risk score, predicts 14-day death, recurrent MI, and urgent revascularization rates (**Table 9**). The GRACE risk score (www.gracescore.org) incorporates examination findings, clinical features, ECG findings, and biomarker variables (creatinine levels, elevated cardiac enzymes) to predict in-house and postdischarge death and MI risk. Prognostic assessment along with serial troponin measurement and clinical status helps determine the most appropriate therapeutic strategy (**Figure 11**).

TABLE 9. 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, 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] doi:10.1001/jama.284.7.835

Invasive Versus Ischemia-Guided Treatment

Urgent 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 high-risk and troponin-positive patients with NSTE-ACS who have been initially stabilized, an early invasive strategy improves the composite clinical end point of death, recurrent MI, and repeat hospitalization compared with an ischemia-guided approach. 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. Other patients, including those with diabetes, stage 2 to 3 chronic kidney disease, LV dysfunction, and recent PCI without elevated risk scores, may be safely evaluated with coronary angiography within 72 hours of presentation (delayed invasive strategy). The choice of revascularization procedure (PCI or CABG) is based on the results of angiography.

With an ischemia-guided strategy, patients undergo noninvasive stress testing with LV function assessment 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), particularly low-risk women, who may have worse outcomes with an early invasive approach. The recommendations for non–low-risk women are identical to those for men.