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Simultaneous with these important advances in the high-income countries, the low- and middle-income countries have moved in the opposite direction. Improvements in agriculture, nutrition, sanitation, prevention and treatment of infections, and management of maternal/ early childhood disorders, urbanization, and a reduction of physical labor have, in combination, led to marked increases in coronary risk factors—hypertension, cigarette smoking, obesity, diabetes mellitus, and elevations of circulating LDL-C. These changes have been most prominent in Central and South Asia, as well as in the more developed regions of sub-Saharan Africa and the Middle East. The current challenge is to apply what was learned in high-income countries to the large populations in the low- and middle-income countries that are now at high risk. This will require large educational efforts directed at both the populations and their caregivers. An addi tional challenge will be to provide the trained specialized personnel, facilities, drugs, and devices to deal with these threats. The successful implementation of these measures is now principally a socio-politicoeconomic issue. One mitigating factor is that many of the important drugs to prevent and treat these disorders, such as statins, ezetimibe, ACE inhibitors, diuretics, beta blockers, and calcium antagonists, are off patent and are now inexpensive. ■ ■FURTHER READING Byrne RA et al: 2023 ESC guidelines for the management of acute coronary syndromes. Eur Heart J 23:44, 2023. Capodanno D et al: Defining strategies of modulation of antiplatelet therapy in patients with coronary artery disease. Circulation 147: 1933, 2023. Hokimoto S et al: JCS/CVIT/JCC 2023 guideline focused update on diagnosis and treatment of vasospastic angina (coronary spastic angina) and coronary microvascular dysfunction. Circ J 87:879, 2023. Kontos MC et al: 2022 ACC Expert Consensus Decision Pathway on the evaluation and disposition of acute chest pain in the emergency department. J Am Coll Cardiol 80:1925, 2022. Lawton JS et al: 2021 ACC/AHA/SCAI guideline for coronary artery revascularization. J Am Coll Cardiol 79:e21, 2021. Mach F et al: ESC/EAS guidelines for the management of dyslipidae mias: Lipid modification to reduce cardiovascular risk. Eur Heart J 41:111, 2020. Martin SS et al: 2024 Heart disease and stroke statistics: A report of US and global data from the American Heart Association. Circulation 149:e347, 2024. Thygesen K et al: Fourth universal definition of myocardial infarction. J Am Coll Cardiol 72:2231, 2018. David A. Morrow,

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ST-Segment Elevation Myocardial Infarction Acute myocardial infarction (AMI) is a common diagnosis in hospital ized patients in industrialized countries. In the United States, ~605,000 patients experience a new AMI and 200,000 experience a recurrent AMI each year. About half of AMI-related deaths occur before the stricken individual reaches the hospital. The in-hospital mortality rate after admission for AMI has declined from 10 to ~5%. The 1-year mortality rate after AMI is ~15%. Mortality is approximately fourfold higher in patients aged >75 years as compared with younger patients. When patients with prolonged ischemic discomfort at rest are first seen, the working clinical diagnosis is that they are suffering from an acute coronary syndrome (Fig. 286-1). The 12-lead electrocardiogram (ECG) is a pivotal diagnostic and triage tool because it is at the center of the decision pathway for management, permitting distinction of

those patients presenting with ST-segment elevation from those pre senting without ST-segment elevation. Circulating cardiac biomarkers of myocardial injury are measured to distinguish unstable angina (UA) from non-ST-segment elevation myocardial infarction (NSTEMI) and to estimate preliminarily the magnitude of myocardial necrosis in an ST-segment elevation myocardial infarction (STEMI). Epidemiologic studies indicate there has been a shift in the pattern of AMI over the past several decades with more patients with NSTEMI than STEMI. This chapter focuses on the evaluation and management of patients with STEMI, while Chap. 286 discusses UA/NSTEMI. PATHOPHYSIOLOGY: ROLE OF ACUTE PLAQUE RUPTURE/EROSION STEMI usually occurs when coronary blood flow decreases abruptly after a thrombotic occlusion of a coronary artery previously affected by atherosclerosis. Slowly developing, high-grade coronary artery stenoses do not typically precipitate STEMI because of the develop ment of a rich collateral network over time. Instead, STEMI occurs when a coronary artery thrombus develops rapidly at a site of vascular injury. This injury is produced or facilitated by factors such as ciga rette smoking, hypertension, lipid accumulation, and inflammation. In most cases, STEMI occurs when the surface of an atherosclerotic plaque becomes disrupted either through erosion or rupture (expos ing its contents to the blood) and conditions (local or systemic) favor thrombogenesis. Histologic studies indicate that the coronary plaques prone to disruption are those with a rich lipid core and a thin fibrous cap. However, current clinical data have demonstrated that less than 5% of such thin-capped fibroatheromas are a nidus for AMI during long-term follow-up. Other morphologic characteristics associated with rupture-prone plaque include expansive remodeling, neovascular ization (angiogenesis), plaque hemorrhage, adventitial inflammation, and a “spotty” pattern of calcification.

CHAPTER 286 ST-Segment Elevation Myocardial Infarction A mural thrombus forms at the site of plaque disruption, and the involved coronary artery becomes occluded. After an initial platelet monolayer forms at the site of the disrupted plaque, various agonists (collagen, ADP, epinephrine, serotonin) promote platelet activation. After agonist stimulation of platelets, thromboxane A2 (a potent local vasoconstrictor) is released, further platelet activation occurs, and potential resistance to fibrinolysis develops. In addition to the generation of thromboxane A2, activation of plate lets by agonists promotes a conformational change in the glycoprotein IIb/IIIa receptor (Chap. 120). Once converted to its functional state, this receptor develops a high affinity for soluble adhesive proteins

(i.e., integrins) such as fibrinogen. Since fibrinogen is a multivalent mol ecule, it can bind to two different platelets simultaneously, resulting in platelet cross-linking and aggregation. The coagulation cascade is activated on exposure of tissue factor in damaged endothelial cells at the site of the disrupted plaque. Fac tors VII and X are activated, ultimately leading to the conversion of prothrombin to thrombin, which then converts fibrinogen to fibrin (Chap. 121). Fluid-phase and clot-bound thrombin participate in an autoamplification reaction, leading to further activation of the coagulation cascade. The culprit coronary artery eventually becomes occluded by a thrombus containing platelet aggregates and fibrin strands (Fig. 286-2). In rare cases, STEMI may be due to coronary artery occlusion caused by coronary emboli, congenital coronary abnormalities, coro nary spasm, or spontaneous coronary artery dissection. The amount of myocardial damage caused by coronary occlusion depends on (1) the territory supplied by the affected vessel, (2) whether or not the vessel becomes totally occluded, (3) the duration of coronary occlusion, (4) the quantity of blood supplied by collateral vessels to the affected tis sue, (5) the demand for oxygen of the myocardium whose blood supply has been suddenly limited, (6) endogenous factors that can produce early spontaneous lysis of the occlusive thrombus, and (7) the adequacy of myocardial perfusion in the infarct zone when flow is restored in the occluded epicardial coronary artery. Patients at increased risk for developing STEMI include those with multiple coronary risk factors and those with UA (Chap. 285). Less

PART 6 Disorders of the Cardiovascular System Ischemic Discomfort Presentation Working diagnosis Supply-demand imbalance (nonthrombotic Acute coronary syndrome (atherothrombotic) ECG No ST elevation ST elevation – + + + – Biomarkers Final diagnosis Unstable angina (demand related) Non-ST elevation MI (type 2) Non-ST elevation MI (type 1) ST elevation MI (type 1) Unstable angina (thrombotic mediated) Final ECG manifestation FIGURE 286-1 Acute coronary syndromes. Following disruption of a vulnerable plaque, patients experience ischemic discomfort resulting from a reduction of flow through the affected epicardial coronary artery. The flow reduction may be caused by a completely occlusive thrombus (right) or subtotally occlusive thrombus (middle). Patients with ischemic discomfort may present with or without ST-segment elevation. Of patients with ST-segment elevation, the majority ultimately develop a Q wave on the electrocardiogram (ECG; Q-wave myocardial infarction [MI]), while a minority do not develop Q waves and, in the past, were said to have sustained a non-Q-wave MI (NQMI). Patients who present without ST-segment elevation are suffering from either unstable angina or a non-ST-segment elevation MI (NSTEMI), a distinction that is ultimately made based on the presence or absence of a biomarker of myocardial injury such as cardiac troponin detected in the blood. (Reproduced with permission from Hamm Scirica BM, Libby P, Morrow DA: ST-elevation myocardial infarction: Pathophysiology and clinical evolution, in Braunwald’s Heart Disease, 12th ed, Libby P et al (eds). New York, Elsevier, 2022, Figure 37-1, pp 636-661.) common underlying medical conditions predisposing patients to STEMI include hypercoagulability, collagen vascular disease, systemic inflammatory diseases, cocaine abuse, and intracardiac thrombi or masses that produce coronary emboli. There have been major advances in the management of STEMI with recognition that the “chain of survival” involves a highly integrated system starting with prehospital care and extending to early hospital management so as to provide expeditious implementation of a reperfu sion strategy. CLINICAL PRESENTATION In up to one-half of cases, a precipitating factor appears to be present before STEMI, such as vigorous physical exercise, emotional stress, or a medical or surgical illness. Although STEMI may commence at any time of the day or night, circadian variations have been reported such that clusters are seen in the morning within a few hours of awakening.

Plaque rupture with thrombus Vasospasm or endothelial dysfunction Causes of myocardial oxygen supply-demand imbalance Fixed atherosclerosis and supply-demand imbalance Supply-demand imbalance alone Q-wave MI Non-Q-wave MI Pain is the most common presenting complaint in patients with STEMI. The pain is deep and visceral; adjectives commonly used to describe it are heavy, squeezing, and crushing; although, occasionally, it is described as stabbing or burning (Chap. 15). It is similar in char acter to the discomfort of angina pectoris (Chap. 284) but commonly occurs at rest, is usually more severe, and lasts longer. Typically, the pain involves the central portion of the chest and/or the epigastrium, and, on occasion, it radiates to the arms. Less common sites of radiation include the abdomen, back, lower jaw, and neck. The frequent location of the pain beneath the xiphoid and epigastrium and the patients' denial that they may be suffering a heart attack are chiefly responsible for the common mistaken impression of indigestion. The pain of STEMI may radiate as high as the occipital area but not below the umbilicus. It is often accompanied by sweating, nausea, vomiting, anxiety, and a sense of impending doom. The pain may commence when the patient is at rest, but when it begins during a period of exertion, it does not usually subside with cessation of activity, in contrast to angina pectoris.

Thrombogenic blood • inflammation • comorbidities • environmental factors • genetic background Vulnerable plaque • inflammation • extension • severity • location plaque ion Vulnerable myocardium • inflammation • ischemia duration/extent • individual susceptibility Cardiomyocyte swelling Interstitial edema Thrombus debris Endothelial dysfunction Leukocyte and platelet activation/interaction FIGURE 286-2 Critical determinants of myocardial infarction injury. The overlapping of vulnerable plaque and thrombogenic blood are critical determinants for myocardial infarction occurrence and extension. In addition, myocardial vulnerability, which is largely due to coronary microvascular dysfunction, contributes to extension and severity of ischemic injury. In the most severe form (known as no-reflow), structural and functional impairments sustain vascular obstruction. Endothelial dysfunction triggers leukocyte and platelet activation/interaction, whereas thrombotic debris may worsen the obstruction. Furthermore, cardiomyocyte swelling, interstitial edema, and tissue inflammation promote extravascular compression. (Modified from F Montecucco, F Carbone, TH Schindler. Pathophysiology of ST-segment elevation myocardial infarction: Novel mechanisms and treatments. Eur Heart J 37:1268, 2016.) The pain of STEMI can simulate pain from acute pericarditis (Chap. 281), pulmonary embolism (Chap. 290), acute aortic dis section (Chap. 291), costochondritis, and gastrointestinal disorders. These conditions should therefore be considered in the differential diagnosis. Radiation of discomfort to the trapezius is not seen in patients with STEMI and may be a useful distinguishing feature that suggests pericarditis is the correct diagnosis. However, pain is not uniformly present in patients with STEMI. The proportion of painless STEMIs is greater in patients with diabetes mellitus, and it increases with age. STEMI may present as sudden-onset breathlessness. Other less common presentations, with or without pain, include sudden loss of consciousness, a confusional state, a sensation of profound weakness, the appearance of an arrhythmia, evidence of peripheral embolism, or merely an unexplained drop in arterial pressure. ■ ■PHYSICAL FINDINGS Most patients are anxious and restless, attempting unsuccessfully to relieve the pain by moving about in bed, altering their position, and stretching. Pallor associated with perspiration and coolness of the extremities occurs commonly. The combination of substernal chest pain persisting for >30 min and diaphoresis strongly suggests STEMI. Although many patients have a normal pulse rate and blood pressure within the first hour of STEMI, patients with anterior infarction may

have manifestations of sympathetic nervous system hyperactivity (tachycardia and/or hypertension), and those with inferior infarction may show evidence of parasympathetic hyperactivity (bradycardia and/or hypotension).

The precordium is usually quiet, and the apical impulse may be difficult to palpate. Other physical signs of ventricular dysfunction include fourth and third heart sounds, decreased intensity of the first heart sound, and paradoxical splitting of the second heart sound (Chap. 246). A transient midsystolic or late systolic apical systolic murmur due to dysfunction of the mitral valve apparatus may be pres ent. A pericardial friction rub may be heard in patients with transmural STEMI at some time in the course of the illness. The carotid pulse is often decreased in volume, reflecting reduced stroke volume. Tem perature elevations up to 38°C may be observed during the first week after STEMI. LABORATORY FINDINGS STEMI progresses through the following temporal stages: (1) acute (first few hours–7 days), (2) healing (7–28 days), and (3) healed (≥29 days). The myocardium undergoes a series of cellular responses in the infarct zone, beginning with recruitment of polymorphonuclear leukocytes (for removal of dead cells and clearance of extracellular macromol ecules) followed by monocytes. Experimental work has now detailed this sequence of accumulation of subpopulations of mononuclear phagocytes with an initial wave of monocytes characterized by high proteolytic and phagocytic capacity and elaboration of proinflamma tory cytokines followed by the repair monocytes that release a media tors that stimulate angiogenesis and extracellular matrix production (Fig. 286-3). New microvessels and fibrosis are key constituents of forming granulation tissue, and these processes establish a foundation for myocardial scar formation, ventricular remodeling, and infarct healing. In addition, emerging evidence reveals a role for an “emer gency hematopoiesis” that mobilizes leukocyte progenitor cells that ultimately participate in myocardial healing. CHAPTER 286 ST-Segment Elevation Myocardial Infarction When evaluating the results of diagnostic tests for STEMI, the tem poral phase of the infarction must be considered. The tests of value in confirming the diagnosis may be divided into four groups: (1) ECG, (2) blood-based cardiac biomarkers, (3) cardiac imaging, and (4) nonspe cific indices of tissue necrosis and inflammation. ■ ■ELECTROCARDIOGRAM The electrocardiographic manifestations of STEMI are described in Chap. 247. During the initial stage, total occlusion of an epicardial coronary artery produces ST-segment elevation. Most patients initially presenting with ST-segment elevation ultimately evolve Q waves on the ECG. However, Q waves in the leads overlying the infarct zone may vary in magnitude and appear only transiently, depending on the reperfusion status of the ischemic myocardium and restoration of transmembrane potentials over time. A small proportion of patients initially presenting with ST-segment elevation will not develop Q waves when the obstructing thrombus is not totally occlusive, obstruction is transient, or a rich collateral network is present. Among patients pre senting with ischemic discomfort but without ST-segment elevation, if a cardiac biomarker of necrosis (see below) is detected, the diagnosis of NSTEMI is ultimately made (Fig. 286-1). A minority of patients who present initially without ST-segment elevation may develop a Q-wave myocardial infarction (MI). Previously, it was believed that transmural MI is present if the ECG demonstrates Q waves or loss of R waves, and nontransmural MI may be present if the ECG shows only transient ST-segment and T-wave changes. However, electrocardiographicpathologic correlations are far from perfect, and terms such as Q-wave MI, non-Q-wave MI, transmural MI, and nontransmural MI have been replaced by STEMI and NSTEMI (Fig. 286-1). Contemporary studies using magnetic resonance imaging (MRI) suggest that the development of a Q wave on the ECG is more dependent on the volume of infarcted tissue rather than the transmurality of infarction. ■ ■CARDIAC BIOMARKERS OF MYOCARDIAL INJURY Certain proteins, referred to as cardiac

biomarkers, are released from necrotic heart muscle after STEMI. The rate of liberation of specific

Polymorphonuclear leukocyte Pro-inflammatory monocyte PART 6 Disorders of the Cardiovascular System • Phagocytosis • Proteolysis-matrix degradation • Pro-inflammatory • Reactive O2 species Early damage clearance phase: • Recruitment of leukocytes • Removal of dead cells • Dissolution and clearance of damaged extracellular matrix macromolecules • Preparing the injured myocardium for repair Monocyte-derived fibroblasts Regulation of the responses to myocardial ischemic injury FIGURE 286-3 Phases of myocardial injury and healing. Immediate recruitment of polymorphonuclear leukocytes precedes the accumulation of proinflammatory monocytes (typically bearing the chemokine receptor 2 [CCR2]). These phagocytic cells release the mediators of the early phase response to ischemic injury by clearing dead cells and debris and prompting additional inflammatory cells to enter the injured area. Reparative monocytes stimulate the production of extracellular matrix macromolecules that reinforce the cardiac skeleton during healing as well as microvessel formation characteristic of granulation tissue. Monocyte-derived fibroblasts are capable of interstitial collagen synthesis that reinforces repair of the myocardial skeleton, potentially mitigating expansive remodeling of the infarct and promoting healing with less risk for chronic heart failure. (Reproduced with permission from P Libby et al: The myocardium: More than just myocytes. J Am Coll Cardiol 74:3137, 2019.) proteins differs depending on their intracellular location, their molecu lar weight, and the local blood and lymphatic flow. Cardiac biomarkers become detectable in the peripheral blood once the capacity of the car diac lymphatics to clear the interstitium of the infarct zone is exceeded and spillover into the venous circulation occurs. The criteria for AMI require a rise and/or fall in cardiac biomarker values with at least one value above the 99th percentile of the upper reference limit for normal individuals. Cardiac-specific troponin T (cTnT) and cardiac-specific troponin I (cTnI) have amino-acid sequences that differ from those of the skeletal muscle forms of these proteins. These differences permitted the devel opment of quantitative assays for cTnT and cTnI using highly specific monoclonal antibodies. cTnT and cTnI may increase after STEMI to levels many times higher than the upper reference limit (set at the 99th percentile of values in a reference population). The measurement of cTnT or cTnI is of considerable diagnostic usefulness, and they are now the preferred biochemical markers for MI when measured with highsensitivity assays (Fig. 286-4 and Chap. 15). In practical terms, the high-sensitivity troponin assays are of less immediate value in patients with STEMI. Contemporary urgent reperfusion strategies necessitate making a decision (based largely on a combination of clinical and ECG findings) before the results of blood tests have returned from the labo ratory. Levels of cTnI and cTnT typically remain elevated for at least 7–10 days after STEMI. Historically, creatine phosphokinase (CK) and its MB isoenzyme (CK-MB) were used for the diagnosis of AMI. A ratio (relative index) of CK-MB mass to CK activity ≥2.5 suggests but is not diagnostic of a myocardial rather than a skeletal muscle source for the CK-MB eleva tion. It is not cost-effective to measure both a cardiac-specific troponin and CK-MB. Because of its more rapid decline after the onset of AMI, CK-MB may be useful for the discrimination of early reinfarction

Reparative monocyte CCR2 F4/80 • Transforming growth factor β • Vascular endothelial growth factor Later repair/healing phase: • Resolution of inflammation • Angiogenesis • Stimulation of extracellular matrix • Interstitial collagen production during the period that cardiac troponin remains elevated following the index event (Fig. 286-3). While it has long been recognized that the total quantity of protein released correlates with the size of the infarct, the peak protein con centration correlates only weakly with infarct size. Recanalization of a coronary artery occlusion

(either spontaneously or by mechanical or pharmacologic means) in the early hours of STEMI causes earlier peaking of biomarker measurements (Fig. 286-4) because of a rapid washout from the interstitium of the infarct zone, quickly overwhelm ing lymphatic clearance of the proteins. The nonspecific reaction to myocardial injury is associated with polymorphonuclear leukocytosis, which appears within a few hours after the onset of pain and persists for 3–7 days; the white blood cell count often reaches levels of 12,000–15,000/μL. The erythrocyte sedimentation rate rises more slowly than the white blood cell count, peaking during the first week and sometimes remaining elevated for 1 or 2 weeks. ■ ■CARDIAC IMAGING Abnormalities of wall motion on two-dimensional echocardiography (Chap. 248) are almost universally present in patients with STEMI. Although acute STEMI cannot be distinguished from an old myo cardial scar or from acute severe ischemia by echocardiography, the ease and safety of the procedure make its use appealing as a screening tool in the emergency department. When the ECG is not diagnostic of STEMI, early detection of the presence or absence of wall motion abnormalities by echocardiography can aid in management decisions, such as whether the patient should receive reperfusion therapy (e.g., percutaneous coronary intervention [PCI] or fibrinolysis). Echocar diographic estimation of left ventricular (LV) function is useful prog nostically; detection of reduced function serves as an indication for

Zone of necrosing myocardium Troponin free in cytoplasm Cardiomyocyte Myosin Actin Troponin complex bound to actin filament Lymphatic system Venous system Myoglobin and CK isoforms

Multiples of the AMI cutoff limit

Troponin (large MI)

CKMB

Troponin (small MI)

99th percentile

Days after onset of AMI FIGURE 286-4 The zone of necrosing myocardium is shown at the top of the figure, followed in the middle portion of the figure by a diagram of a cardiomyocyte that is in the process of releasing biomarkers. The biomarkers that are released into the interstitium are first cleared by lymphatics followed subsequently by spillover into the venous system. After disruption of the sarcolemmal membrane of the cardiomyocyte, the cytoplasmic pool of biomarkers is released first (left-most arrow in bottom portion of figure). Markers such as myoglobin and CK isoforms are rapidly released, and blood levels rise quickly above the cutoff limit; this is then followed by a more protracted release of biomarkers from the disintegrating myofilaments that may continue for several days. Cardiac troponin levels rise to about 20–50 times the upper reference limit (the 99th percentile of values in a reference control group) in patients who have a “classic” acute myocardial infarction (MI) and sustain sufficient myocardial necrosis to result in abnormally elevated levels of the MB fraction of creatine kinase (CK-MB). Clinicians can now diagnose episodes of microinfarction by sensitive assays that detect cardiac troponin elevations above the upper reference limit, even though CK-MB levels may still be in the normal reference range (not shown). CV, coefficient of variation. (Modified from EM Antman: Decision making with cardiac troponin tests. N Engl J Med 346:2079, 2002, and; bottom image: Reproduced with

permission from AS Jaffe: Biomarkers in acute cardiac disease: The present and the future. J Am Coll Cardiol 48:1, 2006.)

therapy with an inhibitor of the renin-angiotensin-aldosterone system. Echocardiography may also identify the presence of right ventricular (RV) infarction, ventricular aneurysm, pericardial effusion, and LV thrombus. In addition, Doppler echocardiography is useful in the detection and quantitation of a ventricular septal defect and mitral regurgitation, two serious complications of STEMI.

CHAPTER 286 Radionuclide imaging techniques (Chap. 248) are available but rarely used for evaluating patients with suspected STEMI. Myocardial perfu sion imaging with [99mTc]-sestamibi, which is distributed in proportion to myocardial blood flow and concentrated by viable myocardium (Chap. 285), reveals a defect (“cold spot”) in most patients during the first few hours after development of a transmural infarct. However, the technique cannot distinguish acute infarcts from chronic scars and, thus, is not specific for the diagnosis of acute MI. ST-Segment Elevation Myocardial Infarction An Expert Consensus Task Force for the Universal Definition of Myocardial Infarction has provided a comprehensive set of criteria for the definition of MI that integrates the clinical and laboratory findings discussed earlier as well as a classification of MI into five types that reflect the clinical circumstances in which it may occur (Table 286-1). INITIAL MANAGEMENT ■ ■PREHOSPITAL CARE The prognosis in STEMI in the era of primary PCI is largely related to the occurrence of two general classes of complications: (1) electri cal complications (arrhythmias) and (2) mechanical complications (“pump failure”). Most out-of-hospital deaths from STEMI result from the sudden development of ventricular fibrillation. The vast majority of deaths due to ventricular fibrillation occur within the first 24 h of the onset of symptoms, and of these, over half occur in the first hour. Therefore, the major elements of prehospital care of patients with sus pected STEMI include (1) recognition of symptoms by the patient and prompt seeking of medical attention; (2) rapid deployment of an emer gency medical team capable of performing resuscitative maneuvers, including defibrillation; (3) expeditious transportation of the patient to a hospital facility that is continuously staffed by physicians and nurses skilled in managing arrhythmias and providing advanced cardiac life support; and (4) expeditious implementation of reperfusion therapy. The greatest delay usually occurs not during transportation to the hos pital but, rather, between the onset of pain and the patient’s decision to call for help. This delay can best be reduced by health care professionals educating the public concerning the significance of chest discomfort and the importance of seeking early medical attention. Regular office visits with patients having a history of, or who are at risk for, ischemic heart disease are important “teachable moments” for clinicians to review the symptoms of AMI and the appropriate action plan. Increasingly, monitoring and treatment are carried out by trained personnel in the ambulance, further shortening the time between the onset of the infarction and appropriate treatment. In areas remote from PCI centers, fibrinolytic therapy may be administered prehospi tal. General guidelines for initiation of fibrinolysis in the prehospital setting include the ability to transmit 12-lead ECGs to confirm the diagnosis, the presence in the ambulance of personnel trained in the interpretation of ECGs and management of STEMI, and online medi cal command and control that can authorize the initiation of treatment in the field. MANAGEMENT IN THE EMERGENCY DEPARTMENT In the emergency department, the goals for the management of patients with suspected STEMI include control of cardiac discomfort, rapid identification of patients who are candidates for urgent reperfu sion therapy, triage of lower-risk patients to the appropriate location in the hospital, and avoidance of inappropriate discharge of patients with STEMI. Many aspects of the treatment of STEMI are initiated in the emergency

department and then continued during the in-hospital phase of management. The overarching goal is to minimize the time from first medical contact to initiation of reperfusion therapy (Fig. 286-5). This may involve transfer from a non-PCI hospital to one

TABLE 286-1 Definitions of Myocardial Injury and Infarction Criteria for Myocardial Injury The term myocardial injury should be used when there is evidence of elevated cardiac troponin (cTn) levels with at least one value above the 99th percentile upper reference limit (URL). The myocardial injury is considered acute if there is a rise and/or fall of cTn values. PART 6 Disorders of the Cardiovascular System Criteria for Acute Myocardial Infarction (types 1, 2, and 3 MI) The term acute myocardial infarction (MI) should be used when there is acute myocardial injury with clinical evidence of acute myocardial ischemia and with detection of a rise and/or fall of cTn values with at least one value above the 99th percentile URL and at least one of the following: • Symptoms of myocardial ischemia • New ischemic electrocardiographic (ECG) changes • Development of pathologic Q waves • Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemic etiology • Identification of a coronary thrombus by angiography or autopsy (not for types 2 or 3 MIs) Postmortem demonstration of acute atherothrombosis in the artery supplying the infarcted myocardium meets criteria for type 1 MI. Evidence of an imbalance between myocardial oxygen supply and demand unrelated to acute atherothrombosis meets criteria for type 2 MI. Cardiac death in patients with symptoms suggestive of myocardial ischemia and presumed new ischemic ECG changes before cTn values became available or abnormal meets criteria for type 3 MI. Criteria for Coronary Procedure–Related MI (types 4 and 5 MI) Percutaneous coronary intervention (PCI)–related MI is termed type 4a MI. Coronary artery bypass grafting (CABG)–related MI is termed type 5 MI. Coronary procedure–related MI <48 h after the index procedure is arbitrarily defined by an elevation of cTn values >5 times for type 4a MI and >10 times for type 5 MI of the 99th percentile URL in patients with normal baseline values. Patients with elevated preprocedural cTn values, in whom the preprocedural cTn levels are stable (<20% variation) or falling, must meet the criteria for a

> 5- or >10-fold increase and manifest a change from the baseline value of 20%. In addition, they must have at least one of the following: • New ischemic ECG changes (this criterion is related to type 4a MI only) • Development of new pathologic Q waves • Imaging evidence of loss of viable myocardium that is presumed to be new and in a pattern consistent with an ischemic etiology • Angiographic findings consistent with a procedural flow-limiting complication such as coronary dissection, occlusion of a major epicardial artery or graft, side-branch occlusion-thrombus, disruption of collateral flow, or distal embolization Isolated development of new pathologic Q waves meets the type 4a MI or type 5 MI criteria with either revascularization procedure if cTn levels are elevated and rising, but less than the prespecified thresholds for PCI and CABG. Other types of type 4 MI include type 4B MI stent thrombosis and type 4C MI restenosis that both meet type 1 MI criteria. Postmortem demonstration of a procedure-related thrombus meets the type 4a MI and type 5 MI criteria if associated with a stent. Criteria for Prior or Silent/Unrecognized MI Any one of the following criteria meets the diagnosis for prior or silent/ unrecognized MI: • Abnormal Q waves

> with or without symptoms in the absence of nonischemic causes • Imaging evidence of loss of viable myocardium in a pattern consistent with ischemic etiology • Pathoanatomical findings of a prior MI Source: Reproduced with permission from K Thygesen et al: Fourth universal definition of myocardial infarction (2018). Circulation 138:e618, 2018. that is PCI capable, with a goal of initiating PCI within 120 min of first medical contact (Fig. 286-5). Aspirin is essential in the management of patients with suspected STEMI and is effective across the entire spectrum of acute coronary syndromes. Rapid inhibition of cyclooxygenase-1 in platelets followed by a reduction of thromboxane A2 levels is achieved by buccal absorp tion of a chewed 160–325-mg tablet in the emergency department. This measure should be followed by daily oral administration of aspirin in a dose of 75–162 mg.

In patients whose arterial oxygen (O2) saturation is normal, supple mental O2 is not recommended. However, when hypoxemia is present (O2 saturation <90%), O2 should be administered to correct the hypox emia; the patient should then be reassessed to determine if there is a continued need for such treatment. CONTROL OF DISCOMFORT Sublingual nitroglycerin can be given safely to most patients with STEMI. Up to three doses of 0.4 mg should be administered at about 5-min intervals in patients with persistent ischemic symptoms. In addi tion to diminishing or abolishing chest discomfort, nitroglycerin may be capable of both decreasing myocardial O2 demand (by lowering pre load) and increasing myocardial O2 supply (by dilating infarct-related coronary vessels or collateral vessels and by improving subendocardial perfusion). In patients whose initially favorable response to sublingual nitroglycerin is followed by the return of chest discomfort, particularly if accompanied by other evidence of ongoing ischemia such as further ST-segment or T-wave shifts, the use of intravenous nitroglycerin may be considered. Therapy with nitrates should be avoided in patients who present with low systolic arterial pressure (<90 mmHg) or in whom there is clinical suspicion of RV infarction (inferior infarction on ECG, elevated jugular venous pressure, clear lungs, and hypotension). Nitrates should not be administered to patients who have taken a phos phodiesterase-5 inhibitor for erectile dysfunction within the preceding 24 h because it may potentiate the hypotensive effects of nitrates. An idiosyncratic reaction to nitrates, consisting of sudden marked hypo tension, sometimes occurs but can usually be reversed promptly by the rapid administration of intravenous atropine. Morphine is a very effective analgesic for the pain associated with STEMI. However, it may reduce sympathetically mediated arteriolar and venous constriction, and the resulting venous pooling may reduce cardiac output and arterial pressure. These hemodynamic distur bances usually respond promptly to elevation of the legs, but in some patients, volume expansion with intravenous saline is required. The patient may experience diaphoresis and nausea, but these events usually pass and are replaced by a feeling of well-being associated with the relief of pain. Morphine also has a vagotonic effect and may cause bradycardia or advanced degrees of heart block, particularly in patients with inferior infarction. These side effects usually respond to atropine (0.5 mg intravenously). Morphine may also slow the gastrointestinal absorption of oral medicines, which may delay the onset of action of orally administered antiplatelet therapy; however, currently available clinical data have not demonstrated an increase in the risk of adverse clinical outcomes as a result of any interaction between morphine and antiplatelet agents. Therefore, it is reasonable to use morphine in patients

with STEMI to relieve pain. Morphine is administered by repetitive (every 5 min) intravenous injection of small doses (2–4 mg). Intravenous beta blockers are also useful in mitigating the ischemic pain of STEMI. These drugs control pain effectively in some patients, presumably by diminishing myocardial O2 demand and hence isch emia. More important, there is evidence that intravenous beta blockers reduce the risks of reinfarction and ventricular fibrillation (see “BetaAdrenoceptor Blockers” below). A commonly employed regimen is metoprolol, 5 mg every 2–5 min for a total of three doses, provided the patient has a heart rate >60 beats/min, systolic pressure >100 mmHg, a PR interval <0.24 s, and no signs of acute heart failure. Patient selection is important when considering beta blockers for STEMI. Oral beta blocker therapy should be initiated in the first 24 h for patients who do not have any of the following: (1) signs of acute heart failure, (2) evidence of a low-output state, (3) increased risk for cardiogenic shock, or (4) other relative contraindications to beta blockade (bradycardia, PR interval >0.24 s, second- or third-degree heart block, active asthma, or reactive airway disease). In eligible patients, 15 min after the last intravenous dose, an oral regimen is initiated with 50 mg every 6 h for 48 h, followed by 100 mg every 12 h. Unlike beta blockers, calcium antagonists are of little value in the acute setting, and there is evidence that short-acting dihydropyridines may be associated with an increased mortality risk.

STEMI patient who is a candidate for reperfusion Initially seen at a PCI-capable hospital Send to cath lab for primary PCI FMC-device time ≤90 min (Class I, LOE: A) Diagnostic angiogram Medical therapy only PCI CABG *Patients with cardiogenic shock or severe heart failure initially seen at a non–PCI-capable hospital should be transferred for cardiac catheterization and revascularization as soon as possible, irrespective of time delay from myocardial infarction (MI) onset (Class I, LOE: B). †Angiography and revascularization should not be performed within the first 2–3 h after administration of fibrinolytic therapy. FIGURE 286-5 Reperfusion therapy for patients with ST-segment elevation myocardial infarction (STEMI). Performance of percutaneous coronary intervention (PCI) is dictated by an anatomically appropriate culprit stenosis. CABG, coronary artery bypass graft; DIDO, door-in–door-out; FMC, first medical contact; LOE, level of evidence. (Reproduced with permission from PT O’Gara: 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction. Circulation 127:e362, 2013.) MANAGEMENT STRATEGIES The primary tool for screening patients and making triage decisions is the initial 12-lead ECG. When ST-segment elevation meeting the Universal Definition of MI criteria (Table 286-2) is present, a patient should be considered a candidate for reperfusion therapy (Figs. 286-1 and 286-5). The process of selecting patients for fibrinolysis versus primary PCI (Chap. 287) is discussed below. In the absence of STsegment elevation, fibrinolysis is not helpful, and evidence exists sug gesting that it may be harmful. LIMITATION OF INFARCT SIZE The quantity of myocardium that becomes necrotic as a consequence of a coronary artery occlusion is determined by factors other than just the location of occlusion. While the central zone of the infarct contains necrotic tissue that is irretrievably lost, the fate of the surrounding isch emic myocardium (ischemic penumbra) may be improved by timely restoration of coronary perfusion, reduction of myocardial O2 demands, prevention of the accumulation of noxious metabolites, and blunting of the impact of mediators of reperfusion injury (e.g., calcium overload and oxygen-derived free radicals). Up to one-third of patients with STEMI may achieve spontaneous reperfusion of the infarct-related coronary artery within 24 h and experience improved healing of infarcted tissue. TABLE 286-2 Electrocardiographic Criteria for ST-Elevation Myocardial Infarction New ST-elevation at the J-point in 2 contiguous leads with the cut-point: • In all leads other than leads V2–V3: ≥0.1 mV (1 mm on standard scale) • In leads V2–V3: •

≥0.2 mV (2 mm) in men ≥40 years old • ≥0.25 mV (2.5 mm) in men <40 years • ≥0.15 mV (1.5 mm) in women regardless of age Source: Reproduced from K Thygesen et al: Fourth universal definition of myocardial infarction (2018). Circulation 138:e618, 2018.

Initially seen at a non–PCI-capable hospital* CHAPTER 286 DIDO time ≤30 min ST-Segment Elevation Myocardial Infarction Transfer for primary PCI Administer fibrinolytic agent within 30 min of arrival when anticipated FMCdevice >120 min (Class I, LOE: B) FMC-device time as soon as possible and ≤120 min (Class I, LOE: B) Transfer for angiography and revascularization within 3–24 h for other patients as part of an invasive strategy† Urgent transfer for PCI for patients with evidence of failed reperfusion or reocclusion (Class IIa, LOE: B) (Class IIa, LOE: B) Reperfusion, either pharmacologically (by fibrinolysis) or by primary PCI, accelerates the opening of infarct-related arteries in those patients in whom spontaneous fibrinolysis ultimately would have occurred and also greatly increases the number of patients in whom restoration of flow in the infarct-related artery is accomplished. Timely restoration of flow in the epicardial infarct–related artery combined with improved perfusion of the downstream zone of infarcted myocardium results in a limitation of infarct size. Protection of the ischemic myocardium by the maintenance of an optimal balance between myocardial O2 supply and demand through pain control, treatment of heart failure (HF), and minimization of tachycardia and hypertension extends the “window” of time for the salvage of myocardium by reperfusion strategies. Glucocorticoids and nonsteroidal anti-inflammatory agents, with the exception of aspirin, should be avoided in patients with STEMI. They can impair infarct healing and increase the risk of myocardial rupture, and their use may result in a larger infarct scar. In addition, they can increase coronary vascular resistance, thereby potentially reducing flow to ischemic myocardium. ■ ■PRIMARY PERCUTANEOUS CORONARY INTERVENTION (See also Chap. 287) PCI, usually stenting without preceding fibrino lysis, referred to as primary PCI, is effective in restoring perfusion in STEMI when carried out on an emergency basis in the first few hours of MI. It has the advantage of being applicable to patients who have contraindications to fibrinolytic therapy (see below) but otherwise are considered appropriate candidates for reperfusion. Primary PCI is more effective than fibrinolysis in opening occluded coronary arteries and, when performed by experienced teams in dedicated medical centers, is associated with better short-term and long-term clinical outcomes. Compared with fibrinolysis, primary PCI is preferred unless the time to delivery of the first coronary device is anticipated to be longer than 120 min. Primary PCI is also preferred when the diagnosis is in doubt, cardiogenic shock is present, bleeding risk is high, or symptoms have

been present for longer than 2–3 h, at which time the clot is less easily lysed by fibrinolytic drugs. Contemporary studies (PRAMI, CvLPRIT, COMPLETE) provide evidence that, in patients with STEMI without shock, performing PCI on nonculprit coronary vessels, either during the index procedure or within 45 days, results in a lower rate of car diovascular events and a lower need for subsequent ischemia-driven revascularization. In contrast, among patients with cardiogenic shock, routine PCI of nonculprit arteries during the initial primary PCI is contraindicated due to an increase in the rate of death or severe renal failure compared with culprit-only PCI.

PART 6 Disorders of the Cardiovascular System ■ ■FIBRINOLYSIS If timely primary PCI is not available and no contraindications are present (see below), fibrinolytic therapy should ideally be initiated within 30 min of presentation (i.e., door-to-needle time ≤30 min). The principal goal of fibrinolysis is prompt restoration of full coronary arterial patency. The fibrinolytic agents tissue

plasminogen activator (tPA), streptokinase, tenecteplase (TNK), and reteplase (rPA) have been approved by the U.S. Food and Drug Administration for intra venous use in patients with STEMI. These drugs all act by promoting the conversion of plasminogen to plasmin, which subsequently lyses fibrin thrombi. Although considerable emphasis was first placed on a distinction between more fibrin-specific agents, such as tPA, and non-fibrin-specific agents, such as streptokinase, it is now recognized that these differences are only relative, as some degree of systemic fibrinolysis occurs with the former agents. TNK and rPA are referred to as bolus fibrinolytics since their administration does not require a prolonged intravenous infusion. When assessed angiographically, flow in the culprit coronary artery is described by a simple qualitative scale called the Thrombolysis in Myocardial Infarction (TIMI) grading system: grade 0 indicates com plete occlusion of the infarct-related artery; grade 1 indicates some penetration of the contrast material beyond the point of obstruction, but without perfusion of the distal coronary bed; grade 2 indicates per fusion of the entire infarct vessel into the distal bed, but with flow that is delayed compared with that of a normal artery; and grade 3 indicates full perfusion of the infarct vessel with normal flow. The latter is the goal of reperfusion therapy, because full perfusion of the infarct-related coronary artery yields far better results in terms of limiting infarct size, maintenance of LV function, and reduction of both short- and longterm mortality rates. tPA and the other relatively fibrin-specific plasminogen activators, rPA and TNK, are more effective than streptokinase at restoring full perfusion—i.e., TIMI grade 3 coronary flow—and have a small edge in improving survival as well. The recommended regimen of tPA consists of a 15-mg bolus followed by 50 mg intravenously over the first 30 min, followed by 35 mg over the next 60 min. Streptokinase is administered as 1.5 million units (MU) intravenously over 1 h. rPA is administered in a double-bolus regimen consisting of a 10-MU bolus given over 2–3 min, followed by a second 10-MU bolus 30 min later. TNK is given as a single weight-based intravenous bolus of 0.53 mg/kg over 10 s. In addition to the fibrinolytic agents discussed earlier, pharmacologic reperfusion typically involves adjunctive antiplatelet and antithrom botic drugs, as discussed subsequently. Clear contraindications to the use of fibrinolytic agents include a history of cerebrovascular hemorrhage at any time, a nonhemor rhagic stroke or other cerebrovascular event within the past year, marked hypertension (a reliably determined systolic arterial pressure

> 180 mmHg and/or a diastolic pressure >110 mmHg) at any time during the acute presentation, suspicion of aortic dissection, and active internal bleeding (excluding menses). While advanced age is associated with an increase in hemorrhagic complications, the benefit of fibrinolytic therapy in the elderly appears to justify its use if no other contraindications are present, the amount of myocardium in jeopardy appears to be substantial, and timely access to primary PCI is not available. Relative contraindications to fibrinolytic therapy, which require assessment of the risk-to-benefit ratio, include current use of anti coagulants (international normalized ratio ≥2), a recent (<2 weeks)

invasive or surgical procedure or prolonged (>10 min) cardiopulmo nary resuscitation, known bleeding diathesis, pregnancy, a hemor rhagic ophthalmic condition (e.g., hemorrhagic diabetic retinopathy), active peptic ulcer disease, and a history of severe hypertension that is currently adequately controlled. Because of the risk of an allergic reac tion, patients should not receive

streptokinase if that agent had been received within the preceding 5 days to 2 years. Allergic reactions to streptokinase occur in ~2% of patients who receive it. While a minor degree of hypotension occurs in 4–10% of patients given this agent, marked hypotension occurs, although rarely, in association with severe allergic reactions. Hemorrhage is the most frequent and potentially the most serious complication. Because bleeding episodes that require transfusion are more common when patients require invasive procedures, unneces sary venous or arterial interventions should be avoided in patients receiving fibrinolytic agents. Hemorrhagic stroke is the most serious complication and occurs in ~0.5–0.9% of patients being treated with these agents. This rate increases with advancing age, with patients

> 70 years experiencing roughly twice the rate of intracranial hemor rhage as those <65 years. Large-scale trials have suggested that the rate of intracranial hemorrhage with tPA or rPA is slightly higher than with streptokinase. ■ ■INTEGRATED REPERFUSION STRATEGY Timely performance of PCI is the preferred reperfusion strategy in the management of STEMI. Prior approaches that segregated the pharma cologic and catheter-based approaches to reperfusion have now been replaced with an integrated approach to triage and transfer STEMI patients to receive PCI (Fig. 286-5). To achieve the degree of integra tion required to care for a patient with STEMI, all communities should create and maintain a regional system of STEMI care that includes assessment and continuous quality improvement of emergency medi cal services and hospital-based activities. In patients who have been treated with a fibrinolytic, urgent coro nary angiography should be performed if there is evidence of either (1) failure of reperfusion (persistent chest pain and ST-segment eleva tion >90 min), in which case a rescue PCI should be considered; or (2) coronary artery reocclusion (re-elevation of ST segments and/or recurrent chest pain) or the development of recurrent ischemia. More over, transfer to a PCI-capable center is recommended in all patients immediately after fibrinolysis with intent for angiography and PCI of the infarct-related artery, if indicated, between 3 and 24 h after suc cessful fibrinolysis. Coronary artery bypass surgery should be reserved for patients whose coronary anatomy is unsuited to PCI but in whom revascularization appears to be advisable because of extensive jeopar dized myocardium or recurrent ischemia. HOSPITAL PHASE MANAGEMENT ■ ■CARDIAC INTENSIVE CARE UNITS These units, previously described as coronary care units, are routinely equipped with continuous monitoring of the cardiac rhythm of each patient and hemodynamic monitoring in selected patients. Equally important is the organization of a highly trained team of nurses who can recognize arrhythmias and perform cardiac resuscitation, includ ing electroshock, when necessary. The availability of electrocardio graphic monitoring and trained personnel outside the coronary care unit has made it possible to admit lower-risk patients (e.g., those not hemodynamically compromised and without active arrhythmias) to “intermediate care units.” However, it remains reasonable to admit patients with STEMI to a cardiac intensive care unit when high-risk features are present (e.g., hemodynamic or

> electrical instability) or when suitably equipped and staffed intermediate care units are not available. The duration of stay in the coronary care unit is dictated by the ongoing need for intensive care. In general, patients with STEMI who remain at low risk (no persistent chest discomfort, HF, hypotension, or cardiac arrhythmias) may be safely transferred out of the coronary care unit within 24–48 h.

Activity Factors that increase the work of the heart during the ini tial hours of infarction may increase the size of the infarct. Therefore, patients with STEMI should generally be kept at bed rest for the first 6–12 h. However, in the absence of complications, patients should be encouraged, under supervision, to resume an upright posture by dangling their feet over the side of the bed and sitting in a chair within the first 24 h. This practice is psychologically beneficial and usually results in a reduction in the pulmonary capillary wedge pressure. In the absence of hypotension and other complications, patients typically are ambulating with increasing duration, anticipating that they may be discharged after 3–5 days. Diet Because of the risk of emesis and aspiration soon after STEMI, patients should receive either nothing or only clear liquids by mouth for the first 4–12 h. The typical diet after AMI should provide ≤30% of total calories as fat and have a cholesterol content of ≤300 mg/d. Complex carbohydrates should make up 50–55% of total calories. Por tions should not be unusually large, and the menu should be enriched with foods that are high in potassium, magnesium, and fiber, but low in sodium. Diabetes mellitus and hypertriglyceridemia are managed by restriction of concentrated sweets in the diet. PHARMACOTHERAPY ■ ■ANTITHROMBOTIC AGENTS The use of antiplatelet and anticoagulant therapy during the initial phase of STEMI is based on extensive laboratory and clinical evidence that thrombosis plays an important role in the pathogenesis of this condition. The primary goal of treatment with antiplatelet and antico agulant agents is to maintain patency of the infarct-related artery, in conjunction with reperfusion strategies. A secondary goal is to reduce the patient’s tendency to thrombosis and, thus, the likelihood of mural thrombus formation or deep-venous thrombosis. The degree to which antiplatelet and anticoagulant therapy achieves these goals partly determines how effectively it reduces the risk of mortality from STEMI. As noted previously (see “Management in the Emergency Depart ment” earlier), aspirin is the standard antiplatelet agent for patients with STEMI. The most compelling evidence for the benefits of anti platelet therapy (mainly with aspirin) in STEMI is found in the com prehensive overview by the Antiplatelet Trialists’ Collaboration. Data from nearly 20,000 patients with MI enrolled in 15 randomized trials were pooled and revealed a relative reduction of 27% in the mortal ity rate, from 14.2% in control patients to 10.4% in patients receiving antiplatelet agents. Inhibitors of the P2Y12 ADP receptor prevent activation and aggre gation of platelets. The addition of the P2Y12 inhibitor clopidogrel to background treatment with aspirin to STEMI patients reduces the risk of clinical events (death, reinfarction, stroke) and, in patients receiving fibrinolytic therapy, has been shown to prevent reocclusion of a suc cessfully reperfused infarct artery. Third-generation oral P2Y12 ADP receptor antagonists, such as prasugrel and ticagrelor, are more effec tive than clopidogrel in preventing ischemic complications in STEMI patients undergoing PCI but are associated with an increased risk of bleeding. Glycoprotein IIb/IIIa receptor inhibitors may be used when thrombotic complications occur during PCI. The anticoagulant agent most commonly used in clinical practice is unfractionated heparin (UFH). Use of UFH is recommended in patients with STEMI undergoing primary PCI. In addition, the avail able

data suggest that when UFH is added to a regimen of aspirin and a non-fibrin-specific thrombolytic agent such as streptokinase, addi tional mortality benefit occurs (about 5 lives saved per 1000 patients treated). The immediate administration of intravenous UFH, in addi tion to a regimen of aspirin and relatively fibrin-specific fibrinolytic agents (tPA, rPA, or TNK), helps to maintain patency of the infarctrelated artery. This effect is achieved at the cost of a small increased risk of bleeding. The recommended dose of UFH is an initial bolus of 60 U/kg (maximum 4000 U) followed by an initial infusion of 12 U/kg per h (maximum 1000 U/h). The activated partial thromboplastin time during maintenance therapy should be 1.5–2 times the control value.

Alternatives to UFH for anticoagulation of patients with STEMI are the low-molecular-weight heparin (LMWH) preparations, a synthetic version of the critical pentasaccharide sequence (fondaparinux), and the direct antithrombin bivalirudin. Advantages of LMWHs include high bioavailability permitting administration subcutaneously, reliable anticoagulation without monitoring, and greater anti-Xa:IIa activity. Enoxaparin has been shown to reduce significantly the composite endpoints of death/nonfatal reinfarction and death/nonfatal reinfarc tion/urgent revascularization compared with UFH in STEMI patients who receive fibrinolysis. Treatment with enoxaparin is associated with higher rates of serious bleeding, but net clinical benefit—a composite endpoint that combines efficacy and safety—still favors enoxaparin over UFH. Interpretation of the data on fondaparinux is difficult because of the complex nature of the pivotal clinical trial evaluating it in STEMI (OASIS-6). Fondaparinux appears superior to placebo in STEMI patients not receiving reperfusion therapy, but its relative efficacy and safety compared with UFH are less certain. Owing to the risk of catheter thrombosis, fondaparinux should not be used alone at the time of coronary angiography and PCI but should be combined with another anticoagulant with antithrombin activity such as UFH or bivalirudin. Trials of bivalirudin used an open-label design to evaluate its efficacy and safety compared with UFH plus a glycoprotein IIb/ IIIa inhibitor. Bivalirudin was associated with a lower rate of bleeding, largely driven by reductions in vascular access site hematomas ≥5 cm or the administration of blood transfusions. Bivalirudin is an alterna tive to UFH in patients undergoing primary PCI.

CHAPTER 286 ST-Segment Elevation Myocardial Infarction Patients with an anterior location of the infarction, severe LV dys function, HF, a history of embolism, or two-dimensional echocardio graphic evidence of mural thrombus are at increased risk of systemic or pulmonary thromboembolism. Patients with suspected mural throm bus should receive full therapeutic levels of anticoagulant therapy (LMWH or UFH) while hospitalized, followed by at least 3 months of oral anticoagulant therapy. It is reasonable to consider extended oral anticoagulant therapy (i.e., up to 3 months after presentation with STEMI) in patients with a high risk of developing systemic thrombo embolism because of a large area of akinetic myocardium. ■ ■BETA-ADRENOCEPTOR BLOCKERS The benefits of beta blockers in patients with STEMI can be divided into those that occur immediately when the drug is given acutely and those that accrue over the long term when the drug is given for second ary prevention after an infarction. Acute intravenous beta blockade, although no longer routinely recommended because of the risk of precipitating heart failure, improves the myocardial O2 supply-demand relationship, decreases pain, reduces infarct size, and decreases the incidence of serious ventricular arrhythmias. In patients who undergo fibrinolysis soon after the onset of chest pain, no incremental reduction in mortality rate is seen with beta blockers, but recurrent ischemia and reinfarction are reduced. Oral beta-blocker therapy after STEMI is useful for most patients (including those treated with an angiotensin-converting enzyme

[ACE] inhibitor) except those in whom it is specifically contraindicated (patients with HF or severely compromised LV function, heart block, orthostatic hypotension, or a history of asthma) and perhaps those whose excellent long-term prognosis (defined as an expected mortality rate of <1% per year, patients <55 years, no previous MI, with normal ventricular function, no complex ventricular ectopy, and no angina) markedly diminishes any potential benefit. ■ ■INHIBITION OF THE RENIN-ANGIOTENSINALDOSTERONE SYSTEM ACE inhibitors reduce the mortality rate after STEMI, and the mortality benefits are additive to those achieved with aspirin and beta blockers. The maximum benefit is seen in high-risk patients (those who have an anterior infarction, a prior infarction, and/or globally depressed LV function), but evidence suggests that a short-term benefit occurs when ACE inhibitors are prescribed unselectively to all hemodynamically stable patients with STEMI (i.e., those with a systolic pressure >100 mmHg). The mecha nism involves a reduction in ventricular remodeling after infarction (see

“Ventricular Dysfunction” later) with a subsequent reduction in the risk of HF. The rate of recurrent infarction may also be lower in patients treated chronically with ACE inhibitors after infarction.

ACE inhibitors should be continued indefinitely in patients who have clinically evident HF, in patients in whom an imaging study shows a reduction in global LV function or a large regional wall motion abnormality, or in those who are hypertensive. PART 6 Disorders of the Cardiovascular System Angiotensin receptor blockers (ARBs) should be administered to STEMI patients who are intolerant of ACE inhibitors and who have either clinical or radiologic signs of HF. Long-term mineralocorticoid receptor inhibition (spironolactone, eplerenone) should be prescribed for STEMI patients who are already receiving therapeutic doses of an ACE inhibitor, have an LV ejection fraction ≤40%, and have either symptomatic HF or diabetes mellitus and do not have significant renal dysfunction (creatinine ≥2.5 mg/dL in men and ≥2.0 mg/dL in women) or hyperkalemia (potassium ≥5.0 mEq/L). Although angiotensin receptor–neprilysin inhibition with sacubi tril/valsartan is more effective than ACE inhibitor therapy in patients with symptomatic HF with a reduced ejection fraction, sacubitril/val sartan was not more effective than an ACE inhibitor in preventing the development of incident HF in patients early post-MI. ■ ■OTHER AGENTS Favorable effects on the ischemic process and ventricular remodeling (see below) previously led many physicians to routinely use intravenous nitroglycerin (5–10 μg/min initial dose and up to 200 μg/min as long as hemodynamic stability is maintained) for the first 24–48 h after the onset of infarction. However, a subsequent large, randomized trial demonstrated no benefit of intravenous nitroglycerin with respect to major outcomes in patients with STEMI. Use of intravenous nitroglyc erin may be considered in patients with STEMI who have persistent hypertension, HF, or ongoing ischemia. Results of multiple trials of different calcium antagonists have failed to establish a role for these agents in the treatment of most patients with STEMI. Therefore, the routine use of calcium antagonists can not be recommended. Targeted control of blood glucose in diabetic patients with STEMI has been shown to reduce the mortality rate. Serum magnesium should be measured in all patients on admission, and any demonstrated deficits should be corrected to minimize the risk of arrhythmias. COMPLICATIONS AND THEIR MANAGEMENT Recognition and management of the complications of STEMI are essential elements of the care of this patient population (Table 286-3). TABLE 286-3 Mechanical Complications of ST-Elevation Myocardial Infarction CHARACTERISTIC VENTRICULAR SEPTAL RUPTURE RUPTURE OF THE VENTRICULAR FREE WALL PAPILLARY MUSCLE RUPTURE Incidence 0.2–3% without reperfusion therapy, 0.2–0.34% with fibrinolytic therapy, 3.9% in patients with cardiogenic shock Approximately 0.3–1%; fibrinolytic

therapy does not reduce risk; primary PCI seems to reduce risk Time course Bimodal peak; within 24 h and 3–5 days; range, 1–14 days Bimodal peak; within 24 h and 3–5 days; range, 1–14 days Clinical manifestations Chest pain, shortness of breath, hypotension Anginal, pleuritic, or pericardial chest pain; syncope; hypotension; restlessness; sudden death Physical findings Harsh holosystolic murmur, thrill, S3, accentuated S2, pulmonary edema, RV and LV failure, cardiogenic shock Jugular venous distention (29% of patients), pulsus paradoxus (47%), electromechanical dissociation, cardiogenic shock Echocardiographic findings Ventricular septal rupture, left-to-right shunt on color flow Doppler echocardiography through the ventricular septum, pattern of RV overload

> 5 mm pericardial effusion not visualized in all cases; layered, high-acoustic echoes within the pericardium (blood clot); direct visualization of tear; signs of tamponade Right-heart catheterization Increase in oxygen saturation from the RA to RV, large v waves Ventriculography insensitive, classic signs of tamponade not always present (equalization of diastolic pressures in the cardiac chambers) Abbreviations: LV, left ventricle; PCI, percutaneous coronary intervention; PCWP, pulmonary capillary wedge pressure; RA, right atrium; RV, right ventricle. Source: Reproduced with permission from Bohula EA, Morrow DA: ST-elevation myocardial infarction: Management, in Braunwald's Heart Disease, 12th ed, Libby P et al (eds). New York, Elsevier, 2022, pp 662-713.

■ ■VENTRICULAR DYSFUNCTION After STEMI, the left ventricle undergoes a series of changes in shape, size, and thickness in both the infarcted and noninfarcted segments. This process is referred to as ventricular remodeling and generally precedes the development of clinically evident HF in the months to years after infarction. Soon after STEMI, the left ventricle begins to dilate. Acutely, this results from expansion of the infarct, i.e., slip page of muscle bundles, disruption of normal myocardial cells, and tissue loss within the necrotic zone, resulting in disproportionate thinning and elongation of the infarct zone. Later, lengthening of the noninfarcted segments occurs as well. The overall chamber enlarge ment that occurs is related to the size and location of the infarct, with greater dilation following infarction of the anterior wall and apex of the left ventricle and causing more marked hemodynamic impair ment, more frequent HF, and a poorer prognosis. Progressive dilation and its clinical consequences may be ameliorated by therapy with ACE inhibitors. In patients with an ejection fraction <40%, regard less of whether or not HF is present, ACE inhibitors or ARBs, and eventually a beta blocker, should be prescribed (see "Inhibition of the Renin-Angiotensin-Aldosterone System" earlier). ■ ■HEMODYNAMIC ASSESSMENT Pump failure is now the primary cause of in-hospital death from STEMI. The extent of infarction correlates well with the degree of pump failure and with mortality, both early (within 10 days of infarction) and later. The most common clinical signs are pulmo nary rales and an S3 gallop sound. Pulmonary congestion is also frequently seen on the chest roentgenogram. Elevated LV filling pressure and elevated pulmonary artery pressure are the charac teristic hemodynamic findings, but these findings may result from a reduction of ventricular compliance (diastolic failure) and/or a reduction of stroke volume with secondary cardiac dilation (systolic failure) (Chap. 264). A classification originally proposed by Killip divides patients into four groups: class I, no signs of pulmonary or venous congestion; class II, moderate HF as evidenced by rales at the lung bases, S3 gallop, tachypnea, or

signs of failure of the right side of the heart, including venous and hepatic congestion; class III, severe HF and pulmonary edema; and class IV, shock with systolic pressure <90 mmHg and evidence of peripheral vasoconstriction, peripheral cyanosis, mental confusion, and oliguria. When this classification was estab lished in 1967, the expected hospital mortality rate of patients in these classes was as follows: class I, 0–5%; class II, 10–20%; class III, 35–45%; and class IV, 85–95%. With advances in management, the mortality rate in each class has fallen, perhaps by as much as Approximately 0.1–1% (posteromedial more frequent than anterolateral papillary muscle rupture) Bimodal peak; within 24 h and 3–5 days; range, 1–14 days Abrupt onset of shortness of breath and pulmonary edema; hypotension A soft murmur in some cases, no thrill, variable signs of RV overload, severe pulmonary edema, cardiogenic shock Hypercontractile LV, torn papillary muscle or chordae tendineae, flail leaflet, severe mitral regurgitation on color flow Doppler echocardiography No increase in oxygen saturation from the RA to RV, large v waves, very high PCWP

one-third to one-half. However, the mortality rate for patients with cardiogenic shock (class IV) has plateaued without additional improvement for the past 25 years. Hemodynamic evidence of abnormal global LV function appears when contraction is seriously impaired in 20–25% of the left ventricle. Infarction of ≥40% of the left ventricle usually results in cardiogenic shock (Chap. 316). Positioning of a balloon flotation (Swan-Ganz) catheter in the pulmonary artery permits monitoring of LV filling pressure as well as estimation of the cardiac output; this technique may be useful in patients who exhibit hypotension and/or clinical evidence of HF. With the addition of intraarterial pressure monitoring, systemic vascular resistance can be calculated as a guide to adjusting vasopres sor and vasodilator therapy. Some patients with STEMI have markedly elevated LV filling pressures (>22 mmHg) and normal cardiac indices (2.6–3.6 L/[min/m2]), while others have relatively low LV filling pres sures (<15 mmHg) and reduced cardiac indices. The former patients usually benefit from diuresis, while the latter may respond to volume expansion. ■ ■HYPOVOLEMIA This is an easily corrected condition that may contribute to the hypo tension and vascular collapse associated with STEMI in some patients. It may be secondary to previous diuretic use, to reduced fluid intake during the early stages of the illness, and/or to vomiting associated with pain or medications. Consequently, hypovolemia should be identified and corrected in patients with STEMI and hypotension by cautious fluid administration during continuous monitoring of oxygenation before more vigorous forms of therapy are begun. Eventually, the cardiac output plateaus, and further increases in LV filling pressure only increase congestive symptoms and decrease systemic oxygenation without raising arterial pressure. TREATMENT Heart Failure The management of HF in association with STEMI is similar to that of acute HF secondary to other forms of heart disease (avoidance of hypoxemia, diuresis, afterload reduction, inotro pic support) (Chap. 264), except that the benefits of digitalis administration to patients with STEMI are unimpressive. By contrast, diuretic agents are extremely effective, as they diminish pulmonary congestion in the presence of systolic and/or diastolic HF. LV filling pressure falls, and orthopnea and dyspnea improve after the intravenous administration of furosemide or other loop diuretics. Nitrates in various forms may be used to decrease pre load and congestive symptoms. Oral isosorbide dinitrate, topical nitroglycerin ointment, and intravenous nitroglycerin all have the advantage over a diuretic of lowering preload through veno dilation without decreasing the total plasma volume. In addition, nitrates may improve ventricular compliance if ischemia is pres ent, as ischemia causes an elevation of LV filling pressure. Vasodi lators must be used with caution to prevent serious hypotension. As noted earlier, ACE inhibitors are an ideal class of drugs for management of

ventricular dysfunction after STEMI, especially for the long term. (See “Inhibition of the Renin-AngiotensinAldosterone System” earlier.) ■ ■CARDIOGENIC SHOCK Prompt reperfusion, efforts to reduce infarct size, and treatment of ongoing ischemia and other complications of MI appear to have reduced the incidence of cardiogenic shock from 20 to ~7%. Among those who exhibit cardiogenic shock, only 10% of patients with this condition present with it on admission, while 90% develop it during hospitalization. Typically, patients who develop cardiogenic shock have severe multivessel coronary artery disease with evidence of “piece meal” necrosis extending outward from the original infarct zone. The evaluation and management of cardiogenic shock after STEMI are discussed in detail in Chap. 316.

■ ■RIGHT VENTRICULAR INFARCTION Approximately one-third of patients with inferior infarction demon strate at least a minor degree of RV necrosis. An occasional patient with inferoposterior LV infarction also has extensive RV infarction, and rare patients present with infarction limited primarily to the RV. Clinically significant RV infarction causes signs of severe RV failure (jugular venous distention, Kussmaul’s sign, hepatomegaly [Chap. 246]) with or without hypotension. ST-segment elevations of right-sided precordial ECG leads, particularly lead V4R, are fre quently present in the first 24 h in patients with RV infarction. Twodimensional echocardiography is helpful in determining the degree of RV dysfunction. Catheterization of the right side of the heart often reveals a distinctive hemodynamic pattern resembling constrictive pericarditis (steep right atrial “y” descent and an early diastolic dip and plateau in RV waveforms) (Chap. 281). Therapy consists of volume expansion to maintain adequate RV preload and efforts to improve LV performance with attendant reduction in pulmonary capillary wedge and pulmonary arterial pressures.

CHAPTER 286 ST-Segment Elevation Myocardial Infarction ■ ■ARRHYTHMIAS (See also Chaps. 251 and 253) The incidence of arrhythmias after STEMI is higher in patients seen early after the onset of symptoms. The mechanisms responsible for infarction-related arrhythmias include autonomic nervous system imbalance, electrolyte disturbances, isch emia, and slowed conduction in zones of ischemic myocardium. An arrhythmia can usually be managed successfully if trained personnel and appropriate equipment are available when it develops. Since most deaths from arrhythmia occur during the first few hours after infarc tion, the effectiveness of treatment relates directly to the speed with which patients come under medical observation. The prompt manage ment of arrhythmias constitutes a significant advance in the treatment of STEMI. Ventricular Premature Beats Infrequent, sporadic ventricular premature depolarizations occur in almost all patients with STEMI and do not require therapy. Whereas in the distant past, frequent, multifocal, or early diastolic ventricular extrasystoles (so-called warn ing arrhythmias) were routinely treated with antiarrhythmic drugs to reduce the risk of development of ventricular tachycardia and ventricular fibrillation, pharmacologic therapy is now reserved for patients with sustained ventricular arrhythmias. Prophylactic antiar rhythmic therapy (either intravenous lidocaine early or oral agents later) is contraindicated for ventricular premature beats in the absence of clinically important ventricular tachyarrhythmias because such therapy may increase the mortality rate. Beta-adrenoceptor block ing agents are effective in abolishing ventricular ectopic activity in patients with STEMI and in the prevention of ventricular fibrillation. As described earlier (see “Beta-Adrenoceptor Blockers”), they should be used routinely in patients without contraindications. In addition, hypokalemia and hypomagnesemia are risk factors for ventricular fibrillation in patients with STEMI; to reduce the risk, the serum potassium concentration should be adjusted to ~4.5 mmol/L and magnesium to ~2.0 mmol/L. Ventricular Tachycardia and Fibrillation Sustained

ventricular tachycardia that is well tolerated hemodynamically should be treated with an intravenous regimen of amiodarone (bolus of 150 mg over 10 min, followed by infusion of 1.0 mg/min for 6 h and then 0.5 mg/ min). A less desirable but alternative regimen is procainamide (bolus of 15 mg/kg over 20–30 min; infusion of 1–4 mg/min). If ventricular tachycardia does not stop promptly, electrical cardioversion should be used (Chap. 253). An unsynchronized discharge of 200 J (biphasic waveform) is used immediately in patients with ventricular fibrillation or when ventricular tachycardia causes hemodynamic deterioration. Ventricular tachycardia or fibrillation that is refractory to electroshock may be more responsive after the patient is treated with amiodarone (150-mg bolus). Ventricular arrhythmias, including the unusual form of ventricular tachycardia known as torsades des pointes (Chaps. 259 and 261), may occur in patients with STEMI as a consequence of ongoing ischemia or

other concurrent problems (e.g., hypoxia, hypokalemia, or other elec trolyte disturbances) or of the toxic effects of a QT-prolonging agent being administered to the patient. A search for such secondary causes should always be undertaken.

Although the in-hospital mortality rate is increased, the long-term survival is excellent in patients who survive to hospital discharge after primary ventricular fibrillation; i.e., ventricular fibrillation that is a primary response to acute ischemia that occurs during the first 48 h and is not associated with predisposing factors such as HF, shock, bundle branch block, or ventricular aneurysm. This natural history is in sharp contrast to the poor prognosis for patients who develop ventricular fibrillation secondary to severe pump failure. For patients who develop ventricular tachycardia or ventricular fibrillation late in their hospital course (i.e., after the first 48 h), the mortality rate is increased both in-hospital and during long-term follow-up. Such patients should be considered for implantation of a cardioverter-defibrillator (ICD) (Chap. 259). A more challenging issue is the prevention of sudden cardiac death from ventricular fibrillation late after STEMI in patients who have not exhibited sustained ventricular tachyarrhythmias during their index hospitalization. An algorithm for selection of patients who warrant prophylactic implantation of an ICD is shown in Fig. 286-6. PART 6 Disorders of the Cardiovascular System Accelerated Idioventricular Rhythm Accelerated idioventricu lar rhythm (AIVR, “slow ventricular tachycardia”), a ventricular rhythm with a rate of 60–100 beats/min, often occurs transiently during fibrinolytic therapy at the time of reperfusion. For the most part, AIVR, whether it occurs in association with fibrinolytic therapy or spontaneously, is benign, and does not presage the development of classic ventricular tachycardia. Most episodes of AIVR do not require treatment if the patient is monitored carefully, as degeneration into a Yes Primary prevention in pts with IHD, LVEF ≤40% EP study (especially in the presence of NSVT) MI <40 d and/or revascularization <90 d Yes* No NYHA class II or III LVEF ≤35% LVEF ≤40%, NSVT, inducible sustained VT on EP study NYHA class I LVEF ≤30% Yes Yes No No ICD (Class I)* ICD (Class I) ICD (Class IIa) GDMT ICD should not be implanted (Class III: No benefit) FIGURE 286-6 Primary prevention of SCD in patients with ischemic heart disease, including recent MI. *Scenarios exist for early ICD placement in select circumstances such as patients with a pacing indication or syncope. †Advanced HF therapy includes CRT, cardiac transplant, and left ventricular assist device. CRT, cardiac resynchronization therapy; EP, electrophysiologic; GDMT, guideline-directed management and therapy; HF, heart failure; ICD, implantable cardioverter-defibrillator; IHD, ischemic heart disease, LVEF, left ventricular ejection fraction; MI, myocardial infarction; NSVT, nonsustained ventricular tachycardia; NYHA, New York Heart Association; pts, patients; SCD, sudden cardiac death; VT, ventricular tachycardia; WCD, wearable cardioverter-defibrillator. The

available evidence does not suggest there is a survival advantage to the use of an ICD early after MI, and the WCD is a potential option while waiting until the ejection fraction is reassessed (see figure). While the WCD appears to be effective in patients who wear the device, it is associated with frequent alarms, skin irritation, and emotional distress, which results in reduced wear time in a large number of patients. (Reproduced with permission from SM Al-Khatib et al: 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. Circulation 138:e272, 2018.)

more serious arrhythmia is rare; overly aggressive treatment can lead to complete heart block. Supraventricular Arrhythmias Sinus tachycardia is the most common supraventricular arrhythmia. If it occurs secondary to another cause (such as anemia, fever, HF, or a metabolic derangement), the primary problem should be treated first. However, if it appears to be due to sympathetic overstimulation (e.g., as part of a hyperdynamic state), then treatment with a beta blocker is indicated. Other common arrhythmias in this group are atrial flutter and atrial fibrillation, which are often secondary to LV failure. Digoxin may be considered for supraventricular arrhythmias if HF with reduced ejection fraction is present. If left ventricular systolic dysfunction is absent, beta blockers, verapamil, and diltiazem are suitable alternatives for controlling the ventricular rate, as they may also help to control ischemia. If the abnor mal rhythm persists for a prolonged period with a high ventricular rate (e.g., >120 beats/min) or if tachycardia induces HF, shock, or ischemia (as manifested by recurrent pain or ECG changes), a synchronized electroshock should be used. Accelerated junctional rhythms have diverse causes but may occur in patients with inferoposterior infarction. Digitalis excess must be ruled out. In some patients with severely compromised LV function, the loss of appropriately timed atrial systole results in a marked reduc tion of cardiac output. Right atrial or coronary sinus pacing is indicated in such instances. Sinus Bradycardia Treatment of sinus bradycardia is indicated if hemodynamic compromise results from the slow heart rate. Atro pine is the most useful drug for increasing heart rate and should be given intravenously in doses of 1.0 mg initially. If the rate remains Inducible sustained VT ICD (Class I) No GDMT (Class I) Reassess LVEF >40 d after MI and/or >90 d after revascularization WCD (Class IIb) NYHA class IV candidate for advanced HF therapy† Yes

<50–60 beats/min, additional doses, up to a total of 3.0 mg, may be given. Persistent bradycardia (<40 beats/min) despite atropine may be treated with electrical pacing. Atrioventricular and Intraventricular Conduction Disturbances

(See also Chap. 251) Both the in-hospital mortality rate and the post discharge mortality rate of patients who have complete atrioventricular (AV) block in association with anterior infarction are markedly higher than those of patients who develop AV block with inferior infarction. This difference is related to the fact that heart block in inferior infarc tion is commonly a result of increased vagal tone and/or the release of adenosine and, therefore, is transient. In anterior wall infarction, however, heart block is usually related to ischemic malfunction of the conduction system, which is commonly associated with extensive myocardial necrosis. Temporary electrical pacing provides an effective means of increas ing the heart rate of patients with bradycardia due to AV block. How ever, acceleration of the heart rate may have only a limited impact on prognosis in patients with anterior wall infarction and complete heart block in whom the large size of the infarct is the major factor determin ing outcome. It should be carried out if it improves hemodynamics. Pacing does appear to be beneficial in patients with inferoposterior infarction who have complete

heart block associated with HF, hypo tension, marked bradycardia, or significant ventricular ectopic activity. A subgroup of these patients, those with RV infarction, often respond poorly to ventricular pacing because of the loss of the atrial contribu tion to ventricular filling. In such patients, dual-chamber AV sequen tial pacing may be required. External noninvasive pacing electrodes should be positioned in a “demand” mode for patients with sinus bradycardia (rate <50 beats/ min) that is unresponsive to drug therapy, Mobitz II second-degree AV block, third-degree heart block, or bilateral bundle branch block (e.g., right bundle branch block plus left anterior fascicular block). Retrospective studies suggest that permanent pacing may reduce the long-term risk of sudden death due to bradyarrhythmias in the rare patient who develops combined persistent bifascicular and transient third-degree heart block during the acute phase of MI. ■ ■OTHER COMPLICATIONS Recurrent Chest Discomfort Because recurrent or persistent ischemia often heralds extension of the original infarct or reinfarc tion in a new myocardial zone and is associated with a near tripling of mortality after STEMI, patients with these symptoms should be referred for prompt coronary arteriography and mechanical revascu larization. Administration of a fibrinolytic agent is an alternative to early mechanical revascularization in patients with recurrent ischemic ST-segment elevation. Pericarditis (See also Chap. 281) Pericardial friction rubs and/or pericardial pain are frequently encountered in patients with STEMI involving the epicardium. This complication can usually be managed with aspirin (650 mg four times daily). It is important to diagnose the chest pain of pericarditis accurately because failure to recognize it may lead to the erroneous diagnosis of recurrent ischemic pain and/or infarct extension, with resulting inappropriate use of anticoagulants, nitrates, beta blockers, or coronary arteriography. When it occurs, complaints of pain radiating to either trapezius muscle is helpful because such a pattern of discomfort is typical of pericarditis but rarely occurs with ischemic discomfort. Anticoagulants potentially could cause tamponade in the presence of acute pericarditis (as manifested by either pain or persistent rub) and therefore should not be used unless there is a compelling indication. Thromboembolism Clinically apparent thromboembolism com plicates STEMI in ~10% of cases, but embolic lesions are found in 20% of patients in necropsy series, suggesting that thromboembolism is often clinically silent. Thromboembolism is considered to be an important contributing cause of death in 25% of patients with STEMI who die after admission to the hospital. Arterial emboli originate from LV mural thrombi, while most pulmonary emboli arise in the leg veins.

Thromboembolism typically occurs in association with large infarcts (especially anterior), HF, and an LV thrombus detected by echocardiog raphy. The incidence of arterial embolism from a clot originating in the ventricle at the site of an infarction is small but real. Two-dimensional echocardiography reveals LV thrombi in about one-third of patients with anterior wall infarction but in few patients with inferior or poste rior infarction. Arterial embolism often presents as a major complica tion, such as hemiparesis when the cerebral circulation is involved. When a thrombus has been clearly demonstrated by echocardiographic or other techniques, systemic anticoagulation should be undertaken (in the absence of contraindications), as the incidence of embolic complica tions appears to be markedly lowered by such therapy. The appropriate duration of therapy is unknown, but 3–6 months is reasonable.

CHAPTER 286 ST-Segment Elevation Myocardial Infarction Left Ventricular Aneurysm The term ventricular aneurysm is usually used to describe dyskinesis or local expansile paradoxical wall motion. Normally functioning myocardial fibers must shorten more if stroke volume and cardiac output are to be maintained in patients with ventricular aneurysm; if they cannot, overall ventricular function is impaired. True aneurysms are composed of scar tissue and neither

predispose to nor are associated with cardiac rupture. The complications of LV aneurysm do not usually occur for weeks to months after STEMI; they include HF, arterial embolism, and ven tricular arrhythmias. Apical aneurysms are the most common and the most easily detected by clinical examination. The physical finding of greatest value is a double, diffuse, or displaced apical impulse. Ven tricular aneurysms are readily detected by two-dimensional echocar diography, which may also reveal a mural thrombus in an aneurysm. Rarely, myocardial rupture may be contained by a local area of peri cardium, along with organizing thrombus and hematoma. Over time, this pseudoaneurysm enlarges, maintaining communication with the LV cavity through a narrow neck. Because a pseudoaneurysm often ruptures spontaneously, it should be surgically repaired if recognized. POSTINFARCTION RISK STRATIFICATION AND MANAGEMENT Many clinical and laboratory factors have been identified that are associated with an increase in cardiovascular risk after initial recovery from STEMI. Some of the most important factors include persistent ischemia (spontaneous or provoked), depressed LV ejection fraction (<40%), rales above the lung bases on physical examination or con gestion on chest imaging, and symptomatic ventricular arrhythmias. Other features associated with increased risk include a history of previous MI, age >75, diabetes mellitus, prolonged sinus tachycardia, hypotension, ST-segment changes at rest without angina (“silent isch emia”), an abnormal signal-averaged ECG, nonpatency of the infarctrelated coronary artery (if angiography is undertaken), and persistent advanced heart block or a new intraventricular conduction abnormal ity on the ECG. Therapy must be individualized on the basis of the relative importance of the risk(s) present. The goal of preventing reinfarction, pump failure, and death after recovery from STEMI has led to strategies to evaluate risk after infarction. The risk of early recurrent ischemic events has diminished substantially in the era of primary PCI, with further reduction in the setting of current practice recommendations for routine revascular ization of suitable severely stenosed nonculprit coronary arteries. In contrast, in stable patients after fibrinolysis who have not undergone revascularization, submaximal exercise stress testing may be carried out before hospital discharge to detect residual ischemia and ven tricular ectopy and to provide the patient with a guideline for exercise in the early recovery period. Alternatively, or in addition, a maximal (symptom-limited) exercise stress test may be carried out 4–6 weeks after infarction. Patients in whom angina is induced at relatively low workloads, those who have a large reversible defect on perfusion imag ing, those with demonstrable ischemia, and those in whom exercise provokes symptomatic ventricular arrhythmias should be considered at high risk for recurrent MI or death from arrhythmia. Cardiac catheter ization with coronary angiography and/or invasive electrophysiologic evaluation is advised.

Revision #1
Created 2026-01-06 16:33:57 UTC by Omar Ayman
Updated 2026-01-06 16:33:57 UTC by Omar Ayman