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ACUTE CORONARY SYNDROME

2025/March/05

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Approach to the Patient with Chest Pain

Acute chest pain remains one of the most common reasons for seeking care in the emergency department (ED), Such pain suggests acute coronary syndrome (ACS), but after diagnostic evaluation, only 10% to 15% of patients with acute chest pain actually have ACS

2–5% It is difficult to differentiate patients with ACS or other life-threatening conditions from those with non cardiovascular, non-life- threatening chest pain. The diagnosis of ACS is missed in approximately 2% of patients

Myocardial Ischemia or Infarction

The most common serious cause of acute chest discomfort is *myocardial ischemia or infarction* , which occurs when the supply of myocardial oxygen is inadequate for the demand. The classic manifestation of ischemia is angina, which is usually described as a heavy chest pressure or squeezing, a burning feeling, or difficulty breathing. The discomfort often radiates to the left shoulder, neck, or arm. It typically builds in intensity over a period of a few minutes. The pain may begin with exercise or psychological stress, but ACS most commonly occurs without obvious precipitating factors.

Clinicians should be mindful of *"angina equivalents"* such as jaw or shoulder pain in the absence of chest pain or dyspnea, nausea or vomiting, and diaphoresis. In particular, women, older persons, and individuals with diabetes may experience atypical symptoms of myocardial ischemia or infarction

Atypical descriptions of chest pain reduce the likelihood of myocardial ischemia or injury. The American College of Cardiology (ACC) and American Heart Association (AHA) guidelines list the following as pain descriptions uncharacteristic of myocardial ischemia:

- *Pleuritic pain* (i.e., sharp or knifelike pain brought on by respiratory movements or coughing)
- Primary or sole location of the discomfort *in the middle or lower abdominal region*
- Pain that may be localized by the tip of one finger, particularly over the left ventricular apex
- Pain *reproduced with movement or palpation* of the chest wall or arms
- *Constant pain* that persists for many hours
- *Very brief* episodes of pain that last a few seconds or less
- Pain that *radiates into the lower extremities*

TABLE 35.2 **Value of Elements of the Chest Pain History for the Diagnosis of Acute Coronary Syndrome**

PAIN DESCRIPTOR	POSITIVE LIKELIHOOD RATIO (95% CI)
Increased Likelihood of AMI	
Radiation to the right arm or shoulder	4.7 (1.9-12.0)
Radiation to both arms or shoulders	4.1 (2.5–6.5)
Associated with exertion	2.4 (1.5–3.8)
Radiation to the left arm	2.3 (1.7–3.1)
Associated with diaphoresis	2.0 (1.9–2.2)
Associated with nausea or vomiting	1.9 (1.7–2.3)
Worse than previous angina or similar to previous MI	1.8 (1.6–2.0)
Described as pressure	1.3 (1.2–1.5)
Decreased Likelihood of AMI	
Described as pleuritic	0.2 (0.1–0.3)
Described as positional	0.3 (0.2–0.5)
Described as sharp	0.3 (0.2–0.5)
Reproducible with palpation	0.3 (0.2–0.4)
Inframammary location	0.8 (0.7–0.9)
Not associated with exertion	0.8 (0.6–0.9)

AMI, Acute myocardial infarction; *CI,* confidence interval; *MI,* myocardial infarction.
Modified from Swap CJ, Nagurney JT. Value and limitations of chest pain history in the evaluation of patients with suspected acute coronary syndromes. *JAMA*. 2005;294:2623.

TABLE 35.1 Common Causes of Acute Chest Pain

SYSTEM	SYNDROME	CLINICAL DESCRIPTION	KEY DISTINGUISHING FEATURES
Cardiac	Angina	Retrosternal chest pressure, burning, or heaviness; radiating occasionally to the neck, jaw, epigastrium, shoulders, left arm	Precipitated by exercise, cold weather, or emotional stress; duration of 2–10 min
	Rest or unstable angina	Same as angina, but may be more severe	Typically <20 min; lower tolerance for exertion; crescendo pattern
	Acute myocardial infarction	Same as angina, but may be more severe	Sudden onset, usually lasting ≥30 min; often associated with shortness of breath, weakness, nausea, vomiting
	Pericarditis	Sharp, pleuritic pain aggravated by changes in position; highly variable duration	Pericardial friction rub
Vascular	Aortic dissection	Excruciating, ripping pain of sudden onset in the anterior aspect of the chest, often radiating to the back	Marked severity of unrelenting pain; usually occurs in the setting of hypertension or underlying connective tissue disorder such as Marfan syndrome
	Pulmonary embolism	Sudden onset of dyspnea and pain, usually pleuritic with pulmonary infarction	Dyspnea, tachypnea, tachycardia, signs of right-sided heart failure
	Pulmonary hypertension	Substernal chest pressure, exacerbated by exertion	Pain associated with dyspnea and signs of pulmonary hypertension
Pulmonary	Pleuritis and/or pneumonia	Pleuritic pain, usually brief, over the involved area	Pain pleuritic and lateral to the midline, associated with dyspnea
	Tracheobronchitis	Burning discomfort in the midline	Midline location, associated with coughing
	Spontaneous pneumothorax	Sudden onset of unilateral pleuritic pain, with dyspnea	Abrupt onset of dyspnea and pain
Gastrointestinal	Esophageal reflux	Burning substernal and epigastric discomfort, 10–60 min in duration	Aggravated by a large meal and postprandial recumbency; relieved by antacid
	Peptic ulcer	Prolonged epigastric or substernal burning	Relieved by antacid or food
	Gallbladder disease	Prolonged epigastric or right upper quadrant pain	Unprovoked or following a meal
	Pancreatitis	Prolonged, intense epigastric and substernal pain	Risk factors, including alcohol, hypertriglyceridemia, medications
Musculoskeletal	Costochondritis	Sudden onset of intense fleeting pain	May be reproduced by pressure over the affected joint; occasionally, swelling and inflammation over the costochondral joint
	Cervical disc disease	Sudden onset of fleeting pain	May be reproduced with movement of the neck
	Trauma or strain	Constant pain	Reproduced by palpation or movement of the chest wall or arms
Infectious	Herpes zoster	Prolonged burning pain in a dermatomal distribution	Vesicular rash, dermatomal distribution
Psychological	Panic disorder	Chest tightness or aching, often accompanied by dyspnea and lasting 30 min or more, unrelated to exertion or movement	Patient may have other evidence of an emotional disorder

The ACC and AHA guidelines suggest an **approach to the immediate management of patients with possible ACS** that integrates information from the *history*, *physical examination*, *12-lead ECG*, and *initial cardiac marker tests* to assign patients to four categories—non cardiac related diagnosis, chronic stable angina, possible ACS, and definite ACS

Electrocardiography

For patients with ongoing chest discomfort, an ECG, which is a source of decisive data, should be obtained within 10 minutes after arrival, The ECG aids in both diagnosis and prognosis. ST segment elevation ≥1 mm in ≥2 contiguous leads is required for the diagnosis of STEMI.

ST segment depression as little as 0.5 mm is suggestive of ischemia. T wave inversions of at least 2 mm can also indicate ischemia but are less specific.

Chest Radiography

A chest radiograph is typically obtained for all patients with chest pain. It is usually non diagnostic in patients with ACS but can show pulmonary edema secondary to ischemia-induced diastolic or systolic dysfunction. It is more useful for diagnosing or suggesting other disorders; for example, it may show a widened mediastinum or aortic knob in patients with aortic dissection. The chest radiograph is generally normal in PE but can show atelectasis, an elevated hemi diaphragm, a pleural effusion, or more rarely, a Hampton hump or Westermark sign. The chest radiograph can reveal pneumonia or pneumothorax.

Biomarkers

Patients with chest discomfort possibly consistent with ACS should undergo measurement of biomarkers of myocardial injury. The preferred biomarker is cardiac troponin (cTn: T or I; cTnT or cTnI); creatine kinase MB isoenzyme (CK-MB) is less sensitive and is no longer recommended

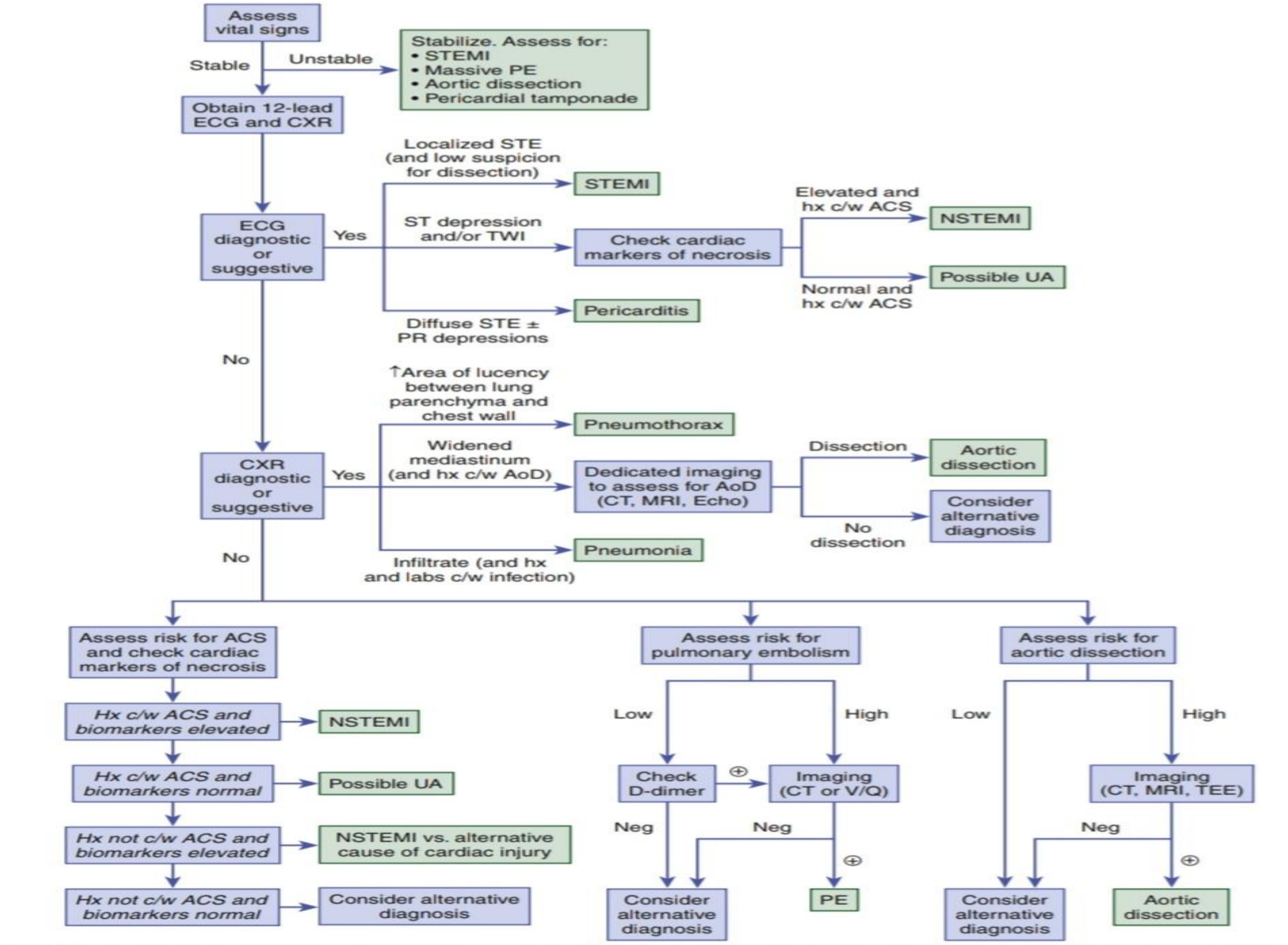

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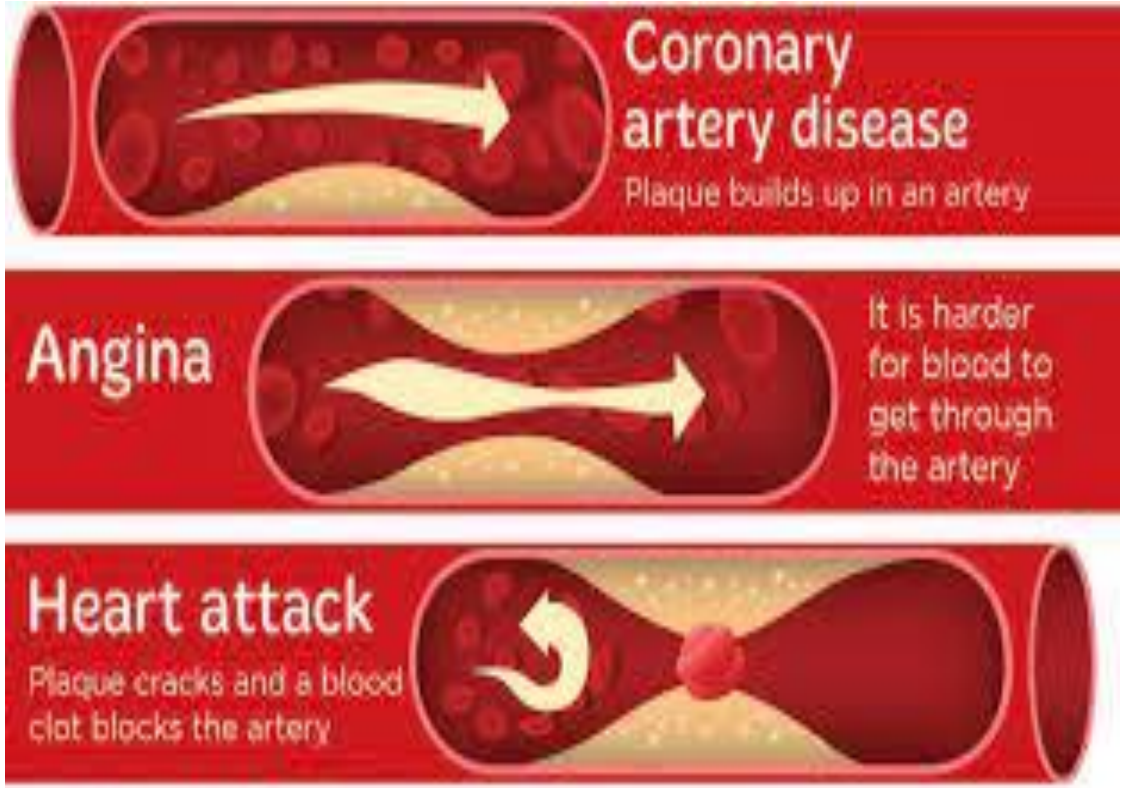
TABLE 37.2 Causes of Myocardial Injury

Myocardial injury related to acute myocardial ischemia
Atherosclerotic plaque disruption with thrombosis
Myocardial injury related to acute myocardial ischemia because of oxygen supply/demand imbalance
Reduced myocardial perfusion
• Coronary artery spasm, microvascular dysfunction
• Coronary embolism
• Coronary artery dissection
• Sustained bradyarrhythmia
• Hypotension or shock
• Respiratory failure
• Severe anemia
Increased myocardial oxygen demand
• Sustained tachyarrhythmia
• Severe hypertension with or without left ventricular hypertrophy
Other causes of myocardial injury
Cardiac conditions
• Heart failure
• Myocarditis
• Cardiomyopathy (any type)
• Takotsubo syndrome
• Coronary revascularization procedure
• Cardiac procedure other than revascularization
• Catheter ablation
• Defibrillator shocks
• Cardiac contusion
Systemic conditions
• Sepsis, infectious disease
• Chronic kidney disease
• Stroke, subarachnoid hemorrhage
• Pulmonary embolism, pulmonary hypertension
• Infiltrative diseases, e.g., amyloidosis, sarcoidosis
• Chemotherapeutic agents
• Critically ill patients
• Strenuous exercise

From Thygesen K, Alpert JS, Jaffe AS, et al. Fourth universal definition of myocardial

Ischemic heart disease

may manifest clinically as either chronic stable angina or an acute coronary syndrome (ACS).
The spectrum of ACS includes ST-segment elevation myocardial infarction (STEMI) and the non–ST elevation acute coronary syndromes (NSTE-ACS). The latter consist of non–ST elevation myocardial infarction (NSTEMI) and unstable angina (UA), which have indistinguishable clinical presentations at the initial evaluation.



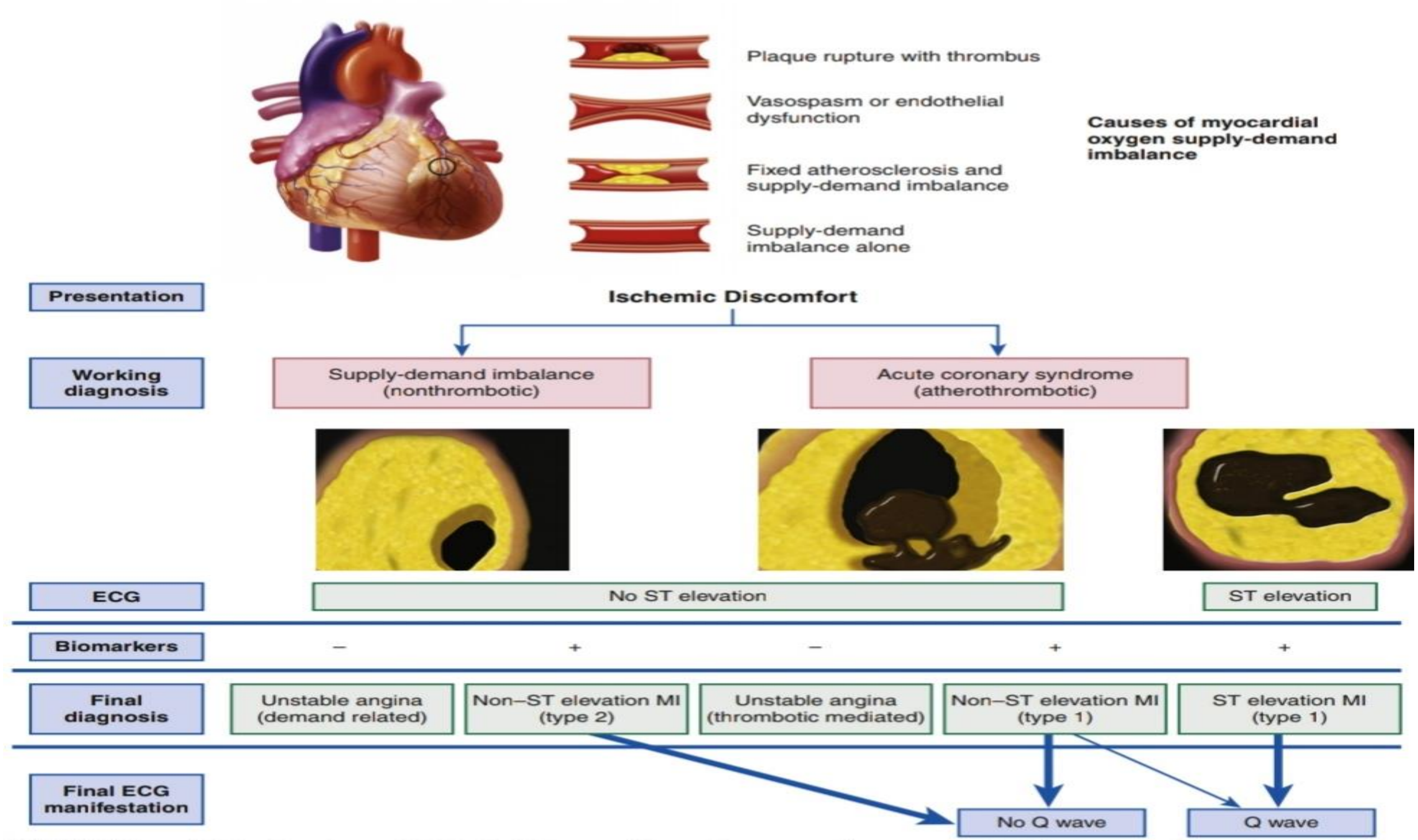
Several features help to differentiate ACS from chronic stable angina, including:

(1) sudden onset of symptoms at rest (or with minimal exertion) that last at least 10 minutes unless treated
promptly;

(2) severe pain, pressure, or discomfort in the chest; and

(3) an accelerating pattern of angina that develops more frequently, with greater severity, or that awakens the patient from sleep.

The 12-lead electrocardiogram (ECG) and markers of myocardial necrosis are essential tools in distinguishing between the three types of ACS mentioned previously. Patients with typical symptoms *without* persistent (>20 minutes) ST-segment elevation in at least two contiguous electrocardiographic leads, but with elevation of myocardial biomarkers (>99% of the normal range), are classified as having NSTEMI. Patients with typical symptoms and serial negative markers of myocardial necrosis are classified as having UA



Plaque rupture with thrombus
Vasospasm or endothelial dysfunction
Fixed atherosclerosis and supply-demand imbalance
Supply-demand imbalance alone
Causes of myocardial oxygen supply-demand imbalance
Presentation
Ischemic Discomfort
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)
Unstable angina (thrombotic mediated)
Non–ST elevation MI (type 1)
ST elevation MI (type 1)
Final ECG manifestation
No Q wave
Q wave

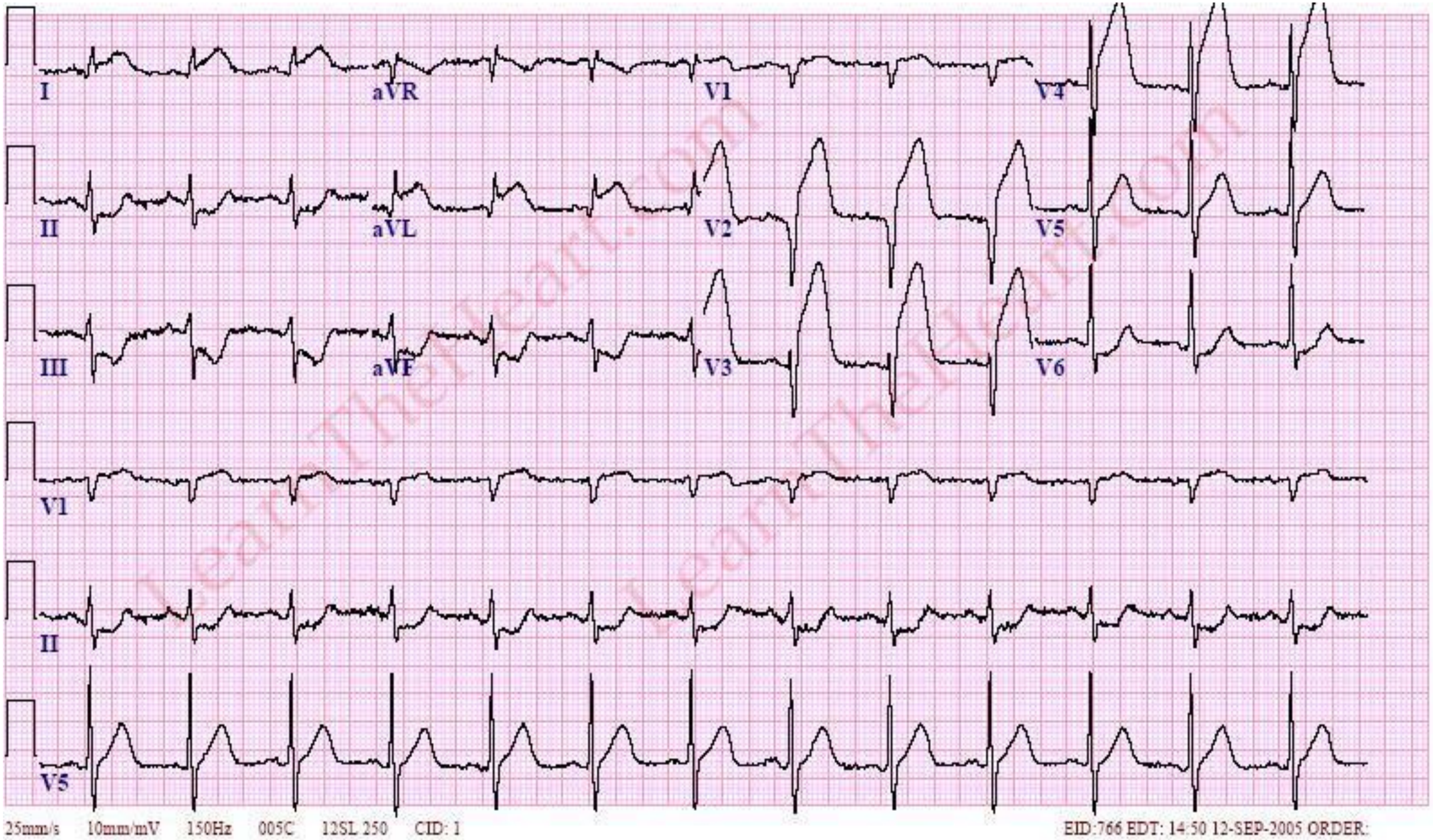
ST-Elevation Myocardial Infarction

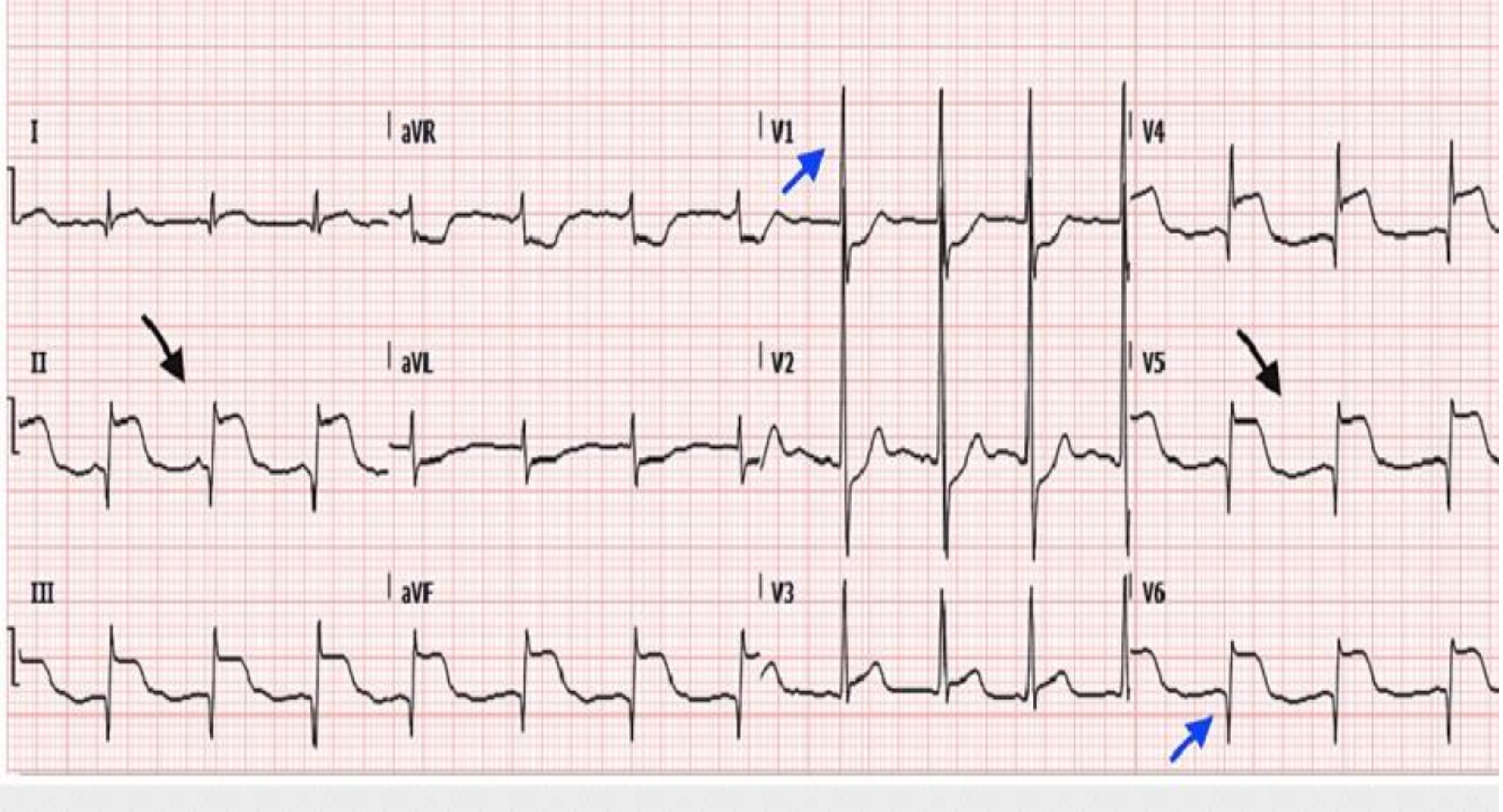
TABLE 37.3 Electrocardiographic Manifestations of Myocardial Infarction

Electrocardiographic Manifestations of Acute Myocardial Ischemia (in the Absence of Left Bundle Branch Block)	
ST Elevation	

New ST elevation at the J point in two contiguous leads with the following cut points:
• ≥0.1 mV in all leads (except V_2–V_3)
• In leads V_2–V_3 the following cut points apply:
  • ≥0.2 mV in men ≥40 years
  • ≥0.25 mV in men <40 years
  • ≥0.15 mV in women	

ST Depression and T Wave Changes	
• New horizontal or downsloping ST depression ≥0.05 mV in two contiguous leads • T wave inversion ≥0.1 mV in two contiguous leads with a prominent R wave or R/S ratio >1	
Electrocardiographic Manifestations of Ischemia in the Setting of Left Bundle Branch Block	
Electrocardiographic Criterion	***Points***
ST-segment elevation ≥1 mm and concordant with the QRS complex	5
ST-segment depression ≥1 mm in lead V_1, V_2, or V_3	3
ST-segment elevation ≥5 mm and discordant with the QRS complex	2
A score of ≥3 had a specificity of 98% for acute MI	
Electrocardiographic Changes Associated With Previous Myocardial Infarction (in the Absence of Left Ventricular Hypertrophy and Left Bundle Block)	
Any Q wave in leads V_2–V_3 ≥0.02 sec or a QS complex in leads V_2 and V_3	
Q wave ≥0.03 sec and ≥0.1-mV deep or QS complex in leads I, II, aVL, aVF, or V_4–V_6 in any 2 leads of a contiguous lead grouping (I, aVL; V_1–V_6; II, III, aVF)	
R wave ≥0.04 sec in V_1–V_2 and R/S ≥1 with a concordant positive T wave in absence of a conduction defect	


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
V1
II
V5
25mm/s 10mm/mV 150Hz 005C 12SL 250 CID: 1
EID:766 EDT: 14:50 12-SEP-2005 ORDER:


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6

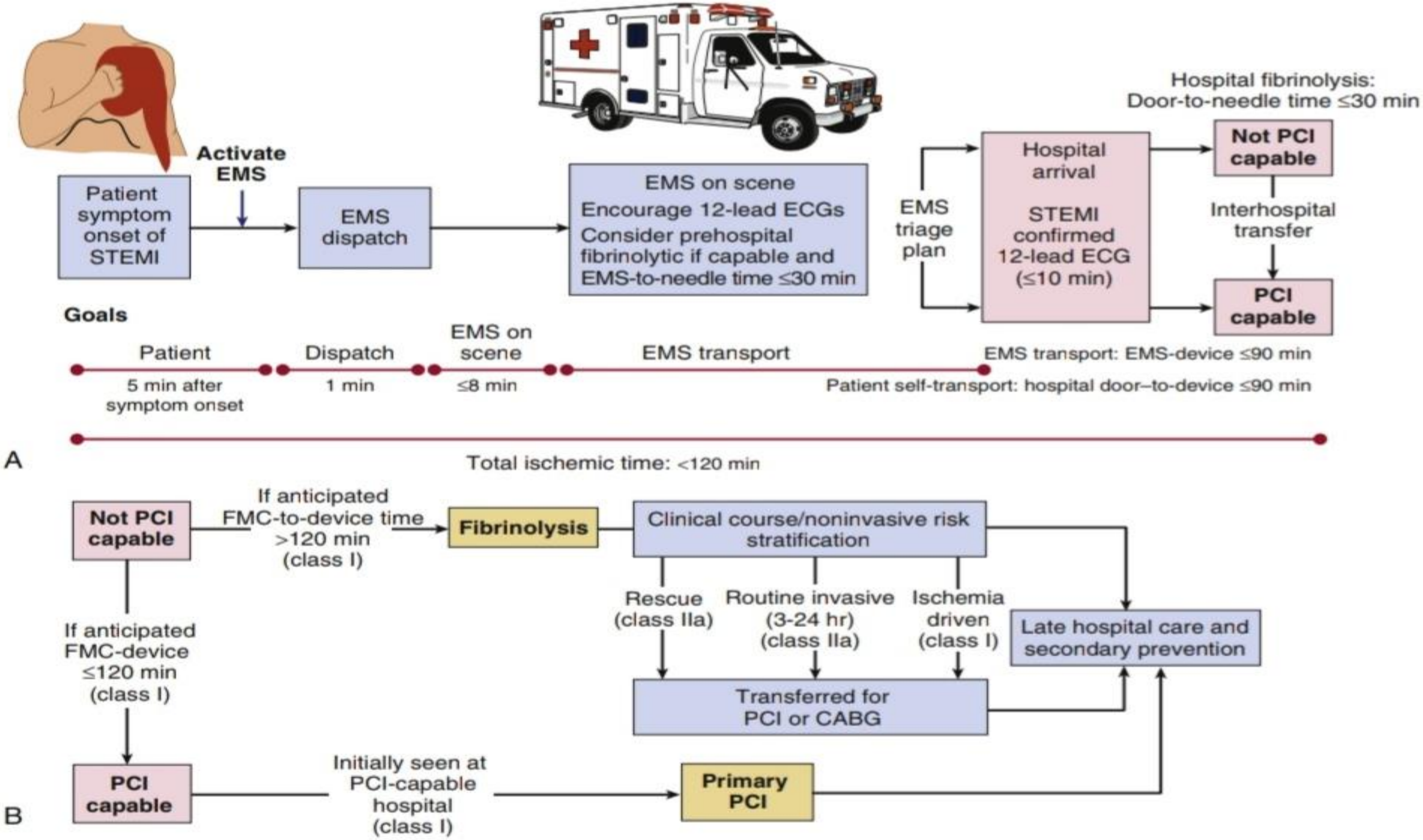

Patient symptom onset of STEMI
Activate EMS
EMS dispatch
EMS on scene
Encourage 12-lead ECGs
Consider prehospital fibrinolytic if capable and EMS-to-needle time ≤30 min
EMS triage plan
Hospital arrival
STEMI confirmed 12-lead ECG (≤10 min)
Hospital fibrinolysis: Door-to-needle time ≤30 min
Not PCI capable
Interhospital transfer
PCI capable
Goals
Patient
5 min after symptom onset
Dispatch
1 min
EMS on scene
≤8 min
EMS transport
EMS transport: EMS-device ≤90 min
Patient self-transport: hospital door–to-device ≤90 min
Total ischemic time: <120 min
A
Not PCI capable
If anticipated FMC-to-device time >120 min (class I)
Fibrinolysis
Clinical course/noninvasive risk stratification
Rescue (class IIa)
Routine invasive (3-24 hr) (class IIa)
Ischemia driven (class I)
Late hospital care and secondary prevention
Transferred for PCI or CABG
If anticipated FMC-device ≤120 min (class I)
PCI capable
Initially seen at PCI-capable hospital (class I)
Primary PCI
B

TABLE 38.3 **Contraindications to and Cautions in the Use of Fibrinolytics for Treating ST-Elevation Myocardial Infarction***

Absolute Contraindications
Any previous intracranial hemorrhage
Known structural cerebral vascular lesion (e.g., arteriovenous malformation)
Known malignant intracranial neoplasm (primary or metastatic)
Ischemic stroke within 3 months *except* acute ischemic stroke within 4.5 hr
Suspected aortic dissection
Active bleeding or bleeding diathesis (excluding menses)
Significant closed-head or facial trauma within 3 months
Intracranial or intraspinal surgery within 2 months
Severe uncontrolled hypertension (unresponsive to emergency therapy)
For streptokinase, previous treatment within the previous 6 months
Relative Contraindications
History of chronic, severe, poorly controlled hypertension
Significant hypertension at initial evaluation (SBP >180 mm Hg or DBP >110 mm Hg)[†]
History of previous ischemic stroke >3 months
Dementia
Known intracranial pathology not covered in Absolute Contraindications
Traumatic or prolonged (>10 min) cardiopulmonary resuscitation
Major surgery (<3 weeks)
Recent (within 2 to 4 weeks) internal bleeding
Noncompressible vascular punctures
Pregnancy
Active peptic ulcer
Oral anticoagulant therapy

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TABLE 38.4 Comparison of Approved Fibrinolytic Agents

FIBRINOLYTIC AGENT	DOSE	FIBRIN SPECIFICITY *	FIBRINOGEN DEPLETION	ANTIGENIC	PATENCY RATE (90-MIN TIMI 2 OR 3 FLOW)
Fibrin Specific					
Tenecteplase (TNK)	Single IV weight-based bolus †	++++	Minimal	No	85%
Reteplase (r-PA)	10 units + 10-unit IV boluses given 30 min apart	++	Moderate	No	84%
Alteplase (t-PA)	90-min weight-based infusion ‡	++	Mild	No	73–84%
Non-Fibrin Specific					
Streptokinase §	1.5 million units IV given over 30–60 min	No	Marked	Yes ¶	60–68%

General Treatment Measures

1)Aspirin: 162 to 325 mg should be administered at the first opportunity after initial medical contact.1 To achieve therapeutic blood levels rapidly, the patient should chew a non–enteric-coated tablet

2) Control of Cardiac Pain: Initial management of patients with STEMI should target relief of pain and its associated heightened sympathetic activity. Control of cardiac pain uses a combination of analgesics (e.g., morphine) and interventions to improve the balance of myocardial oxygen supply and demand, including oxygen (in the setting of hypoxia), nitrates, and in appropriately selected patients, beta-adrenergic receptor-blocking agents (beta blockers)

- ✓ **Morphine:** an initial dose of 4 to 8 mg can be administered intravenously initially, followed by doses of 2 to 8 mg repeated at intervals of 5 to 15 minutes until the pain is relieved or side effects emerge—hypotension, depression of respiration, or vomiting

- ✓ **Nitrates*:*** sublingual (SL) nitrates are indicated for most patients with an ACS. the only groups of patients with STEMI in whom SL nitroglycerin should *not* be given are those with suspected right ventricular (RV) infarction or marked hypotension (e.g., systolic BP <90 mm Hg), especially if accompanied by bradycardia. In patients with a prolonged period of waxing and waning chest pain, continuous IV nitroglycerin infusion may help control the symptoms and lessen the ischemia, but this requires frequent BP monitoring

- ✓ **Beta-Adrenergic Blocking Agents:** aid in the relief of ischemic pain, reduce the need for analgesics in many patients, and reduce infarct size and life-threatening Arrhythmias. First, exclude patients with heart failure (HF), hypotension (systolic BP <90 mm Hg), bradycardia (HR <60 beats/min), or significant atrioventricular (AV) block

TABLE 38.6 Recommendations for Beta-Blocker Therapy for ST-Elevation Myocardial Infarction (STEMI)

RECOMMENDATION	COR	LOE
Oral beta blockers should be initiated in the first 24 hr in patients with STEMI who do not have any of the following:	I	B
Signs of heart failure or evidence of a low-output state		
Increased risk for cardiogenic shock*: • Age >70 years • Systolic blood pressure <120 mm Hg • Sinus tachycardia >110 beats/min or heart rate <60 beats/min • Increased time since the onset of symptoms of STEMI Other relative contraindications to use of oral beta blockers: • PR interval longer than 0.24 second • Second- or third-degree heart block • Active asthma or reactive airways disease		
Beta blockers should be continued during and after hospitalization for all patients with STEMI and no contraindications to their use.	I	B
Patients with initial contraindications to the use of beta blockers in the first 24 hours after STEMI should be reevaluated to determine their subsequent eligibility.	I	C
It is reasonable to administer IV beta blockers at initial encounter to patients with STEMI and no contraindications to their use who are hypertensive or have ongoing ischemia.	IIa	B

COR, Class of recommendation; LOE, level of evidence.

3)Anticoagulant Therapy
The rationale for administering anticoagulant therapy acutely to patients with STEMI includes establishing and maintaining patency of the infarct-related artery, regardless of whether a patient receives fibrinolytic therapy, and preventing deep venous thrombosis, pulmonary embolism, ventricular thrombus formation, and cerebral embolization.

4)Antiplatelet Therapy: All patients with STEMI should receive aspirin as soon as possible after an initial encounter in the absence of contraindications. Adding the P2Y12 inhibitor clopidogrel to aspirin appears to offer additional benefit in patients undergoing PCI after STEMI

5)Modification of Lipid Profile:
High-intensity statin therapy should be initiated or continued in all patients with STEMI and no contraindications to its use. Ezetimibe, a nonstatin lipid lowering agent, may be added during hospitalization for STEMI based on IMPROVE-IT

6)Inhibition of the Renin-Angiotensin- Aldosterone System:

To prevent late remodeling of the left ventricle and to decrease the likelihood of recurrent ischemic events, we advocate indefinite therapy with an ACE inhibitor in patients with HF, a moderate decrease in global EF, or a large regional wall motion abnormality even in the presence of a normal global EF

Non–ST Elevation Acute Coronary Syndromes

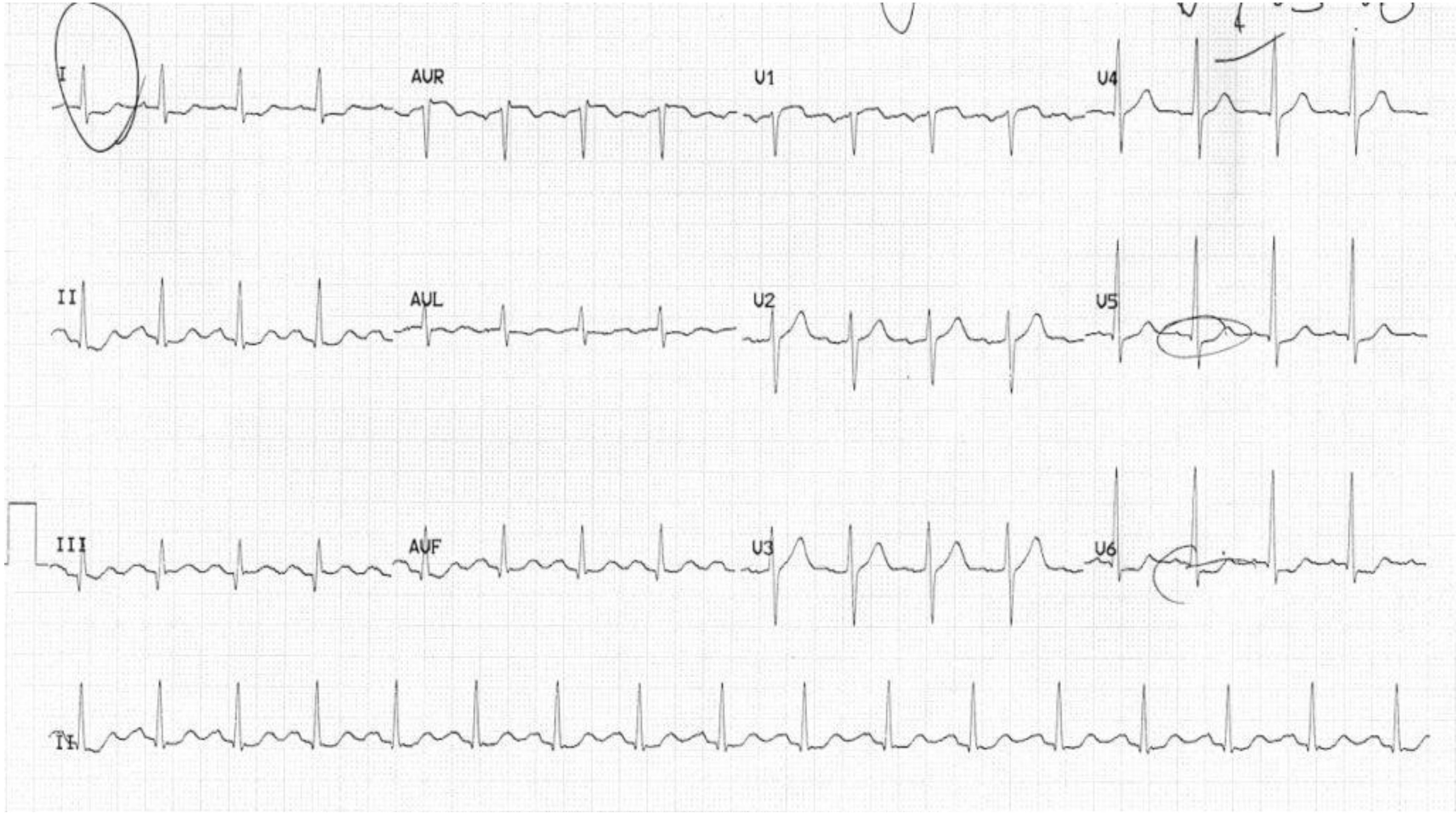

TABLE 39.5 Pharmacologic Anti-Ischemic Therapies in Non–ST Elevation Acute Coronary Syndromes

CLASS OF MEDICATION	MECHANISM OF ACTION	CLINICAL EFFECTS IN NSTE-ACS
Traditional Therapies		
Beta blockers	Decrease heart rate, blood pressure, and contractility through antagonism of $beta_1$ receptors	Decrease mortality[51]
Nitrates	Decrease preload through venodilation; vasodilate coronary arteries	No benefit on mortality
Calcium channel blockers	May vasodilate, reduce heart rate, or decrease contractility depending on specific drug	No clear benefit on mortality or reinfarction Increased reinfarction rate when short-acting nifedipine is used alone
Newer and Experimental Therapies		
Ranolazine	Inhibits late inward sodium current	Decreases recurrent ischemia and arrhythmias
Trimetazidine	Shifts myocardial metabolism from fatty acid to glucose use	Decreases short-term mortality
Nicorandil	Activates ATP-sensitive K^+ channels and dilates arterioles; may have ischemic precondition-like effect	Decreases arrhythmias and transient ischemia

From Soukoulis V, et al. Nonantithrombotic medical options in acute coronary syndromes: old agents and new lines on the horizon. Circ Res 2014;114:1944–1958.

ANTITHROMBOTIC TREATMENTS

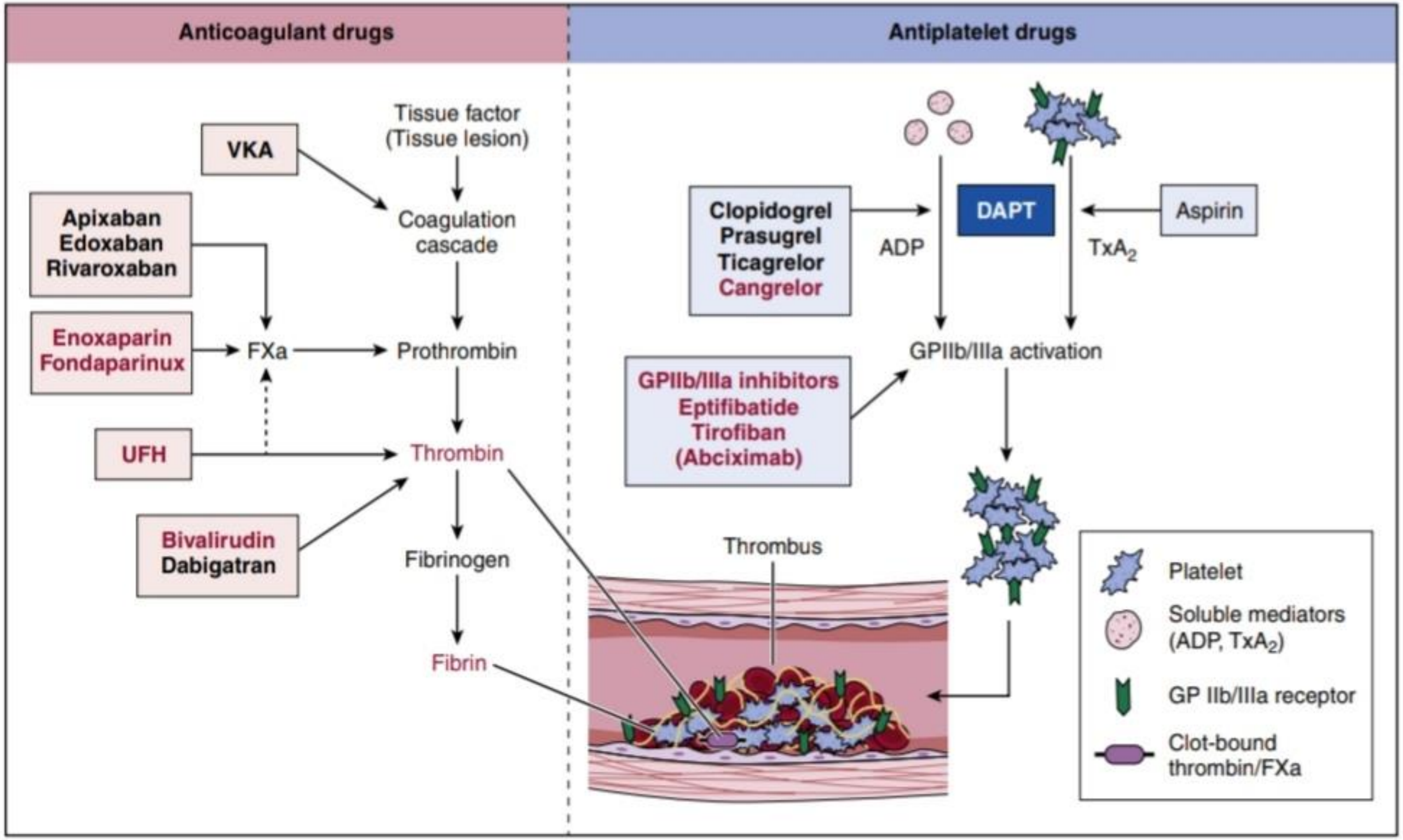

FIGURE 39.7 Antithrombotic treatments in non–ST-segment elevation acute coronary syndrome patients: pharmacologic targets. Drugs with oral administration are shown

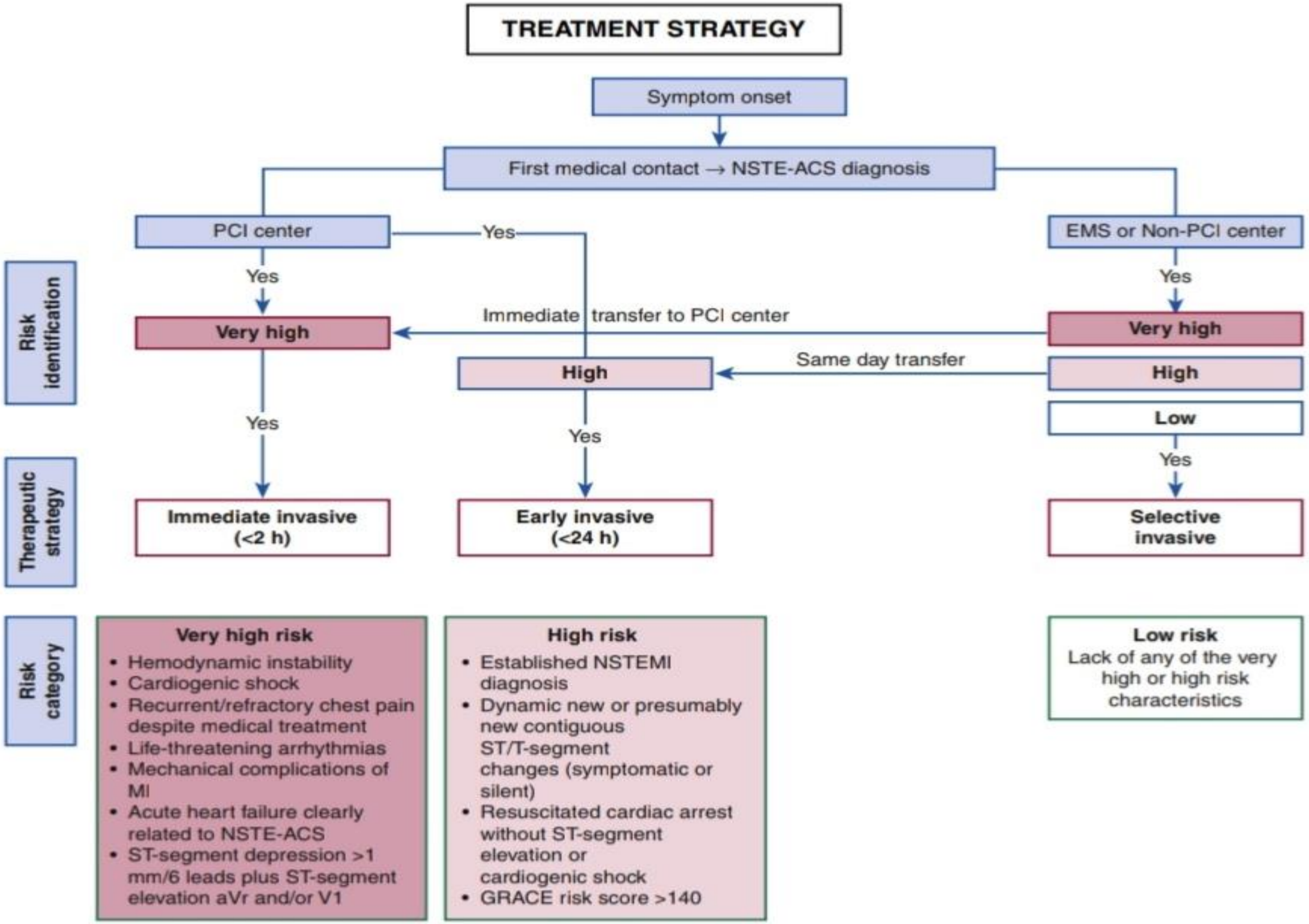

FIGURE 39.10 Selection of non–ST-segment elevation acute coronary syndrome treatment strategy and timing according to initial risk stratification. (Adapted from Collet J-P, et al. 2020 ESC Guideline for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J 2020; 42(14):1289–1367.)

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