SECTION XII CARdioVASCuLAR disease and dysFUNCTION

CHAPTER 118 EVALUATION OF CHEST PAIN AND ACUTE CORONARY SYNDROME IN THE ICU
GIUSEPPE DE LUCA • SALVATORE CASSESE • PAOLO MARINO

This chapter deals with the clinical presentation and evaluation of chest pain in the intensive care unit (ICU). Please see Chapters 119 and 120 for a full discussion of non-ST-segment elevation myocardial infarction and ST-segment elevation myocardial infarction.

EVALUATION OF CHEST PAIN

Immediate Concerns

Despite insights and innovations over the last decades, acute nontraumatic chest pain still represents one of the most difficult diagnostic challenges in medicine. In fact, it is commonly observed in several life-threatening illnesses, including cardiovascular, pulmonary, and gastrointestinal diseases and, when symptoms are atypical, it may be difficult to interpret (Table 118.1) (1). Algorithms have been proposed to improve the accuracy of diagnosis and the patient’s risk stratification via the integrated use of clinical data, biomarkers, and noninvasive diagnostic tests (2,3) (Fig. 118.1).

Main Tips

When confronted with a patient suffering from acute chest pain:

1. First, exclude major life-threatening processes, such as myocardial infarction, pulmonary embolism (PE), or aortic dissection.
2. Obtain a careful history and perform a meticulous physical examination, particularly in patients with atypical chest pain, which is commonly seen in the emergency department (Table 118.2).
3. Use this information to select the most appropriate tests or procedures needed to confirm or reject the suspected diagnosis.

Clinical Evaluation

The evaluation of patients with acute chest pain should include the following.

History

1. Symptoms and description of the current illness: The patient should be allowed to describe the character (pressure, sharp, burning, pleuritic), duration (minutes, hours, days), intensity (scale of 0–10), location (radiation), and onset (sudden, gradual) of the pain. Associated symptoms and signs such as nausea, vomiting, diaphoresis, dyspnea, presyncope, and syncope should be noted. Factors that worsen or relieve the symptoms should be obtained (Table 118.2).
2. Past medical history: A thorough investigation on history of cardiopulmonary and gastrointestinal disease is mandatory (Table 118.1).
3. Family history: A family history of glucose intolerance, coronary artery disease, and sudden or premature death should be investigated.
4. Social history: A history of alcohol, cigarette, cocaine, or other drug use should be sought.

Physical Examination

1. Vital signs: Changes in heart rate, blood pressure, pulse pressure, pulmonary artery waveforms and pressure, ventilatory parameters, temperature, and urine output should be noted.
2. Inspection and palpation: Examination of the head, neck, chest, and abdomen may reveal significant disease. Disrobe the patient and visually inspect for obvious deformities and asymmetry. Significant point tenderness and crepitation should be sought by applying firm pressure to the anterior, lateral, and posterior chest wall. Cardiac impulses may reveal significant underlying disease. Palpate and note the symmetry of all upper and lower extremity pulses. Palpation of the abdomen for tenderness and pulsatile masses is vital in making the diagnosis of thoracic and intra-abdominal disease.
3. Auscultation: The neck should be auscultated to evaluate for the presence of significant upper airway obstruction (stridor). Careful auscultation of the chest should assess symmetry of breath sounds. Abnormal sounds (i.e., rales, wheezing, rhonchi, friction rubs) and their location should be noted. Heart sounds should be carefully studied. The cardiac rate and rhythm should be noted. Close attention to findings suggestive of valvular heart disease is important. The abdomen should be auscultated, and the presence and quality of bowel sounds should be noted.
### TABLE 118.1

<table>
<thead>
<tr>
<th>DIFFERENTIAL DIAGNOSIS OF CHEST PAIN</th>
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<tbody>
<tr>
<td><strong>CARDIOVASCULAR</strong></td>
</tr>
<tr>
<td>Myocardial infarction</td>
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<tr>
<td>Angina pectoris</td>
</tr>
<tr>
<td>Aortic valve disease</td>
</tr>
<tr>
<td>Hypertrophic cardiomyopathy</td>
</tr>
<tr>
<td>Myocarditis</td>
</tr>
<tr>
<td>Pericarditis</td>
</tr>
<tr>
<td>Dressler syndrome</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
</tr>
<tr>
<td>Aortic dissection</td>
</tr>
<tr>
<td>Thoracic aneurysm</td>
</tr>
<tr>
<td>Pericardial effusion</td>
</tr>
<tr>
<td>Mitral valve prolapse</td>
</tr>
<tr>
<td><strong>PULMONARY</strong></td>
</tr>
<tr>
<td>Pulmonary embolism</td>
</tr>
<tr>
<td>Pneumothorax</td>
</tr>
<tr>
<td>Atelectasis</td>
</tr>
<tr>
<td>Pleuritis</td>
</tr>
<tr>
<td>Pneumonia</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
</tr>
<tr>
<td>Infratracheal tumor</td>
</tr>
<tr>
<td>Tracheitis</td>
</tr>
<tr>
<td>Tracheobronchitis</td>
</tr>
<tr>
<td><strong>GASTROINTESTINAL</strong></td>
</tr>
<tr>
<td>Esophageal spasm</td>
</tr>
<tr>
<td>Esophageal reflux</td>
</tr>
<tr>
<td>Esophagitis</td>
</tr>
<tr>
<td>Esophageal rupture</td>
</tr>
<tr>
<td>Foreign bodies (food, pills)</td>
</tr>
<tr>
<td>Peptic ulcer disease</td>
</tr>
<tr>
<td>Nassocystic tube erosions</td>
</tr>
<tr>
<td>Gastritis</td>
</tr>
<tr>
<td>Colonic distention</td>
</tr>
<tr>
<td>Biliary disease</td>
</tr>
<tr>
<td><strong>MUSCULOSKELETAL</strong></td>
</tr>
<tr>
<td>Costochondritis</td>
</tr>
<tr>
<td>Intercostal muscle cramps</td>
</tr>
<tr>
<td>Rib fractures</td>
</tr>
<tr>
<td>Trauma</td>
</tr>
<tr>
<td><strong>OTHER</strong></td>
</tr>
<tr>
<td>Herpes zoster</td>
</tr>
<tr>
<td>Myositis</td>
</tr>
<tr>
<td>Diaphragmatic flutter</td>
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<tr>
<td>Psychoneurosis</td>
</tr>
</tbody>
</table>

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**Diagnostic Tests for Acute Chest Pain**

1. **Electrocardiogram (ECG):** An electrocardiogram should be obtained as soon as possible, particularly in patients with persistent chest discomfort at the time of evaluation. Non-diagnostic ECG changes (i.e., old left bundle branch block) or a normal ECG may neither prove nor disprove significant cardiac ischemia. Right axis deviation, right bundle branch block, and inversion of T waves in chest (V₁)-leads may be observed in acute pulmonary embolism. Difusely concave ST-segment elevation or inversion of T waves may be observed in patients with pericarditis.

2. **Biomarkers:**
   - **A** Markers of myocardial injury: Several markers are currently available that allow accurate identification of patients with myocardial injury. Cardiac troponin I and T represent a more accurate and sensitive marker of myocardial injury (3,4). It is imperative to consider that a single negative troponin assay at the time of a patient’s admission cannot always be relied upon to exclude myocardial infarction. In this setting, it is recommended to repeat the test 6 to 12 hours after admission and after any further episode of chest pain. Myoglobin might be considered between 2 and 6 hours from symptom onset, as compared to creatine kinase (CK)-MB mass and troponin, but the maximal negative predictive value of myoglobin reaches only 89% during this time frame (5). Elevation of troponin may be observed also in patients with acute pulmonary embolism, where it correlates well with the extent of right ventricular dysfunction and prognosis (6,8), and in patients with myocarditis, pericarditis, or acute heart failure (4).
   - **B** Natriuretic peptides: Cardiac natriuretic peptides are useful diagnostic and prognostic markers for patients with heart failure (6,9). Similar to cardiac troponin, elevations in brain natriuretic peptide (BNP) and in N-terminal proBNP (the prohormone) are associated with right ventricular dysfunction in acute pulmonary embolism, and may help to identify a subgroup of hemodynamically stable patients at especially high risk for adverse clinical events (8) (Fig. 118.2).
   - **C** D-dimer: Fibrin d-dimer (DD) has been proposed as a diagnostic tool in patients with suspected pulmonary embolism (Fig. 118.2) (10). In fact, the dimeric D-domain serves as an indicator of in vivo fibrin formation. However, many conditions are associated with fibrin formation:
     - **Nonpathologic:** Cigarette smoking, aging, functional impairment, pregnancy, and postoperative state
     - **Pathologic:** Trauma, pre-eclampsia, malignancy, infection, disseminated intravascular coagulation, arterial or venous thromboembolism, atrial fibrillation, acute coronary syndromes, stroke, and acute upper gastrointestinal hemorrhage
   - Because of this low specificity, DD testing may not be helpful in hospitalized patients in whom comorbidities are common. In addition, DD assays (especially qualitative latex agglutination assays) are not 100% sensitive, limiting their utility as a single screening test.

3. **Imaging techniques:**
   - **A** Echocardiography: The echocardiogram plays an important role in evaluating chest pain and is frequently used to diagnose regional wall motion abnormalities, aortic stenosis, dissecting aortic aneurysm, pericardial effusion, and cardiac tamponade. Preserved regional wall motion occasionally occurs early in the process of significant cardiac ischemia. Contrast echocardiography may further improve diagnostic accuracy in the evaluation of acute chest pain (11). Transesophageal echocardiography (TEE) has a sensitivity approaching 100% for aortic dissection (12).
   - **B** Radionuclide myocardial perfusion imaging: Tc-99m-based tracers have been shown to be highly sensitive in the detection of myocardial infarction, although
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somewhat less specific. However, data acquisition in a gated mode for additional wall motion score information results in a significant increase in specificity (13). The most suitable population for this method are patients judged at low to intermediate probability of having myocardial ischemia, with an atypical chest pain and a normal or nondiagnostic ECG (14,15).

C) Chest radiography: The chest radiograph may provide important clues regarding the cause of chest pain. The presence or absence of the following radiographic abnormalities should be determined: subcutaneous air, rib fractures, pneumothorax, pulmonary infiltrates, widened mediastinum, pleural effusions, and intraperitoneal free air.

TABLE 118.2
CLINICAL FEATURES OF CHEST PAIN ACCORDING TO THE ETIOLOGY

<table>
<thead>
<tr>
<th>Cause of chest pain</th>
<th>Type of pain</th>
<th>Referred pain</th>
<th>Posture/movement</th>
<th>Food/fluid</th>
<th>Nitroglycerin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic cardiac pain</td>
<td>Visceral</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Nonschismic cardiac pain</td>
<td>Visceral</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Pulmonary disease</td>
<td>Visceral/cutaneous</td>
<td>Usually no</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>Visceral/cutaneous</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>Cutaneous</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Visceral</td>
<td>Sometimes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Aortic aneurys</td>
<td>Visceral</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

FIGURE 118.1. Diagnostic flow chart in patients with chest pain. ECG, electrocardiogram; TTE, transthoracic echocardiography; TEE, transesophageal echocardiography; CT, computed tomography; STEMI, ST-segment elevation myocardial infarction; ACS, acute coronary syndrome; GI, gastrointestinal.
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Suspicion of Acute PE

Chest radiograph — ECG

(a) Signs and symptoms of deep vein thrombosis; (b) Heart rate >100; (c) immobilization (bedrest) >3 days; (d) previous diagnosis of PE or DVT; (e) malignancy; (f) PE more likely than alternative diagnosis

Low probability

Non-low probability

PE excluded

D-dimer

CT scan or V/Q Scan

D-Dimer

No evidence of DVT: Manage according to pretest probability

Leg-vein ultrasound

Low probability

Non-low probability

D-dimer

Pulmonary angiogram or repeat leg-vein ultrasound within 1 week

Treat for PE

No shock

BNP

Troponin

Echocardiography

No RV dysfunction

Consider thrombolysis of embolectomy

Anticoagulation alone

Shock

BNP

Troponin

Echocardiography

RV dysfunction

FIGURE 118.2. Algorithm on diagnosis and management of patients with acute pulmonary embolism (PE). ECG, electrocardiogram; DVT, deep vein thrombosis; CT, computed tomography; V/Q, ventilation/perfusion; BNP, brain natriuretic peptide; RV, right ventricle.

D) Radionuclide perfusion lung scan: Intubated patients or patients too ill for transport who are believed to have PE may undergo bedside perfusion lung scanning. Whereas this test is often nondiagnostic, a normal scan result is a sensitive negative predictor for the presence of pulmonary emboli. This test is no longer a principal diagnostic test in PE, being supplanted by computed tomography (CT) scan, unless patients are too unstable for transportation.

E) Radionuclide ventilation/perfusion (V/Q) lung scan: Normal- and high-probability findings on V/Q scan often are sensitive enough to dictate therapy without further evaluation. Patients with low- and intermediate-probability V/Q scan results, depending on the level of clinical suspicion, frequently require additional examinations (see Chapter 144). This is no longer a principal diagnostic test in PE, being supplanted by CT scan. It is usually reserved for patients with renal insufficiency, contrast allergies, or pregnancy (because of lower radiation exposure as compared to CT scan).

F) Duplex ultrasound of the lower extremities: Venous ultrasonography is useful if it demonstrates deep venous thrombosis (DVT) in patients with suspected PE. However, the majority of patients with PE have no imaging evidence of DVT. Therefore, if clinical suspicion of PE is high, patients without evidence of DVT should still be investigated for PE.

G) CT scan: Iris readily available in most emergency departments, and performed rapidly. It may help in challenging cases when the chest radiograph is not conclusive (e.g., pneumothorax). Furthermore, CT angiography scan may evaluate coronary, aortic, and pulmonary anatomy with great clarity. Several studies have shown that 64-slice computed tomography coronary angiography
is very accurate in the diagnosis of coronary artery disease (16). The multidetector CT seems at least as good as stress nuclear imaging for the detection and exclusion of an acute coronary syndrome in low-risk chest pain patients (17). A recent large study has shown that CT scan is effective in the evaluation and management of patients with clinically suspected pulmonary embolism (18). In cases of acute aortic syndromes, in addition to making the initial diagnosis, CT angiography can assess the extent of aortic involvement and depict involvement of visceral and iliac arteries. The average sensitivity exceeds 95%, with specificities of 87% to 100%, and may be more accurate than magnetic resonance imaging (MRI) or TEE in the detection of aortic arch vessel involvement (19).

Typical Chest Pain

As shown in Figure 118.1, the approach to patients with chest pain can be systematic and organized. Musculoskeletal or cutaneous causes of atypical chest pain should be excluded. An ECG and cardiac enzymes should thus be obtained. If the index of suspicion for cardiac ischemia is high, irrespective of the ECG and cardiac enzymes, one should proceed with further studies to either confirm or negate the suspected diagnosis. If the index of suspicion for cardiac ischemia is low, causes of chest pain such as PE, aortic dissection, pleural inflammation, pneumomediastinum, and gastroesophageal disease should be considered. If the ECG reveals new ischemic changes, one may assume that this is the primary cause of the patient's discomfort. Many patients in the adult ICU have significant undiagnosed coronary artery disease. An echocardiogram, unless the result is totally normal, usually is not sensitive enough to exclude acute and significant cardiac ischemia. Stress echocardiography, nuclear medicine studies, angio-CT, and, finally, cardiac catheterization may be necessary under these circumstances. The urgency with which to pursue these tests depends on the acuity of illness.

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Pulmonary Embolism

Approximately 200,000 patients die yearly from PE. The mortality of untreated PE is five times greater than treated cases (24). The multiple factors that appear to predispose to pulmonary thromboembolism are detailed in Table 118.3. The multiple factors that appear to predispose to pulmonary thromboembolism are detailed in Table 118.3. The multiple factors that appear to predispose to pulmonary thromboembolism are detailed in Table 118.3. The multiple factors that appear to predispose to pulmonary thromboembolism are detailed in Table 118.3. The multiple factors that appear to predispose to pulmonary thromboembolism are detailed in Table 118.3. The multiple factors that appear to predispose to pulmonary thromboembolism are detailed in Table 118.3. The clinical presentation of acute PE includes the following:

- Abrupt onset of dyspnea
- Chest pain unrelied with nitroglycerin
- Apprehension
- Tachypnea
- Diaphoresis
- Fever
- Tachycardia
- Increased P2
- Dyspnea at rest
- Thrombophlebitis of the lower extremity
- Decreasing PaO2

The most common complaint is the sudden onset of pleuritic chest pain; nonpleuritic discomfort occurs less frequently. Approximately 84% of patients complain of dyspnea, and apprehension, cough, and hemoptysis are noted in 50% of patients. Syncope may also be a presenting sign. On physical examination, most patients have tachycardia and tachypnea. Fever is seen in nearly half of affected patients. Patients with large or multiple emboli often have evidence of

CheST PAIN SYNDROMES

Pitfalls in the clinical presentation of acute PE can be systematic and organized. Musculoskeletal or cutaneous causes of atypical chest pain should be directed to specifically confirm or exclude the suspected diagnosis.
TABLE 118.3

| PREDISPOSING FACTORS TO ACUTE AORTIC SYNDROME, PULMONARY EMBOLISM, AND ACUTE CORONARY SYNDROME |
|--------------------------------------------------|--------------------------------------------------|--------------------------------------------------|
| Acute aortic syndrome                          | Pulmonary embolism                               | Acute coronary syndrome                          |
| Long-standing arterial hypertension            | Hereditary                                        | Hereditary                                        |
| Connective tissue disorders                    | - Factor V mutation                               | - Factor V mutation                               |
| Hereditary vascular disease                     | - Protein C mutation                              | - Protein C mutation                              |
| Marfan syndrome                                | - Protein S deficiency                            | - Protein S deficiency                            |
| Vascular Ehlers-Danlos syndrome                 | - Antithrombin III deficiency                     | - Antithrombin III deficiency                     |
| - Bicuspid aortic valve, coarctation of the aorta | - Plasminogen deficiency                          | - Plasminogen deficiency                          |
| Hereditary thoracic aortic aneurysm/dissection  | - Factor VIII overexpression                      | - Factor VIII overexpression                      |
| Vascular inflammation                          | - Hyperhomocysteinemia                            | - Hyperhomocysteinemia                            |
| - Giant cell arteritis                          | - Acquired - Antithrombin III deficiency          | - Obesity                                        |
| - Takayasu arteritis                            | - Orthopedic or pelvic surgery                    | - Advanced age                                    |
| - Behcet's disease                              | - Protein C mutation                              | - Antithrombin III deficiency                      |
| Deceleration trauma                             | - Protein S deficiency                            | - Plasminogen deficiency                          |
| Iatrogenic factors                              | - Marfan syndrome                                 | - Factor VIII overexpression                      |
| Diagnostic catheterization or intervention      | - Vascular Ehlers-Danlos syndrome                 | - Hyperhomocysteinemia                            |
| Advanced age                                    | - Bicuspid aortic valve, coarctation of the aorta | - Obesity                                        |
| - Atherosclerotic disease                       | - Hereditary                                      | - Advanced age                                    |

hypoperfusion. A narrowed pulse pressure, poor peripheral perfusion, hypotension, low urine output, and mental status changes are common signs of hypoperfusion. Once a suspicion of PE is entertained, one should proceed with further diagnostic studies (Fig. 118.2) (26–28) (see Chapter 144).

Pneumothorax

Pneumothorax, a common entity in the ICU setting, is an abnormal collection of air between the parietal and visceral pleurae, which may be, if undiagnosed, rapidly fatal. Pneumothoraces are either spontaneous, traumatic, or iatrogenic. Irrespective of the etiology, a pneumothorax can have a significant impact on oxygenation and hemodynamics. The array of clinical presentations ranges from mild pleuritic chest pain with the sensation of shortness of breath to cardiac arrest. The clinician should look for the following signs and symptoms when pneumothorax is suspected:

- Tachypnea
- Dyspnea at rest
- Dyspnea with exertion
- Localized decrease in breath sounds
- Unilateral hyperresonance to chest percussion
- Dyspnea of abrupt onset
- Increased peak airway pressure
- Sudden hemodynamic instability
- Arterial desaturation

Patients who are critically ill and undergoing mechanical ventilation are at risk for a pneumothorax. Such patients may have increased peak airway pressures, arterial desaturation, and increased oxygen extraction. Despite sedation, some patients may become agitated and diaphoretic. Compression of the mediastinal structures with a subsequent decrease in preload may result in a significant decrease in the cardiac output and hemodynamic instability. If a ball-valve mechanism occurs during positive-pressure ventilation, a life-threatening tension pneumothorax may rapidly develop.

A pneumothorax in a patient with severe underlying pulmonary disease may be extremely difficult to diagnose (29,30). Loculated pneumothoraces are frequently missed on portable radiographs of critically ill patients. Once suspected, this diagnosis must be confirmed or negated, as nearly half of all untreated pneumothoraces progress to tension pneumothorax. In these circumstances, a CT scan of the chest often is necessary to make the diagnosis.
Tachycardia

β  Knifelike or tearing substernal chest pain
Severe back pain
Chest pain unrelieved by nitroglycerin
Elevated diastolic blood pressure
Diaphoresis
Fever
Abrupt onset
Maximal severity at onset

PROPOSED CLASSIFICATIONS OF AORTIC DISSECTION

| STANFORD CLASSIFICATION       | Type A: Dissection of the ascending and descending aorta |
| TYPICAL CLASSIFICATION        | Type B: Dissection of the descending aorta |

| DEBAKEY CLASSIFICATION       | Type 1: Dissection of the entire aorta |
| TYPICAL CLASSIFICATION        | Type 2: Dissection of the ascending aorta |
| TYPICAL CLASSIFICATION        | Type 3: Dissection of the descending aorta |

NEW CLASSIFICATION
Class 1: Classic aortic dissection with an intimal flap between true and false lumen
Class 2: Medial disruption with formation of intramural hematoma/hemorrhage
Class 3: Discrete/subtle dissection without hematoma, eccentric bulge at tear site
Class 4: Plaque rupture leading to aortic ulceration, penetrating aortic atherosclerotic ulcer with surrounding hematoma, usually subadventitial
Class 5: Iatrogenic and traumatic dissection

Aortic IMH is considered a precursor of dissection, originating from ruptured vasa vasorum in medial wall layers and resulting in an aortic wall infarct that may provoke a secondary tear, causing a classic aortic dissection. It is similar to classic dissection in its natural history in that IMH may extend, progress, regress, or reabsorb. Whereas IMH resorption has been reported in about 10% of cases, resorption of aortic dissection has rarely been so reported (12,39,40). Most IMHs (50%–85%) are located in the descending aorta and are typically associated with hypertension (41,42). Although clinical manifestations of IMH are similar to acute aortic dissection, IMH tends to be a segmental process; therefore, radiation of pain to the head or legs is less common. Chest pain is more common with ascending (type A) IMH; upper or lower back pain is more common with descending (type B) lesions. Nonetheless, the diagnosis of IMH versus acute aortic dissection cannot be made clinically. IMH is a tomographic imaging diagnosis in the appropriate clinical setting. These patients should be managed as those with classic aortic dissection.

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Plaque Rupture/Penetrating Atherosclerotic Ulcer

Deep ulceration of atherosclerotic aortic plaques can lead to IMH, aortic dissection, or perforation (43–46). Noninvasive imaging has further elucidated this disease process that often further complicates IMH and appears as an ulcer-like projection into the hematoma. In association with IMH, limited series have reported penetrating atherosclerotic ulcers almost exclusively in patients with type B IMH (46). Symptomatic ulcers with signs of deep erosion are more prone to rupture than others. In these patients, endovascular stent grafting is emerging as an attractive therapeutic modality.

Acute Pericarditis

Acute pericarditis is an inflammatory process of the pericardium caused by a variety of disorders. It is the most common disease of the pericardium. Pericarditis is commonly caused by infection, trauma, autoimmune disease, or neoplasm (see Chapter 127).

The diagnosis of acute pericarditis is established by the presence of chest pain, pericardial friction rub, and ECG abnormalities. A more complete list of the clinical features of acute pericarditis is as follows:

- Chest pain at rest
- Exacerbation of chest pain with breathing
- Chest pain lasting longer than 20 minutes
- Chest pain unrelieved with nitroglycerin
- Fever; sinus tachycardia
- ST-segment elevation without reciprocal depression
- Inverted T waves
- Pericardial friction rub
- Leukocytosis

Pericardial effusions of various sizes are seen by echocardiography (47). The pain of acute pericarditis is pleuritic in nature and often is described as a sharp, retrosternal discomfort radiating to the back and shoulders. This pain is relieved by leaning forward and worsened by recumbency, inspiration, and cough. The chest pain of acute pericarditis may be hand-like with radiation to the arms, similar to that of a myocardial infarction.

Pathognomonic for acute pericarditis is a three-component friction rub that is heard best over the left sternal border and other related studies.

Cardiac Ischemia

An imbalance between myocardial oxygen supply and demand is the basic pathophysiologic process for a variety of disease entities. Myocardial infarction, myocardial ischemia, aortic stenosis, hypertrophic cardiomyopathy, right ventricular hypertension, and severe anemia all are associated with the development of such an imbalance. The distinction between these disease processes is made by medical history, symptoms, physical examination, ECG, cardiac enzymes, chest radiographs, and other related studies.

Acute Coronary Syndrome (see below and Chapters 121 and 122)

ST-segment Elevation Myocardial Infarction (see Chapter 122)

Aortic Stenosis

Aortic stenosis is a narrowing of the aortic valve orifice secondary to congenital abnormality, valvular degeneration (calculus), or rheumatic heart disease (see Chapter 125). Discomfort associated with aortic stenosis mimics typical angina pectoris. The clinical presentation of aortic stenosis includes the following:

- Exertional dyspnea
- Chest pain at rest

Most patients who are diagnosed with acute pericarditis have an uneventful recovery with bedrest and anti-inflammatory drug therapy. However, a substantial number of individuals have persistent chest discomfort, fever, leukocytosis, generalized illness, or hemodynamically significant pericardial effusions. In these patients, aggressive diagnostic strategies including pericardiocentesis are warranted (Table 118.5). Despite an aggressive search, a diagnosis is obtained in only approximately 20% of cases (50,51).

Table 118.5

<table>
<thead>
<tr>
<th>Table 118.5: Diagnostic Tests for Acute Pericarditis</th>
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<tbody>
<tr>
<td><strong>Echocardiogram</strong></td>
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<tr>
<td><strong>Pericardiocentesis</strong></td>
</tr>
<tr>
<td><strong>Evaluation of pericardial fluid</strong></td>
</tr>
<tr>
<td>The following suggests bacterial pericarditis:</td>
</tr>
<tr>
<td>Greater than 2,000 WBCs</td>
</tr>
<tr>
<td>Positive Gram stain/culture</td>
</tr>
<tr>
<td>CBC with differential</td>
</tr>
<tr>
<td>Serum urea and creatinine</td>
</tr>
<tr>
<td>Blood cultures</td>
</tr>
<tr>
<td>Tuberculin skin test</td>
</tr>
<tr>
<td>Antinuclear antibodies</td>
</tr>
<tr>
<td>Rheumatoid factor</td>
</tr>
<tr>
<td>Serologic tests for Brucella</td>
</tr>
<tr>
<td>Salmonella</td>
</tr>
<tr>
<td>Toxoplasma</td>
</tr>
<tr>
<td>Mycoplasma</td>
</tr>
<tr>
<td>Human immunodeficiency virus</td>
</tr>
<tr>
<td>Thyrotrypin</td>
</tr>
</tbody>
</table>

| WBCs, white blood cells; CBC, complete blood cell count. |

WBCs, white blood cells; CBC, complete blood cell count.
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Nonlife-Threatening Causes of Chest Pain

**Costochondritis**

Inflammation of the costochondral joints frequently results in chest wall pain. This pain is exacerbated by applying pressure over the affected area, by deep breathing, or by coughing. Often, patients can point to the exact area of inflammation.

**Herpes Zoster**

Reactivation of latent varicella-zoster virus with subsequent posterior root neuronal viral replication and inflammation can result in severe chest pain. This process can be triggered by trauma, surgery, immunosuppression, and a multitude of other immunologic stresses. The distribution of pain is usually along a particular dermatome, with eventual eruption of vesiculopustules on an erythematous base. The Tzanck test demonstrating multinucleated giant epidermal cells is diagnostic.

**Asthma and Chronic Obstructive Lung Disease**

A well-known association exists between atypical chest pain and obstructive lung disease. Patients describe a variety of symptoms ranging from sharp stabbing discomfort to pressure-like sensations. Bronchodilators may provide relief in some patients.

**Psychosomatic Chest Pain**

Psychosomatic chest pain is a diagnosis of exclusion. Patients may present with either classic or atypical symptoms. Significant coronary artery disease is frequently excluded by coronary angiography. Many of these patients have clinical depression and need aggressive intervention.

Summary

The evaluation of patients with chest pain should be organized and proceed rapidly in logical sequence. The evaluation should include a review of the patient's past medical history, history of present illness, risk factors, and a detailed physical examination. This initial evaluation should narrow the differential diagnosis and direct the clinician so that appropriate tests or procedures are performed.
EVALUATION OF ACUTE CORONARY SYNDROMES

Immediate Concerns

Acute coronary syndrome (ACS) is a broad term that encompasses a range of acute manifestations of coronary atherosclerosis, including ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (N-STEMI), and unstable angina (UA) (see Chapter 123). The diagnosis and the optimal treatment of these patients may be associated with significant improvement in outcome and survival. We focus on patients with UA/N-STEMI, although, as noted above, there are separate chapters within this textbook that will deal with these topics in detail.

Main Tips

When confronted with a patient suffering from acute coronary syndrome (UA/N-STEMI):

1. Obtain a careful history and perform a meticulous physical examination (Table 118.1), particularly in patients with atypical chest pain, which is commonly seen in the ICU, to exclude:
   - Noncardiac causes of chest pain
   - Nonischemic cardiac disorders (pericarditis, valvular disease)
   - Precipitating extracardiac causes (anemia)

2. Monitor ECG and repeat marker of myocardial ischemia if initially negative (at least 6 hours after initial measurement).

3. Perform echocardiography to identify regional dysfunction and/or nonischemic disorders.

4. After confirmation of the diagnosis, start medical therapy as soon as possible.

5. Risk stratification: high-risk patients may benefit from aggressive antplatelet therapy and early angiography and revascularization.

Clinical Evaluation

Patients with acute coronary syndromes should undergo rapid and accurate evaluation (see Chapters 120, 121 and 122). Obtaining a careful history and a meticulous physical examination are mandatory as a guide toward a definite diagnosis, which may influence therapeutic strategies.

Unstable angina is defined as angina pectoris (or equivalent type of ischemic discomfort) with at least one of the three features:

1. Occurrence at rest (or with minimal exertion) and lasting more than 20 minutes (if not interrupted by nitroglycerin)
2. Severe new-onset chest pain (i.e., within 1 month)
3. Occurrence with a crescendo pattern (i.e., more severe, prolonged, or frequent than previously) (53,54)

These symptoms may be associated with ECG changes, such as inversion of T waves or ST-segment depression, and elevation of cardiac biomarkers of necrosis (such as CK-MB or troponin T or I, or both); when this is the case, the condition is defined as non-ST-segment elevation myocardial infarction (33,34). Asymptomatic patients with ECG changes and/or elevation of cardiac enzymes are also included in these categories.

ST-segment elevation myocardial infarction is defined as prolonged chest pain at rest (greater than 30 minutes), the presence of ST-segment elevation in the 12-lead ECG (more than 0.1 mV in at least two contiguous peripheral leads or more than 0.2 mV in at least two contiguous chest leads), or new-onset left bundle branch block (see Chapter 122).

The discomfort associated with acute coronary syndromes typically radiates to the left shoulder and the left arm, and may be associated with diaphoresis, nausea, and vomiting. Left ventricular failure—manifested by pulmonary edema and shock—may occur. During attacks, increased heart rate, distant heart sounds, and a diffuse apical impulse may develop. Localized papillary muscle dysfunction may cause the late systolic murmur of mitral regurgitation. The tools for diagnosing the problem include ECG changes during attacks, biomarkers, echocardiography, nuclear medicine scan, exercise stress testing, CT scan, and cardiac catheterization.

Risk Stratification

Due to differences in the extent and severity of underlying coronary artery disease, and the different degree of thrombotic risk, identification of high-risk patients is of high clinical relevance in order to prevent, by adequate pharmacologic therapies and mechanical revascularization, the progression and the extent of myocardial infarction and the risk of death (53–55). As previously noted, medical history, clinical examination, ECG, and biomarkers provide key elements for risk assessment (Fig. 118.3).

The characteristics of patients with non-ST-segment elevation ACS at high risk for rapid progression to myocardial infarction or death who should undergo coronary angiography within 48 hours include:

- Recurrent rest pain
- Dynamic ST-segment changes: ST-segment depression of more than or equal to 0.1 mV or transient (less than 30 minutes) ST-segment elevation more than or equal to 0.1 mV
- Elevated troponin-I, troponin-T, or CK-MB levels
- Hemodynamic instability within the observation period
- Major dysrhythmias (ventricular tachycardia, ventricular fibrillation)
- Early postinfarction unstable angina (56–60)

Furthermore, the following markers of severe underlying disease (i.e., a high long-term risk) might also be helpful for risk assessment in non-ST-segment elevation ACS:

- Age older than 65 to 70 years
- History of known coronary artery disease, previous MI, prior percutaneous coronary intervention (PCI), or coronary artery bypass grafting (CABG)
- Congestive heart failure, pulmonary edema, and new mitral regurgitant murmur
- Elevated inflammatory markers (i.e., C-reactive protein [CRP], fibrinogen, interleukin (IL)-6)
- BNP or NT-proBNP in upper quartiles
- Renal insufficiency
Chapter 118: Evaluation of Chest Pain and Acute Coronary Syndrome in the ICU

Diagnosis of ACS

STEMI

UA/N-STEMI

Aspirin, clopidogrel, unfractionated heparin, β-blockers, nitrates

GP IIb/IIIa inhibitors/coronary angiography/revascularization

High risk clinical features or positive troponin and/or ST-segment depression

Immediate angiography (<3 hours)

GP IIb/IIIa inhibitors postponed

Low risk

Second troponin

Positive

Negative

Noninvasive imaging

Positive

Negative

Conservative management

Lysis or primary PCI

The Thrombolysis in Myocardial Infarction (TIMI) risk score has been shown to be an accurate tool for risk stratification that can be easily applied at the bedside of a patient with N-STEMI (61).

Perioperative Management

Cardiac Surgery

Despite improvements in intraoperative myocardial protection, between 5% and 15% of patients undergoing cardiac surgery actually experience a perioperative myocardial infarction due to diffuse atherosclerotic disease of the distal coronary arteries, spasm, embolism, thrombosis of native coronary vessels or bypass graft, technical problems with graft anastomoses, or increased myocardial oxygen need (as in left ventricular hypertrophy).

The diagnosis of postoperative MI is difficult because of the nonspecific ST–T-wave abnormalities frequently present in those patients. In addition, troponins are elevated in almost all patients who undergo CABG. A 12-lead ECG should be obtained upon arrival in the ICU after surgery and every 24 hours, since it represents the most reliable tool to diagnose perioperative MI. CK and CK-MB should be evaluated every 8 hours for the first 36 hours, if postprocedural MI is suspected. Bedside echocardiography, by detecting new regional wall motion abnormalities, represents a major diagnostic tool, particularly when ECG and serum marker measurements are unclear. The appropriate management strategy should be defined according to an integrated evaluation of clinical findings and diagnostic tests (Fig. 118.4).

Major Noncardiac Surgery

Myocardial infarction and ischemia occurring during or after major noncardiac surgery are difficult to diagnose, since they are often silent and because of the confounding effects of analgesics and postoperative surgical pain. The diagnosis is often based on evaluation of cardiac troponins, since CK and CK-MB are less specific and may be elevated during aortic surgery or mesenteric ischemia. Furthermore, most perioperative MIs are non–Q wave, and nonspecific ST changes are common after surgery with or without MI. Echocardiography may certainly help by identifying new wall motion abnormalities.
Section XII: Cardiovascular Disease and Dysfunction

Cardiovascular Disease and Dysfunction

ST elevation after CABG

Cardiac index >2.0

Echocardiography

No new wall-motion abnormalities

Nitroglycerin

ECG normalized or improved

Observation

New wall-motion abnormalities

1) Nitroglycerin

2) IABP

3) Coronary angiography

Indotropes + nitroglycerin

Cardiac index <2.0

Still unstable

IABP, angiography

FIGURE 118.4. Algorithm on management of patients with ST-segment elevation myocardial infarction after coronary artery bypass grafting (CABG). IABP, intra-aortic balloon pump; ECG, electrocardiogram.

The management of these patients should be based on the extension and severity of ischemia, weighing the risk of bleeding complications and the benefits from an aggressive therapy. Patients in stable hemodynamic condition, without severe ischemia, may be managed conservatively with administration of acetylsalicylic acid (ASA), β-blockers (if not contraindicated), nitroglycerin, and low-molecular-weight heparin (LMWH). In patients with large STEMI or who are hemodynamically unstable, immediate coronary angiography and PCI should be the preferred strategy.

Drug Therapy

The main objectives of medical therapy in patients with ACS are to stabilize and “cool” the culprit lesion, treat residual ischemia, and prevent long-term complications.

Antiplatelet and Anticoagulation Therapies

Aspirin and clopidogrel, as shown by several large randomized trials (62,63), improve the outcome, and thus represent a cornerstone in the initial treatment of ACS. Glycoprotein IIb/IIIa inhibitors have been shown to reduce mortality. However, the benefits were restricted to patients with positive troponin. A strategy of upstream administration—starting 48 hours before angiography—is currently recommended with epifibatide or tirofiban. Abciximab may be considered for downstream administration in the catheterization laboratory in patients with positive troponin undergoing percutaneous intervention due to the significant benefits shown in a recent randomized trial (64).

Intravenous heparin or LMWH are considered a fundamental therapy for treating ACS and are a class IA therapy when given in conjunction with antiplatelet agents (53–55). However, it seems that LMWH further improves the outcome as compared to intravenous unfractionated heparin (65).

Anti-ischemic Drugs

Relief of the symptoms of acute myocardial ischemia requires the use of drugs that correct the imbalance that exists between myocardial oxygen supply and demand. In the absence of contraindications, β-adrenergic blockers should be first-line anti-ischemic therapy and should be given intravenously in high-risk patients, particularly if ischemia is ongoing. A meta-analysis of three randomized clinical trials comparing β-blockers with placebo in unstable angina showed a significant reduction in rates of progression to acute myocardial infarction, but not death, by active treatment (66).

There are no randomized, placebo-controlled trials investigating the effect of nitrates on symptoms or prognosis in ACS. A number of small, uncontrolled datasets have been published (67,68), but the routine use of this group of drugs is almost entirely based on anecdotal experience of their efficacy in relieving symptoms. It is recommended that sublingual glyceryl trinitrate should be given in all cases where ischemic chest discomfort is present at the time of initial clinical assessment. If symptoms are not relieved rapidly thereafter and after administration of intravenous β-blockers, an intravenous nitrate infusion should be started.

Randomized studies of calcium channel blockers in ACS have shown their efficacy in relieving symptoms (69,70). In addition, diltiazem may have a protective effect (71,72), whereas there is strong evidence that immediate-release nifedipine (a dihydropyridine) increases mortality rate, particularly if given without β-blockers (73,74). Current guidelines recommend reserving the dihydropyridine calcium antagonists for use as second- or third-line therapy after β-blockers and nitrates,
whereas the rate-limiting, nonhydroxypropionate agents (diltiazem and verapamil) may be reasonable alternatives when \( \beta \)-blockers are contraindicated.

**Statins** represent the main agents for treatment of hypercholesterolemia today. Recent studies have shown that their effects on progression of atherosclerosis can be explained by additional properties beyond lowering cholesterol (75–77). In particular, their antithrombotic and anti-inflammatory properties may explain the effects observed in ACS patients. In fact, early statin therapy has been shown to be associated with a significant improvement in clinical outcome (78), and is strongly recommended after ACS (53,54).

**SUMMARY**

The evaluation of patients with ACS should be organized and proceed rapidly in logical sequence. The evaluation should include a review of the patient’s past medical history, history of present illness, risk factors, and a detailed physical examination, to exclude noncardiac or nonischemic disorders and precipitating extracardiac causes. After confirmation of the diagnosis, all patients should be treated with optimal medical therapy. Risk stratification is mandatory, since high-risk patients may benefit from aggressive antithrombotic therapy and early angiography and revascularization, whereas patients at lower risk should undergo early, noninvasive testing for inducible myocardial ischemia, followed by coronary angiography when such testing is positive.

**References**


Section XIII: Cardiovascular Disease and Dysfunction


