Cardiology in the ER

A Practical Guide

Carlos Jerjes-Sánchez

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For my beloved family, my dear wife Alicia and my two dear children, Carlos and Alicia, thank you for accompanying me in this life and to the time we have spent together

Preface

The book *Cardiology in the ER* attempts to link advances made in the management of patients with cardiovascular emergencies. The main characteristic of the last decade was the acquisition of new knowledge and technologic advances to improve patients' care in the emergency room. In this book, we cover the broad spectrum of cardiovascular emergencies and highlight a practical approach to patient assessment and therapy.

The book was enriched with our 30-year experience in treating cardiovascular emergencies at large cardiology hospitals in Mexico, from 1982 to 1995 in the emergency room department in the Cardiology Hospital, National Medical Center, IMSS, Mexico City, and from 1996 to 2010 in the emergency room department in the Cardiology Hospital No. 34, IMSS, Monterrey City. In both hospitals, I had the opportunity to perform the first fast-track programs in cardiology hospitals on ST-elevation myocardial infarction and submassive and massive pulmonary embolism patients to perform systemic thrombolysis in <30 minutes and <90 minutes, respectively. Also, I had active participation in patient care and decision-making in the setting of different cardiovascular emergencies in all these years.

Cardiology in the ER provides a current and comprehensive update of the most frequent clinical presentation symptoms (dyspnea, chest pain, and syncope) and acute cardiovascular events. The clinical spectrum of the acute vascular syndromes (acute coronary syndromes, acute aortic syndromes, and acute pulmonary embolism), cardiac tamponade, cardiogenic shock, hypertensive crisis, arrhythmias, as well as acute heart failure, cardiac arrest, and prosthetic valve dysfunction is fully explored. Finally, the chapter related to pacemaker emergencies presents current knowledge and gives to the emergency room physician a quick review of the complications, clinical diagnostic keys, high clinical suspicion signs, and possible treatments. Additionally, a brief section about the basis of pacing is included.

Our contribution is targeted to a broad group of physicians, including cardiologists, internists, and first-contact physicians involved in the emergency room patient care. In addition, it serves as a resource for medical students, interns, residents, and fellows.

A deep recognition to all coauthors for their contributions that made this book possible; especially Dr. David Rodriguez for the excellent coordination.

We hope that this book enables physicians to make the best decisions for their patients in the field of cardiovascular emergencies. It is my profound hope that *Cardiology in the ER* will in some measure improve the quality of care for all patients in the emergency room. Finally, thanks to all those patients whom we were able to help but especially to those whom we could not.

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Chapter 1
Chest Pain in the ER

Carlos Jerjes-Sánchez and Francisco Nevarez

1.1 The Scope of the Problem

Chest pain (CP) management is one of the biggest challenges in the emergency room (ER), being the second most common cause of ER presentation among adults in the United States [1, 2]. Causes of this symptom range from musculoskeletal CP to potentially life-threatening emergencies, such as coronary artery disease (CAD) [2]. For this reason, good clinical evaluation is mandatory; although most patients presenting with classical CP and accompanying symptoms are easily diagnostic-oriented, there is an important fraction of patients that will not have the typical presentation. It is essential to accurately stratify risk for this patients to improve ER efficiency and avoid unnecessary tests and admissions [3].

1.2 Prevalence

CP accounts for 5.5 million (9%) of all noninjury-related ER visits for adults in the United States each year [1]. This symptom accounts from 5% to 20% of all ER admissions [2]. Among those without diagnostic ECGs and/or cardiac biomarkers, only 1–4% have angiographic evidence of significant CAD [4], so although CP is related to very serious complications, most of its causes are non-cardiac of origin. Although one of the most urgent and treatable causes for CP is the acute coronary syndrome (ACS), it only accounts for a small percentage (9%) of all the ER visits with this symptom [1], and it is the cause with more fatal-preventable "management."

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1.3 High-Clinical Suspicion for Cardiac-Related Causes of CP in the ER

Clinicians in the ER must focus on the immediate recognition and exclusion of life-threatening causes of CP, although patients with life-threatening etiologies may appear deceptively well, manifesting neither vital sign nor physical examination abnormalities [5]. Therefore, the recognition of the cause of CP based on the patients' medical history and semiology of the symptom is imperative. Since there are several causes for CP, and some patients will have atypical signs, clinicians should be able to suspect a cardiac cause if it presents with coronary risk factors, typical pain characteristics, and ECG findings positive for ACS [6]. In all age ranges, an ischemic chest pain (see below) should suggest structural or nonstructural heart disease. In young, middle age, or elderly population, physicians in charge should be in warning about pulmonary arterial hypertension, hypertrophic cardiomyopathy, congenital coronary abnormalities, pulmonary embolism, ischemic heart disease, Takotsubo syndrome, etc.

1.4 Chest Pain and Risk Factors for Acute Coronary Syndromes

The coronary risk factors of CP of ACS origin are as follows [6].

Medical History

- A familiar history of myocardial infarction (MI), >60 years, smoking, high arterial blood pressure, dyslipidemia, < LDL cholesterol, diabetes mellitus, periphery vascular disease, prior history of MI, male sex

Risk Factors

- Obesity, hypertension, diabetes, dyslipidemia, visceral fat, insulin resistant, metabolic syndrome, low HDL cholesterol, stress, cocaine abuse

Triggers

- The sudden lowering of body temperature, traffic pollution, intense tobacco abuse, and infections

1.4.1 Pathophysiology

The underlying cause for CP is in relation with its cause, whether for the aortic dissection or the lack of oxygen in myocardial cells. Each of these causes will have a different onset and evolution of the signs and symptoms and different

pathophysiology. To cover all the different theories for the onset of CP for each given cause is far beyond the scope of this chapter, it will instead analyze which characteristics can guide us to a correct and prompt diagnosis. In subsequent chapters, we will address the cardiovascular pathologies seen in the ER.

1.4.2 Clinical Presentation

Since each cause of CP has a different clinical presentation, we will mainly focus on life-threatening cardiovascular causes.

Characteristics of Ischemic CP [6]

- Oppressive or sibling pain (from the chest to the back)
- Localization: precordial, retrosternal, anterior face of the neck, inferior mandible
- With or absent irradiation: left arm, both arms, scapulae, neck, dorsal region
- With or without adrenergic symptoms (nausea, vomit, diaphoresis)
- The sense of imminent death
- Length > 1 min

In Table 1.1, characteristics and related symptoms of CP are shown, along with their positive likelihood ratio and their association with an increased probability of MI [1].

The chest discomfort or pain that occurs in ACS is generally accompanied by an autonomic nervous system stimulation, which in turn makes the patient appear pale, cold, diaphoretic, and clammy to touch [7]. However, we can identify a similar chest pain in non-cardiac disorders such as aortic dissection [7]. Nausea and vomiting are associated with the cardiac cause of the CP. Nausea and vomiting associated with dyspnea are more frequent in women with MI, whereas sweating is more frequent in men. Associated symptoms should always be assessed together with signs of other diseases, such as infection, fever, anxiety, and nervousness [7].

Physicians in charge must be in warning about that the severity of symptoms and the outcome are not related in some cases of ACS. Also, the clinician must have in mind that women suffering from MI have been reported to have pain more frequently in the back, in the neck, and in the jaw [7].

Table 1.1 Chest pain characteristics and related symptoms that are associated with increased odds of MI

Characteristic	+ LR
Pain radiation to both arms	7.1
Right shoulder	2.9
Left arm	2.3
Chest pain as most important symptom	2.0
Diaphoresis	2.0
Nausea or vomiting	1.9

MI myocardial infarction, *+ LR* positive likelihood ratio

Table 1.2 Causes of chest pain and its characteristics

Cause	Characteristic of chest pain
Acute aortic dissection	Pain most often occurs in the chest and most often present as a sharp, severe pain with changing localization, described by patients as tearing, or ripping; auscultation of aortic valve regurgitation
Pulmonary embolism	Pulmonary infarction: worsen with inspiration, anterior or lateral chest wall, associated with transitory or persistent dyspnea. Submassive or massive: retrosternal oppression without irradiation accompanied by persistent dyspnea, tachypnea, desaturation
Pneumothorax	<50%: ipsilateral chest pain bound to respiration, initially sharp and pleuritic, but may become dull or achy over time. >50% retrosternal oppression, in hypertensive modality a circulatory collapse is a clinical presentation. Sudden dyspnea is the main symptom in both conditions
Pericarditis	Classically positional worsening when lying supine and relieved when leaning forward; also, it is possible to identify a friction sound
Musculoskeletal cause	Sharp, well localized, reproduced with movement or palpation
Esophageal rupture	Can cause identical symptoms as cardiac disease but more commonly cause burning pain in the chest and epigastrium

In Table 1.2, other probable causes for CP and the characteristics that can help differentiate the underlying pathology are listed [5, 7].

1.4.3 Physical Examination

For most cases, a physical examination is not helpful distinguishing patients with ACS from those with non-cardiac CP [5]. Although, the approach for a stable and an unstable patient should be different to guide our clinical diagnoses. Physical examination findings associated to MI are shown in Table 1.3 [1].

1.4.4 Electrocardiogram

An ECG is mandatory in all patients with suspected CP from cardiac origin. The findings in the ECG may variate depending on the underlying cause.

1.4.4.1 Acute Coronary Syndromes

ECG remains the best immediately available test for detecting ACS, but its sensitivity for MI is low; a single ECG performed during the initial clinical presentation detects fewer than 50% of AMIs. Patients with normal or nonspecific ECGs have a 1–5% incidence of MI and a 4–23% incidence of unstable angina. The ECG must

Table 1.3 Physical examination findings associated with increased or decreased likelihood of MI

Characteristic	+ LR
Increase probability of MI	
Include a third heart sound on auscultation	3.2
Hypotension with a systolic blood pressure of 80 mmHg or lower	3.1
Pulmonary crackles on auscultation	2.1
Decrease probability of MI	
Pleuritic chest pain	0.2
Pain that is sharp or stabbing	0.3
Pain that is positional	0.3
Pain reproduced by palpation	0.2–0.4

MI acute myocardial infarction, *+ LR* positive likelihood ratio

repeat every 10 minutes when it is not diagnostic and in symptomatic patients with high-clinical suspicion for MI. Prior ECGs are important for determining whether abnormalities shown are new [5].

1.4.4.2 Pulmonary Embolism

ECG has a high sensitivity to pressure overload but low specificity. The most common findings in patients with severe pulmonary hypertension are sinus tachycardia, "S1Q3T3", prominent S wave in lead I, Q wave in lead III, and inverted T wave in lead III (right heart strain). Also aVR ST elevation (right ventricular ischemia), V1 qR and ST elevation (right atrial dilatation and right myocardial infarction), V1 to V4, ST dynamic changes as elevation or depression and V1 to V4 negative T waves, or complete or incomplete right bundle branch, (right ventricular ischemia), and atrial fibrillation as consequence of right ventricular strain [8]. Patients with acute pulmonary embolism (PE) rarely have a normal ECG, but a wide range of abnormalities are possible, and most are equally likely to be seen in other patients [5].

1.4.4.3 Pericarditis and Pericardial Tamponade

Pericarditis, or inflammation of the pericardium, has typical ECG findings. These findings occur in progressive stages, all of which are seen in about 50% of cases of pericarditis.

Stage I (Acute Phase)

- Diffuse concave upward ST elevation in most leads, PR depression in most leads (maybe subtle), and sometimes nothing at the end of the QRS complex

Stage II

- ST elevation and PR depression have resolved, and T waves may be normal or flattened.

Stage III

- T waves are inverted, and the ECG is otherwise normal.

Stage IV

- T waves return to the upright position, and thus the ECG is back to normal [5, 9, 10].

The ECG changes with pericarditis must be distinguished from those of early repolarization. The ST elevation seen in early repolarization is very similar: diffuse and concave upward. However, three things may help to distinguish pericarditis from early repolarization [5, 9, 10]:

- The ratio of the T wave amplitude to the ST elevation should be greater than four if early repolarization is present, meaning the T wave in early repolarization is usually four times the amplitude of the ST elevation. Another way to describe this would be that the ST elevation is less than 25% of the T wave amplitude in early repolarization.
- The ST elevation in early repolarization resolves when the person exercises.
- Early repolarization, unlike pericarditis, is a benign ECG finding that should not be associated with any symptoms.

Also, ECG findings in patients with pericarditis may mimic MI. ST dynamic changes suggest an acute coronary syndrome. ECG findings suggestive of tamponade include low voltage and electrical alternans [5].

1.4.4.4 Acute Aortic Dissection

ECG tracing can range from completely normal, left ventricular hypertrophy or ST elevation if the dissection involves the origin of the right coronary artery [5].

1.5 Imaging Studies

1.5.1 Chest X-ray

It is one of the most taken studies in the ER when CP is present; the findings may vary depending on the underlying cause.

1.5.1.1 Acute Coronary Syndromes

A normal chest X-ray is characteristic. Signs of the pulmonary capillary wedge pressure rises and ACS complicated with heart failure [5].

1.5.1.2 Acute Aortic Dissection

Widened mediastinum or aortic knob occurs in up to 76% of patients; if we add high-clinical suspicion, these three findings give an odds ratio of 11 (95% CI 6.1–19.8) for aortic dissection. Displacement of the aorta and pleural effusion may also have a finding. Around 90% show some abnormality [5].

1.5.1.3 Acute Pulmonary Embolism

The study could be normal in low-risk PE (segmental or subsegmental); however, it is always abnormal in lobar, submassive, and massive PE. Main pulmonary artery dilatation and right ventricular dilatation are infrequent, mainly in those who early arrival after onset symptoms. It is possible to identify classic radiographic findings such as the Westermark sign (a clarified area with diminished vascularity), Hampton sign (a triangle with a base to the pleura and the vertex directed to a branch of the pulmonary artery), elevated diaphragm, and small pleural effusion which are findings related with pulmonary infarction [8].

When the pulmonary obstruction is >25%, acute pulmonary arterial hypertension occurs inducing pulmonary artery and right ventricular remodeling; its radiographic expression is right and/or left pulmonary artery dilatation, main pulmonary artery dilatation, as well as right ventricular dilatation. Also, left or right elevated diaphragms are findings. Most chest X-rays are bedside in submassive or massive PE patients, so it is not easy to identify classic signs. However in this condition chest radiograph allows to exclude another clinical situation mimicking PE (acute pulmonary edema, COPD exacerbation, cardiac tamponade, extensive pneumothorax, etc.) [8].

1.5.2 Echocardiogram

ED clinicians should perform a bedside echocardiogram study in every patient with acute CP and clinical instability, hypotension, severe respiratory failure, aborted cardiac arrest, or acute pulmonary edema if it is available [5]. This non-expensive and accessible tool provides unique insight into the pathophysiology of the CP extending our clinical sensitivity beyond the usual clinical perception. Bedside transthoracic echocardiography can rapidly differentiate conditions inducing clinical instability as PE, myocardial infarction, aortic dissection, and pericardial tamponade, also allowing a rapid lifesaving treatment. Since it is an "operator dependent" tool, is mandatory a clinicians with experience in its use in stable and unstable patients.

1.5.3 Immediate Exercise Stress Echocardiogram

Immediate exercise stress echocardiogram in the ER is a suggestion that has been made by certain studies [11]. Usual common management of a patient who presents with CP to the ER, with a low-risk score, includes a 23-h observation unit admission, with serial biomarkers to rule out MI. Stress echocardiography has several advantages as an imaging modality for low-risk CP patients. Studies report sensitivity 86% and specificity 81% for detecting coronary disease via stress echocardiography, which is superior to an exercise ECG and comparable to myocardial perfusion scintigraphy. Stress echocardiography can also provide findings to diagnose nonischemic causes of CP, including PE, valvular heart disease, pericardial disease, and cardiomyopathy. A final consideration is that there is no radiation. One disadvantage in this technique is the fact that the echocardiography, similar to ECG interpretation, is "operator dependent" [11]. We recommended this approach to patients with risk factors, ischemic chest pain, and normal or non-specific ECG.

1.5.4 Cardiac Computed Tomography (CCT) and Other Imaging Tests

The increase in CCT use is appropriate, given the finding of three major randomized trials that included ER patients with CP. CCT to evaluate patients with this symptom in the ER is performed as a so-called triple rule-out examination; it can be used to exclude other causes of acute CP, such as PE, acute aortic dissection, cardiac tamponade, pericardial effusion, and pneumothorax. Myocardial perfusion imaging and stress echocardiography are not widely accepted for this purpose [12].

Several modalities diagnose acute aortic dissection with high sensitivity, including computed tomography (98%), magnetic resonance imaging (98%), and transesophageal echocardiography (94%) [5].

Computed tomography is the most widely used study for the diagnosis of PE, and it will also provide information about alternative etiologies of CP. On the downside, it exposes patients to radiation and contrast dye, which can limit its use [5].

1.6 Laboratory Evaluation

1.6.1 Cardiac Biomarkers in the Context of Acute Coronary Syndromes

Cardiac Troponins

- Elevate within 3 hours, peak at 12 hours, and remain elevated for 7 to 10 days.
- Preferred test for the diagnosis of MI.

- Highly sensitive troponin assays become detected more rapidly including unstable angina [5].
- In the majority of cases, a single set of negative cardiac biomarkers is insufficient to rule out MI; however, using the high-sensitivity troponin assays, this approach is now possible in select patients [5].

D-dimer

- In patients with a low pretest probability for PE, this test that has high sensitivity can rule out the diagnosis, obviating the need for further testing [5].
- The utility of the D-dimer test depends upon both, patient baseline characteristics and the sensitivity and specificity of the test employed [5].
- Precaution at interpreting this test may be needed in recent major surgery, trauma, pregnancy, and those with malignancy because they are likely to have an elevated D-dimer at baseline [5].

Complete Blood Count

- White blood cell count elevated in any of the inflammatory or infectious etiologies, such as myocarditis, pericarditis, ST-elevation MI, PE, mediastinitis, and pneumonia [5].
- Anemia in exertional CP is suggestive of myocardial ischemia but also consistent with aortic rupture [5].

B-Type Natriuretic Peptide and N-Terminal Pro-BNP

- B-type natriuretic peptide levels >100 pg/mL are highly sensitive for acute heart failure. Levels <50 pg/mL have high negative predictive value for heart failure [5].
- N-terminal pro-BNP levels >500 pg/mL are highly sensitive for acute heart failure. Levels <500 pg/mL also have a high negative predictive value for heart failure [5].

1.6.2 Differential Diagnosis

In all patients with acute onset of CP, ACS must be ruled out; however, other more frequent clinical conditions should be considered and excluded. In Table 1.4, we can find the final diagnosis found in a multicenter registry [1] with suspected ACS that includes 15,608 patients (being CP the main complaint in the 71% of ACS visits).

1.6.3 Clinical Approach

When confronted with a patient suffering from acute CP, the first important task is to decide whether the patient has a life-threatening disease or not, so judgment is based on the patient's previous history, actual symptoms, and clinical signs on admission [7]. We will consider an unstable patient when it presents these characteristics:

Table 1.4 Final diagnosis of the Internet Tracking Registry of Acute Coronary Syndrome

Final diagnosis	Percentage
Chest pain not otherwise specified + another diagnostic	70%
Unstable angina	6.3%
Congestive heart failure	4.0%
STEMI	1.6%
Pneumonia	1.5%
Stable angina	1.2%
NSTEMI	1.0%
Pulmonary embolism	0.4%
Pericarditis	0.3%
Dissecting aneurysm	0.1%

STEMI ST-elevation myocardial infarction, *NSTEMI* non-ST-elevation myocardial infarction

- Blood pressure < 90 mmHg
- Severe respiratory distress
- Oxygen saturation < 90%
- Tachycardia > 100 bpm

When approaching this unstable patient, immediate actions are required, to stabilize airway, breathing, and circulation; start assessing the probable cause according to the presentation, ECG, and characteristics of CP; and treat accordingly.

For a stable patient, the use of a fast stratification is necessary for their management, mainly to identify those with immediate risk of complications, as those with ACS. The HEART score in low-risk patients allows to rule out a cardiac cause without further planned cardiac testing. In several studies, this score has been accurate in predicting a low risk of 60-day MACE (>99% NPV) [4]. Further evidence suggests that the use of HEART score obtains a higher diagnostic value than troponin or clinical evaluation solely [13]. Tables 1.5 and 1.6 describe the variables of the HEART score and how to interpret each value, respectively.

The currently most used risk scores are the TIMI score and the GRACE score; each can give an idea of the 30-day mortality for the patient varying its prognostic value whether if there is an ST-elevation myocardial infarction or a non-ST-elevation myocardial infarction.

Where the clinician should always focus their attention first on are the patient's history, comorbidities, and description of symptoms, to help narrow the scope of potential diagnosis and to stratify patient's risk for life-threatening disease. Physical examination focuses on vital sign abnormalities and cardiac or pulmonary findings [5].

Any patient without a clear explanation for their CP even after the initial workup including chest X-ray and ECG will be considered to have an ACS until proven; otherwise, in these patients, serial ECGs and risk assessment (HEART, TIMI scores) are cornerstones for management [5].

Table 1.5 HEART score for chest pain patients at the ER

Variable		Points
History (anamnesis)	Highly suspicious	2
	Moderately suspicious	1
	Slightly or non-suspicious	0
ECG	Significant ST-depression	2
	Non-specific repolarization disturbance	1
	Normal	0
Age	≥65 years	2
	45–65 years	1
	≤45 years	0
Risk factors	≥3 risk factors, or history of atherosclerotic disease	2
	One or two risk factors	1
	No risk factors are known	0
Troponin	≥3x normal limit	2
	1–3x normal limit	1
	≤normal limit	0

Score: low risk, <4; intermediate risk, 4–6; high risk, >7

Table 1.6 How to interpret the HEART score

HEART score	MACE	Death	Decision
0–3	1.9%	0.05%	Discharge
4–6	13%	1.3%	Observation with noninvasive stress testing or imaging, risk management
7–10	50%	2.8%	Early invasive diagnostics and treatment

MACE major adverse cardiac event

Another pathology outcome time depending on that we must rule-out acute aortic dissection. In a prospective observational study, its probability significantly increases with the presence of the following variables [14]:

- Abrupt onset of thoracic or abdominal pain with a sharp, tearing, and/or ripping character
- Variation in pulse (absence of a proximal extremity or carotid pulse) and/or blood pressure (>20 mmHg difference between the right and left arm)
- Mediastinal and/or aortic widening in the chest X-ray

Acute aortic dissection occurs in approximately 83% of patients with variables 1 and 3 and approximately 92% of patients with variables 1 and 2. When all three variables coexist, diagnosis of acute aortic dissection is present in all patients; when no variable is present, approximately 7% of patients were found with the diagnosis [14].

Clinicians frequently overlook acute PE in the ER, and it always should be considered in the acute chest discomfort or dyspnea who lacks a firm alternative diagnosis. The approach is based on risk stratification, with symptoms suggestive of PE and right ventricular heart dysfunction or hemodynamic instability are at high risk. Several scoring systems exist to characterize patient risk for PE, including the Wells score, the Charlotte criteria, the revised Geneva score, and the PERC rule [5].

For diagnosing or rule-out cardiac tamponade, a bedside echocardiogram is an ideal tool, especially in any patient with suggestive historical, examination, or electrocardiogram findings [5].

Tension pneumothorax is diagnosed clinically combining: a suggestive history, hemodynamic compromise, and unilateral diminished breath sounds. This triad is the usual presentation. Treatment should not be delayed while awaiting confirmation from chest X-ray. This tool or bedside echocardiogram may be used to make the diagnosis in patients without signs of tension. The treatment is immediate needle thoracostomy, followed by tube thoracostomy [5].

The initial chest X-ray is almost always abnormal in patients with esophageal perforation and mediastinitis and usually reveals mediastinal or free peritoneal air as the initial radiologic manifestation. CT scan may show extraesophageal air, periesophageal fluid, mediastinal widening, and air and fluid in the pleural spaces, retroperitoneum, or lesser sac. The diagnosis is confirmed with the oral administration of a water-soluble contrast agent followed by chest X-ray looking for extravasation [5].

To find more about each specific treatment of pathologies causing CP, go to the corresponding chapter of your suspected diagnosis in this book.

To find a more visual way to the approach to CP patients, look for the algorithm in Fig. 1.1.

1.7 Additional Clinical Practice Takeaway

- CP is one of the most common complaints in the ER; its wide variety of causes forces a well-structured workup to find its diagnosis.
- The first step is to detect stable and unstable patients; in some cases, the underlying cause is obvious, for example, in trauma-related CP.
- It is necessary to determine whether CP is from a cardiac, pulmonary, musculoskeletal, or another source and do it with proper speed.
- The clinician should have a structured approach when encountered with CP and know if there is a code response team available at the hospital.
- Precaution at interpreting D-dimer in patients with recent major surgery, trauma, pregnancy, and those with malignancy.
- We recommended stress test in ER in those with risk factors, ischemic chest pain, and normal or non-specific ECG.
- An echocardiogram provides unique insight into the pathophysiology of the CP extending our clinical sensitivity beyond the usual clinical perception.

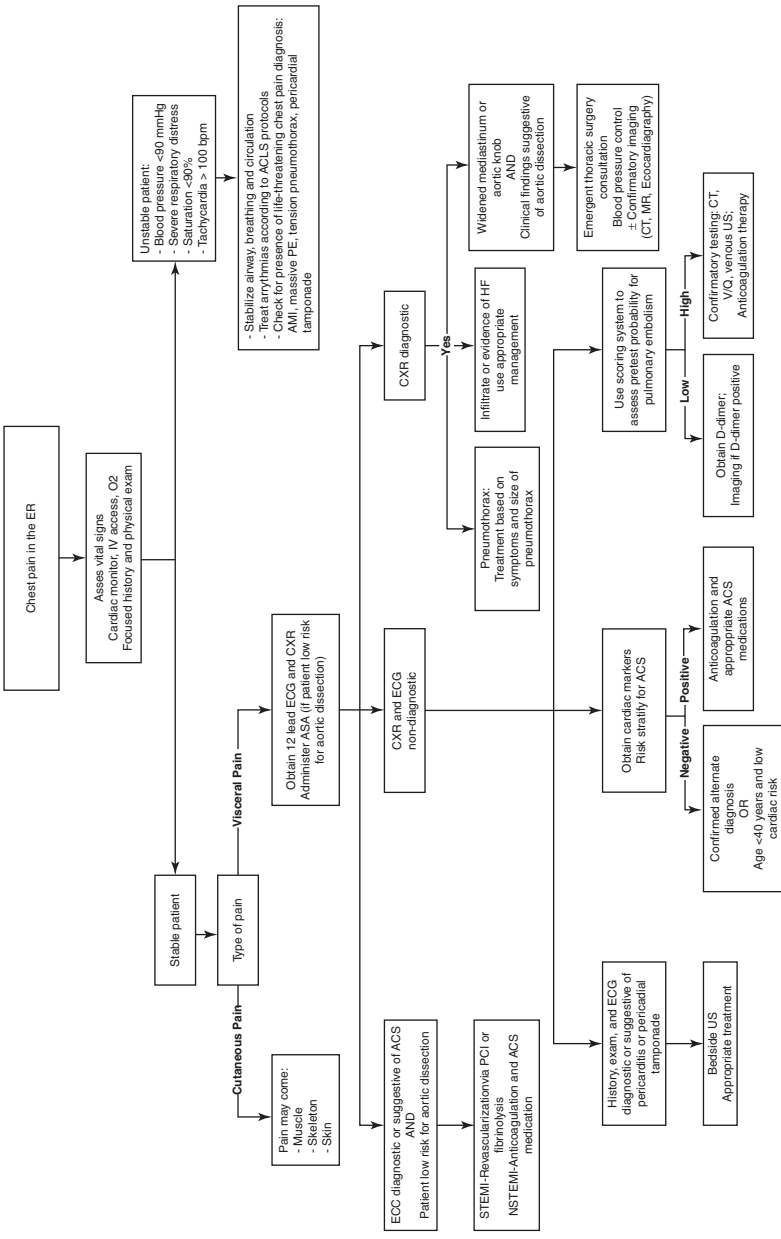

Fig. 1.1 Approach to the patient with chest pain in the emergency room

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Chapter 2
Dyspnea in the ER

Carlos Jerjes-Sánchez and Francisco Nevarez

2.1 The Scope of the Problem

Dyspnea or shortness of breath is defined by the American Thoracic Society as "a subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity and derives from interactions among multiple physiological, psychological, social, and environmental factors, and may induce secondary physiological and behavioral responses" [1]. Dyspnea may also be considered as the perception of an inability to breathe comfortably, which adds subjectivity to the symptom which may be challenging to the clinician when managing an acutely dyspneic patient [2]. Dyspnea may occur either at rest or at lower than expected levels of exertion [3]. One of its main difficulties is the subjectivity of this symptom, because of the impossibility for the clinician to assess the severity and to make it accountable for the diagnosis process. Dyspnea at rest or effort may be the clinical presentation of a life-threatening event.

2.2 Prevalence

Dyspnea is a common chief complaint among patients in the emergency room (ER). A chief complaint of dyspnea, "shortness of breath," and "labored or difficult breathing" made up for 3.7 million visits (2.7%) of the more than 136 million visits in the United States ERs in 2011 [2, 4]. It also affects up to 50% of patients admitted acutely to tertiary care hospitals and a quarter of patients seeking care in ambulatory settings. Population-based studies have shown a prevalence of 9%–13% for mild to moderate dyspnea among community-residing adults, 15%–18% among community-residing adults aged 40 years or older, and 25%–37% of adults aged 70 years and older [4]. In a more recent study, when

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taking all hospital admissions into consideration, within 12 hours of admission, 11% of all hospitalized patients reported current dyspnea >0 on admission and 4% (2483/67,362) of patients reported a rating of 4 or greater (out of 10) on admission [5].

2.3 High-Clinical Suspicion for Dyspnea of Cardiac Origin

When the clinical presentation is dyspnea and respiratory distress, the primary task of the emergency physician is to assess and ensure for patient's airway, breathing, and circulation stability [6]. Since dyspnea is one of the most common symptoms in patients with cardiac diseases, it is necessary to establish steps to evaluate a patient. The first step is to differentiate between acute from chronic worsening dyspnea. Acute dyspnea may be a manifestation of a life-threatening condition, so the potential threat should be assessed at once [1].

It is helpful to be familiar with the various differential diagnoses for dyspnea, which may include many disorders that can be divided based on obstructive, parenchymal, cardiac, and compensatory features. Risk factors such as past medical and family history, trauma, travel, medications, and exposures should be considered [6].

Some of the more relevant causes for acute dyspnea in the ER are [2]:

Cardiac

- Heart failure (HF) with or without preserved ejection fraction
- Flash cardiac, pulmonary edema
- Acute coronary syndromes
- Ischemic heart disease
- Emergency or uncontrol hypertension
- Cardiac arrhythmia
- Critical aortic stenosis
- Severe mitral or tricuspid regurgitation
- Prosthetic valve dysfunction
- Cardiac tamponade
- Pulmonary embolism (PE)
- Pulmonary hypertension

Respiratory

- Aspirated foreign body
- Airway trauma
- Direct pulmonary injury
- Anaphylaxis with angioedema
- Non-cardiogenic pulmonary edema
- Acute respiratory distress syndrome
- Pulmonary hemorrhage
- Pneumothorax

Psychiatric

- Hyperventilation
- Anxiety attacks

Steps to take when evaluating dyspnea are showing in Fig. 2.1

2.3.1 Pathophysiology

Dysfunctions of the respiratory system could be secondary by alterations in either the controllers, ventilatory pumps, or gas exchangers. Dyspnea as a clinical presentation of cardiovascular diseases is the consequence of left or right ventricular dysfunction with low- cardiac output syndrome, increase in pulmonary venous or capillary pressure, as well as, increase of arterial and venous vascular resistance.

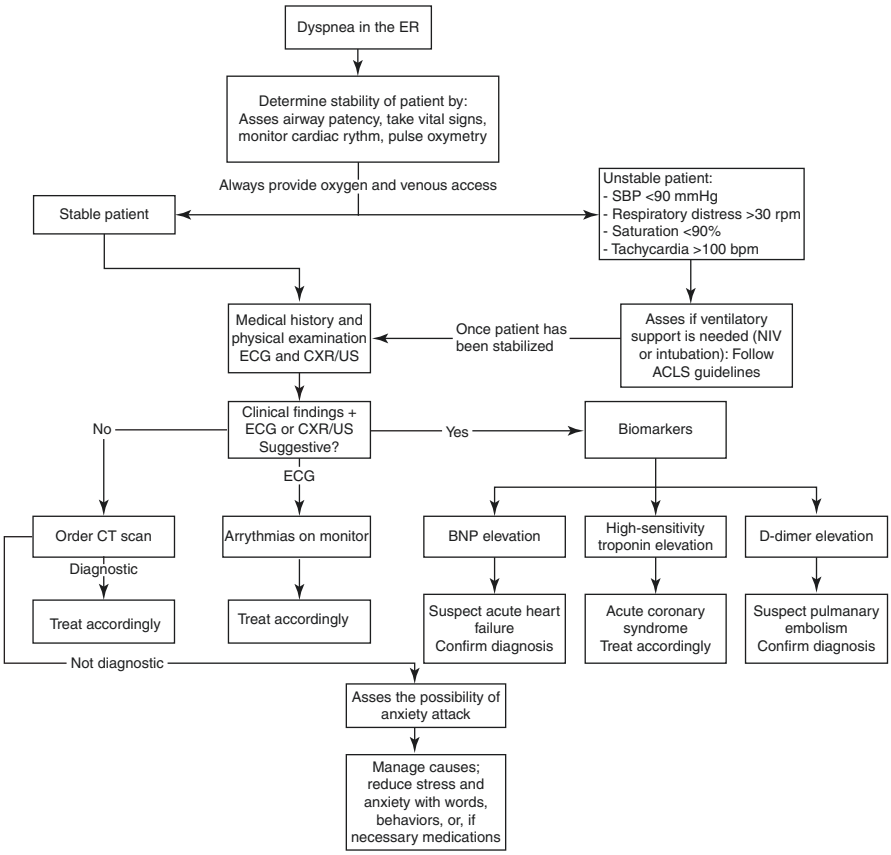

Fig. 2.1 Algorithm for evaluating dyspnea

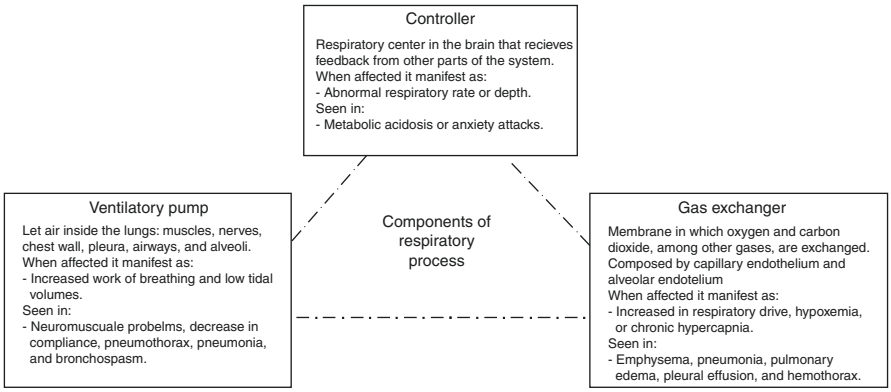

Fig. 2.2 Assessing the components of the respiratory process

Anemia through non-cardiogenic mechanisms can induce dyspnea, and similarly, decreased oxygen carrying capacity in anemia explains the dyspnea that presents [6]. Figure 2.2 describes the three components of the respiratory process.

2.3.2 Clinical Presentation

Vital signs (heart rate, blood pressure, oxygen saturation) are necessary for timely decision-making, particularly whether if the patient acutely needs noninvasive or invasive assisted ventilation [1]. Once the patient is stable, the diagnostic workup will proceed.

To evaluate a patient with dyspnea, a thorough medical history must be made to guide clinician's judgment: events and symptoms prior/accompanying acute dyspnea, past history (to identify acute, subacute or chronic dyspnea), history of intubation, onset (suddenly or gradually), severity (recommended to use a scale of 1 to 10), presence of chest pain and its characteristics, history of trauma, fever, paroxysmal nocturnal dyspnea, cough, sputum, hemoptysis, medications, tobacco and/or drug abuse, and any psychiatric conditions [2].

In a recent systematic review, there was not a single sign or symptom accompanying dyspnea that had acceptable sensitivity to be useful in ruling out the diagnosis of heart failure, chronic obstructive pulmonary disease, asthma, or PE. However, it was found that elevated jugular venous pressure (pooled specificity: 0.88, pooled odds ratio: 7), third heart sound (pooled specificity: 0.97), and lung crepitation (pooled specificity: 0.7, OR 7, pooled OR 11) are useful in ruling in heart failure [7]. Restless or effort, acute, or subacute dyspnea is a symptom that may be the first expression of severe ventricular dysfunction that can be life-threatening, so following a systematized approach is mandatory (Fig. 2.1).

2.3.3 Dyspnea Approach

Evaluating clinical stability: assess airway patency and auscultate lungs and accessory muscles, monitor cardiac rhythm, measure vital signs and pulse oximetry, and evaluate mental status [8]. Provide oxygen, IV access, cardiac pulse, oximetry monitoring, airway management equipment to the bedside, and screening examination (assess for causes for airway difficulty and search for rapidly reversible causes) [2].

In an unstable patient, the ACLs guidelines should be followed, before investigating the symptom of dyspnea. Once the patient is stable, an ECG and CXR should be obtained, and the rest of the clinical history should be assessed. Considering clinical presentation patient should be referred to intensive care unit, cardiology, pneumology, etc. Clinicians most to determine diagnosis or need for admission based on history, physical examination, CXR, and ECG, although often the cause for dyspnea cannot be determined with certainty in the ER [2].

Management Recommendations of the Airway

- Mild dyspnea and normal room-air arterial oxygenation saturation (SpO2): 2 L/min of oxygen via nasal cannula is adequate [2].
- Hypoxic patients with respiratory distress: 50–60 L/min of oxygen provided via nonrebreather mask [2].
- Target oxygen saturation to COPD 90–94% [2].

Noninvasive and invasive mechanical ventilation should be considered in cases with severe respiratory distress independent of the etiology [2] (Fig. 2.1).

2.3.4 Physical Examination

Respiratory rate and oxygen saturation should be obtained along with vital signs. The clinician should look for any tripoding or retractions, conjunctival pallor, capillary refill, and temperature of extremities, which can provide clues about blood volume and general circulation [6].

It is important to conduct a systematic physical examination to obtain the most information possible. It is suggested that the order of the physical examination is always maintained the same, starting cranially and proceeding caudally [8]:

- *Neck*: venous jugular distention, thyroid enlargement (HF may result from hyperthyroidism or hypothyroidism), assess midline trachea, and auscultate for stridor
- *Cardiac and pulmonary examination*: palpate chest for subcutaneous emphysema and crepitus and percuss for dullness. Auscultate heart and lungs for murmurs or extra heart sounds, absent breath sounds, wheezing, rales, rapid or irregular pulse, left or right S3 third sound or gallop, S4 gallop, loud P2, murmurs, and distant heart sounds

- *Abdominal examination*: hepatomegaly, ascites, and hepato-jugular reflux
- *Extremities*: edema in lower extremities and any signs of deep venous thrombosis and examine the digits for clubbing or cyanosis

Symptoms may differ depending on the type of dyspnea; parenchymal dyspnea can be caused by cardiac pathology; 80% of patients with acutely decompensated HF present through the ER with a chief complaint of dyspnea [6]. When circulatory perfusion is compromised, dyspnea can occur, which is where we can find PE, which interferes with ventilation and perfusion, ultimately causing circulatory collapse [6].

Dyspnea and clinical instability related to [8]:

- Hypotension with or without altered mental status
- Stridor and breathing effort without air movement (suspect upper way obstruction)
- Unilateral tracheal deviation, hypotension, and unilateral breath sounds (suspect tension pneumothorax)
- Respiratory rate above 40 bmp, retractions, cyanosis, low oxygen saturation

Signs suggestive of severe respiratory distress [2]:

- Retractions and the use of accessory muscles
- Brief, fragmented speech
- Inability to lie supine
- Profound diaphoresis, dusty skin
- Agitation or depressed mental status
- Cyanosis
- Inability to maintain the respiratory effort

Tables 2.1 and 2.2 shown cardiac and non-cardiac signs and symptoms accompanying dyspnea, and possible diagnosis or findings. Occasionally COPD due to viscous respiratory secretions can mimic orthopnea.

2.3.5 Electrocardiogram

Electrocardiogram must be obtained in all patients with dyspnea. ECG is accessible, cheap, and easy to repeat several times bedside. It has high sensitivity but low specificity to myocardial ischemia, volume and pressure overload, and ventricular hypertrophy.

In the ER setting, its main strengths are:

- Very useful to identify arrhythmias and ST- dynamic changes [6].
- A careful analysis can identify right ventricular dysfunction in high clinical suspicion PE patients [9].

Table 2.1 Cardiac symptoms and signs accompanying dyspnea and possible diagnosis [1, 2, 6, 8]

Symptoms and signs	Clinical conditions
Cardiac wheeze	Heart failure with or without preserved ejection fraction
Orthopnea	Acute heart failure, toxic pulmonary edema, COPD
Dizziness, syncope	Pulmonary embolism, pulmonary hypertension, valvular heart disease, hypertrophic or dilated cardiomyopathy, paroxysmal cardiac arrhythmia, severe anemia, anxiety disorder, hyperventilation
Cyanosis	Acute respiratory failure, heart defect with right to left shunt, Eisenmenger syndrome
Hypertension	Uncontrol hypertension or hypertensive emergency, panic attack, acute coronary syndrome
Hypotension	Severe right or left heart failure, acute right or left ventricular dysfunction, metabolic disturbance
Peripheral edema	Right or left ventricular heart failure
Pulmonary edema	Cardiogenic: acute or chronic left ventricular heart failure. Non-cardiogenic: non-cardiogenic acute pulmonary edema, acute respiratory distress syndrome
Bradycardia	Sinoatrial or atrioventricular block, an overdose of drugs that slow heart rate
Pulsus paradoxus	Right heart failure, acute right ventricular dysfunction, cardiogenic shock, pericardial tamponade, asthma exacerbation
Heart murmur	Valvular heart disease, acute mitral or tricuspid regurgitation, prosthetic valve dysfunction, rupture of the intraventricular septum, obstructive myocardiopathy
Hepatojugular reflux	Acute right or left heart failure with or without preserved ejection fraction
JVD with clear lungs	Cardiac tamponade, PE
JVD with crackles	Acute left heart failure with or without preserved ejection fraction, acute left ventricular dysfunction
Left or right S3 sound or gallop	Suggests left or right heart failure with or without preserved ejection fraction; acute left or right ventricular dysfunction
S4 sound	Suggests left ventricular dysfunction, severe hypertension, aortic stenosis, hypertrophic cardiomyopathy, ischemic heart disease, acute mitral regurgitation
Muffled or distant heart sounds	Pericardial effusion or cardiac tamponade

JVD jugular venous distension

- Persistent ST elevation establish myocardial infarction to mechanical or pharmacological reperfusion [2].
- Initial ECG is normal in 20% of patients with myocardial infarction [2].
- PR depression suggests auricular infarction, myocarditis, or pericarditis and diffuses low voltage and electrical alternans, pericardial effusion, or tamponade [2].

Table 2.2 Non-cardiac symptoms and signs accompanying dyspnea and possible diagnosis [1, 2, 6, 8]

Symptoms and signs	Clinical conditions
Wheeze	COPD/emphysema, asthma, allergic reaction, foreign body
Inspiratory stridor	Croup, foreign body, bacterial tracheitis
Expiratory/combined	Foreign body, epiglottitis, angioedema
Cough	Pneumonia, asthma, COPD/emphysema
Pleuritic chest pain	Pneumonia, pneumothorax, COPD, asthma, pulmonary infarction
Pain on respiration	Pneumothorax, pleuritic, pleural effusion, pneumonia
Pain independent of respiration	Acute coronary syndromes, aortic aneurysm, pulmonary hypertension, PE, Roemheld syndrome, renal or biliary colic, acute gastritis
Auxiliary muscles of respiration	Respiratory failure/acute respiratory distress, severe COPD or asthma
Hoarseness	Disease of glottis or trachea, recurrent laryngeal nerve palsy, recurrent compression secondary pulmonary artery dilatation, aortic aneurysm
Fever	Pneumonia, tuberculosis, malignancy, bronchitis, thyrotoxicosis
Pallor	Severe anemia
Impairment of consciousness	Psychogenic hyperventilation, cerebral or metabolic disturbance, pneumonia
Hemoptysis	Pneumonia, TB, malignancy, pulmonary infarction, bronchiectasis
Platypnea	Hepatopulmonary syndrome, intrapulmonary shunting
Tachypnea (hyperventilation)	PE, acidosis (including aspirin toxicity), psychogenic (includes anxiety), sepsis
Absent/diminished breath sounds	COPD, severe asthma, pneumothorax, tension pneumothorax, hemothorax, pleural effusion
Crackles (rales)	Acute left heart failure, acute respiratory distress syndrome, pneumonia
Indigestion, dysphagia	Gastroesophageal reflux disease, aspiration
Urticaria	Angioedema
Brainstem signs, neurologic deficits	Brain tumor, cerebral hemorrhage, cerebral vasculitis, encephalitis
Vegetative symptoms (trembling, cold sweats)	Respiratory failure, anxiety disorder, acute myocardial infarction

COPD chronic obstructive pulmonary disease, *PE* pulmonary embolism

2.4 Imaging Diagnosis Approach

2.4.1 Chest X-Ray

It must be obtained in all patients with dyspnea; it is often the first image technique in the ER. Strengths: low radiation, identifying a pulmonary disease as consolidation, pleural effusion, hyperinflation, pneumothorax, chronic pulmonary disease,

and subcutaneous air; also, the heart size may be apparent. Weakness: low sensitivity in acute dyspnea (it only detected 8/26 cases of pneumonia that were diagnosed with tomography) [6]. It should be stated that the chest X-ray may be normal at first, and it must always be interpreted once a full history and physical examination have been completed.

There are specific findings from the chest X-ray to establish a diagnosis or a high-clinical suspicion:

- *Acute HF*: cardiomegaly; cephalization of blood vessels; venous helium; Kerley A, B, and C lines; peribronchial cuffing; and interstitial or alveolar edema [2]. In elderly patients (> 75 years), interstitial or alveolar edema could have irregular distribution secondary pulmonary degenerative changes suggesting chronic pulmonary diseases.
- *Pneumonia*: infiltrate or consolidation with segmental, lobar, or over in the location and air bronchogram is considered a "gold standard" [2].
- *Pneumothorax*: total or partial lung collapse usually induces dyspnea [2]. Physicians in charge should be in a warning with the peripheral collapse.
- *COPD and asthma*: large lung volumes and a flattened diaphragm bilaterally suggest air trapping; unilateral air trapping suggests a foreign body, mainly in lateral view [2].
- *PE*: normal in segmental or subsegmental PE; submassive or massive: Hampton sign, Fleischner lines, significative or small right or left pleural effusion, Westermark sign, left or right or both pulmonary artery cutoff, left or right or both pulmonary artery dilatation, main pulmonary artery dilatation, elevated right diaphragm [10].

2.4.2 Echocardiogram

This imaging tool has broad and global accepted for its use in the ER. Strengths: no radiation, fast, reproducible bedside test, and semi-recumbent position which is useful in unstable patient [6]. Weaknesses: operator depending, poor window (COPD), other factors which may limit the images (subcutaneous air, body habitus, and so forth) [6].

In the ER identify [2, 11]:

- HF preserved ejection fraction (> 50%), HF intermediate range (40–49%), HF reduced ejection fraction (< 40%)
- Submassive PE by right ventricular dysfunction with or without wall motion abnormalities
- In-transit thrombus: thrombi in the right atrial or ventricle
- Clinical conditions mimicking a massive PE (pericardial tamponade, acute prosthetic valve dysfunction)
- In acute coronary syndromes jeopardized the myocardial area
- In patients with clinical instability and ST-elevation myocardial infarction mechanical complications

Table 2.3 PoC echocardiogram vs. ER workup diagnosis [12][a]

Sensibility in favor of	Diagnosis
PoC echocardiogram	Heart failure
ER diagnosis	COPD, asthma, and PE
No statistical difference	Acute coronary syndrome, pneumonia, pleural effusion, pericardial effusion, pneumothorax, and dyspnea from other causes

[a]All diagnosis have an appropriate range of accuracy

Recently, echocardiogram systematically reduces the time to diagnosis with an acceptable safety profile in the ER (PoCUS study; integrated point-of-care ultrasonography). The time required to establish diagnosis in patients with dyspnea was significantly lower (24 ± 10 min vs. 186 ± 72 min, p = 0.025) compared with standard ER diagnosis. The study also shows that the use of echocardiogram has an appropriate range of accuracy compared to the clinical evaluation [12]. Table 2.3 shows sensibility between point of care echocardiogram and other ER work-up diagnosis.

2.4.3 Cardiac Computed Tomography

This image technique provides detailed imaging of the cardiorespiratory system, offering sensitive and specific results, although clinicians should maintain clinical context and consider whether other modalities can answer the clinical question. Weaknesses: significant radiation exposure, contrast nephropathy, and intravenous contrast dye reactions [6]. Cardiac CT has low sensitivity in subsegmental PE. In patients with clinical instability, cardiac CT triage, including aorta and pulmonary and coronary arteries, reduces diagnosis time. However, the quality of acquired image could be affected. Also, if the institute does not have agile protocols to readily deliver patients to the imaging department and effectuate the study, time could be an important factor to consider.

2.4.4 Ventilation/Perfusion Lung Scan

In the context of the ER, the V/Q scan is not the most common nor precise study for the workup of dyspnea. Its use is reserved for PE diagnosis. Radiolabeled aerosols and albumin aggregates are used to study ventilation and perfusion. The V/Q lung scan should be interpreted as diagnostic or non-diagnostic. Diagnosis of PE: one segmental or two subsegmental defects or over. Main strength: low dose of radiation [6]. In patients with, PE high-clinical suspicion, abnormal D-dimer, and non-diagnosis CT, V/Q lung scan is the next step.

2.5 Laboratory Evaluation

A complete blood count identifies low hemoglobin and leukocytosis suggesting anemia or infections as responsible of dyspnea [6]. The World Health Organization defines anemia as a hemoglobin value <8.06 mmoL/L (13 g/dL) in men or 7.44 mmoL/L (12 g/dL) in women. Unfortunately, the threshold value of hemoglobin below which anemic patients become dyspneic is unknown [1].

2.5.1 Cardiac Biomarkers

High-Sensitive Troponin I [1, 6]

- Abnormal measurements suggest myocardial infraction or myocardial injury.
- Useful in patients with chest pain approach or acute coronary syndromes.
- We recommend basal and 3-hour measurements.
- Considering the clinical context high-sensitive troponin I assay with a coefficient of variance of <10% at the 99th percentile value suggests left or right myocardial infarction type I or II.
- There are several clinical conditions related to abnormal measurements of high-sensitive troponin I, called myocardial injury possible secondary to ischemia, apoptosis or necro-apoptosis.
- Useful in patients with or without risk factors, ischemic chest pain, and normal or unspecific ECG.
- Independent to the clinical context, abnormal high-sensitive troponin I expression is related with poor outcome.
- The positive predictive value of serial high-sensitive troponin I measurement for myocardial ischemia is 75–80%.

B-Type Natriuretic Peptide (BNP) and N-Terminal Pro-BNP [1, 2, 6, 11, 13]

- Abnormal measurements suggest cardiomyocyte stretch.
- Both biomarkers are useful to exclude HF and to identify its severity.
- BNP < 100 pg/mL or N-terminal pro-BNP < 500 pg/mL excluded HF.
- BNP measurements < 100 pg/mL has an NPV > 90% to exclude HF and >500 pg/mL PPV > 90% (European Society of Cardiology recommend <300 pg/mL).
- In patients with dyspnea BNP measurements >100 pg/mL suggests right or left ventricular dysfunction.
- BNP discordantly low (< 100 pg/mL) has been seen in flash pulmonary edema (onset 1 hour), acute pulmonary edema secondary to papillary muscle rupture with mitral regurgitation (onset <2 hours), massive PE (onset 1 hour) and RV myocarditis secondary to systemic lupus erythematosus (unknown mechanism).
- Considering that the half-life of PNC is 23 minutes and therefore approximately 2 hours are required to reflect changes in the setting of the acute left of right ventricular

dysfunction. Physicians in charge should be aware of this 2-hour lag period before the onset of PNC to avoid underdiagnosing ventricular dysfunction.
- In HF, BNP subexpression is possible in elderly and morbid obesity patients.

D-Dimer [1, 2]

- Abnormal measurements suggest endogenous fibrinolysis activation.
- D-Dimer < 500 ng/dL rule out PE in low-high clinical suspicion patient.
- We recommend standard D- dimer cutoff in all age ranges and its analysis in the first blood sample.
- As an expression of a hypercoagulative state, abnormal D-dimer measurements are possibly in elderly, cancer, coagulopathy, infection, trauma, pregnant, etc.

Arterial Blood Gases [6]

- In most patients with dyspnea and tachypnea, with or without clinical stability, oximetry drives decision-making to oxygen, noninvasive or invasive mechanical ventilation.
- Useful in those patients with suspicion of respiratory or metabolic acidosis.
- Careful in patients on anticoagulation or thrombolysis.
- We do not recommend femoral access in patients on anticoagulation or thrombolysis.
- There is limited evidence for its routine use in undifferentiated dyspnea patients.

Recently in a biomarkers study to evaluate short-term mortality in dyspneic patients, the association of MR-proADM, copeptin, and troponin added significant prognostic information (Table 2.4) [14]. The clinical application of these biomarkers is yet an unanswered question.

2.5.2 Differential Diagnosis

Differential diagnosis categorized by organ systems is shown in Table 2.5. Cardiac causes for dyspnea and its clinical presentation are shown in Table 2.6.

The most common causes of dyspnea in the ER [1]:

- COPD: 16.5%
- Heart failure: 16.1%

Table 2.4 Biomarkers for short-term mortality of dyspneic patients [14]

Biomarker	Cutoff value	MP AUC	*P* value
MR-proADM	2.143 nmol/L	0.805	0.0048
Copeptin	138.31 pmol/L	0.801	0.0055
Troponin	0.03 μg/L	0.807	0.0464

MR-proADM mid-regional pro-adrenomedullin, *MP AUC* area under the curve for model of prognosis

Table 2.5 Differential diagnosis of dyspnea in the ER [3, 8]

Cardiac	Cardiac disorders: ischemic and nonischemic cardiomyopathies Valvular heart disease: aortic stenosis/insufficiency, congenital heart disease, mitral valve stenosis/regurgitation Arrhythmia: atrial fibrillation or flutter, paroxysmal atrial tachycardia, ventricular tachycardia, sick sinus syndrome, bradycardia Restrictive causes: constrictive pericarditis, pericardial effusion/tamponade
Pulmonary	COPD, asthma, pneumonia, pneumothorax, PE, pleural effusion, metastatic disease, pulmonary edema, gastroesophageal reflux, restrictive lung disease, non-cardiac pulmonary edema, acute respiratory distress syndrome
Upper way obstruction	Epiglottitis, foreign body, croup, Epstein-Barr virus
Endocrine	Metabolic acidosis, medications, thyrotoxicosis
Central	Neuromuscular disorders, pain, aspirin overdose
Psychogenic	Panic attacks, hyperventilation, pain, anxiety

COPD chronic obstructive pulmonary disease, *PE* pulmonary embolism

Table 2.6 Life-threating cardiac causes of dyspnea and their possible presentation [2]

Disease	Clinical presentation and causes in the ER
Acute coronary syndrome	Ischemic chest pain associated with dyspnea. Unstable angina, non-ST-elevation myocardial infarction, ST-elevation myocardial infarction
Acutely decompensated heart failure	Dyspnea at rest or effort with tachypnea, S3 gallop, pulmonary crackles, peripheral edema. Ischemic heart disease, valvular disease, restrictive cardiomyopathy, hypertensive emergencies
Flash pulmonary edema	Orthopnea, severe respiratory failure, alveolar rales. Non-ST-elevation myocardial infarction, ST-elevation myocardial infarction, ischemic heart disease, valvular disease, restrictive cardiomyopathy, hypertensive emergencies, mechanical valvular obstruction
High output heart failure	Dyspnea at rest or effort with tachypnea, S3 gallop, pulmonary crackles, peripheral edema. Precipitated by anemia, Beriberi, pregnancy, and thyrotoxicosis
Cardiomyopathy	Dyspnea at rest or effort with tachypnea, S3 gallop, pulmonary crackles, peripheral edema or orthopnea, severe respiratory failure, alveolar rales
Valvular dysfunction	Dyspnea at rest or effort with tachypnea, S3 gallop, pulmonary crackles, peripheral edema or orthopnea, severe respiratory failure, alveolar rales secondary to Aortic stenosis or regurgitation, mitral stenosis or regurgitation, or ruptured chordae tendinae
Cardiac tamponade	Dyspnea at rest or effort, hypotension, cardiac collapse, jugular venous distention, clear lung secondary to hemopericardium post-surgery or secondary to anticoagulation, immunologic diseases, tuberculosis

- Pneumonia: 8.8%
- Myocardial infarction: 5.3%
- Atrial fibrillation or flutter: 3.3%
- Malignant tumor: 3.3%
- PE: 3.3%

Table 2.7 Use of arterial blood pH and hypoxemia to rule-in anxiety disorders [15]

	Specificity	Sensitivity	Cutoff value	Odds ratio	Combined AUC
pH	75%	72%	7.45	4.50, 95% CI 2.27–8.92	0.86 (95% CI 0.82–0.88)
Hypoxemia	NA	NA	PaO2 < 10.8 kPa	0.21, 95% CI 0.07–0.65	NA

NA not available

The iatrogenic (pharmacological) causes for dyspnea need to identified. Nonselective beta-blockers can cause bronchospasm via B2-blocking effect; nonsteroidal anti-inflammatory drugs that inhibit COX-1 lead to increased conversion of arachidonic acid to leukotriene, which in turn can cause bronchoconstriction [1].

The last diagnosis to consider in the diagnostic workup is psychological causes. Acute anxiety and panic disorders can present as shortness of breath, tachypnea, or hyperventilation [2]. The pathophysiology suggests abnormal proprioception, experimenting dyspnea without the usual abnormal stimulus [2]. Improvement of dyspnea with distraction or physical exercise may be a clue to pathology of a psychological cause. An arterial blood gas may be useful in diagnosing anxiety-related hyperventilation [2].

Table 2.7 shows the accuracy of pH and hypoxemia use to diagnose anxiety disorders [15]. Anxiety disorders can be managed by managing their causes and reduce stress and anxiety with words, behaviors, or, if necessary, medications. Finally, always keep in mind that patients who suddenly develop dyspnea feel themselves to be in danger, so it is often that emotional factors such as panic, anxiety, and frustration additionally worsen the patient's subjective distress [1]. That is why it is emphasized to avoid a premature diagnosis of anxiety-based dyspnea without first ruling out other diagnostics [2].

2.6 Additional Clinical Practice Takeaway

- Dyspnea is a common symptom in the ER, whether it is the main complaint or associated with other symptoms, so an excellent diagnostic workup is needed.
- The evaluation of dyspnea in the ER is complex and should be addressed promptly and efficiently, to avoid life-threatening situations.
- Dyspnea at rest or effort may be the clinical presentation of a life-threatening event.
- B-type natriuretic peptide <100 pg/dL excluded heart failure.
- BNP discordantly low (<100 pg/mL) has been seen in flash pulmonary edema (onset 1 hour), acute pulmonary edema secondary to papillary muscle rupture with mitral regurgitation (onset <2 hours), massive PE (onset 1 hour), and RV myocarditis secondary to systemic lupus erythematosus (unknown mechanism).
- D-Dimer <500 ng/dL excluded pulmonary embolism.

- High-sensitive troponin assays with a coefficient of variance of <10% at the 99th percentile value, myocardial infarction.
- Anxiety is the last diagnosis after a careful cardiac ruled out.
- Noninvasive or invasive mechanical ventilation are the foundation of the workup in cases with severe respiratory distress.
- Noninvasive ventilation requires a medical staff and patient cooperation; if this approach fails, invasive mechanical ventilation is the next step.
- A multifocal approach including clinical examination, ECG, chest X-ray, biomarkers, echocardiogram, cardiac, or pulmonary CT should be obtained when the mechanisms of dyspnea are uncertain.

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Chapter 3
Suspected Cardiovascular Syncope in the ER

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3.1 The Scope of the Problem

Syncope is a sudden, transient episode of complete loss of consciousness with spontaneous recovery caused by a brief interruption of cerebral oxygen supply [1]. The most common cause is an abrupt drop in systemic blood pressure (reflex or orthostatic faints); however, in some cases, the cause requires immediate workup and treatment, especially when it is related to cardiac etiology. Although mortality in syncope is low, a 1-year mortality rate can reach almost 33% in some subgroups with cardiac syncope [2]. Syncope is an important and frequent complaint in the ER. Its cause, however, often remains unclear. So, management should be focused on risk stratification to single out those patients that warrant immediate workup and investigation to define a cause for syncope. Syncope can be classified into three groups: reflex or neurally mediated, secondary to orthostatic hypotension, and cardiac syncope. This chapter focuses mainly on cardiac syncope.

3.2 Prevalence

A report from the Framingham Heart Study showed that the incidence of syncope was 6.2 per 1000 person-years, with 9.5% being of cardiac etiology. A multivariable-adjusted hazard ratio in this group was 2.01 (95% CI 1.48–2.73) for the death of any cause, 2.66 (95% CI 1.69–4.19) for death from coronary heart disease or myocardial infarction, and 2.01 (95% CI 1.06–3.80) for a fatal or nonfatal stroke [2]. The prevalence of syncope as a presenting symptom to the ER ranged from 0.8 to 2.4% [3] or 1% to 1.5% of all emergency department visits, 250,000 annual hospital admissions, and a median hospital cost of $8500 [4].

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Approximately 40% of the US population will experience a syncopal episode in their lifetimes, and 30%–50% will be admitted to the hospital for further evaluation. The etiology is unexplained in up to one-third of cases. Although syncope is associated with serious risks, short-term mortality is low (i.e., 0.7% at 10 days and 1.6% at 30 days). At 1 year, the mortality rate is 8.4%; one-third of these are attributed to cardiovascular causes. Approximately 25% of patients with syncope will experience another event [4].

3.3 Syncope Risk Factors

- Neurologic conditions (seizures, migraine)
- Elderly age and drugs affecting blood pressure
- Diabetes
- Intoxications
- Antihypertensive or antiarrhythmic drugs
- The family history of sudden cardiac death at a young age
- The family or personal history of cardiomyopathy or channelopathy

3.4 Pathophysiology

A fall in systemic BP predisposes cerebral hypoperfusion. Only 6–8 s of cessation in cerebral blood flow is needed to cause a complete loss of consciousness [5]. True syncope usually lasts 1–2 minutes with the loss of postural tone allowing for restoration of blood flow to the brain [6]. Table 3.1 shows cardiac syncope causes.

Table 3.1 Cardiovascular syncope causes [5]

Irregular heart rhythm	Structural
Bradycardia Sinus node dysfunction Atrioventricular conduction system disease Implanted device malfunction	*Cardiac* Cardiac valvular disease Myocardial infarction Hypertrophic cardiomyopathy Pericardial disease Arrhythmogenic right ventricular dysplasia Congenital coronary anomalies Cardiac tumors
Tachycardia Supraventricular, including atrial fibrillation Ventricular (secondary to structural heart disease or due to channelopathies)	*Other* Pulmonary embolism Pulmonary hypertension Acute aortic dissection

3.5 Clinical Presentation

3.5.1 Presyncope

Although this clinical presentation is poorly studied and true incidence is unknown, rates of adverse outcomes are similar in patients with presyncope and syncope. A prospective observational study in 244 patients compared adverse outcomes and hospitalizations in patients who presented with presyncope and syncope. Results showed adverse outcomes in 20% with presyncope compared with 23% of syncope and admission rates of 49% and 69% respectively. Therefore, emphasis should be made on the fact that both groups should receive a similar evaluation. However, this continues to be a challenge given the difficulty to stratify patients at increased risk of adverse outcomes, regardless of presumed etiology [4].

3.5.2 Syncope

The initial syncope evaluation should accomplish both diagnostic and prognostic objectives. The clinician should take a complete and careful clinical history with special interest on previous attacks and eyewitnesses accounts to ascertain whether the collapse was a true syncope or not. This clinical history should be able to determine if the patient can be managed as an outpatient or an immediately workup in-hospital. Presyncope carries the same prognosis as syncope, and for this reason, it should be managed with the same accuracy and similar evaluation [5].

In patients with cardiac syncope, the presence of premonitory symptoms like those seen in vasovagal syncope (lightheadedness, sweating, palpitations, nausea, visual blurring) is not common. Other nontraumatic losses of conscience syndromes include seizures, cataplexy, metabolic disorders, acute intoxications, vertebrobasilar insufficiency, transient ischemic attack, cerebrovascular accident, and psychogenic pseudosyncope. A standardized approach to the evaluation of syncope reduces hospital admissions and medical costs and increases diagnostic accuracy [4].

Syncope is generally expected to occur in patients with pulmonary embolism if they have a sudden obstruction of the most proximal pulmonary arteries that leads to a transient depression in cardiac output. Recently, syncope was the clinical presentation in segmental low-risk pulmonary embolism patients secondary to vasodepressor or cardioinhibitory mechanisms or can also occur when a clot dislodges from venous system and lodges in the pulmonary circulation, inducing arrhythmias when it passes through the heart [7]. D-Dimer normal values excluded pulmonary embolism (Fig. 3.1).

At any age, syncope is a medical emergency until proven otherwise, and clinicians should always exclude structural or nonstructural heart disease. A transient loss of conscience suggests cardiac origin. A systematic clinical analysis, risk stratification, and careful evaluation decide outpatient or in-hospital evaluation.

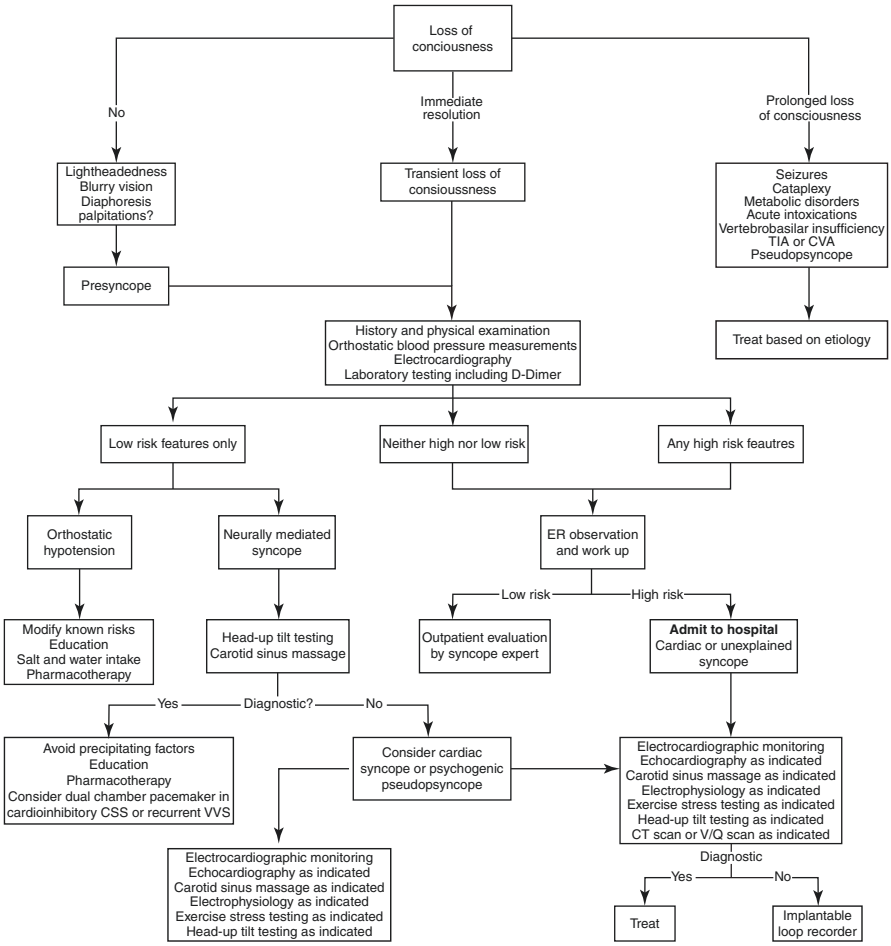

Fig. 3.1 Intial management of suspected cardiovascular syncope

Table 3.2 highlights pathology-specific signs and symptoms that may be related to syncope and that clinicians should be aware of during initial evaluation.

3.5.3 Main Clinical Characteristics

Some clinical features that can suggest a cardiac syncope in the initial evaluation are family history of sudden death at a young age (<40 years), familial or personal cardiomyopathy or channelopathy, syncope during exertion, sudden palpitation followed by syncope, and ECG with arrhythmic findings.

Table 3.2 Symptoms and signs related to syncope [8]

Pathology	Symptom	Sign
Pulmonary embolism	Dyspnea with or without chest pain	Accentuated S_2,S_3, or S_4 gallop, Sat O_2 desaturation
Acute coronary syndromes	Chest pain, anxiety, diaphoresis	Hyper-/hypotension,a systolic murmur, rales
Arrhythmias	Palpitations, syncope with exertion	ECG abnormalities
Aortic stenosis	Syncope with exertion, ischemic chest pain, dyspnea	Hypertension, S_4, crescendo-diminuendo murmur, pulsus parvus et tardus
Aortic dissection	Chest, neck, or jaw pain;cerebrovascular symptoms	Inter-arm blood pressure differential >20 mm Hg, asymmetrical pulses, diastolic murmur
Hypertrophic cardiomyopathy	Dyspnea, angina, palpitations	S_4, systolic murmur, *bisferiens* pulse

3.5.3.1 Physical Examination

Most patients with syncope will have normal physical examination findings, except for any trauma incurred from the syncopal event. Any new focal neurologic findings suggest a primary central nervous system lesion [4].

The physical examination must include:

- A complete neurological examination.
- Orthostatic blood pressure.
- BP measurements with special attention to a difference in BP between both arms.
- Carotid bruits.
- Careful carotid sinus massage in patients >40 years. It is diagnostic of carotid sinus hypersensitivity if we identify a ventricular pause of more than 3 s or if systolic BP decreases by >50 mm Hg.
- Search for murmurs at the time of heart auscultation.
- Evaluation of pulses intentionally looking for the presence of *pulsus parvus et tardus* when on palpation the pulse is late and weak, *pulsus alternans* a regular rhythm alternating strong and weak pulse, bounding pulses or *pulsus paradoxus* a drop in the pressure more than 10 mmHg during inspiration.
- Cardiac and pulmonary examination locking to evidence of heart failure.
- Abdominal, rectal, and skin/nail (anemia signs).

3.5.3.2 Electrocardiogram

This accessible tool generally has a low diagnostic yield (approximately 3%–5%) but is recommended for all patients with presyncope or syncope. Although arrhythmias are unlikely to be detected on a single ECG, it is possible to identify ischemic,

structural, or conduction abnormalities. Any ECG abnormality or change from baseline increases the risk of arrhythmia or death within 1 year of the syncopal event [4].

The main electrocardiogram patterns suggesting arrhythmic syncope are:

- Bifascicular block or other intraventricular conduction abnormalities (QRS > 0.12 s)
- Second-/third-degree atrioventricular block and 1°degree AV block with a prolonged PR interval
- Asymptomatic sinus bradycardia (<40 bpm), sinoatrial block, or sinus pause >3 s in the absence of physical training
- Atrial fibrillation <40 bpm

Non-sustained Ventricular Tachycardia

- VT or rapid paroxysmal supraventricular tachycardia
- Long or short QT intervals
- Pre-excited QRS complexes (Wolff-Parkinson-White syndrome)
- Early repolarization
- Brugada pattern (right bundle branch block pattern with ST-elevation in leads V1–V3)
- Negative T waves in the right precordial leads, epsilon waves, and late ventricular potentials suggestive of arrhythmogenic right ventricular cardiomyopathy
- Q waves suggesting myocardial infarction
- Left ventricular hypertrophy suggesting hypertrophic cardiomyopathy
- Right ventricular strain pattern suggesting high pulmonary artery pressures

3.5.4 Risk Stratification

Physicians should determine the severity of the episode to dictate further evaluation. Patients with high-risk, requiring hospital admission and further investigation, intermediate-risk, hospital admission and evaluation a case-by-case dependent, finally those with a low-risk could have outpatient evaluation (Table 3.2). The patients with intermediate-risk syncope are those with a history of structural heart disease without signs of unstable cardiac disease, no major ECG abnormalities, and no family history of sudden death [8]. Patients with low-risk features do not need further workup in the ER, and they should consider counseling. High-risk patients need an intensive diagnostic approach and should be monitored up to 6 hours in the ER and up to 24 hours as inpatients [5] (Fig. 3.1, Table 3.3).

3.6 Multimodal Diagnosis Approach

Due to syncope being caused by multiple etiologies, the most important goal in the ER is to ensure the stability of the patient. Once it has been classified as a high or intermediate-risk syncope that needs further investigation, proceed to hospitalize the patient and begin to uncover the cause (Fig. 3.1).

Table 3.3 Risk stratification [5]

Low-risk	High-risk
Presence of prodrome symptoms	Sudden onset of chest discomfort, dyspnea, headache, or abdominal pain
Prolonged standing or being in a crowded place	During exertion or while supine or sitting
Triggered by a cough, defecation, or micturition	Palpitations at the time of syncope
Standing from a supine position	Known structural or coronary artery disease
After head rotation or pressure on carotid sinus	Unexplained SPB < 90 mmHg
History of recurrent syncope with the same characteristics	Findings pointing toward gastrointestinal bleed
The absence of structural heart disease	Persistent bradycardia (<40 bpm)
No findings in the physical examination	Undiagnosed systolic murmur
No findings in the ECG	ECG changes explained previously
Minor risk (high-risk if there is association with SHD or abnormal ECG)	
The family history of SHD at a young age while in a sitting position	

SHD structural heart disease

Some tests that can be of use are:

- Transthoracic echocardiogram if structural heart disease is suspected
- Blood tests when clinically indicated
- Holter monitoring
- Electrophysiological study when there is a history of previous myocardial infarction, bifascicular bundle branch block, and asymptomatic sinus bradycardia or when sudden palpitations precede syncope

Echocardiography is essential to evaluate suspected structural abnormalities, but it generally has low diagnostic yield. Two studies (>310 patients) found echocardiography to be clinically useful in patients with syncope if there is a history of cardiac disease, abnormal ECG findings, or suspected significant valvular disease [4].

Continuous cardiac monitoring is the diagnostic standard to establish a correlation between symptoms and ECG findings. Devices include Holter monitors (up to 72 hours), external loop recorders (4–6 weeks), and implantable loop recorders (up to 3 years). The diagnostic yield improves with prolonged monitoring. Up to 50% of patients who present with presyncope or syncope in the absence of heart disease will have an arrhythmia when an implantable loop recorder is placed [4].

3.7 Laboratory Evaluation

Routine laboratory studies have low diagnostic yield and should be ordered only if clinically indicated. Laboratory tests can distinguish syncope from other suspected nontraumatic etiologies. Abnormal troponin and B-type natriuretic peptide measurements have a close relationship with a higher likelihood of adverse outcomes and

should be indicated if cardiovascular disease is clinically suspected [4]. A negative D-dimer excludes pulmonary embolism as the cause of presyncope or syncope [7].

3.7.1 Differential Diagnosis of Cardiac Syncope

The clinician should be warning about conditions that mimic syncope but are not true syncope. The most common causes of pseudosyncope are seizures, intracerebral or subarachnoid hemorrhage, metabolic disorders (hypoglycemia, hypoxia, hyperventilation with hypocapnia), intoxication, cardiac arrest, falls, and coma. Table 3.4 shows other causes of non-cardiac syncope [1].

3.8 Treatment

3.8.1 Neurally Mediated Syncope

Explanation of the diagnosis, provision of reassurance, and explanation of the risk of recurrence are indicated in all patients (Class I, level B). In situational syncope, it is important to avoid potential triggers [5]. Physical counter pressure maneuvers such as leg crossing, squatting, and tensing the lower extremities are effective at the onset of prodromal symptoms and reduce syncope by 39%. Tilt training involves standing for prolonged periods, and compliance is generally poor [4].

Pharmacologic therapy with beta-blockers, alpha agonists, and fludrocortisone has shown no effectiveness or conflicting results in reducing vasovagal syncope. The recommendation of the use of beta-blockers differs between the ACC/AHA and ESC guidelines (Table 3.5), but it might be reasonable to use in patients >42 years of age with recurrent vasovagal syncope [3].

Table 3.4 Differential diagnosis [8]

Neurally mediated syncope	Orthostatic hypotension syncope
Vasovagal Secondary to emotional distress Secondary to orthostatic stress	*Drug-induced* Vasodilator, diuretics, beta-adrenergic blockers, alcohol
Situational Cough, sneeze Gastrointestinal stimulation Micturition Pain Fear	*Autonomic failure* Primary: Pure autonomic failure, multiple system atrophy, Parkinson's disease, Lewy dementia Secondary: diabetes, amyloidosis, spinal cord injuries
Carotid sinus syncope	Volume depletion: low fluid intake

Table 3.5 Current international guidelines recommendations for syncope [3, 5]

	COR	LOE
European Society of Cardiology		
Patients with high-risk features receive an early intensive and prompt evaluation in a syncope unit or an ED observation unit (if available), or in-hospital	I	B
Intermittent determination by sphygmomanometer of BP and HR while supine and during active standing for 3 minutes is indicated at initial syncope evaluation	I	C
Immediate in-hospital monitoring (in bed or by telemetry) is indicated in high-risk patients	I	C
Tilt testing should be considered in patients with suspected reflex syncope, OH, POTS, or PPS	IIa	B
Echocardiography is indicated for diagnosis and risk stratification in patients with suspected structural heart disease	I	B
For OH, explanation of the diagnosis, provision of reassurance, and explanation of the risk of recurrence and the avoidance of triggers and situations, as well as adequate hydration and salt intake, are indicated in all patients	I	C
Beta-blockers are not indicated	III	A
Cardiac pacing is indicated when there is an established relationship between syncope and symptomatic bradycardia, BBB, and a positive EPS or ILR-documented AV block	I	B
Cardiac pacing is indicated with intermittent/paroxysmal intrinsic third or second degree AV block (including AF with slow ventricular conduction), although there is no documentation of a correlation between symptoms and ECG	I	C
An ICD is indicated in patients with syncope due to VT and EF $\leq$ 35% and in patients with unexplained syncope, symptomatic HF (NYHA cClasses II–III), and LVEF $\leq$35% after $\geq$3 months of optimal medical therapy who are expected to survive for $\geq$1 year with good functional status	I	A
An ICD is indicated in patients with syncope and previous myocardial infarction who have VT induced during EPS	I	C
American Heart Association/American College of Cardiology		
A detailed history and physical examination should be performed in patients with syncope	I	B-NR
In the initial evaluation of patients with syncope, a resting 12-lead ECG is useful	I	B-NR
Evaluation of the cause and assessment for the short- and long-term morbidity and mortality risk of syncope are recommended	I	B-NR
Hospital evaluation and treatment are recommended for patients presenting with syncope who have a serious medical condition potentially relevant to the cause of syncope	I	B-NR
Continuous ECG monitoring is useful for hospitalized patients admitted for syncope evaluation with suspected cardiac etiology	I	B-NR
If the diagnosis is unclear after the initial evaluation, tilt-table testing can be useful for patients with suspected VVS	IIa	B-R

(continued)

Table 3.5 (continued)

	COR	LOE
Beta-blockers might be reasonable in patients 42 years of age or older with recurrent VVS	IIb	B-NR
Acute water ingestion is recommended in patients with syncope caused by neurogenic OH for occasional temporary relief	I	B-R
For bradycardia, SVT, VA, ischemic and non-ischemic cardiomyopathy, valvular heart disease, and HCM, GDMT is recommended	I	C-EO
ICD is recommended in patients with ARVC and cardiac sarcoidosis with syncope and sustained VA	I	B-NR

COR class of recommendation, *LOE* level of evidence, *ED* emergency department, *BP* blood pressure, *HR* heart rate, *OH* orthostatic hypotension, *POTS* postural orthostatic tachycardia syndrome, *PPS* psychogenic pseudosyncope, *BBB* bundle branch block, *EPS* electrophysiological study, *ILR* implantable loop recorder, *AV* atrioventricular, *ECG* electrocardiogram, *ICD* implantable cardiac defibrillator, *VT* ventricular tachycardia, *EF* ejection fraction, *NYHA* New York Heart Association, *LVEF* left ventricle ejection fraction, *VVS* vasovagal syncope, *SVT* supraventricular tachycardia, *VA* ventricular arrhythmia, *HCM* hypertrophic cardiomyopathy, *GDMT* guideline-directed medical therapy, *ARVC* arrhythmogenic right ventricular cardiomyopathy

There is enough evidence that dual-chamber cardiac pacing should be considered to reduce recurrence of syncope when the correlation between symptoms and ECG is established in patients ≥40 years of age with the clinical features of those in the Third International Study on Syncope of Uncertain Etiology (ISSUE) studies. In patients with severe asystole from neurally mediated syncope, two observational studies showed that cardiac pacing reduced syncope burden by 92% and 83%, respectively, but did not prevent all syncopal events.

In the ISSUE-3 trial, 77 patients who had documentation, using implantable loop recorder (ILR) of syncope and asystole >3 s or >6 s asystole without syncope, were randomly assigned to receive either dual-chamber pacing with rate drop response or sensing only. During the 2-year follow-up, the estimated rate of syncope recurrence was 57% in pacemaker off and 25% in pacemaker on ($p = 0.039$). In the ILR subgroup of the multicenter Syncope Unit Project 2 study, the estimated rates of syncope recurrence with pacing were 11% at 1 year, 24% at 2 years, and 24% at 3 years, significantly lower than the corresponding rates observed in untreated control patients [5].

3.8.2 Orthostatic Hypotension

Treatment includes education and lifestyle modifications, such as slowly transitioning from a supine or sitting position to standing and increasing fluid and sodium intake. Contributing medications should be discontinued or decreased, if possible. Other treatment modalities include elevating the head of the bed by 10 degrees, compression stockings/abdominal binders, and counterpressure maneuvers. If these do not mitigate symptoms, midodrine and fludrocortisone are effective treatments [4].

3.8.3 Cardiac Syncope

Management of cardiac syncope is directed at the underlying etiology. Options include antiarrhythmic drugs, cardiac pacing, catheter-directed ablation, and, rarely, implantable cardioverter-defibrillator placement [4]. Permanent pacemaker therapy may be effective if asystole is a dominant feature of reflex syncope. Establishing a relationship between symptoms and bradycardia should be the goal of the clinical evaluation of patients with syncope and a normal baseline ECG. The efficacy of pacing depends on the clinical setting [9].

Table 3.5 summarizes the most current recommendations from the AHA/ACC and ESC guidelines for the approach and treatment of syncope.

3.9 Additional Clinical Practice Takeaways

- It is more common that a syncope neutrally mediated or due to orthostatic hypotension occurs with the presence of various factors at the same time as drugs causing low BP (diuretics), electrolyte disturbances (hypokalemia, diuretics), hypotension (all antihypertensive agents) volume depletion due to hemorrhage, low fluid intake (especially in elderly people), and alcohol consumption.
- The longer the period over which episodes have occurred, the less likely that the cause of syncope is life-threatening.
- Diagnostic radiology, routine laboratory tests, and cardiac biomarkers should be routinely used when an underlying cardiac cause is suspected.
- Presyncope or syncope could be the clinical presentation of segmental low-risk or submassive or massive pulmonary embolism.
- Elderly patients who present syncope related to defecation are mandatory to rule out pulmonary embolism.
- Negative D-dimer could exclude pulmonary embolism as a cause of presyncope or syncope.
- Patients with presyncope have similar prognoses to those with syncope and should undergo a similar evaluation.
- A standardized approach to syncope evaluation reduces hospital admissions and medical costs and increases diagnostic accuracy.

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Chapter 4
Optimizing the Use of Biomarkers in the ER

Carlos Jerjes-Sánchez and David Rodríguez

Medicine is a science of uncertainty and an art of probability
–Sir William Osler.

4.1 Introduction

Acute cardiovascular emergencies requiring rapid, complex, and resource-intensive care and conferring a high risk of mortality represent approximately four million annual visits to the emergency room (ER) in the United States [1]. Cardiac biomarkers have emerged as reliable tools for integral diagnosis and the treatment of acutely ill cardiac patients and are one of the most critical advances in medicine, enabling rapid identification of ischemia, micronecrosis or necrosis, ventricular dysfunction, and endogenous fibrinolysis activation, stratifying in-hospital and follow-up risk [2]. On the other hand, although there have been enormous advances in the improvement of their analytical and clinical operating characteristics, we are still far from the ideal biomarker, since all tests produce false-positive and false-negative results. The seriousness of the potential consequences relates to the performed test, the extent of the difference between the reported result and the true result, as well as the ability of clinicians and laboratory personnel to recognize these obstacles [3].

Despite biomarkers being used to increase physician skill and judgment, it use should be supported by common sense and the clinical context of each patient. Also, biomarkers should not be used as stand-alone tests for clinical diagnosis but rather additional tools for clinical decision-making [4]. Bayesian reasoning is a heuristic method that enables clinicians to incorporate their original thinking about the condition of a patient with a test result to determine the posttest probability of a suspected diagnosis (anchoring and adjusting) [4]. It is essential that clinicians know about the analytical and clinical operating characteristics of biomarkers and how to integrate them with Bayesian reasoning to support and optimize daily clinical decision-making. Therefore, with many biomarkers now or soon to be available, an understanding of the basis of biomarkers and their role in cardiovascular care is decisive. Accordingly, in this chapter, we will discuss the basic principles for the

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proper use of cardiac biomarkers focused on their pre-analytical and analytical characteristics, as well as the clinical operating characteristics. Mainly, we will focus on cardiac troponins (cTn), natriuretic peptides (NPs), and D-dimer (DD) and their utility at the ER. Also, we will address the concepts of predictive values and likelihood ratios as the essential elements of Bayesian reasoning and its application in the ER.

4.2 The Scope of the Problem

In overcrowded ERs, the need for rapid turnover times drives the inappropriate practice of initial bundling of laboratory tests to eliminate time-consuming sequential processes (clinical evaluation followed by testing) [4]. Thus, cardiac biomarkers often are drawn before the attending physician even assesses the patient through a meticulous physical examination and detailed history [4]. The indiscriminate use of biomarkers in a broad range of patients yields a large number of false-positive results [5]. Therefore, clinicians must be familiar with the pre-analytical and analytical characteristics of biomarkers, as well as their clinical operating characteristics and should always use them in combination with the available diagnostic armamentarium, especially clinical judgment. However, how should these elements affect our thinking about an individual patient [4].

4.2.1 Pre-analytical Operating Characteristics

How samples are obtained is critical to the measurement of every analyte [6]. The term "pre-analytical phase" describes all actions and aspects of the medical laboratory diagnostic procedure and is recognized as the most vulnerable part of the total testing process [7, 8]. The determinants of the pre-analytical phase are listed in Table 4.1. Pre-analytical problems can arise at any point before sample testing, including (but not limited to) sample collection and quality, handling, transportation, processing, and storage [3], interfering in the results of the test. This issue may not be important for studies of low sensitivity; however, in the ER, where the evaluation of change in the expression of cardiac biomarkers is critical, this problem becomes relevant [6].

Table 4.1 Determinants of pre-analytical characteristics of biomarkers

Parameter	Examples
Collection and quality	Arterial or venous line, hemolysis, clotting, lipemia
Processing	Inadequate filling, incorrect tube, expired additives
Storage	Inadequate or prolonged freezing

4.2.2 Analytical Operating Characteristics

Clinicians need to be familiar with the terms of analytical sensitivity and specificity of an assay. Analytical sensitivity represents the smallest amount of substance in a sample that can accurately be measured by an assay and is expressed in concentration (a.k.a. limit of detection (LoD)). Analytical specificity refers to the ability of an assay to measure on particular organism or substance, rather than others, in a sample [9]. Both depend on the characteristics of the equipment and methodology used. Table 4.2 shows the analytical characteristics of biomarkers.

4.2.3 Clinical Operating Characteristics

Sensitivity and specificity are the clinical operating characteristics of any test. Sensitivity refers to the rate of correctly identifying a subject with a disease (true positive rate (TPR)); likewise, specificity refers to the rate of correctly identifying a subject without disease (true negative rate (TNR)). Sensitivity and specificity vary with the cutoff value chosen for a diagnostic test and are not intrinsic to the test but critically dependent upon the clinical context [10]. The ideal biomarker correctly identifies all subjects with the disease and similarly correctly identifies all subjects who are disease free [11] (Table 4.3). Clinicians in the ER should be familiar with

Table 4.2 Analytical characteristics of biomarkers [9]

Characteristics	Definition
Sensitivity	The ability to detect a low concentration of a given substance in a biological sample. Also, be expressed in terms of an assay's ability to detect a change in concentration. The lower the detectable concentration, the greater the analytical sensitivity. The smaller the detectable change, the greater the analytical sensitivity
Specificity	The ability to exclusively identify a target substance or organism rather than similar but different substances B-type natriuretic peptide (BNP) rather than N-terminal proBNP (NT-proBNP) in a sample or specimen. Analytically nonspecific produces a positive result when the specimen is truly negative for the exact biomarker. In highly sensitivity analytical assays, the slightest variation causes a false-positive test result in an assay that is "very highly specific"

Table 4.3 Operating characteristics of clinical tests

Characteristic	Definition	Question solved	Formula
Sensitivity or TPR	The ability to correctly identify those patients with the disease	How much is the detection ability of the test for those true *positive* subjects?	$\frac{TP}{TP+FP}$
Specificity or TNR	The ability to correctly identify those patients without the disease	How much is the detection ability of the test for those false-*negative* subjects?	$\frac{TN}{TN+FN}$

TPR true positive rate, *TNR* true negative rate, true *positives* (TP), the patient has the disease, and the test is *positive;* false *positives* (FP), the patient does not have the disease, and the test is *positive;* true *negatives* (TN), the patient does not have the disease, and the test is *negative;* false *negatives* (FN), the patient has the disease, but the test is *negative*

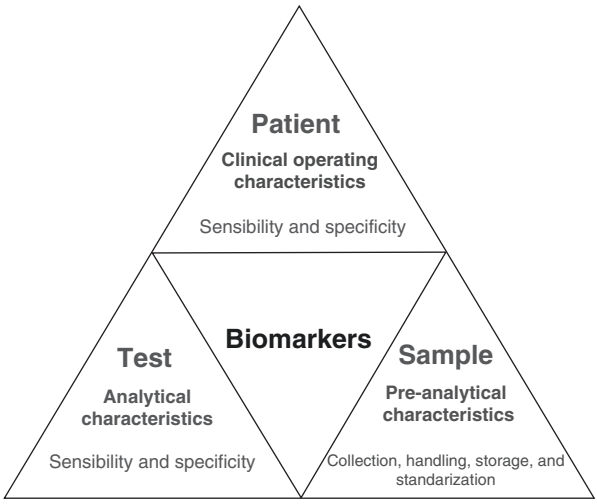

Fig. 4.1 Pre-analytical, analytical, and clinical operating characteristics of biomarkers

characteristics shown in Table 4.3, since they are leading a fast-paced multidisciplinary team in critical scenarios where every second counts (Fig. 4.1).

4.2.4 Principles for the Proper Use of Cardiac Biomarkers at the ER

- Cardiac biomarkers are not markers of disease but pathophysiological processes related to different clinical entities; therefore, they must be used together with adequate clinical judgment and other available diagnostic tools [12].
- To maximize the diagnostic and prognostic performance of biomarkers, they must be interpreted as quantitative variables. For example, a cTn expression which is 50 times the upper limit of normal has a much higher PPV for the presence of myocardial infarction (MI) compared to a level just above the upper limit [6]
- A systematic approach first considers a test with high sensitivity/low specificity and then uses a test with low sensitivity/high specificity. This way nearly all the false positives may be correctly identified as disease negative.

4.3 Cardiac Troponins

Given their superior clinical specificity and sensitivity compared with other biomarkers (such as creatine kinase, lactate dehydrogenase, and myoglobin) that have been routinely used in clinical practice [17], these biomarkers are recommended by the European Society of Cardiology and the American Heart Association/American

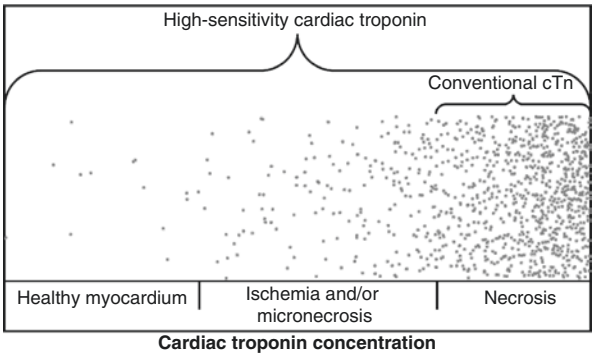

Fig. 4.2 Cardiac troponin concentration and detection range of conventional cTn and HS-cTn

College of Cardiology as the gold standard for the detection of ischemia, micronecrosis, or necrosis, with at least one value above the 99th percentile upper reference limit [13–16]. This recommendation acknowledges the fact that laboratory methods for cardiac troponins (cTn) testing have markedly improved over the past two decades, resulting in lower LoD and improved assay precision [4] (Fig. 4.2). However, these advances should be integrated with good clinical reasoning by physicians both to know when to request them as well as to interpret the results accurately, especially since high-sensitivity tests allow us to identify many reasons for cTn elevations and thus reduce the specificity of any given elevation for unstable ischemic heart disease [6].

4.3.1 Physiology

cTn is a complex of three proteins that regulate the excitation and contraction of the striated muscle troponins C, I, T, and I. cTnI and cTnT have amino acid sequences specific to cardiac tissue, although cTnT has also been found occasionally in diseased skeletal muscle [4, 17]. After damage to myocardial cells (i.e., ischemia), the systemic blood concentrations of these proteins increase, making them useful markers of ischemia, micronecrosis, or necrosis while being independent of the cause of the damage [17] (Fig. 4.3).

4.3.2 Pre-analytical Considerations

Pre-analytical factors that interfere with cTn include hemolysis and heparin, leading to false-positive results [18]. Also, there can be differences between serum and plasma samples, independent of heparin [6]. On the other hand, erroneous calibration, analyzer malfunction, reagent deterioration, instrumental carry-over, and

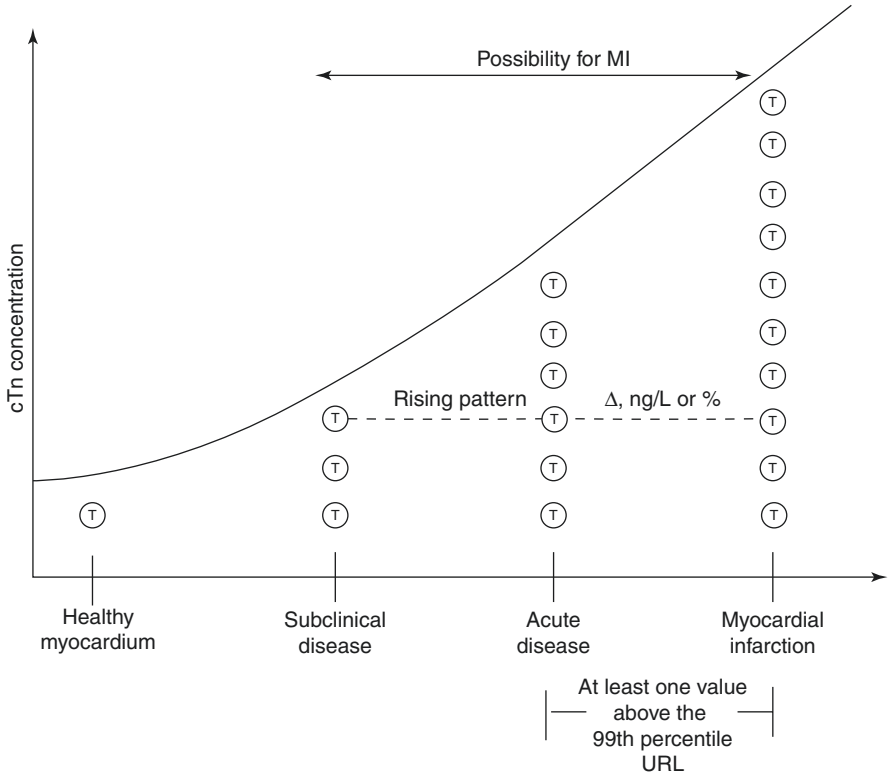

Fig. 4.3 Troponin expression and pathophysiological context. Considering the rising pattern and the likelihood of MI based on cTn expression. (Adapted from Westermann et al. [17])

Table 4.4 Pre-analytical factors that interfere with cTn [6, 18, 19]

Factors	
Storage	*HS-cTnT*: stable for at least 24 h in whole blood at room temperature. Currently no ideal tube type for minimizing inconsistent, but heterophile blocking tubes could be useful increasing the cost of testing
Sample	Hemolysis, serum or plasma sample, heparin or non-heparinized sample
Standardization	Erroneous calibration, analyzer malfunction, reagent deterioration, instrumental carry-over, and inappropriate sample dilution

HS-cTnT high-sensitivity cardiac troponin T

inappropriate sample dilution, all of which concern laboratory of biochemistry, can also directly affect the clinician performance and patient care [18]. Table 4.4 further describes pre-analytical factors that interfere with cTn.

4.3.3 Analytical Characteristics

The term "high-sensitivity tests" refers to the increase in the detection capacity of lower concentrations compared with conventional assays with a coefficient of variability (CV) ≤ 10%, depending on each laboratory assay, increasing their ability to determine small differences in cTn over time [4, 20] (Fig. 4.2). An overview of selected available assays, their specific LoD, and 99th percentile value is given by Westermann et al. [17]. On the other hand, despite point-of-care assays being of great clinical importance, because complete triaging of patients with chest pain in the ER would be feasible within minutes [17], they should not be used for serial cTn measurements because the imprecision of these assays could give the misleading appearance of a rise or fall in the cTn level [4, 20]. Nonetheless, each center should identify the 99th percentile value for the used assay, from either the assay manufacturer's guidelines or laboratory reference literature.

On the other hand, in patients with acute coronary syndromes (ACS), the prevalence of cTnI autoantibodies is ~20%. These affect the assay performance with false-negative and false-positive results, delaying diagnosis and treatment of ACS patients. Although studies to investigate the interference of autoantibodies have been limited in sample size, and clinical implications cannot be determined, clinicians in the ER should consider this possibility when testing results do not match with the clinical presentation [17]. In the case of cTn, the prevalence of false-positive test was estimated at 3% of the general population [18]. Current Food and Drugs Administration recommendation establishes a sex-specific cutoff of 14 ng/L for women, 22 ng/L for men, and 19 ng/L for both sexes for high-sensitivity cTnT [17, 21].

4.3.4 Clinical Relevance

The term MI should be used when there is evidence of micronecrosis or necrosis (one value above the 99th percentile upper reference limit) in a clinical setting consistent with myocardial ischemia [14, 16]. However, high-sensitivity assays can detect troponin in the bloodstream of patients without micronecrosis or necrosis, perhaps due to normal myocardial cell turnover or formation of exosomes that release small amounts of free troponin into the bloodstream [4]. Like patients with renal dysfunction, mild HS-cTn elevation is commonly observed in elderly non-MI patients, COPD, dementia, peripheral vascular artery, as well as in those patients submitted to non-cardiac surgery in whose worsening outcome was observed compared with those without HS-cTn expression [22–25]. Although the mechanisms are not well known, they may suggest chronic cardiomyocyte injury secondary to

subclinical events of coronary artery disease [26]. One way to differentiate HS-cTn expression in stable and unstable patients is analysis the rising pattern values. Some patients with stable angina and HF have chronic troponin elevations as a subclinical expression of a cardiovascular event [6, 17]. A significant troponin change, consistent with an ACS, may be expressed as the absolute (Δ, ng/L) or relative (%) change (Δ,%), where the former shows diagnostic advantage [27]. Figure 4.3 shows the troponin expression in the pathophysiological context of myocardial necrosis or micronecrosis.

Some authors suggest that a 20% change with some assays and a 30% change with others are significant [6]. From a diagnostic perspective, it is recommended to use cTn as a quantitative tool and avoid interpreting results in a binary fashion, using the term "cTn-positive." At higher concentrations of cTn, the possibility of MI is greater; at lower concentrations, the possibility is remote [28]. Despite this marked relationship between concentration and the likelihood of an event, clinicians must consider the possibility of analytical "false positive," especially when there is striking discordance between cTn measurements and clinical presentation. For this scenario, Twerenbold et al. proposed the following algorithm [28].

Physicians should retesting with the same assay, if there is a significative change, and MI must be excluded by imaging or invasive strategy.

- No evidence of MI and serial cTn measurements remains below the 99th percentile upper reference limit: false positive due to no repeatable outlier.

If no change after retesting, cTn should be measured using an alternative assay (if available). In the case of cTn mismatch, assess the possibility of analytical interferences.

- In case of a match, chronic necrosis or micronecrosis must be suspected and should be evaluated using imaging techniques.

4.3.5 Clinical Conditions Associated with Increased Expression of cTn

Regardless of the cause, elevations of cTn values are associated with an adverse clinical outcome in most clinical conditions as in patients with MI, chronic heart failure, pulmonary embolism (PE), or pulmonary arterial hypertension [12]. Abnormal cTn measurements in patients with stable angina suggest subclinical acute events [29]. Table 4.5 shows the differential diagnosis for elevated cTn.

ACS, acute coronary syndrome; PE, pulmonary embolism; PAH, pulmonary hypertension; CS, cardiac surgery; HF, heart failure; PCI, percutaneous coronary intervention; CNS, central nervous system; CVA, cerebrovascular accident; BSA, body surface area; DM, diabetes mellitus

Table 4.5 Clinical conditions associated with elevated cardiac troponins [20, 30]

System	Clinical conditions
Cardiovascular	ACS, PE, severe PAH, cardiac contusion resulting from trauma, ablation, pacing, implantable cardioverter, defibrillator, CS, cardioversion, endomyocardial biopsy, acute and chronic HF, aortic dissection, aortic valve disease, hypertrophic cardiomyopathy, tachy-or bradyrhythmia, Takotsubo syndrome, post-PCI, rhabdomyolysis, myocarditis or endocarditis/pericarditis, Kawasaki disease, interventional closure of atrial septal defects
CNS	Acute CVA, subarachnoid bleeding
Pulmonary	Respiratory failure
Renal	Renal failure
Metabolic/inflammatory	Burns, especially if total BSA ≥ 30%, sepsis, DM, drug toxicity (i.e., adriamycin, 5-fluorouracil, Herceptin, snake venoms). Hypothyroidism, infiltrative diseases including amyloidosis, hemochromatosis, sarcoidosis, and scleroderma, vital exhaustion/strenuous exercise, inflammatory diseases, parvovirus B19, sarcoid, smallpox vaccination, postoperative major no cardiac surgery patients

Table 4.6 0/1 h and 0/3 h ESC algorithm for triaging of patients with suspected ACS [28]

	HS-cTnT	HS-cTnI
	0/1 h	
Rule-out	0 h < 12 ng/L AND 1 h change <3 ng/L	0 h < 5 ng/L AND 1 h change <2 ng/L
Rule-in	0 h ≥ 52 ng/L OR 1 h change ≥5 ng/L	0 h ≥ 52 ng/L OR 1 h change ≥6 ng/L
	0/3 h	
Rule-out	0 h and 3 h < 14 ng/L	0 h and 3 h < 26 ng/L

HS-cTnT high-sensitivity cardiac troponin T, *HS-cTnI* high-sensitivity cardiac troponin I

4.3.6 Diagnostic Algorithms and Prediction Scores

Several HS-cTn-based strategies rely on serial testing. Two of them, 0/1 h algorithm and a 0/3 h algorithm, are recommended by the European Society of Cardiology (ESC) with a Class I recommendation with negative predictive value (NPV) of 99.1% to 100% and 99.6% to 100%, respectively [28]. However, these strategies should be considered triage strategies rather than definitive diagnostic strategies, because additional imaging tests, such as invasive coronary angiography, stress testing, echocardiography, or computed tomography angiography, are mandatory for a definite diagnosis [28]. Table 4.6 shows the ESC rule-in and rule-out criteria for rapid assessment of patients with potential ACS at the ER.

Clinical risk scores provide an alternative approach to identifying patients at low risk of MI who might be suitable for early discharge. The addition of the GRACE, TIMI, HEART, and EDACS scores to the ESC 3 h algorithm showed to be beneficial for risk stratification. However, clinical scores do not improve the performance of pathways which apply a low concentration of cTn to risk stratification, such as High-STEACS score or the ESC 0/1 h algorithm [31].

4.3.7 Foresight, Challenges, and Limitations at the ER

HS-cTn assays improve and accelerate the early management of patients presenting at the ER with suspected ACS. In daily practice, the criteria for ordering cTn in ER are less stringent than in the clinical research setting; therefore, clinicians must consider the clinical background of each patient [4]. Indiscriminate cTn testing can cause clinicians to jump to conclusions and specifically treat patients who would not stand to benefit and may be harmed [19, 26]. Many factors other than MI may cause ischemia, necrosis, or micronecrosis, and therefore mild HS-cTn elevations could be observed in heart and renal failure, drug toxicity, COPD, peripheral artery disease, dementia, non-cardiac surgery patients, etc. In these cases, serial measurements are key to distinguish the dynamic changes of subclinical or acute events. Also, clinicians should be aware of the many factors that could interfere with testing results, so good clinical reasoning and standardized procedures are the cornerstones to maximize the biomarker performance, translating to increased safety for patients and substantially reducing the duration of stay in the ER.

4.4 Natriuretic Peptides, Cardiac Stress, and Heart Failure

Natriuretic peptides (NPs) are of enormous clinical value in diagnosing HF in patients with dyspnea of unknown etiology; in patients with heart disease without clinical manifestations of, but also in those who are at risk for HF; and in apparently healthy patients who are at higher risk for HF. Although atrial NP was the first NP elaborated by stretched cardiac tissue to be identified and studied in patients with HF, due to its instability and other analytic problems, it was soon replaced by BNP and its prohormone fragment, NT-proBNP, both peptides mainly derived from the ventricles [32]. NPs have been successfully evaluated for predicting complications, survival, and re-hospitalization in HF, and particularly mid-regional pro-atrial natriuretic peptide for long-term outcome prediction [33]. However, this section is only focused on NT-proBNP and BNP.

In adult patients, BNP concentration >100 ng/L is considered as abnormal; recent evidence suggests that a reference interval <50 ng/L would increase clinical sensitivity and negative predictive value. For instance, both in nonpregnant and pregnant women, as well as in healthy newborns, the reference interval is <20 and <34 ng/L, respectively [34]. Therefore, there are still unanswered questions, such as if concentrations between 50 and 100 ng/L are reflective of subclinical ventricular failure. On the other hand, the reference interval of NT-proBNP is 300 ng/L, with a negative predictive value of 90–98% (in a meta-analysis) for ruling out HF [35].

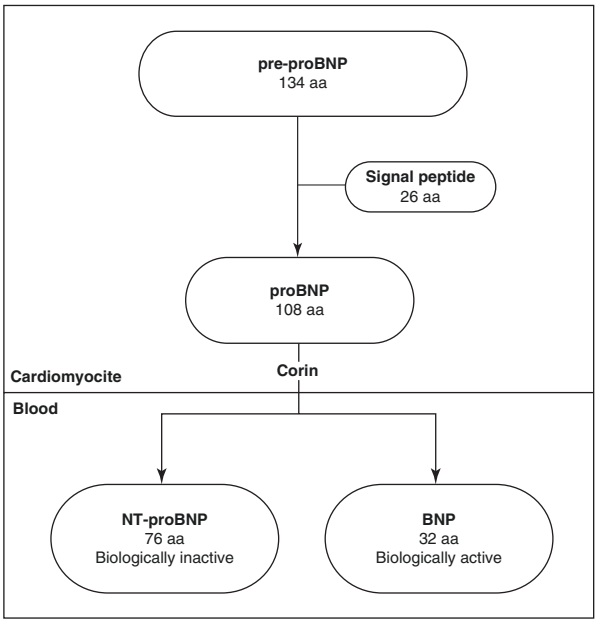

Fig. 4.4 Synthesis of NT-proBNP and BNP

4.4.1 Physiology

The main mechanisms of BNP expresion are increase of myocardial wall stress secondary to volume or pressure overload states [36]. BNP derives from the pre-proBNP, which contains a signal peptide sequence at the N-terminal end. After the signal peptide is cleaved, proBNP is further split proteolytically into an inactive N-terminal fragment (NT-proBNP) and the biologically active peptide hormone, BNP [37]. The half-life of BNP is 20 minutes, whereas NT-proBNP has a half-life of 120 minutes, which explains why NT-proBNP serum values are approximately six times higher than BNP values, even though both molecules are released in equimolar proportions [38] (Fig. 4.4). This process requires de novo synthesis to be released in substantial amounts and has biological activity in stimulation of natriuresis and diuresis, inhibition of renin-angiotensin-aldosterone system and sympathetic nervous system, vascular and pulmonary smooth muscle relaxation, vasodilation. Increase in endothelial permeability, increased lipolysis in adipose tissue, and inhibition of cardiac and vascular remodeling and cytoprotective effects [2].

4.4.2 Pre-analytical Considerations

Clinicians must know how to prepare for blood sampling, how the sample is collected, and some of the analytical fundamentals for proper test interpretation [2]. Proteolytic degradation of the BNP molecule appears to occur as soon as blood is

Table 4.7 Pre-analytical factors that interfere with NT-proBNP and BNP [2]

Factors	
Sample	*NT-pro-BNP*: Stable at room temperature for at least 2 days. The long-term stability is at least 4 months at -20 °C and at least 1 year at -80 °C. *BNP*: Proteolysis degradation of the BNP molecule occurs as soon as blood is collected. Assay dependent. Stable for at least 4 h at room temperature. For the long-term, values diminish, even at -80 °C. Instability of EDTA plasma samples with high BNP concentrations has been reported even at -80 °C. To be safe, a protease inhibitor cocktail including kallikrein- and serine-specific protease inhibitors should be added
Storage	*NT-pro-BNP*: Serum or heparin plasma is choice, either glass or plastic tubes are acceptable. EDTA plasma gives a negative bias of 8–10% compared with serum
Standardization	Currently available assays are not standardized, which means that results are not comparable in each patient. Further, BNP and NT-proBNP values in each sample may differ between assays using the same antibodies due to matrix effects

NT-proBNP N-terminal pro B-type natriuretic peptide, *BNP* B-type natriuretic peptide, *EDTA* ethylenediaminetetraacetic acid

collected. Sample stability appears to be method dependent, evidently because of the different stabilities of epitopes targeted by different assays. Furthermore, BNP is reportedly unstable when collected in glass tubes because of activation of kallikreins of the extrinsic clotting pathways, but this phenomenon may be dependent on the specificities of antibodies used in the measurement method. NT-proBNP appears to be relatively stable during sample storage. For BNP assays, EDTA plasma is the only suitable specimen [37]. Table 4.7 summarizes the factors that could interfere with the test results.

4.4.3 Analytical Characteristics

In the acute setting, NPs blood sampling conditions do not require special considerations. Currently available assays are not standardized, which means that results are not comparable in each patient. Further, BNP and NT-proBNP values in each sample may differ between assays using the same antibodies due to matrix effects [2]. The characteristics of each assay depend on the manufacturer, and detailed recommendations have been issued by both International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) Committee on the Standardization of Markers of Cardiac Damage (C-SMCD) and the National Academy of Biochemistry (NACB) [37, 39]. Regarding sex differences, data suggest that the production and release of NT-proBNP are decreased by testosterone and increased by estrogen [40]. Although there are several clinical conditions associated with peptides increase such as advanced age, renal failure, cerebrovascular accident,

critical illnesses, high-output states, etc., it is important to consider secondary ventricular dysfunction as the main mechanism [41]. Also, the use of novel neprilysin inhibitors, such as sacubitril-valsartan, leads to pharmacologic "raising" of BNP values by interfering with clearance and inhibition of the renin-angiotensin-aldosterone system by blocking the angiotensin II receptor [35]. Notably, these drugs do not affect NT-proBNP levels. On the other hand, some conditions are associated with lower than expected NP expression: HF with preserved ejection fraction (HFpEF) compared with HF with reduced ejection fraction, obesity (with a lower sensitivity) [41], black population, which has been associated with lower concentration, without clinical relevance, likely due to the suppression of natriuretic peptide synthesis or release. Moreover, other conditions associated with lower than expected NP expression include flash pulmonary edema (<1 h), acute pulmonary edema secondary to papillary muscle rupture with mitral regurgitation (onset <2 h), and right ventricular myocarditis secondary to systemic lupus erythematosus. Also, in PE with severe right ventricular dysfunction (<1 h symptoms onset), BNP expression could be reduced, which highlights that the time between the onset of symptoms to testing (<2 h) may also interfere with the results, since it is possible that BNP gene expression has had insufficient time, between the initial trigger of increased ventricular wall stress and the measurement of BNP concentration, since the half-life of BNP is 23 minutes, and therefore, it is expected that approximately 2 h are required to fully reflect changes due to RV dysfunction [42].

4.4.4 Clinical Relevance

The addition of testing for BNP or NT-proBNP to standard clinical assessment has been shown to be valuable in the ER setting for an accurate and efficient diagnosis and prognosis of HF, improving clinical outcomes [36]. Clinicians must consider the clinical context and even the time of the onset of symptoms to testing. NT-proBNP has excellent sensitivity, specificity, and area under the receiver operating curve (ROC) for diagnosis of acute HF, and the age-adjusted cutoff had an OR >10 for the diagnosis of HF, substantially stronger than traditional variables from history, physical examination, or another laboratory testing [43]. Moreover, the diagnostic and exclusionary performance of NT-proBNP remained accurate with consistent effects of sex and race, abnormal renal function, obesity, and atrial fibrillation on the sensitivity or specificity of NT-proBNP [43], but detection and/or exclusion of HF is less accurate in patients with GFR = 30 mL/min/1.73m^2 [2]. On the other hand, NPs performance is maximized as continuous variables in patients with an intermediate pretest probability. Thus, routine use in low- and high-risk groups is controversial. The strength of NPs in HF is their high NPV, although cannot be used to distinguish diastolic from systolic HF [2].

Table 4.8 Differential diagnosis by the system for elevated NT-proBNP and BNP [2, 44–46]

System	Clinical conditions
Cardiovascular	Coronary artery disease, hypertrophic heart muscle diseases, infiltrative cardiomyopathies (i.e., amyloidosis), Takotsubo syndrome, myocarditis, chemotherapy-induced cardiotoxicity, valvular heart disease (aortic or mitral stenosis and regurgitation), arrhythmia (atrial fibrillation and flutter), pulmonary embolism, pulmonary hypertension, congenital heart disease
CNS	Acute cerebrovascular disease
Hematology	Anemia
Nephrology	Renal failure
Pulmonary	Adult respiratory distress, chronic obstructive pulmonary disease, sleep apnea
Metabolic/inflammatory	Sepsis, burns, transfusion-associated circulatory overload, snake venoms, cirrhosis, hyperaldosteronism, hyperthyroidism

4.4.5 Clinical Conditions Associated with Increased Expression of NP

Also, NPs are increased in all edematous disorders with salt and fluid overload and those with increased atrial or ventricular wall tension [2]. The predominant stimulus for release of BNP is end-diastolic wall stress myocardial ischemia evoking BNP secretion and paracrine factors, such as angiotensin II, endothelin, and cytokines [2]. Table 4.8 summarizes the differential diagnosis associated with elevated NT-proBNP and BNP.

4.4.6 Diagnostic Algorithms and Prediction Scores

NPs aid in the diagnosis of acute HF and are embedded as Class of Recommendation I, Level of Evidence A in clinical practice guidelines [43]. There are no differences in the diagnostic use of BNP and NT-proBNP except when using nesiritide and neprilysin inhibitors [2, 35]. As discussed with cTn, the higher the NP level, the higher the likelihood of HF. However, applying an only decision limit for all situations is imprudent, and absolute levels are not interchangeable between assays. In the ER, identifying HF in patients with only dyspnea as clinical presentation is challenging; therefore, clinical research in the emergency setting has validated the high diagnostic accuracy of NPs. Also, NT-proBNP and BNP are comparable, with sensitivities of ~ 90% and specificities ~70%, enhancing the diagnostic accuracy of clinical judgment from 74% to 81% [2]. Figure 4.5 illustrates the decision limits of NT-proBNP and BNP for patients with acute dyspnea without renal failure [43].

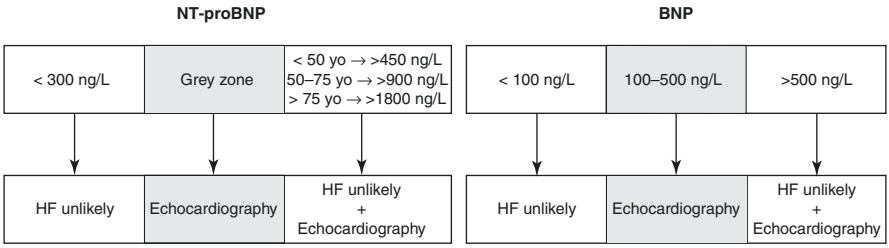

Fig. 4.5 Decision limits for NT-proBNP and BNP in patients with acute dyspnea

4.4.7 Foresight, Challenges, and Limitations at the ER

NPs are secreted from the cardiomyocyte in response to hemodynamic stress mediated by volume and/or pressure overload and thus related to the extent of atrial, ventricular, and valvular dysfunction but are neither HF nor heart disease-specific [2]. The release of these molecules activates various compensatory mechanisms, representing a useful tool for early identification and risk stratification. Also, NPs are valuable tools for estimating the prognosis of patients. The kidneys clear both NPs to a similar extent; both are increased with renal failure, but NT-proBNP values are higher than BNP values due to the longer biological half-life [2]. Both are predictors of morbidity and mortality in acute HF; therefore, it is a useful and decisive tool in the context of the patient in the ER. In addition to these considerations, the time of onset of symptoms upon arrival at the ER should also be considered when there is a mismatch between clinical presentation and NPs measurements.

4.5 D-Dimer and Endogenous Fibrinolysis Activation

D-Dimer (DD) is a product generated during fibrinolysis. It is a marker of thrombin activity and fibrin turnover and thus reflects both hemostasis and fibrinolysis and is currently considered the biochemical gold standard for the laboratory exclusion of low clinical suspicion of VTE, which comprises deep vein thrombosis (DVT) and PE [47]. These molecules are the smallest cross-linked degradation products of cross-linked fibrin and are also found in increased concentrations in the plasma of patients with arterial thrombosis (including MI and stroke), recurrent thrombotic risk following anticoagulation, and disseminated intravascular coagulation [48]. Also, it has been associated with healthy pregnancy, or during the postoperative state, and in patients with the significant liver disease, malignancy, and sepsis [49], highlighting the relationship with thrombosis and inflammation, also known as immunothrombosis [50]. In the ER, its role to rule out a thrombotic event is critical. Clinicians must know their applications and their limitations, as well as the factors that could interfere with the proper interpretation of the results, leading to adverse clinical outcomes.

4.5.1 Physiology

The formation of fibrin clots by the coagulation system in response to vascular injury and intravascular tissue factor expression is balanced by the breakdown of the clot by the fibrinolytic system. DD is one of several fragments that is released when plasmin, an enzyme activated through the fibrinolytic pathway, cleaves fibrin to break down clots. It consists of two covalently bound fibrin D domains that were cross-linked by factor XIII when the clot was formed. This fragment forms unique epitopes that can be targeted by monoclonal antibodies in DD assays to confirm that the coagulation cascade is generating thrombin [51]. After index thrombus formation, time to detection of DD in blood is approximately 2 h, with a half-life of 4–6 h, and could remain increased for at least 1 week after the resolution of a VTE event, returning to normal values even after 3 months of the acute event [47, 52]. Figure 4.6. shows the synthesis of DD.

4.5.2 Pre-analytical Considerations

DD samples must be collected before other test samples are drawn, or any procedure is performed, even minimally invasive ones, such as canalization. Also, it should be processed as quickly as possible (ideally within 1 h after collection) and testing performed within 4 h of procurement (or else be processed by centrifugation and plasma frozen) [8]. Table 4.9 shows the pre-analytical factors that interfere with DD testing.

4.5.3 Analytical Characteristics

DD is one of the products of endogenous fibrinolysis. Depending upon the degree of lysis of cross-linked fibrin, a heterogeneous mixture of fibrin-degradation products containing the DD moiety will be formed [52]. Since a wide variety of assays for DD are available, there is no standard against which all assays can be calibrated; thus, significant differences can be observed in the clinically significant threshold and reference interval values across systems, leading to inconsistencies across assays. Also, different assay kits may report DD in either FEU or DDU, using various units of measure (i.e., ng/mL, μg/mL, μg/L). These inconsistencies have led to confusion in some institutions, especially for cases in which the threshold for the exclusion of VTE must be defined [8, 52].

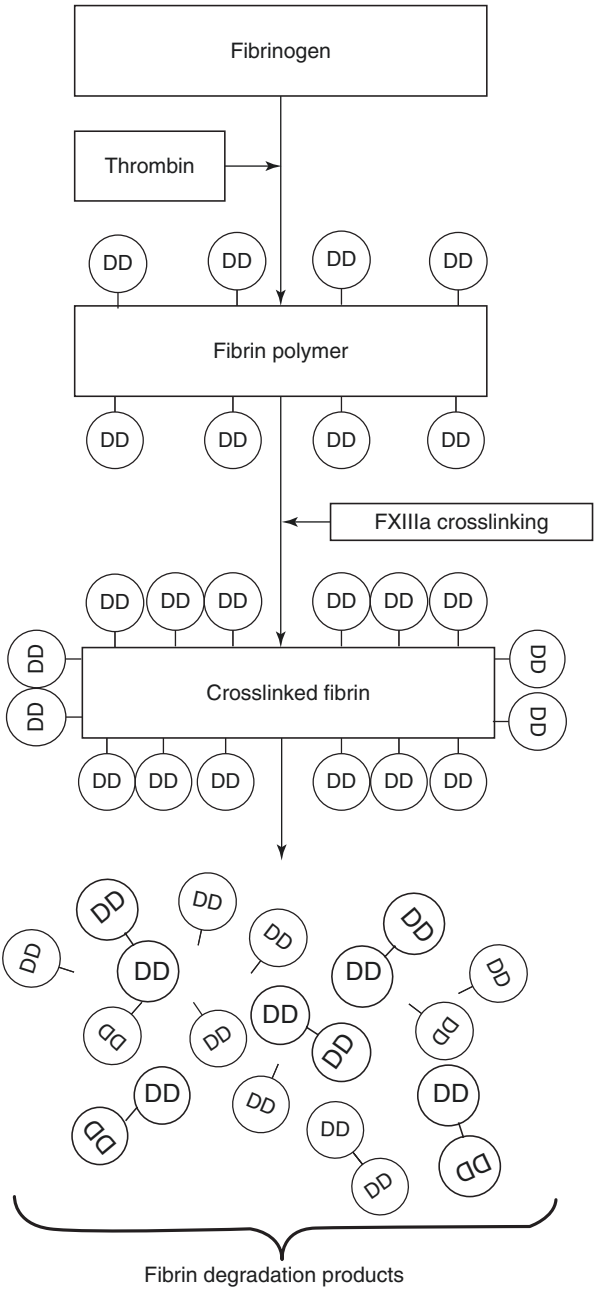

Fig. 4.6 Synthesis of DD

Table 4.9 Pre-analytical factors that interfere with D-dimer [3]

Factors	
Sample	The collection should be drawn before any procedure or test and should be processed as quickly as possible (ideally within 1 h of collection). Testing performed within 4 h procurement (or else be processed by centrifugation and plasma frozen). DD can be measured in whole blood, heparinized, or citrated plasma (specimen of choice). EDTA plasma influence results. Samples derived from central venous lines, leading to partially clotted, hemolyzed, or activated samples or samples diluted by saline or contaminated with heparin
Storage	Underfilling may cause significant sample dilution and will also lead to underestimation of quantitative test results. Samples should be mixed thoroughly (but gently) by 3 to 6 end-over-end tube inversions to ensure adequate mixing of the test sample with anticoagulant and to prevent sample clotting
Standardization	While a wide variety of antibody-based assays for DD are available, there is no standard against which all assays can be calibrated; thus, significant differences can be observed in the clinically important threshold and reference interval values across systems. This variability contributes to inconsistency across assays performed with different methods in different laboratories, as do the variety of specificities of the antibodies used

EDTA ethylenediaminetetraacetic acid, *FEU* fibrinogen equivalent units, *DDU* DD units

4.5.4 Clinical Relevance

DD is a marker of thrombosis with subsequent activation of endogenous fibrinolysis, and its primary clinical use of the DD assay has been as a screening test for the presence of VTE [47, 52]. However, DD levels may be increased in any condition involving activation of endogenous fibrinolysis, such as VTE, pulmonary embolism, infections, cancer, surgery, cardiac or renal failure, acute coronary syndromes, acute non-lacunar stroke, pregnancy, and sickle cell crises [53]. On the other hand, the use of a DD assay in combination with an evidence-based clinical algorithm in outpatients who have not undergone anticoagulation procedures but are suspected of having DVT or PE can effectively exclude the presence of disease without using imaging techniques [54]. Although the sensitivities and NPVs for DD regarding DVT and PE differ slightly, logic has it that they should be similar, because the diseases often overlap in the form of a thrombus or thromboses [52]. Regarding AAS, DD might be of diagnostic as well as prognostic value. Furthermore, DD levels correlate with the anatomic extension of the dissection [49]. DD has been shown to be a prognostic marker in ST-elevation myocardial infarction undergoing PCI, as well as in AF, especially in patients with multiple risk factors for embolism and exclusion of intra-atrial thrombus and previous catheter ablation. Moreover, it has a high NPV in thrombosis of the cerebral venous sinus [53, 55–57]. Clinical sensitivity and specificity of DD measurements are markedly reduced in-hospital patients, since most patients have multiple comorbidities, in consequence they are also high-risk patients, which represents a challenge for the diagnosis of a thrombotic event [54–57]. Age is a factor that should be considered when interpreting the

results of the test, since the incidence of hypercoagulable states and chronic inflammation such as cancer may increase with age [47]. In fact, in patients older than 80 years, the clinical specificity could decrease up to 15%, increasing the number of patients with false positives results [49]. Therefore, DD threshold for patients above 50 years of age could be safely increased by multiplying their age in years by 10 (i.e., DD threshold for a 60 years patient would be 600 μg/L instead of the manufacturer's threshold of 500 μg/L), with a slight increase in the sensitivity of the test [47, 49, 58]. In pregnant patients, DD test result is more likely to be positive since concentration increases progressively throughout pregnancy, especially in the third trimester until the first 45 days of puerperium. This result is challenging due to PE; it is the leading cause of pregnancy-related maternal death in developed countries [59, 60]. Therefore, the clinician must consider that, as in previously discussed biomarkers, the higher the DD level, the higher is the likelihood for the presence of thrombosis-related event as well as the lower the DD blood concentration, the lower the likelihood for a thrombosis-related event.

4.5.5 Clinical Conditions Associated with Increased Expression of DD

4.5.5.1 Hypercoagulability States

Due to the relationship between thrombosis and inflammatory processes, hypercoagulability states associated with abnormal DD measurements include MI, peripheral artery diseases, acute hemorrhage, acute aortic syndrome, atrial fibrillation, acute cerebral events, and Alzheimer's disease, severe inflammatory response syndrome, as well as infection or malignancy. Table 4.10 shows a summary of DD differential diagnosis.

Table 4.10 Hypercoagulability states for elevated D-dimer [47, 61, 62]

System	Clinical conditions
Cardiovascular	Myocardial infarction, peripheral artery disease, acute hemorrhage, acute aortic syndromes, arterial or venous thromboembolism, intravascular thrombosis (catheters, pacemakers, artificial valves) fibrinolytic therapy, abnormal fibrinolysis, atrial fibrillation
CNS	Alzheimer's disease, acute cerebral vascular events, cerebral venous thrombosis
Hematology	Disseminated intravascular coagulopathy, sickle cell disease, hemolysis, superficial thrombophlebitis
Nephrology	Acute or chronic renal failure, nephrotic syndrome
Gynecology	Pregnancy, HELP syndrome, preeclampsia, and eclampsia
Pulmonary	Acute respiratory distress syndrome
Systemic/ inflammatory	Severe inflammatory response syndrome, infection, malignancy, old age, neonatal period, disability, hospitalization, surgery, trauma, burns

4.5.6 Diagnostic Algorithms and Prediction Scores

Measurement of DD is not recommended as a stand-alone test for ruling out or diagnosing VTE at ER admission, since without appropriate clinical preselection, the DD results may be a false negative. As outlined above, elevated DD levels are nonspecific; consequently, a positive DD result in a patient suspected to have VTE should be followed by an imaging test to confirm the diagnosis [51].

A negative DD result can exclude the diagnosis of VTE without further testing but only if the sensitivity of the test is high (>98%). Albeit, high sensitivity comes at the cost of specificity [51]. Therefore, to improve the utility of DD testing in patients with suspected VTE, it is essential to assess the patient's clinical probability for VTE and usually combined with imaging tests as part of a diagnostic algorithm [51, 61].

Several clinical decision rules for the diagnosis of DVT and PE have been developed, but the most validated include the Wells score and the Geneva score [51]. The Wells score has two levels, unlikely or likely, and the presence of each clinical feature is given a positive score of +1. A score of −2 is given if an alternative diagnosis is highly likely, which mainly depends on individual physician judgment [47, 61]. Patients who are considered as "low" or "unlikely" to have VTE have a DD level drawn. If the DD result is negative, VTE is considered excluded, and no further testing should be performed [51] Fig. 4.7 shows a diagnostic algorithm for VTE using DD and diagnostic imaging.

4.5.7 Foresight, Challenges, and Limitations at the ER

The use of DD in the ER allows the rapid exclusion in low-high clinical suspicion VTE patients (high negative predictive value). Also, DD has a high negative predictive value to excluded sinus venous thrombosis in young female patients [57]. At present there is not a positive predictive value in pulmonary embolism; however, very high measurements of DD are a constant in massive or submassive PE patients. The accuracy of the DD assay is further compromised by individual patient heterogeneity in DD determined by patient age, genetic influences, disease factors, hereditary and acquired coagulation deficiencies, the size of the blood clot, and the timing of specimen collection regarding the thrombotic event [54]. The goal is to rule out any possibility of a thrombotic event that may have adverse outcomes.

4.6 Bayesian Reasoning and Clinical Decision-Making

In medical decision-making, the clinical estimate of probability strongly affects the physician's belief as to whether or not a patient has a disease, and this belief, in turn, determines actions: to rule out, to treat, or to do more tests [63]. Bayesian reasoning

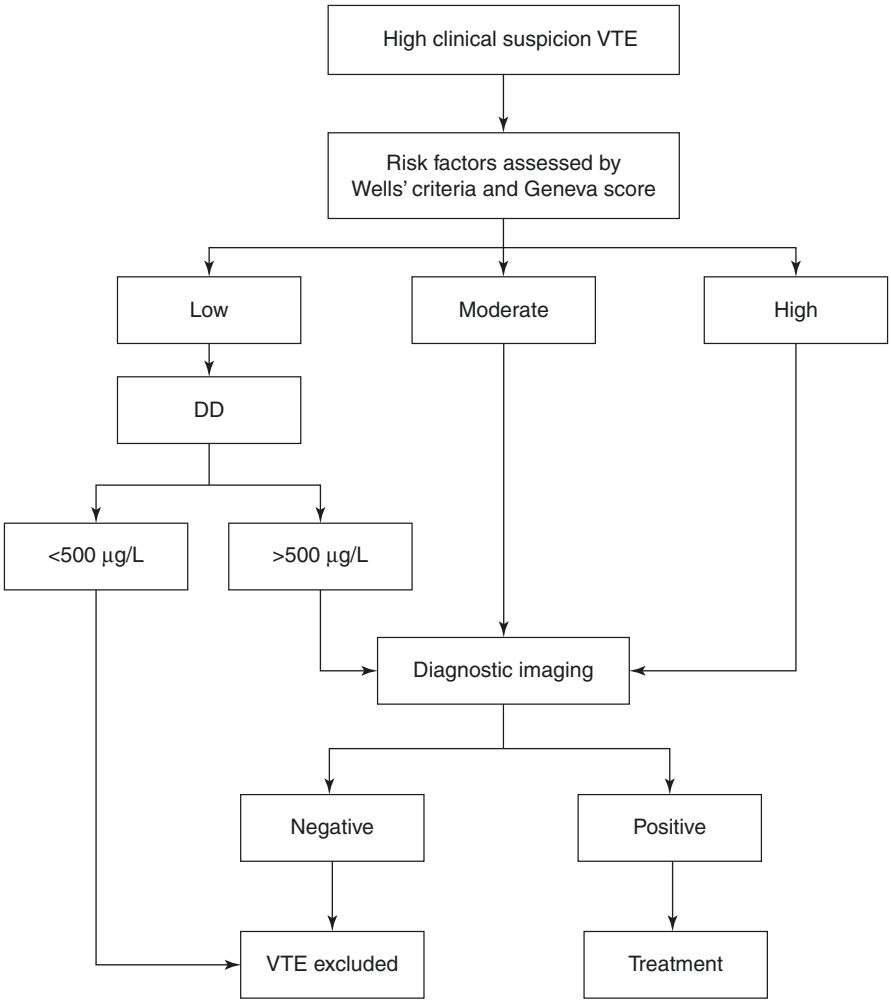

Fig. 4.7 Diagnostic algorithm for VTE using DD and diagnostic imaging

is a method that enables us to incorporate our original thinking about a patient with a test result to determine the posttest probability of diagnosis [5]. First, it requires an estimate of the baseline probability of disease before any test is ordered. This baseline probability goes by the synonyms "prior probability" and "pretest probability" [63]. Accordingly, clinicians must modify the baseline probability based upon the magnitude of "skew" introduced by the test's diagnostic sensitivity (proportion of diseased patients with a positive test – TPR) and specificity (proportion of non-diseased patients with a negative test – TNR). The numeric tool that summarizes this skew is the likelihood ratio (LR) [63]. LRs may be a more intelligible way of conveying the properties of a diagnostic test to clinicians and may merit

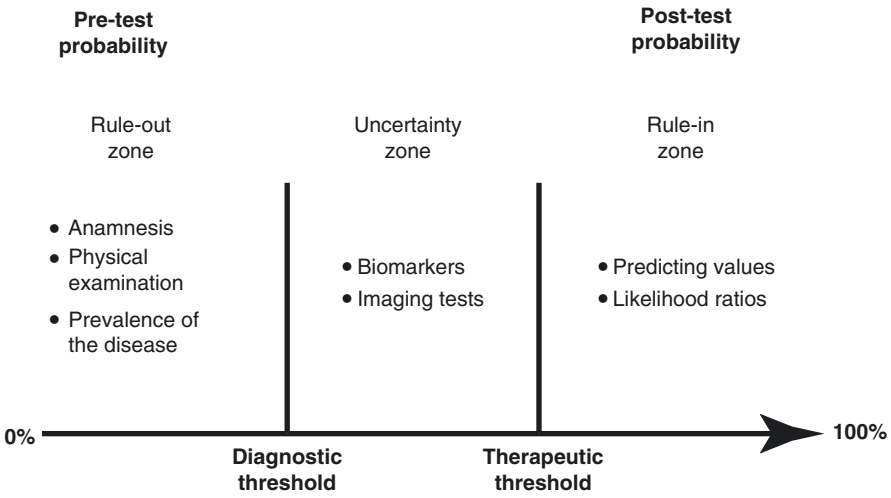

Fig. 4.8 Diagnostic and therapeutic thresholds of clinical decision-making

further adoption into operational practice. An LR is defined as the percentage of diseased patients with a given test result divided by the percentage of well people with the same test result [4]. In Bayesian reasoning, one keeps adjusting the initial probability by gathering new information to the point that one is satisfied with the probability value that can be used to make a final decision (diagnostic threshold) [63]. Figure 4.8 shows the diagnostic and therapeutic thresholds of clinical decision-making.

4.6.1 Rules of Decision-Making Based on Probabilities

- The test should be ordered if they will affect the decision on management only.
- Threshold values should be established before any tests are ordered.
- Thresholds should be individualized for each disease.

4.6.2 Pretest Probability

Pretest probability is the starting point for all clinical decisions [64]. Proficient anamnesis and physical examination allow clinicians to generate a provisional diagnosis that might explain the condition of a subject [4]. Predictive values assess the probability that a subject truly has or not a disease before performing a test. However, the result is dependent on disease prevalence; therefore, the positive predictive value (PPV) will be as high as the prevalence of the disease with a low NPV [10]. If the probability of a disease is so unlikely (below the test threshold), it can be eliminated

Table 4.11 Predictive values of clinical tests

Characteristics	Definition	Probability	Question solved	Formula
Positive predictive value (PPV)	Probability that subjects with a positive test truly have the disease	Pretest	How likely is it that this subject has the disease given that the test result is positive?	$\frac{TP}{TP+FP}$
Negative predictive value (NPV)	Probability that subjects with a negative test truly do not have the disease		How likely is it that this subject does not have the disease given that the test result is negative?	$\frac{TN}{TN+FN}$

True *positives*, the patient has the disease, and the test is *positive;* false *positives*, the patient does not have the disease, and the test is *positive;* true *negatives*, the patient does not have the disease, and the test is *negative;* false *negatives,* the patient has the disease, but the test is *negative*; TPR, true positive rate; TNR, true negative rate

from the potential differential diagnosis. Conversely, if the probability is sufficiently high for treatment to be initiated (above the treatment threshold), then testing is not required. When the probability lies between the two thresholds, further diagnostic testing is indicated. Table 4.11 summarizes PPV and NPV characteristics.

4.6.3 Posttest Probability

We can also express the capability of a test using LRs which are derived from sensitivity and specificity and give us an idea of the strength of a positive or negative test result. LRs may be a more intelligible way of conveying the properties of a diagnostic test to clinicians and may merit further adoption into operational practice. An LR is defined as the percentage of diseased patients with a given test result divided by the percentage of well people with the same test result. Incorporating the test results to our initial diagnosis to adjust the probability that the subject has the disease is known as posttest probability. LRs are advantageous in this regard because they are a measurement of the strength of the test result. They can help us know how much we should adjust our initial probability estimate as we attempt to determine the final probability estimate [3]. For this purpose, the Fagan nomogram is a graphical tool for estimating how much the result of a diagnostic test changes the probability that a patient has a disease [65] (Fig. 4.9). Table 4.12 summarizes the characteristics of LRs.

4.6.4 Clinical Practice Takeaway

- Biomarkers are used to augment physician skill and judgment but are dependent on the clinical context.
- The good clinical reasoning is essential to correctly order and interpret the results.

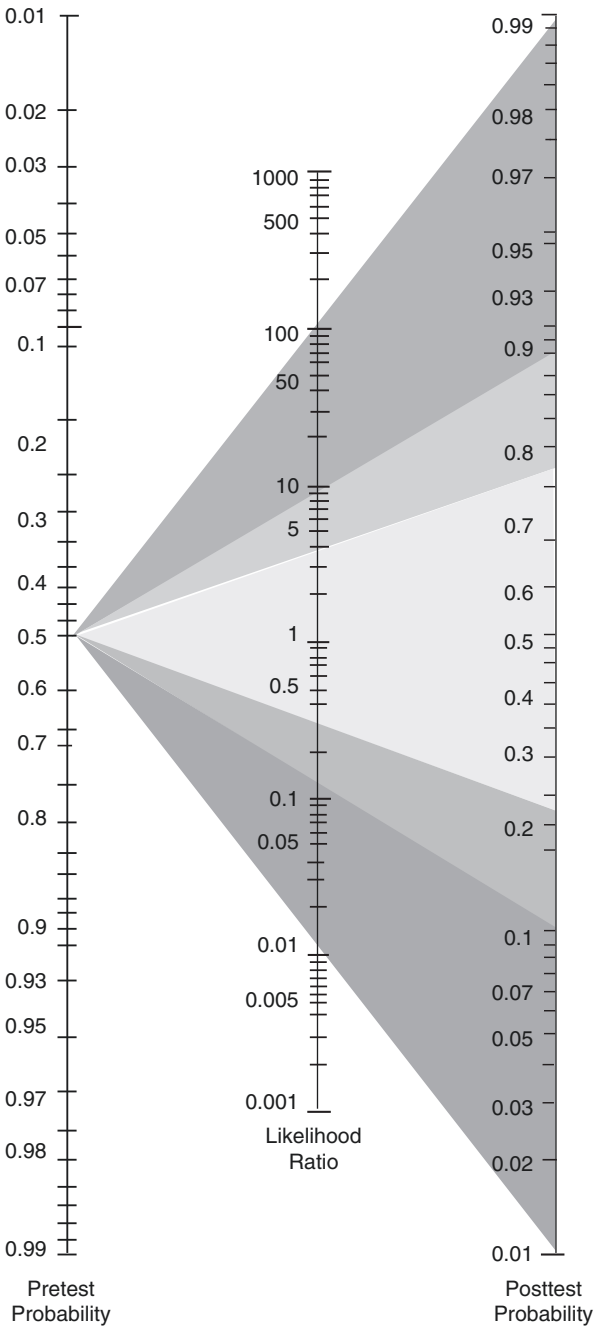

Fig. 4.9 Fagan nomogram

Table 4.12 Likelihood ratios of clinical tests

Characteristics	Definition	Question solved	Formula
Likelihood ratio (+)	Probability of diseased patients with a given test result divided by the percentage of well people with the same test result	How change the posttest possibility after a positive test?	$\frac{\text{sensitivity}}{1-\text{specificity}}$ *or* $\frac{TPR}{1-\text{specificity}}$
Likelihood ratio (−)		How change the posttest possibility after a negative test?	$\frac{1-\text{sensitivity}}{\text{specificity}}$ *or* $\frac{1-\text{sensitivity}}{\text{TNR}}$

True positives, the patient has the disease, and the test is positive; false positives, the patient does not have the disease, and the test is positive; true negatives, the patient does not have the disease, and the test is negative; false negatives, the patient has the disease, but the test is negative; TPR, true positive rate; TNR, true negative rate

- Biomarkers should not be used as stand-alone tests for the diagnosis of cardiovascular disease and should be interpreted as quantitative variables.
- Pre-analytical and analytical characteristics must be in consideration at the interpretation of the results.
- Clinical operating characteristics and predictive values are dependent on cutoff values and prevalence of the disease, respectively.
- Likelihood ratios are a more intelligible way of conveying the properties of a diagnostic test to clinicians.
- HS-cTn is markers of ischemia, micronecrosis, or necrosis, while being independent of the cause of the damage, therefore, will identify new causes for cTn elevations and thus reduce the specificity of any given elevation for ischemic heart disease.
- NPs are neither HF nor heart disease because they have standardized values of cutoff values that allow discarding the possibility of HF. For the predictive value that these molecules add to the integration of decision-making, their use is critical in the ER.
- DD are markers of thrombosis-related event; however, it is not a standardized tool, and each test has its cutoff value. Due to the low specificity, it is necessary to define the pretest probability to increase the performance of this test, as well as to use together with the image tools that allow ruling out the possibility of an event with unfavorable results. Its use in the emergency area is fundamental.

4.7 Suggested Tools

- *MdCalc+*
  MDCalc is the #1 medical reference for clinical decision tools and content used by over one million medical professionals globally, including more than 50% of US physicians, every month. https://www.mdcalc.com
- *DocNomo®*
  DocNomo is a convenient graphical tool to enhance the bedside interpretation of a diagnostic test result. From the diagnostic sensitivity and specificity of the test and the probability of the patient having the target disorder before running the test. DocNomo calculates the posttest probability.
  https://itunes.apple.com/us/app/docnomo/id901279945?mt=8
- *The NNT group®*
  A multidisciplinary team of clinicians that have developed a framework and rating system to evaluate therapies based on their patient-important benefits and harms as well as a system to evaluate diagnostics by patient sign, symptom, lab test, or study. http://www.thennt.com/

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Chapter 5
Acute Coronary Syndromes in the ER

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5.1 The Scope of the Problem

In many undeveloped countries, the incidence of acute coronary syndromes (ACS) is still increasing, while more developed countries report diminished incidence rates [1, 2]. Currently, cardiovascular disease remains the most important cause of mortality among developing and developed countries [3]. Patients who survive an ACS will have a greater long-term risk of recurrent ACS and other cardiovascular conditions such as chronic heart failure, arrhythmia, stroke, peripheral arterial disease, and other cardiovascular complications linked to different arterial territories [4].

The diagnosis of ACS can be a great challenge. Less than 10% to 20% of patients who present to the emergency room (ER) with chest pain and high clinical suspicion will have an ACS [5, 6]. Some other specific patient populations might even not experience chest pain or typical symptoms at all. This peculiar diagnostic difficulty is usually in women, the elderly, and patients with diabetes. Currently, chest pain remains as the most prevalent symptom; however, the clinical expression in special populations (women and elderly) can manifest a wide variety of atypical symptoms such as nausea, dyspnea, weakness, dizziness, syncope/presyncope, abdominal pain, palpitations, cognitive impairment, confusion, or even delirium [7–10]. Selecting the optimal diagnostic and management strategies is crucial for patient survival and long-term prognosis [11]. Physicians in the ER should know all these variations to improve quality care in special populations with a high clinical suspicion of an ACS.

5.2 Classification and Definitions

ACS can be clinically indistinguishable from one another, and the term involved ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), and unstable angina (UA) base on electrocardiographic findings

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and troponin release. STEMI occurs after 100% of coronary artery occlusion and UA/NSTEMI after partial coronary obstruction (Fig. 5.1) [1].

Electrocardiogram (ECG) remains as the main element in the setting of high clinical suspicion in the ER. Per current guidelines and recommendations, every patient in the ER with suspected ACS must have an ECG done and interpreted in less than 10 minutes. With ECG patients can be triaged into the STEMI or NSTEMI/UA categories [12]. Symptomatic patients with nondiagnostic ECGs should be submitted for biomarker analysis, particularly high-sensitivity cardiac troponins (HS-cTn). Detectable troponin levels above the 99th percentile of the upper limit of normal (ULN) have a close relationship with myocardial necrosis and establish the diagnosis of NSTEMI [12]. In a more clinical approach, myocardial necrosis can occur as early as 20 minutes after the onset of pain. Therefore, the setting of high clinical suspicion and ischemic chest pain >20 minutes is highly suspicious of MI (STEMI/NSTEMI) and should be considered in the decision-making [4, 13].

Unstable angina is the clinical expression of myocardial tissue suffering ischemia. Patients deemed to have chest pain, suspicious symptoms, and cardiovascular risk factors, with no ST elevation on their ECGs and with lack of troponin elevation, will be classified into this category. It is important to considered that there are no particular electrocardiographic changes associated with UA; also, some patients can even have normal ECGs upon ER arrival [4].

NSTEMI will be diagnosed in the absence of persistent ST elevation and detectable HS-cTn levels above the 99th percentile ULN (per local central lab)

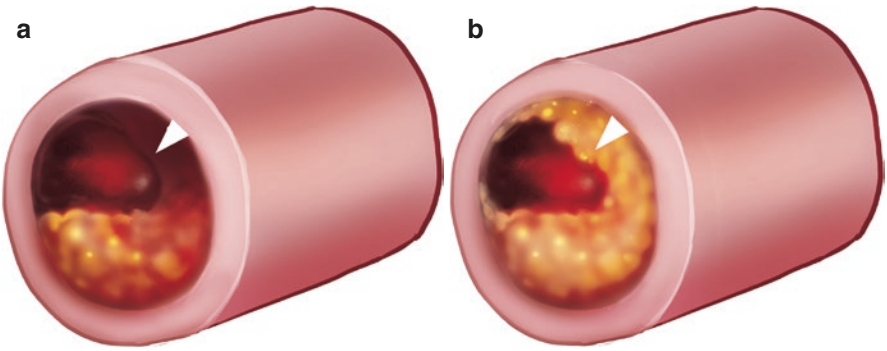

Fig. 5.1 Coronary artery cross-sectional view during ACS. Panel **a** displays a fractured atherosclerotic plaque with exposure of lipid-rich core and thrombus formation conditioning partial occlusion; this phenomenon is most likely seen in NSTEMI/UA. Panel **b** displays complete occlusion, as normally seen in STEMI

or with initial HS-cTn below the ULN but with a delta of at least 20% to 30% by the time of the second blood draw [14]. Troponin elevation can be interpreted as tissue necrosis and established myocardial damage. Just like for UA, up to one-third of patients may present with a normal ECG upon arrival, and the remaining ones may have characteristic ECG abnormalities such as ST depression, T wave changes or inversion, and transient or nondiagnostic high T wave elevation [4].

Finally, the diagnosis of STEMI is established when ST elevation measured at the J point is compatible with a total acute coronary artery occlusion. If there are high clinical suspicion and persistent ischemic symptoms, patients presenting with left or right bundle branch blocks should be treated as STEMI patients. Prompt diagnosis is key to salvage ischemic (at risk) myocardium. STEMI patients in the ER do not need to wait for biomarker (troponin) results to establish the diagnosis of myocardial necrosis. It is crucial that these patients are submitted to any urgent reperfusion therapy [15].

According to the fourth universal definition of myocardial infarction, the term myocardial injury should be used when there is evidence of HS-cTn with at least one value above the 99th percentile ULN. The myocardial injury is considered acute if there is a quick rise and/or fall of cTn values [13]. However, this definition remains unclear, and its clinical utility is questionable.

The term acute myocardial infarction should be used when there is an acute myocardial injury with clinical evidence of acute myocardial ischemia and with detection of a rise and/or fall of HS-cTn values with at least one value above the 99th percentile URL and at least one of the following [13, 15–17]:

- Ischemic symptomatology
- New ST-T wave changes or New LBBB
- New Q waves
- New imaging evidence of loss of viable myocardium
- Motion abnormality consistent with an ischemic etiology
- Coronary thrombus on angiography or autopsy

The classification of MI can be extended to six different subtypes, regardless of the electrocardiographic changes present at the time of diagnosis [1].

- Type 1: MI due to atherothrombosis
- Type 2: MI due to a supply-demand mismatch
- Type 3: MI presenting as sudden death, without ECG nor biomarker confirmation
- Type 4a: MI related to percutaneous coronary intervention (PCI)
- Type 4b: MI related to stent thrombosis
- Type 5: MI related to coronary artery bypass grafting (CABG)

5.3 Prevalence

ACS is an important cause of morbidity and mortality. The prevalence of ACS differs among developed and third world nations [1]. The incidence of ACS in North America and Europe has been declining during the past decades. In the United States, there are reports of a decline in the adjusted incidence for STEMI from 133 per 100,000 in 1999 to 50 per 100,000 patients per year during 2008 [15]. During 2016, in the United States alone, the American Heart Association (AHA) reports an incidence for MI of around 550,000 first episodes and 220,000 recurrent episodes annually [1]. Overall, each year, about three-quarters of a million people will experience an ACS in the United States, of which about 70% will be NSTEMI [12]. The United Kingdom describes a similar situation in which two-thirds of their ACS are NSTEMI and the remaining one third is STEMI, with a 33% reduction in the rates reported in 2010 compared to 2002 [2].

5.4 Pathophysiology

Multiple cardiovascular risk factors promote a persistent proinflammatory state, which triggers deleterious effects inside the blood vessels, particularly on the endothelial walls. Inflammation modulates the overexpression of prothrombotic mediators that increase the risk of thromboembolic events [18].

In addition to this persistent inflammatory environment, which already favors prothrombotic activity and platelet aggregation, atherosclerosis plays an important role in the genesis of ACS. The pathophysiology of atherosclerosis is characterized by the accumulation of lipids along the arterial walls. These lipids stimulate local vascular inflammation and further endothelial dysfunction [1, 18].

As previously described the damaged endothelium becomes highly dysfunctional; endothelial relaxation becomes impaired through a mechanism of low sensitivity and low liberation of thrombo-regulating substances such as nitric oxide, endothelial prostacyclin, and the ectonucleotidase CD39, which constitute our first line of defense against thrombosis [1, 19]. These plaque rupture walls are highly thrombogenic because they attract a wide variety of inflammatory blood cells which favor the release of proinflammatory cytokines and growth factors which enhance platelet adhesiveness and favor chemotaxis of more inflammatory cells such as neutrophils: these processes of cell recruitment and interleukin liberation result in thrombi formation and propagation.

The most common pathologic mechanism responsible for ACS is the erosion or rupture of unstable atherosclerotic plaques which results in plaque rupture and the exposure of core and matrix materials like collagen and intravascular tissue fac-

tor (ITF) into the circulating blood starting the formation of a thrombus. Exposed collagen also triggers the activation and accumulation of platelets, whereas ITF initiates the generation of thrombin, converting fibrinogen to fibrin and activating platelets. The resulting thrombus formation promotes total or partial occlusion of the affected coronary artery [1, 18, 19]. These data establish a relationship between atherothrombotic risk factors and venous thrombosis, as well as with the role of inflammation as a trigger of thrombotic events [19].

5.5 High Clinical Suspicion in ACS

A clinician's initial assessment should focus on the probability of any given patient with a suspected ACS of having the diagnosis. For this purpose, several diagnostic scores have been developed to help doctors safely and efficiently rule out or rule in a potential ACS. The HEART score has several advantages over other risk scores. Thrombolysis in Myocardial Infarction (TIMI) and the Global Registry of Acute Coronary Events (GRACE) scores were based on high-risk populations with known coronary disease. Other scores like the Troponin-only Manchester Acute Coronary Syndromes (T-MACS) and the High-Sensitivity Cardiac Troponin T Assay for Rapid Rule-out of Acute Myocardial Infarction (TRAPID-AMI) involve the use of high-sensitivity cardiac troponins, which might be not readily available in many hospitals [14]. On the other hand, the HEART score was based on a meta-analysis including over 11,000 patients, and the combined result of the studied variables yielded a 96.7% sensitivity for a major adverse cardiovascular event (MACE) [5, 14] (Table 5.1). The HEART score has a greater clinical utility because it is capable of identifying low-risk patients with undifferentiated chest pain who might have an ACS [6, 14, 20].

Diverse conditions determine everyone's cardiovascular risk. In many industrialized and developing countries, important lifestyle changes have a notorious influence on the behavior of systemic atherosclerosis and ischemic heart disease (IHD). The Framingham Cohort initially studied traditional cardiovascular risk factors such as age (>45 years for men or >55 years for women), high blood pressure, diabetes mellitus, dyslipidemia, tobacco use, hyper-caloric diets, sedentarism, obesity, and a positive family history, and they continue to be important milestones that set an individual coronary risk [11]. Nonetheless, new risk conditions have been identified during the last decades, such as chronic kidney disease, stress, depression, inflammatory and autoimmune diseases, cancer, chronic (non-cardiovascular) degenerative diseases, and low socioeconomic income figure among the most important [11]. The combination of cardiovascular risk factors and a suspicious medical history enhance the likelihood for the diagnosis of ACS [1].

Table 5.1 The HEART score [14]

Variable	Points
Clinical suspicion	
High	2
Moderate	1
Low	0
Electrocardiogram	
Significant ST depression	2
Nonspecific repolarization changes	1
Normal	0
Age	
>65 years old	2
45–65 years old	1
<45 years old	0
Risk factors (traditional)	2
≥3 risk factors or history of coronary artery disease1 or 2 risk factors	1
No risk	0
Troponin	
>2× ULN	2
1–2× ULN	1
Normal limit	0

0–3 points = low risk, consider discharge
4–6 points = moderate risk, observation, and further testing
7–10 = high risk, urgent intervention needed
ULN upper limit of normal

5.6 Risk Stratification

Once the diagnosis of an ACS is established, the next step is to determine the patient's risk of cardiovascular complications and mortality. The acute risk stratification during ACS presentation relies on the physician's initial clinical assessment in combination with a few simple tests such as a 12-lead ECG and cTn determination [21]. A patient with nausea/vomiting, dyspnea, tachyarrhythmias, hemodynamic instability, syncope, or aborted sudden death is a high-risk patient, as well as patients with STEMI, who are deemed as high-risk individuals in need for urgent medical care. Finally, the next risk-assessing parameter is the serum troponin levels. Patients presenting with higher levels are linked to worse cardiovascular outcomes [4, 15, 21].

A few morbid-morality risk calculators have been developed to allow physicians to rapidly triage high risk and high mortality. Triage and risk stratification determine which patients will benefit from immediate or early and elective reperfusion and which need to be further studied with invasive diagnostic testing [1]. One of the most widely used scores is the Thrombolysis in Myocardial Infarction (TIMI) score [12] (Tables 5.2 and 5.3). It is used to classify and estimate the risk of death and/or

reinfarction within 30 of the onset of the acute event in the context of STEMI or the risk of death and reinfarction or the need for urgent revascularization within the next 2 weeks in patients with NSTEMI/UA [4].

Another widely used scoring system is the Global Registry of Acute Coronary Events (GRACE) risk score, which predicts in-hospital and 6-month mortality risks (Tables 5.4, 5.5, and 5.6). The GRACE score has a good discriminatory power among all risk groups, notably in low-risk patients. This scoring system considers variables like age, heart rate, systolic blood pressure, creatinine level, Killip and Kimball classification, cardiac arrest at admission, ST deviation, and abnormal cardiac biomarkers [21–24].

In recent years, the development of the GRACE 2.0 algorithm has addressed a major limitation of the first GRACE score which was the patient's initial creatinine levels and Killip and Kimball classification (Table 5.7). This simplified score had

Table 5.2 TIMI non-ST elevation ACS risk stratification [4, 12, 22]

Variable	Points
Age > 65 (years)	1
≥3 Coronary artery disease risk factors:	
Hypertension, hypercholesterolemia, diabetes, family history of CAD, or current smoker	1
Known CAD (stenosis ≥50%)	1
Aspirin use (within the previous 7 days)	1
Severe angina (≥2 episodes in 24 hours)	1
ECG ST dynamic changes (≥0.5 mm)	1
Positive cardiac biomarker (troponin)	1

2-week mortality, reinfarction, revascularization risk. If points 0–1 = 4.7%, 2 = 8.3, 3 = 13.2%, 4 = 19.9%, 5 = 26.2%, 6–7 = 40.9%

Table 5.3 TIMI STEMI risk stratification [4, 12, 22]

Variable	Points
Age (years)	
<65	0
65–74	2
≥75	3
Diabetes, hypertension, or angina (if present)	1
Systolic blood pressure < 100 mmHg	3
Heart rate > 100 beats per minute	2
Killip classes II–IV	2
Weight < 67 kg	1
Anterior ST elevation or LBBB (if present)	1
Time to treatment >4 hours	1

30-day mortality risk. If points 0 = 0.8%, 1 = 1.6%, 2 = 2.2%, 3 = 4.4%, 4 = 7.3%, 5 = 12%, 6 = 16%, 7 = 23%, 8 = 27%, ≥9 = 36%

Table 5.4 GRACE risk score [24]

Age	*Pts*	*HR (bpm)*	*Pts*	*SBP (mmHg)*	*Pts*	*SCr (mg/dL)*	*Pts*
<30	0	<50	0	≥200	0	0–0.39	1
30–39	8	50–69	3	160–199	10	0.40–0.79	4
40–49	25	70–89	9	140–159	24	0.8–1.19	7
50–59	41	90–109	15	120–139	34	1.20–1.59	10
60–69	58	110–149	24	100–119	43	1.6–1.99	13
70–79	75	150–199	38	80–99	53	2.0–3.99	21
80–89	91	≥200	46	<80	58	≥4	28
≥90	100						
Killip and Kimball classification of prior or current congestive HF							*Pts*
No CHF							0
Rales, S3, and/or jugular venous distension							20
Acute pulmonary edema							39
Cardiogenic shock							59
Abnormal cardiac enzymes							14
ST deviation							28
Cardiac arrest at admission							39

HR heart rate, *SBP* systolic blood pressure, *SCr* Serum creatinine, *HF* heart failure, *CHF* congestive heart failure

Table 5.5 GRACE score interpretation for NSTEMI/UA [24]

	In-hospital mortality		6-month mortality	
Risk	Score	Mortality	Score	Mortality
Low	<109	<1%	<89	<3%
Intermediate	109–140	1–3%	89–118	3–8%
High	>140	>3%	>118	>8%

NSTEMI non-ST-elevation myocardial infarction, *UA* unstable angina

Table 5.6 GRACE score interpretation for STEMI [24]

	In-hospital mortality		6-month mortality	
Risk	Score	Mortality	Score	Mortality
Low	<126	<2%	<100	<4.5%
Intermediate	126–154	2–5%	100–127	4.5–11%
High	>154	>5%	>127	>11%

STEMI ST-elevation myocardial infarction

Table 5.7 Killip and Kimball classification [26–28]

Class	Definition	30-day mortality
I	Non-complicated infarct	2.1%–6%
II	Moderate heart failure: rales in pulmonary bases, galloping by S3, tachycardia	6.8%–17%
III	Severe heart failure with acute lung edema	14.4%–38%
IV	Cardiogenic shock	45.9%–81%

a better overall performance than its predecessor regarding mortality prediction at 1- and 3-year post discharge among all ACS (STEMI and NSTEMI/UA) [25]. The GRACE 2.0 is still not universally accepted because it lacks validation in several populations, and it yet has failed to show a good performance predicting in-hospital mortality [25].

In the context of STEMI, a simple clinical scoring system, such as the Killip and Kimball classification, can be used. Patients are classified based on the presence of physical findings that suggest heart failure and ventricular dysfunction. Four main categories are described ranging from an uncomplicated MI up to cardiogenic shock. With each category, there is a substantial increase in the short-term mortality risk [26–28].

5.7 Other Risk Considerations

In recent years, the female population has gained special interest regarding ACS incidence and ACS-associated mortality, due to their higher prevalence of atypical presentation of ischemic heart disease. Recent trends show that women beyond their fifth decade have a particularly higher risk for coronary disease because they often suffer from more comorbid conditions such as diabetes, obesity, chronic kidney disease, hypertension, smoking, and depression. Even women with the same risk factors as men are more prone to ACS, for example, women with diabetes are 1.5 times more likely to develop an ACS than diabetic men, as well as women suffering from depression are twice as likely to develop MI than depressed men [29, 30]. Besides, there are a few identified women-specific risk factors that increase cardiovascular risks such as menopause, a previous medical history of preeclampsia or gestational diabetes and oral contraceptive use [29].

Of all patients, elderly females presenting to the ER with non-chest pain NSTEMI have the highest mortality rate [8]. Perhaps this is due to lack of awareness among the general population and the medical community. Even when patients present with chest pain, ER physicians tend to be less suspicious of ACS when the patient is female than when the patient is male. These kinds of diagnostic delays translate into higher mortality rates and higher long-term morbidity in females [29].

Just as the female population, the elderly and diabetic patients carry a high-risk cardiovascular profile; in these population, the chest pain is the most common presentation of ACS; both groups also exhibit lower rates of chest pain than male adults. Around 40–60% of the geriatric population present with typical chest pain, while in younger patients typical anginal pain is present in up to 80–85% [7–9]. A possible explanation is that they have reduced pain perception, perhaps due to diabetic neuropathy, autonomic nerve dysfunction, or dementia [8]. In general, atypical symptomatology is frequent in diabetics, women, and the elderly patient [7, 9, 10, 17, 20, 29–31].

This behavior is particularly worrisome because non-chest pain NSTEMI carries a mortality risk of five to six times greater than chest pain associated with MI [8]. Overall, NSTEMI is more frequent in women than in men and in patients older than

75 years of age [8, 31, 32]. Timely diagnosis and adequate risk stratification of ACS can appropriately allocate patients that can benefit from an aggressive reperfusion strategy regardless of their age. Even within the geriatric population, robust elderly patients with a diagnosis of MI or UA will benefit from invasive reperfusion, rather than medical therapy alone [9, 33–39].

Another similarity between females, elderly, and diabetic patients is their higher prevalence of comorbid diseases, which has an impact on the incidence of ACS. About 1/3 of all ACS occur among the elderly population, and round 60% of all deaths due to ACS happen among the elderly [9, 32, 40].

5.7.1 Clinical Manifestations

Patients with ACS may present with typical ischemic symptoms including various combinations of the chest, upper extremity, jaw, or epigastric pain and discomfort with exertion or at rest. Chest pain is usually oppressive and tends to radiate to the arms, neck, and jaw, and it usually lasts at least 20 minutes. Pain can be associated with other MI symptomatology such as weakness, nausea, and dyspnea. Recall that special subpopulations such as females, diabetic patients, and the elderly have a higher incidence of atypical presentations of ACS [1, 4].

Physical examination during ACS tends to be normal unless heart failure or mechanical complications are present [20]. Patients can present some clinical characteristics that increase the probability of an ACS (Table 5.8).

Table 5.8 Clinical features that increase ACS likelihood [6, 41]

	Likelihood ratio
Common pain characteristics	
Pain radiation to both arms	2.6–4.3×
Pain resembling previous ischemia	2.2×
Pain's pattern changed over the last 24 hours	2.0×
Oppressive chest pain	1.9×
Pain worse on exertion	1.8×
Pain radiating to the neck	1.5×
Common physical findings	
Hypotension (systolic blood pressure < 100 mmHg)	3.9×
Lung rales	2.0×
Tachypnea	1.9×
Electrocardiogram changes	
ST elevation	15.7×
ST depression	5.3–11.7×
Dynamic ST changes	3.6×
T wave inversion	1.8–3.6×

ACS acute coronary syndromes

Table 5.9 Differential diagnosis of ACS [4, 12]

Cardiovascular	Hypertensive emergency
	Myocarditis
	Pericarditis
	Pulmonary embolism
	Aortic dissection
	Acute heart failure (nonischemic)
Pulmonary	Pleuritis
	Pneumonia
	Pneumothorax
	Bronchitis
Gastrointestinal	Gastroesophageal reflux
	Esophageal spasm
	Gastric/peptic ulcers
	Esophagitis
	Pancreatitis
Musculoskeletal	Costochondritis
	Previous chest trauma
	Muscular injury
Neurologic/psychiatric	Radiculopathy
	Herpes Zoster
	Depression
	Anxiety
Others	Anemia
	Thyrotoxicosis

ACS acute coronary syndromes

5.7.2 Differential Diagnosis

The mainstay symptom of ACS is the chest pain, and patients will manifest it in a wide variety of ways: oppressive, sharp, stabbing, burning, pulsating, and many others. The heart is in intimate contact with other structures inside the chest, and it has a shared innervation with other organs that can mimic chest pain and symptomatology that can resemble an ACS. Pain irradiation or referred pain to different anatomical locations other than the thorax can make the diagnosis of ACS a complex challenge. Multiple conditions can emulate acute heart disease (Table 5.9).

5.8 Multimodal Diagnosis Approach

5.8.1 Electrocardiogram

Patients arriving at the ER complaining of chest pain must have an ECG in under 10 minutes [4]. ST elevation found on an ECG is the hallmark sign of a STEMI**.** Nonetheless, only 1/3 of all ACS are STEMI, the rest of patients can present with a

wide variety of electrocardiographic changes, some suggestive of ischemia, but many others will even have normal ECGs throughout all their in-hospital stay. Like cardiac biomarkers, the ECG alone is often insufficient to make the diagnosis of an acute MI, and serial assessments increase the sensitivity and specificity of ECG. ECG changes such as ST deviation may be present in other conditions, such as left ventricular hypertrophy, left bundle branch block, or acute pericarditis [42, 43]. In ACS, timely diagnosis is essential, since every minute lapsed the myocardial damage increases, evidenced by dynamic changes in the ECG that correlate with histological findings (Table 5.10).

To establish the diagnosis of STEMI, ST changes must be present in at least two contiguous leads, and the ST elevation needs to be of at least ≥0.25 mV in men <40 years, ≥0.2 mV in men ≥40 years, ≥ 0.15 mV in women in leads V2–V3, or ≥0.1 mV in any other leads, as long as these changes do not happen in the context of left bundle branch block (LBBB) [13, 15]. Another pattern of acute STEMI is the presence of tall and symmetric T waves, otherwise called tall hyperacute T waves [44]. In patients without paced rhythms nor LBBB presenting with symptomatology suspicious of coronary ischemia, ECGs have a diagnostic sensitivity of around 75% with a specificity of 85% for the diagnosis of STEMI [44]. The following figures depict the correlation between ECG changes and coronary angiography findings (Figs. 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, and 5.9).

The modified Sgarbossa criteria were developed to improve diagnostic accuracy in patients with STEMI and left bundle branch block (LBBB. A modified rule

Table 5.10 Evolution of the ECG during a myocardial infarct [45]

Time	ECG findings	Histological findings
Minutes	Hyperacute T waves (tall T waves)	Reversible ischemic damage
	ST elevation	
Hours	ST elevation, with terminal negative T waves	The onset of myocardial necrosis
	Negative T waves (these can last for days to months)	
Days	Pathologic Q waves	Scar formation

ECG electrocardiogram

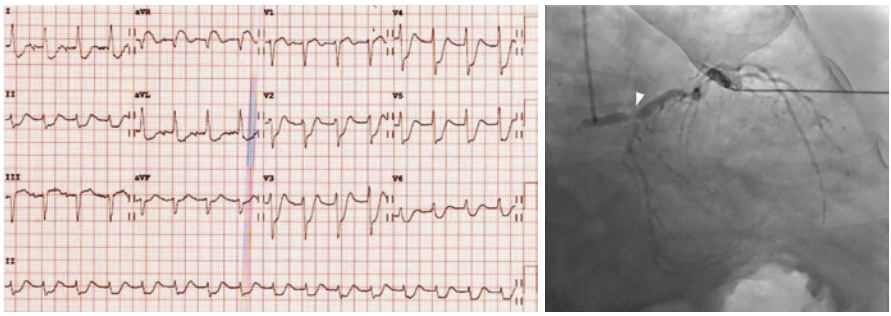

Fig. 5.2 ECG with significant ST depression in lateral and precordial leads and ST elevation in aVR. A corresponding coronary angiography depicts a subocclusive bifurcated Medina 1,1,1 lesion (arrow) on the distal portion of the left main artery extending to the proximal left anterior descending and circumflex arteries

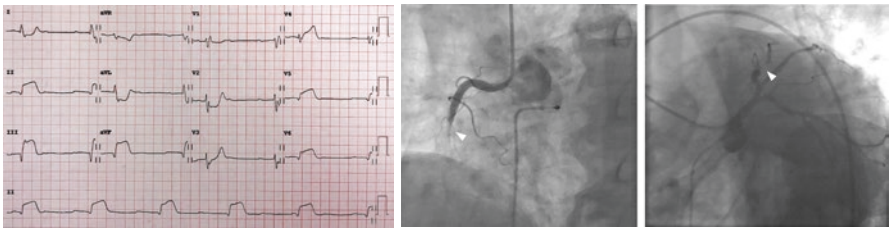

Fig. 5.3 ECG with a third-degree AV block with junctional escape rhythm and ST elevation in inferior leads and V5–V6. The coronary angiography patient shows that the patient had a multivessel disease with a 100% occlusion of the mid-right coronary artery and critical stenosis of a second diagonal artery (arrows)

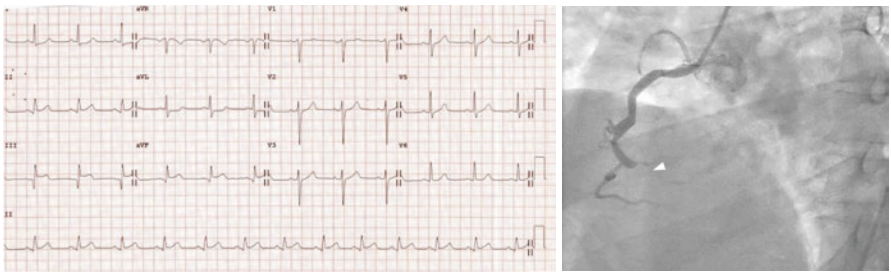

Fig. 5.4 ECG with inferior lead ST elevation (DII, DIII, aVF) corresponding to a complete distal occlusion of the right coronary artery (arrow)

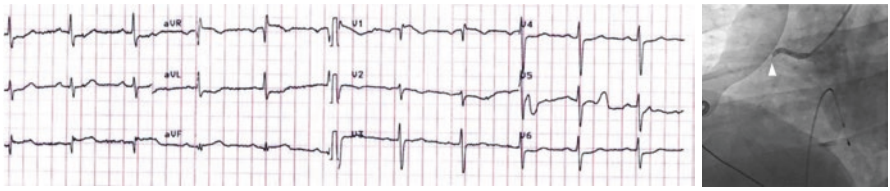

Fig. 5.5 CG shows inferior lead ST elevation (DII, DIII) due to a proximal right coronary artery occlusion

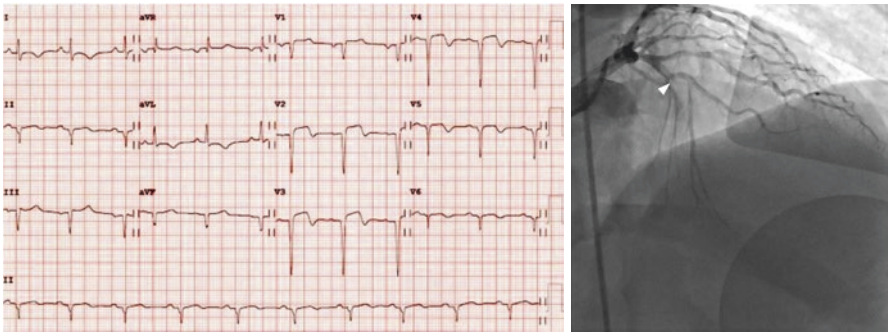

Fig. 5.6 ECG with anterior STEMI. ST elevation is seen on V2, V3, and extending to V4. Coronary angiography showed total occlusion of the distal left anterior descending artery (arrow), just beside the second diagonal artery

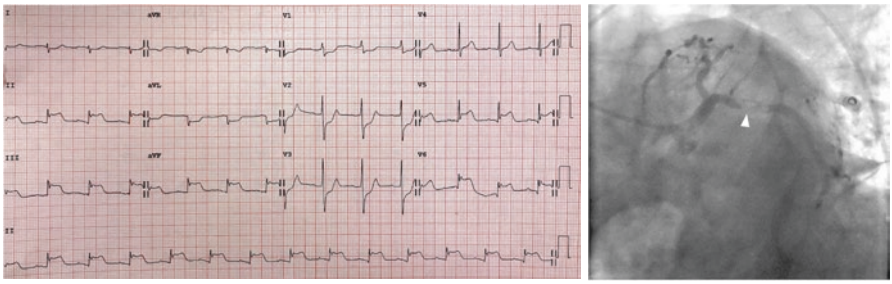

Fig. 5.7 ECG with inferior lead ST elevation as well as ST elevation in V5–V6. Spider view coronary angiography identified a proximal occlusion on the circumflex artery

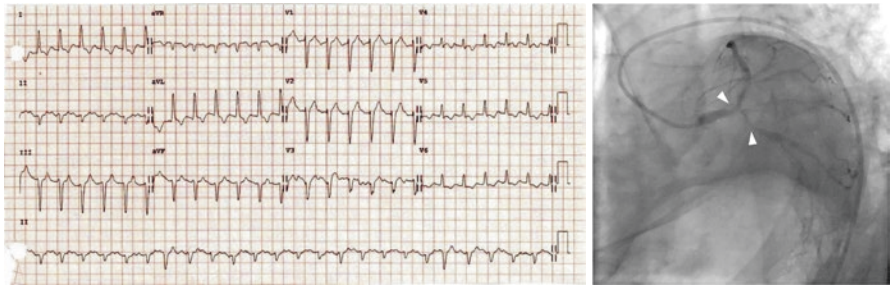

Fig. 5.8 ECG with flutter and new-onset LBBB caused by a bifurcated Medina 1,1,1 lesion located on the distal left main artery and extending to the proximal left anterior descending and circumflex arteries (arrows)

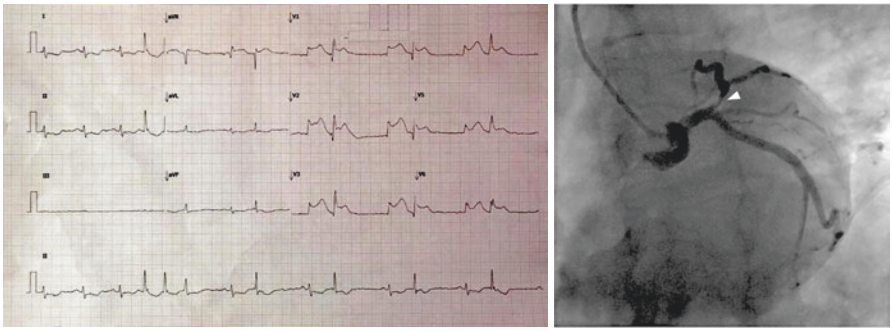

Fig. 5.9 ECG with long DII that shows a couple of premature supraventricular beats, followed by ventricular bigeminy. The basal rhythm and the bigeminy show important ST elevation in all precordial leads and aVR. The corresponding coronary angiography shows a critical stenosis of the proximal left anterior descending artery

describing that there should be discordant ST elevation with amplitude >25% of the depth of the preceding S wave was included for a positive diagnosis of STEMI [15, 44].

Modified Sgarbossa criteria [44, 46]:

- ≥ One lead with ≥1 mm of concordant ST elevation
- ≥ One lead of V1–V3 with ≥1 mm of concordant ST depression
- ≥ One lead anywhere with ≥1 mm ST elevation and proportionally excessively discordant ST elevation, as defined by ≥25% of the depth of the preceding S wave

High-risk patients with right bundle branch blocks (RBBB) and persistent ischemic symptomatology should be considered for a primary revascularization strategy because RBBB in the setting of MI is considered a poor survival indicator.

Paced rhythms mask ECG repolarization changes, posing a remarkable challenge that complicates appropriate ECG interpretation by interfering with ST-segment changes. Patients with pacemakers may require serial troponin determinations to safely rule in or rule out a potential ACS. In unstable patients with rhythm disorders in whom clinical suspicion for an ACS is high, urgent coronary imaging or coronary angiography comes in handy to confirm the diagnosis and initiate treatment [47].

5.8.2 Chest X-Ray

The value of the chest radiography in patients defined as low risk by observing symptoms and physical examination has not yet been well defined. Some series report that only around 12% of the ER chest X-rays (CXR) requested due to chest pain would provide diagnostic information regarding an ACS [48] (Table 5.11). Sometimes, if the patients present with signs and symptoms of an ACS and heart failure, the CXR could help us rule out signs of venocapilar hypertension, pulmonary edema, pleural effusions, and other complications of MI (Fig. 5.10).

Table 5.11 Chest X-ray congestion patterns

Grade	Description
0	No congestion
I	Flow redistribution
II	Interstitial edema
III	Localized alveolar edema
IV	Diffuse alveolar edema

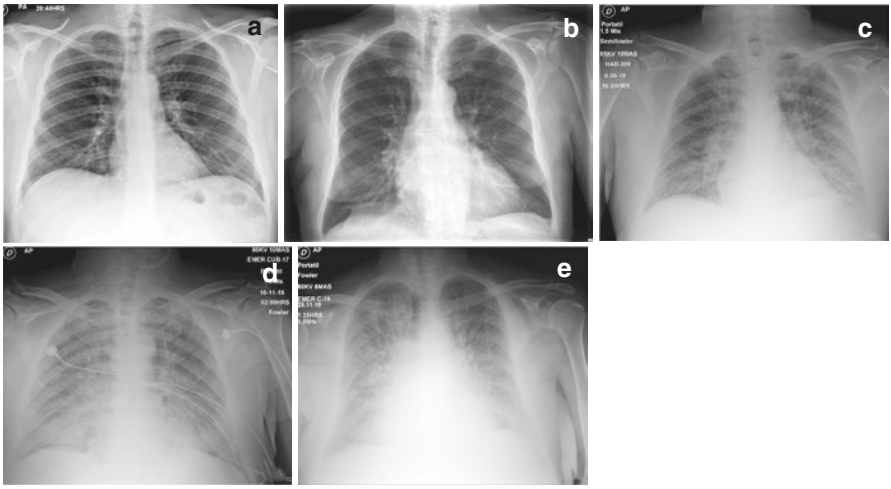

Fig. 5.10 Image **a** depicts a chest X-ray with normal pulmonary circulation. Image **b** has venus hilum and flow redistribution. Image **c** shows signs of interstitial edema. Image **d** has alveolar edema predominantly on the basal portion of the right lung. Image **e** has severe bilateral alveolar edema

5.9 Laboratory Evaluation

Cardiac troponins are biochemical markers of myocardial damage and necrosis. Biomarker elevation does not indicate the underlying mechanism of ischemia or necrosis and does not differentiate between ischemic or nonischemic causes of myocardial damage. Several clinical conditions have the potential to result in myocardial ischemia or necrosis and cause elevations in cardiac biomarkers, including acute pulmonary embolism, heart failure, advanced renal disease, and myocarditis [45, 49].

In patients with a high suspicion of ACS but with an initial negative or non-diagnostic cTn, a second sample should be obtained within 3–6 hours. For high-sensitivity cardiac troponin (HS-cTn) assays, the second sample should be drawn within 1–3 hours (see Fig. 5.11) [14, 20]. Contemporary sensitive troponin I and troponin T assays have a sensitivity of 80% and a specificity of 90% [49, 50]. With a second sample, HS-cTn assays with short time-frame algorithms have a 99.7% negative predictive value for ruling out myocardial infarction [50].

- HS-cTnT 1-hour algorithms exhibit good sensitivity around 88–98% and specificity 86–99% to rule out MI [5, 17].
- HS-cTnI 1-hour algorithms also have good performance ruling out MI, with a sensitivity ranging around 98.4% and a specificity of 99.8% [5, 38].

Other biomarkers that play an important role on the prognosis of patients presenting with ACS, such biomarkers are the B-type natriuretic peptide (BNP), C-reactive protein (CRP), and serum creatinine and cystatin, are among the most commonly used.

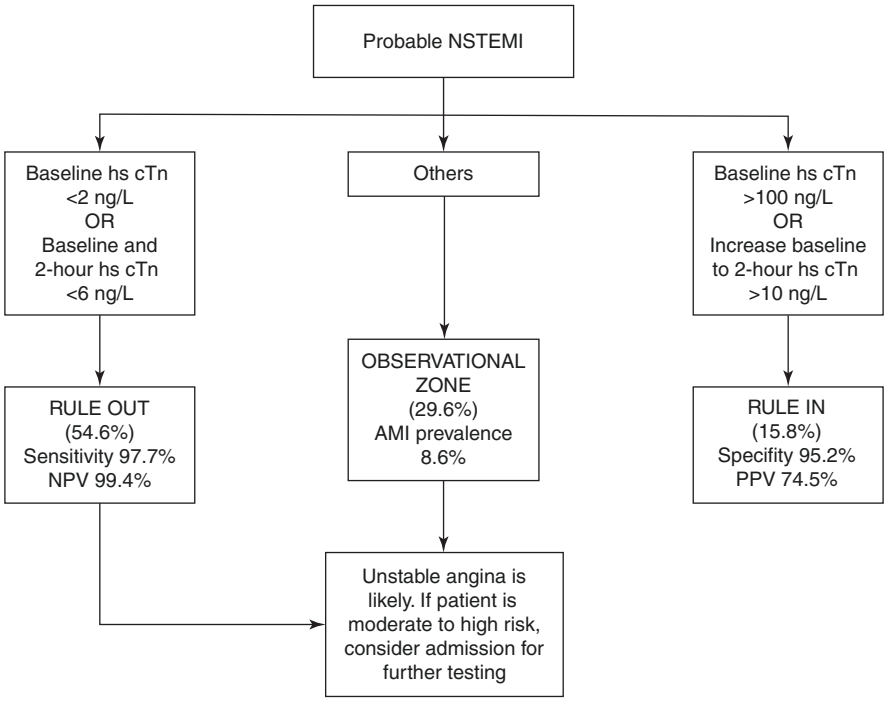

Fig. 5.11 HS-cTn MI 2 hours rule-out algorithm

- BNP can be a helpful biomarker during ACS, providing short- and long-term prognostic information. Its release can be triggered by myocardial ischemia and wall stress. Elevated levels correlate with worse prognosis [4, 51].
- CRP plays a role in ACS as a stressor for endothelial inflammation and thrombus formation. Its elevation can be correlated with increased mayor adverse cardiovascular events and mortality [4, 16, 52].
- Serum creatinine and calculation of the estimated filtration rate (eGFR). The lower the eGFR, the higher associated with cardiovascular complications and mortality rates [15].
- HS-cTn displays an opposite behavior to eGFR; in this case, higher levels mean worse prognosis.
- Contemporary data advocates for increased cardiovascular risk linked to cystatin level elevation [16].

5.9.1 Echocardiogram

Currently, echocardiography is a powerful imaging tool capable of diagnosing and triaging chest-pain patients inside the ER environment. Transthoracic echocardiography (TTE) plays an important role in the setting of nondiagnostic ECGs

among patients with high clinical suspicion for NSTEMI/UA. Its use comes in handy because TTE imaging studies are readily available in most ERs; they are mobile, relatively inexpensive, fast, and easy to use. TTE is a noninvasive tool that can screen for real-time wall-motion abnormalities compatible with diastolic and systolic dysfunction which are some of the earliest changes of the ischemic cascade. During the evaluation of suspicious chest pain, TTE sensitivity ranges around 90%–95% and its specificity 90%–100% [53–57]. New modalities such as contrast TTE have the capability of visualizing wall-motion abnormalities and myocardial perfusion in a simultaneous fashion [54].

Another main use is that TTE has the capability of detecting several acute MI-related mechanical complications. ER TTE during an ACS can assess left ventricular and right ventricular functions and volumes, as well as a wall-motion index, valvular function, mitral regurgitation, papillary muscle rupture, right ventricular infarction (30% of all inferior MI), myocardial rupture, and pericardial effusions and other diseases [53]. Patients with no wall-motion abnormalities during stress echocardiography were found to have a negative predictive value for cardiovascular events >99% [58].

Stress TTE has a sensitivity of 85%–88% and a specificity of 80%–83% [50, 59, 60], which are highly superior to simple treadmill stress testing, which accounts for a sensitivity of 62%–70% with a specificity of 52%–79% [50, 59, 60].

5.9.2 Cardiac Computerized Tomographic Angiography (CTA)

CT angiography is a relatively quick and cheap imaging study that can efficiently rule out coronary disease and other causes of chest pain, therefore reducing ER length of stay and hospital admissions. It has proved its functionality in the rapid evaluation of patients with acute chest pain because it provides a comprehensive look at key coronary anatomic features that are related to occlusive coronary disease. Image acquisition is fast, and computerized image reconstruction has unlimited fields of view. Some drawbacks of CTA are its cost and patient exposure to radiation and IV contrast agents. Overall, CTA has a good sensitivity of 95%–99% and a specificity of 80%–90%, with a negative predictive value of 99%–100%. Perfusion CT can increase test's specificity up to 98% maintaining a similar sensitivity [50, 58–62].

5.9.3 Cardiac Magnetic Resonance (CMR) Imaging

Just as CTA, CMR has imaging reconstruction software that can create unlimited fields of view. CMR can differentiate from old and new myocardial infarctions and even edema. Vasodilator perfusion CMR is capable of detecting stress-induced ischemia. Its disadvantages are it is not a cost-effective alternative, the image acquisition process is time-consuming, some patients get claustrophobic while inside the CMR machine, and

IV contrast agents and vasodilating agents are needed. Contrast CMR sensitivity ranges around 87%–95% and a specificity of 85% [58, 62] (Mahler, Scirica). Vasodilator perfusion CMR has a sensitivity of 99–100% for coronary disease [58].

5.10 Radionuclide Myocardial Perfusion Imaging (MPI)

One of MPI strengths is that it has a negative predictive value for ruling out myocardial infarction that is close to 100% [63]. With the use of more modern radionuclide tracers, its sensitivity for detecting MI is 90%–100%, but its specificity is about 67%–90% [50, 59, 63]. Other downsides of nuclear medicine are its cost and its limited spatial resolution (around 3 mm), and even though it is not as time-consuming as a cardiac magnetic resonance (CMR), patients still need around 15–60 minutes of scan time. Other limitations that affect signal intensity and that could be misinterpreted as a false-negative perfusion-metabolism match is when large patients with excessive thoracic adipose tissue, particularly women, are subject to MPI. The excessive adipose tissue attenuates the radionuclide intensity causing this misinterpretation. Another group of patients subject to this confusion is patients who suffer from the multi-vascular disease. In this group, the tracers' distribution might not generate enough territorial signal intensity difference, and the study could be misinterpreted as normal when perhaps the patient suffers from global ischemia.

5.10.1 Coronary Angiography

Coronary artery angiography is considered the gold standard for the diagnosis of coronary artery disease. Cardiac catheterization has a sensitivity of 86%–95% with a specificity of 89%–100% [50, 59].

5.11 Treatment

5.11.1 Initial ACS Management

It is essential to evaluate patients with suspected ACS immediately to prevent potentially fatal complications and chronic cardiovascular morbidity. Every ER patient complaining of chest pain should undergo early risk stratification based on medical history, physical examination, ECG, and cardiac biomarker measurements, HEART, TIMI, and GRACE scores (Fig. 5.12). Early risk stratification can assist in determining whether a patient should be managed with either an early invasive strategy or an initial conservative strategy and can help determine the pharmacologic therapies that are recommended [15, 64].

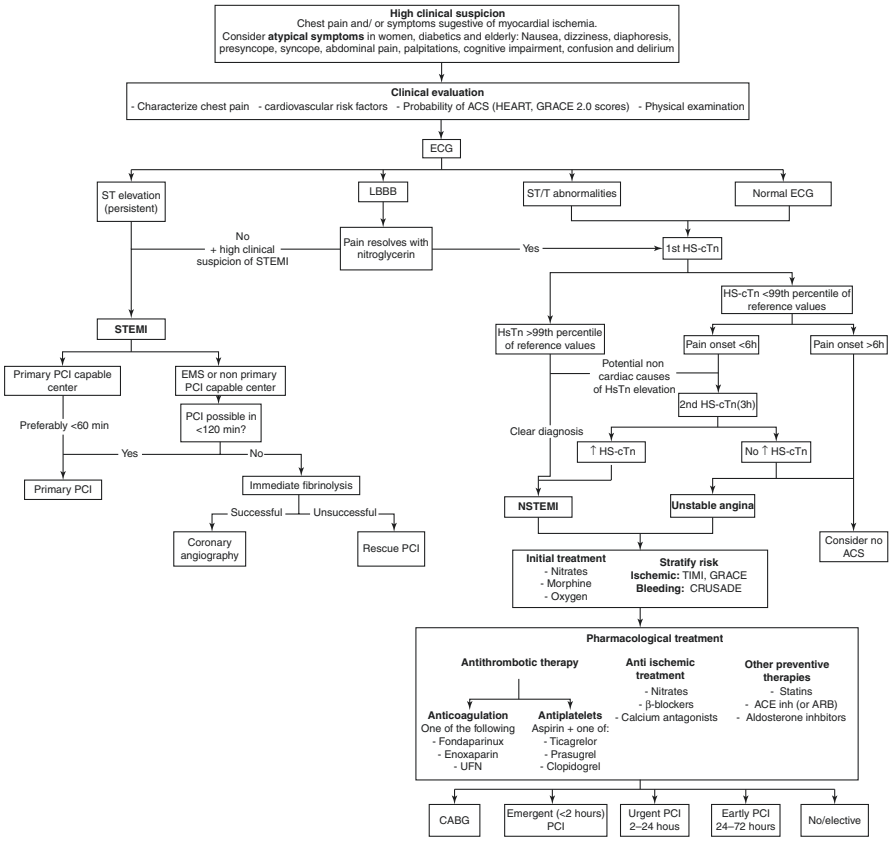

Fig. 5.12 ACS diagnostic and therapeutic algorithm

The initial management of ACS should include patient admission to a coronary care unit or a specially designated area in which patients can receive continuous hemodynamic surveillance. Constant rhythm and vital sign monitoring should be enforced. Hemodynamic instability should be addressed according to the advanced cardiac life-support protocols, though the vast majority of patients are considered hemodynamically stable; hence supportive measures should be instated [1, 4, 20, 65].

If a patient is deemed too anxious, a mild sedative or a benzodiazepine can be of much help if not contraindicated [4]. General oxygen use is not supported by current clinical practice guidelines unless patients are desaturated with O2 saturation levels below 90% [4]. If not contraindicated by the type of ACS (RV infarct) or hemodynamic instability (low blood pressures or extreme bradycardia), pain should be treated using nitrates (sublingual, intravenous, oral), and early beta-blocker use is favored by current evidence in case of refractory angina or hemodynamically stable patients with MI [1, 4, 20, 65]. Cardiac pain is frequently high intensity, and symptomatic relief often needs opioid analgesics.

Table 5.12 Common types of oral P2Y12 inhibitors

	Clopidogrel	Prasugrel	Ticagrelor
Loading dose	PCI: 600 mg	PCI: 60 mg	PCI: 180 mg
	Fibrinolysis: 300 mg	Fibrinolysis: Not recommended	Fibrinolysis: Not recommended
Loading dose in the elderly (≥75 years old)	PCI: 300–600 mg	PCI: 60 mg, use not favored	PCI: 180 mg
	Fibrinolysis: Loading dose not recommended	Fibrinolysis: Loading dose not recommended	Fibrinolysis: Loading dose not recommended
Maintenance dose	75 mg qd	10 mg qd	90 mg bid
Maintenance dosing in the elderly (≥75 years old)	No adjustment necessary	5 mg QD	No adjustment necessary
Dosing in CKD	Caution if eGFR <15 mL/min/1.73 m^2	Do not use if eGFR <15 mL/min/1.73 m^2	Do not use if eGFR <15 mL/min/1.73 m^2
Dosing in hepatic disease	Use with caution	Avoid use in severe hepatic impairment	Avoid use in severe hepatic impairment
Duration	3–10 days	7–10 days	3–5 days

PCI, percutaneous coronary intervention; QD, once daily; BID, twice daily; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate

As soon as a diagnosis of STEMI/NSTEMI/UA is established, patients must be started on antiplatelet therapy. The initial loading dose of non-enteric-coated aspirin should be between 325 and 500 mg. In STEMI patients, the use of a second antiplatelet agent (a P2Y12 inhibitor) can be withheld until coronary anatomy is known (Table 5.12). An anticoagulation strategy must be adopted until the culprit artery is reperfused (Table 5.13). If reperfusion is not achieved or a conservative management strategy was selected, anticoagulant use is recommended for up to 7 days. ACE/ARB use can be of benefit in patients with anterior MI or ventricular dysfunction [1, 4, 20, 65].

Antiplatelet therapy recommendations for the elderly population [34, 66, 67]:

- Prasugrel in elderly 5 mg instead of 10 mg
- Ticagrelor safe in elderly. No increased risk of bleeding
- Clopidogrel preferred in elderly patient which needs concomitant anticoagulation

5.11.2 Coronary Revascularization

Percutaneous coronary intervention (PCI) is favored over fibrinolysis [15]. Independently of the chosen reperfusion strategy, the maximum time for culprit-artery reperfusion should not exceed 90 minutes [1, 4, 15, 20, 65] (Table 5.14). Depending on the diagnosis and the individual risk profile, the timing of PCI can be classified into four categories: immediate, early invasive, invasive, and selective.

Table 5.13 Intravenous and subcutaneous coagulants

	Unfractionated heparin	Enoxaparin	Fondaparinux	Bivalirudin
Loading dose	PCI: 70–100 IU/kg IV Angiography: 60–70 IU/kg IV Max: 5000 IU	PCI: 30 mg IV	N/A	PCI: 0.75 mg/kg IV
Loading dose in the elderly (≥75 years old)	No dose adjustment needed	No IV bolus recommended	No dose adjustment needed	No dose adjustment needed
Maintenance dose	12–15 IU/kg/hours Max: 1000 IU/hours	1 mg/kg SC bid	2.5 mg SC qd	1.75 mg/kg/hours IV
Maintenance dosing in the elderly (≥75 years old)	No dose adjustment needed	0.75 mg/kg SC bid	eGFR 20–50 mL/min/1.73 m^2 use 1.5 mg SC qd	eGFR 30–59 mL/min/1.73 m^2 use 1.4 mg/kg/hours Avoid use if eGFR <30 mL/min/1.73 m^2
Dosing in CKD	No dose adjustment needed	eGFR 15–30 mL/min/1.73 m^2 use 1 mg/kg SC qd eGFR <15 mL/min/1.73 m^2 avoid use	Avoid use if eGFR <20 mL/min/1.73 m^2	eGFR 15–30 mL/min/1.73 m^2 use 1 mg/kg/hours IV Avoid use if eGFR <15 mL/min/1.73 m^2
Dosing in hepatic disease	Use with caution monitor for aPTT 50–70 s	N/A	N/A	No dose adjustment needed
Duration	60–90 minutes	12 hours	17–21 hours	1 hours

PCI percutaneous coronary intervention, *IU* international unit, *IV* intravenous, *SC* subcutaneous, *BID* twice daily, *QD* once daily, *eGFR* estimated glomerular filtration rate, *CKD* chronic kidney disease, *aPTT* activated partial thromboplastin time

A strong indication of the use of a primary reperfusion strategy is in patients with STEMI in whom the onset of ischemic symptoms is <12 hours. If a primary PCI cannot be done within the 12-hour time frame, clinicians should adopt a pharmaco-invasive reperfusion strategy (Table 5.15). Successful pharmaco-invasive reperfusion should be followed by an early PCI (6–24 hours) [15]. In the event of failed fibrinolysis, patients should undergo rescue PCI as soon as possible [15]. Patients with NSTEMI or high suspicion for MI that experience acute heart failure, life-threatening arrhythmias, hemodynamic instability, refractory chest pain (angina), and mechanical complications related to MI should also undergo PCI reperfusion [15].

If needed, elderly patients benefit from primary PCI reperfusion, and in selected, robust, and low-bleeding-risk elders, fibrinolysis has good results [68]. Across all

Table 5.14 Timing of invasive reperfusion therapies

Category	Time frame	Indication
Immediate	<1–2 hours	STEMI
		Complicated MI (hemodynamic instability, mechanical, persistent symptoms, potentially lethal arrhythmias)
Early	<24 hours	NSTEMI
		STEMI (after pharmaco-invasive treatment)
Invasive	<72 hours	NSTEMI patients with intermediate risk (this is the maximal time frame for PCI)
Selective	NA	Unstable angina
		Stable angina
		Patients with recurrent chest pain

STEMI ST-elevation myocardial infarction, *MI* myocardial infarction, *NSTEMI* non-ST-elevation myocardial infarction, *PCI* percutaneous coronary intervention, *NA* not applicable

Table 5.15 Fibrinolytic doses

Fibrinolytic agent	Recommended dosage
Tenecteplase[a]	30 mg for weight < 60 kg
	35 mg for 60–69 kg
	40 mg for 70–79 kg
	45 mg for 80–89 kg
	50 mg for >90 kg
Reteplase	10 Units +10 units IV boluses given 30 minutes apart
Alteplase	Bolus 15 mg, infusion 0.75, infusion 0.75 mg/kg for 30 minutes (maximum 50 mg), then 0.5 mg/kg (maximum 35 mg) over the next 60 minutes
	Total dose should not exceed 100 mg

[a]Half-dose tenecteplase can be used in elderly patients (not yet recommended in clinical practice guidelines)

types of ACS, invasive strategies are associated to lower mortality rates in the geriatric population [34, 39].

Recent trials shed light on the importance of adapting half-dose TNK fibrinolysis in elderly patients with STEMI. Current practice guidelines do not support the use of this therapeutic approach, but preliminary results show similar efficacy outcomes and reduced hemorrhagic complications [67–69].

5.12 Additional Clinical Practice Takeaways

- NSTEMI is more frequent in women than in men and in patients older than 75 years of age [8, 31, 32].
- Chest pain is the most frequent symptom in all populations presenting with ACS [7, 8].

- Atypical symptomatology is frequent in people with diabetes, women, and the elderly patient [7, 9, 10, 17, 20, 29–31].
- Around 40–60% of the geriatric population present with typical chest pain; in younger patients typical anginal pain is present in up to 80–85% [7–9].
- Physical examination during ACS tends to be normal unless heart failure or mechanical complications are present [20].
- In ACS, current evidence suggests that non-fragile elderly patients tend to benefit from an invasive, reperfusion strategy, rather than medical therapy alone [9, 33–39].
- In STEMI, robust elderly patients benefit from aggressive reperfusion strategies [9, 33].
- About 1/3 of all ACS occur among the elderly population [9, 32].
- Around 60% of all deaths due to ACS happen among the elderly [40].
- Recent trials shed light on the importance of adapting half-dose TNK fibrinolysis in elderly patients with STEMI. Current practice guidelines do not support the use of this therapeutic approach, but preliminary results show similar efficacy outcomes and reduced hemorrhagic complication [67–69].
- In patients with a high suspicion of ACS but with an initial negative or nondiagnostic cTn, a second sample should be obtained within 3–6 hours. For HS-cTn assays, the second sample should be drawn within 1–3 hours [14, 20].

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Chapter 6
Acute Aortic Syndromes in the ER

Carlos Jerjes-Sánchez and Felipe Valdés

6.1 The Scope of the Problem

The high mortality rate and the associated morbidity of acute aortic syndromes (AAS) are directly related to diagnostic delay, since the onset of symptoms [1–4]. Acute aortic syndromes are rarely seen outside an ER scenario. Patients presenting with acute aortic dissections (AAD) tend to manifest life-threatening signs and symptoms, which need prompt diagnostic evaluation. Quick detection and expedite treatment are fundamental to reduce morbidity and mortality [5]. If left untreated, mortality can spike from 20% during the first 24 hours after symptom onset up to 62% by the 7th day [6].

Acute aortic syndromes are considered an infrequent spectrum of diseases, perhaps that is why medical personnel rarely consider them as a first-line diagnosis. AAS comprise a series of potentially fatal conditions which include aortic dissection, penetrating aortic ulcer (APU), and intramural aortic hematoma (AIMH). These AAS are clinically indistinguishable one from another, and their cardinal manifestation is acute onset of severe chest pain, probably because AAS share common pathophysiology which relates to the breakdown and tearing of the intima and media [1, 7].

6.2 Prevalence

The incidence of aortic syndromes is roughly around 2.5 to 4 cases per 100,000 patients per year, the vast majority comprised by AD [1, 2, 5, 7–9]. Of all AAS, AAD represent approximately 80% of all cases, followed by AIMH at 15% and APU with less than 5%. Present-day data derived from the International Registry of Acute Aortic Dissections shows that two-thirds of the affected patients are men, about two-thirds also suffer from high blood pressure, and AAD is more common in patients between their sixth and seventh decade of life. Traditionally if the age of presentation is below 40 years, the single most common predisposing condition is connective tissue diseases [1, 2, 7, 8].

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Generally, the ascending aorta is affected in the majority of patients with an estimated incidence of 60–70% [1, 2, 6, 7]. Proper classification is key to determine treatment. Considering the high mortality of AAS, early treatment is one of the main determinants of survival, particularly for AAD, which if left untreated has an average mortality between 1 and 2% per hour during the first 24 hours upon symptom presentation. Survival declines with time since symptom onset and symptomatology progression can be considered a stronger prognostic factor, even more than the selected treatment approach [1, 9].

6.3 Patient-Related Risk Factors

Table 6.1 lists the most important risk factors for AAD patients presenting to the ER.

6.4 Types and Mechanisms of the Problem

According to the anatomical structures affected by the tear (layers of the aorta), acute aortic syndromes can be classified as seen in Table 6.2.

Table 6.1 Prevalent risk factors reported in patients with aortic dissections [1–3, 8]

Risk factor	Prevalence
Hypertension	65–77%
Age (beyond sixth decade of life)	32%
Genetic diseases (bicuspid aortic valve, Marfan syndrome, Ehlers-Danlos, autoimmune disease)	20%
High-speed deceleration (aortic trauma)	15–20%
Sex (male)	66%
Iatrogenic	0.06%
Vasculitis	NA
Other	NA

NA not available

Table 6.2 Classification and characteristics of the aortic syndromes [1, 2, 6]

Aortic dissection 60–70%	Intramural hematoma 5–30%	Penetrating ulcer 2–7%
The formation of true and false lumens	Hematoma formation in the media	Ulceration of atherosclerotic plaque
Intramural bleeding	No blood flow must supply the hematoma.	Penetrates internal lamina
Break in the medial layer	No flap and no intimal tear	Reaches medial layer
Inflammatory response and bleeding cause aortic dilation and eventually rupture	Rupture of the vasa vasorum	Risk of rupture or progression toward acute aortic dissection

6.5 Clinical Presentation

The most common clinical presentation (>75%) for both type A and B dissections is moderate to severe pain, usually abrupt in onset, starting at the chest or abdomen and described as tearing, stabbing, or penetrating. Sometimes the pain tends to radiate to the back and can migrate toward the lower abdomen and legs [1–3, 5, 7, 8].

Accompanying symptoms are very diverse and usually derive from ischemia to affected organs along the tear's path (Table 6.3) or hypotension and circulatory shock due to sudden and massive blood loss. When the tear starts at the aortic root, patients can exhibit aortic regurgitation and acutely decompensated heart failure [1, 2, 5, 7, 8].

6.6 Physical Examination

Usually patients tend to present with a hypertensive response. Nonetheless circulatory shock can be the initial presentation. Physicians should be aware of any neurological manifestation and perform a quick neurological checkup. Aortic murmurs can be present, especially in the setting of acute aortic regurgitation. Patients with aortic regurgitation can present wide pulse pressure variations along with classic aortic regurgitation signs. Others experience heart failure symptoms such as jugular reflux, lung rales, and edema. If the dissection flap excludes limb arteries along the way, pulse deficit can be noted on the affected extremity [1, 5, 7, 8].

Table 6.3 Signs and symptoms of ER patients with acute aortic syndromes

Signs/symptoms	Affected patients (%)
Chest pain	80–89%
Aortic regurgitation (acute)	40–75%
Hypertension (SBP >150 mmHg)	25–65%
Pain migration	15–50%
Back pain	40%
Abdominal Pain	24–41%
Neurological deficit or paraplegia	7–40%
Circulatory shock	5–33%
Pulse deficit	9–36%
Pericardial tamponade	<20%
Pleural effusion	15–20%
Renal failure	10–20%
Syncope	5–20%
Myocardial ischemia	10–<15%
Congestive heart failure	<10%
Tamponade	5%
Mesenteric ischemia	<5%

SBP systolic blood pressure

6.7 Classification

AAS is a spectrum of diseases closely related to pathological vessel walls. The vessel's walls are constantly withstanding variations in hemodynamic sheer stress which favor fluctuations along the disease's spectrum, meaning that no syndrome remains quiescent. AIMH and APU eventually may evolve to the most lethal of all AAS, the AAD.

AAD can also be classified based on different properties, such as its site of origin, extension, time from symptom onset, and etiology of the intimal tear; different schemes are recommended for these purposes [1–3, 9]. Table 6.4 and Fig. 6.1 show DeBakey and Stanford classifications.

Considering the time elapsed since symptom onset, the American Heart Association (AHA), the American College of Cardiology (ACC), and the European Society of Cardiology (ESC) classify AAD into three main categories, acute, subacute, and chronic dissections. Nonetheless, considering more recent data collected by the International Registry of Acute Aortic Dissections, a different and more contemporary chronological classification (Table 6.5) is proposed, adding a new time-based category, the hyper AAD. The global mortality is better matched according to this new arrangement, and it tends to increase substantially as time passes by. The patients whose symptoms have lasted for less than 24 hours and received proper and expeditious treatment exhibit the lowest mortality rates of all [1–3, 8].

Table 6.4 Classification of aortic dissections

DeBakey Origin of the tear	Svensson Etiology	Stanford Extension of the tear
Category 1 Dissection tear starting at the ascending aorta and disseminates to the descending aorta (aortic arch involvement is possible)	*Class 1* Dissection with true and false lumens (classical dissection)	*Type A* All dissections involving the ascending aorta
Category 2 Tear confined to ascending aorta	*Class 2* Intramural hematoma(or hemorrhage)	
Category 3 Tear starts at the descending aorta and propagates distally	*Class 3* Subtle dissection without hematoma	*Type B* All dissections that do not involve the ascending aorta (regardless of aortic arch involvement)
Category 3a Tear limits to the descending thoracic aorta	*Class 4* Penetrating atherosclerotic ulcer	
Category 3b Tear extends beyond the diaphragm	*Class 5* Iatrogenic or traumatic dissection	

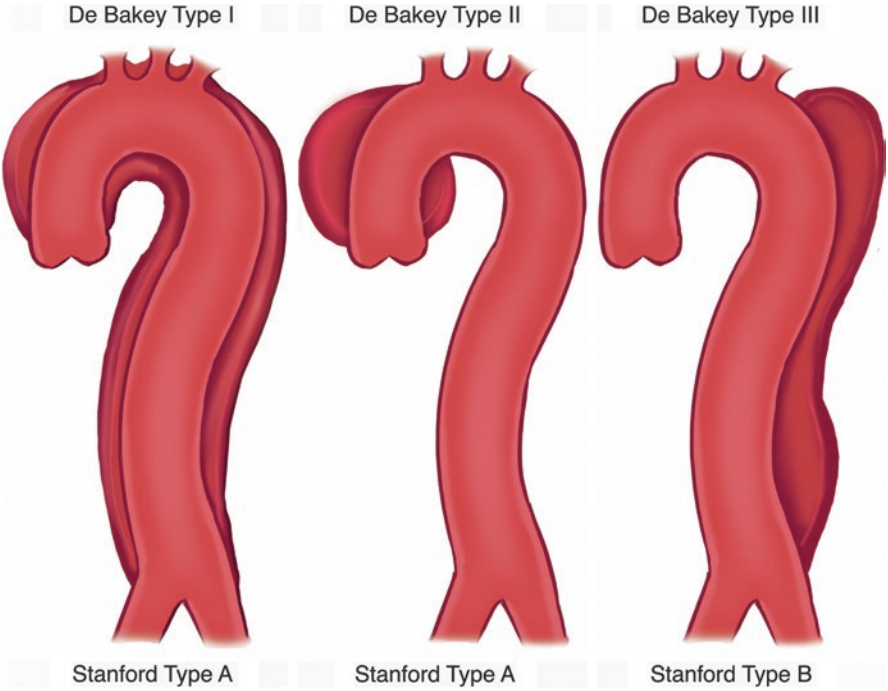

Fig. 6.1 Anatomical classification of aortic dissections. (Courtesy of Celina Ortiz)

Table 6.5 Aortic dissection chronological classification

	Hyperacute	Acute	Subacute	Chronic
AHA/ACC	NA	<2 weeks	2–6 weeks	>6 weeks
ESC	NA	<14 days	15–90 days	>90 days
IRAD[a]	<24 hours	2–7 days	8–30 days	>30 days

Classification is according to time since onset of symptoms
NA not applicable, *ESC* European Society of Cardiology, *AHA* American Heart Association, *ACC* American College of Cardiology, *IRAD* International Registry of Acute Aortic Dissections
[a]New proposed classification

6.8 Differential Diagnosis

The most important differential diagnostics in the ER setting in a patient presenting with sudden-onset chest pain and cardiovascular risk factors are acute coronary syndromes (ACS), pulmonary embolism, hypertensive emergencies, and acute heart failure. Other non-life-threatening conditions are esophageal diseases (spasm, reflux, achalasia) and pleural conditions (pleural effusion, pleuritis); finally we should consider musculoskeletal diseases that can mimic cardiopulmonary pathology.

6.9 Diagnostic Strategy

High-clinical suspicion is key. Patients with risk factors and characteristic symptomatology should undergo urgent contrast angiography CT scan and transthoracic echocardiography. Blood samples should be drawn searching for blood loss, hypoperfusion, and end-organ damage. D-dimer levels below the 500 ng/mL threshold make the diagnosis of aortic syndrome less probable; normal D-dimer does not exclude the possibility of AIMH. Biomarkers such as cardiac troponin I (cTi) and B-type natriuretic peptide (BNP) are of special importance while assessing myocardial stress [1, 5, 7, 8, 10]. High-clinical suspicion for AAD must be considered in all patients with sudden abdominal or chest pain, especially in high-risk populations with or without systemic hypoperfusion syndrome until proven otherwise (Fig. 6.2) [2, 7, 10, 11]. A fast diagnosis, risk stratification, and clinical decision making are mandatory to improve the outcome.

6.10 Multimodal Diagnostic Approach

6.10.1 Electrocardiogram

There is no specific electrocardiographic pattern for the diagnosis of an acute aortic syndrome. Usually nonspecific changes can be observed. Up to 40% of electrocardiograms (ECG) tend to be within normal limits [1, 12]. Around 35% of patients exhibit changes related to left ventricular (LV) hypertrophy, LV strain, or LV overload (Fig. 6.3). LV overload is a regular finding in patients presenting with aortic regurgitation. Less often, myocardial necrosis patterns, Q waves, and bundle branch blocks are seen in up to 5–10% [1, 6, 12]. ST and T wave changes were found in 34–47% of patients; most often ST changes were nonspecific. A smaller portion (around 15–20%) of these patients may exhibit ST depression and T wave inversion compatible with acute ischemia. ST elevation, an uncommon finding, was observed in about 5–8% of all ECGs [8, 9, 12]. This finding is of extreme importance because it should prompt the clinician to rule out acute myocardial infarction as a differential diagnosis and take into consideration that right coronary artery involvement is a possibility, especially in proximal type A dissections. If the coexistence of MI and ADD is confirmed, antiplatelet, anticoagulant, and thrombolytic agents must be avoided because they increase the risk of fatal bleeding boosting in-hospital mortality to numbers more than 70% [9].

6.10.2 Laboratory Tests

Lab testing is usually complimentary since no test offers robust evidence to diagnose an acute aortic syndrome properly. Its usefulness comes in the detection of alternate differential diagnosis. Excluding D-dimer, biomarker and blood analysis

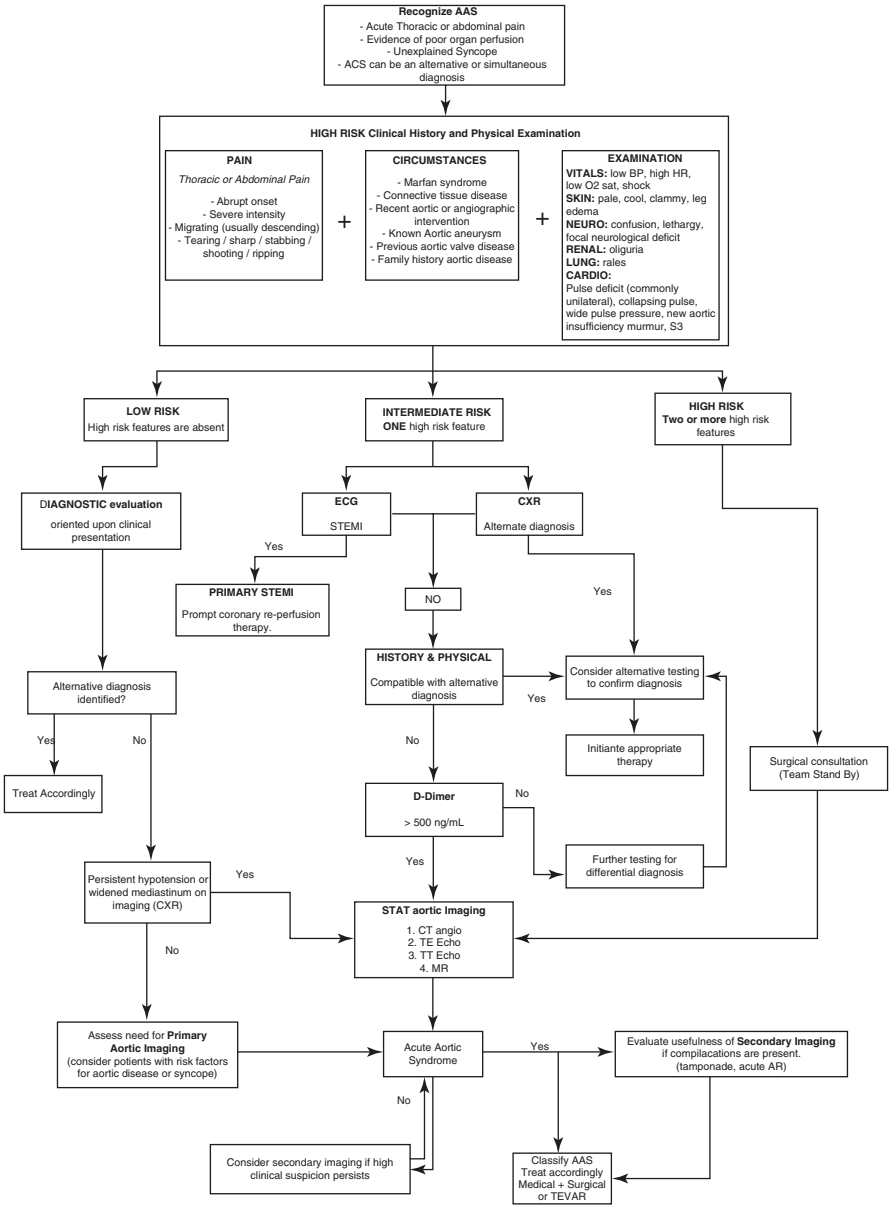

Fig. 6.2 Quick decision ER flowchart. STEMI, ST myocardial infarction. ECG electrocardiogram, CXR chest X-ray, TE echo transesophageal echocardiogram, TT echo transthoracic echocardiogram, MR magnetic resonance, AR aortic regurgitation

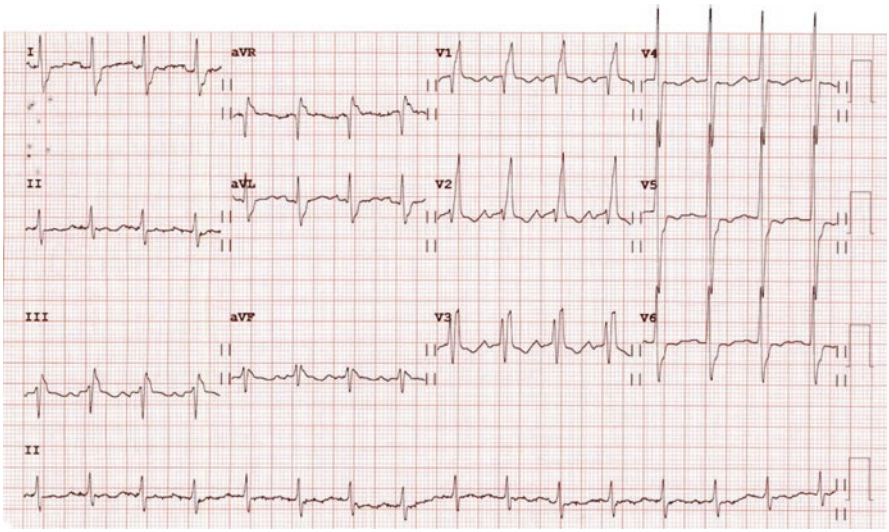

Fig. 6.3 ER ECG of a patient with aortic dissection and acute aortic regurgitation. The ECG shows sinus tachycardia, right bundle branch block and inferior subepicardial ischemia

lack sensitivity and specificity to accurately rule in or rule out AAS. BNP and cTi are adding information about myocardium response to an AAD. In the ER environment, lab results offer clues about blood loss, procoagulant activity, and end-organ damage.

6.10.3 Complete Blood Count

The complete blood count (CBC) is particularly useful for the assessment of dynamic changes in the total red blood cell and platelet count, even though the frequency in which changes are manifested in the CBC has not yet been defined. The detection of thrombocytopenia is an indirect indicator of bleeding which reflects platelet consumption and can be observed in the presence of ADD or large AIMH. Other indicators of hemorrhage are decreased hemoglobin, hematocrit, or a low red blood cell count.

6.10.4 Blood Chemistry

Several other biomarkers can be used as indicators of AAS severity beside CBC for blood loss. Low organ perfusion and ischemia can be inferred in the presence of high serum lactate, creatinine, and transaminase elevations [1].

6.10.4.1 C-Reactive Protein and Procalcitonin

C-reactive protein and white blood cell elevation suggest an inflammatory response. Even so, C-reactive protein and white blood cell tend to be elevated; both are not specific for AAS diagnosis. AAS differentials rarely involve infectious etiologies. Nonetheless, the measurement of procalcitonin and infection-related antibodies or biomarkers can assist clinicians in the differentiation of infection from inflammatory response.

6.10.4.2 Cardiac Troponin I or T

Traditionally myocardial infarction is a differential diagnosis of AAS, but according to the International Registry of Acute Aortic Dissections, up to 7% of acute AAD present with accompanying myocardial infarction. Troponin will always be useful in the context of acute chest pain and differential diagnostic considerations of ACS.

Physicians should invariably acknowledge troponin expression as myocardial ischemia consistent with an AC, particularly in the setting of acute chest pain and/or ST-T wave abnormalities presenting in a patient with cardiovascular risk factors. Current evidence suggests that cardiac troponin elevation can be present in patients with the AD and concomitant myocardial infarction or in patients with aortic regurgitation presenting with pressure/volume overload and hemodynamic stress.

In the ER, cardiac troponins rule out many non-cardiac causes of acute chest pain, but ultimately may not be such a powerful discriminator between AAD and myocardial infarction. High-clinical suspicion is key to quickly identify patients with synchronous AAD and differentiate them from MI. Bear in mind that this binomial condition is of high mortality. Several studies such as an ECG and coronary CT angiogram can aid in the diagnosis, without delaying proper treatment (which is often surgical for type A AAD and endovascular for type B AD). This spike in mortality is often iatrogenic and precipitated by inappropriate administration of anticoagulant and antiplatelet medications before the AAD is adverted. Standard cTi and high-sensitivity cTi expression (up to 25% of patients) have been related to higher in-hospital mortality and longer ICU and hospital stays, as well as elevated creatinine levels and the need for catecholamine infusion therapy [4]. High-sensitivity cTT (found in more than 60% of patients) have shown a similar correlation regarding mortality [13].

Recently, from 6455 consecutive patients with acute chest pain admitted to the ER, 15 (0.23%) of whom had AAD diagnosed and biomarker data collected. AAD was confirmed on transthoracic esophageal echocardiogram and computed tomography. Patients with abnormal cTnI concentrations had a higher rate of mortality. In univariate analysis, elevated.

cTnI was an independent predictor of in-hospital mortality (relative risk 27.46, 95% confidence interval 1.20–629.31). No relationship between mortality and D-dimer, BNP, or the DeBakey classifications was identified. These findings suggest that cTnI may be a promising tool for rapid risk stratification of patients with AAD [14].

6.10.4.3 D-Dimer

D-dimer (DD) elevation is often observed in patients with AAS. A cutoff level of 500 ng/mL has been suggested in several studies [1, 8]. DD is a test that is notably useful within the first 6 hours of symptom onset [6]. DD levels above the 500 ng/mL threshold are known to have a sensitivity ranging amid 96–98% with a low specificity just around 40–60% [5, 15–17]. It is important to take into consideration that a normal DD does not exclude the possibility of an AAS, particularly for those patients with whom there is high-clinical suspicion or for those presenting with AIMH; the displayed values for DD levels tend to be within normal ranges (below 500 ng/mL).

Recently, we observed concentrations above the upper limit of the assay in all patients with AAD except one, who had localized intramural hematoma. As previously reported, a trend toward higher DD levels in patients who died was detected; however, no relationship with mortality was observed. The results confirm previous observations and suggest that testing for DD should become part of the initial screening of patients with the suspicion of AAD. A negative test result makes the presence of the disease unlikely [14].

6.10.4.4 B-Type Natriuretic Peptide

Frequently, an acute heart failure syndrome is a clinical complication of patients with proximal AAD; BNP could offer a secondary phenomenon biomarker to understand this complication better. Recent evidence linking BNP and AAD showed high plasma concentrations in patients with AAD (667 ± 703 pg/mL) or a chronic aneurysm (593 ± 964 pg/mL) compared with a control group [14].

Recently, BNP concentrations identified a subgroup with acute heart failure syndrome and preserved ejection fraction. BNP concentrations established severe ventricular dysfunction and adrenergic, renin-angiotensin-aldosterone systems and vasopressin activation in some patients, but not in others. Although abnormal BNP concentrations could be attributed to heart failure secondary to aortic valve disruption and/or acute ischemia, long-standing hypertension and subclinical heart failure has to be considered in some cases. Diagnosis of heart failure with preserved ejection fraction could be established through normal ejection fraction and elevated plasma BNP concentrations. Although BPN determination does not replace echocardiography in the diagnostic approach to AAD, adding a rapid plasma BNP assay could be useful for detecting early ventricular dysfunction stages when an echocardiogram is not available or the ejection fraction is normal. Although BNP values had no relationship with in-hospital mortality, these findings could be the first clinical evidence linking BNP and ejection fraction in AAD patients [14].

6.11 Imaging Modalities

Aortic imaging is the most reliable approach to the diagnosis of aortic pathology. Imaging techniques are not only used for the detection of aortic pathology but rather can be used for monitoring purposes as well. Imaging can diagnose disease in at-risk patients, or patients with known stable aortic diseases (like aneurysms) can benefit from repeated imaging and anatomical landmark measurement and comparison [3].

6.11.1 Chest X-Ray

The chest X-ray (CXR) is a broadly available imaging study. Its chief advantages are its speed and its cheap cost; nonetheless, it has a low diagnostic performance in the detection of aortic dissections. CXR's poor sensibility around 64% and specificity of 86% and high observer variability represent a diagnostic challenge while searching for aortic pathology [18]. A normal CXR may be observed up to 20–50% of patients, while a widened mediastinum is the most common finding in around 50–60% of patients [1, 6]. Other frequent findings in CXR of patients presenting with AAD are changes in the aortic contour, an enlarged aortic knob (double density), aortic silhouette dilation (due to hematoma, aneurysm or edema), and mass effects that usually displace contralaterally structures such as the trachea and esophagus [18] (Fig. 6.4).

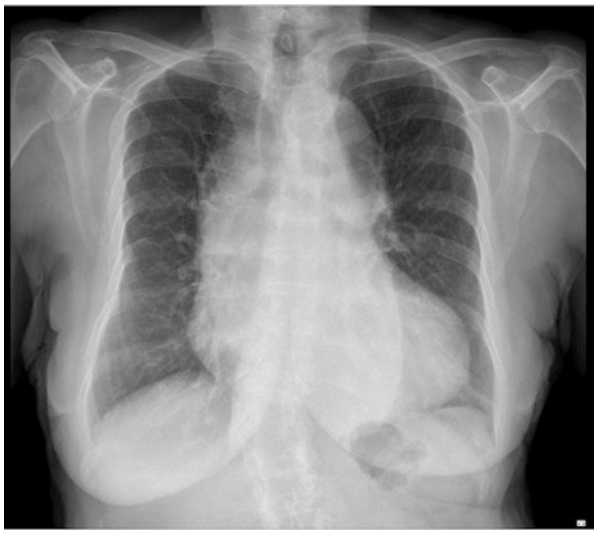

Fig. 6.4 Chest X-ray of a patient presenting with a dissected thoracic aneurysm. A widened mediastinum is observed. A prominent aorta and cardiomegaly are also distinctive features

6.11.2 Echocardiography

Ultrasonographic imaging comes in handy in the approach of a hemodynamically unstable patient inside the emergency room because it is quick, cheap, and mobile. These studies are safe, lack the added risk of radiation exposure, and can be performed bedside [1, 3]. A minor inconvenience is that both echo modalities are operator-dependent [9].

Transthoracic echocardiography (TTE) has a sensitivity which ranges around 77–100% for AAS type A AAD with a specificity of 93–96% and sensitivity around 31–55% for AAS type B AAD. Its usefulness comes to play as a quick screening tool for the detection of proximal (or type A) AAD [3, 7, 9]. TTE is particularly advantageous in the ER because it offers a fast approach to the patients' anatomy [1, 7]. TTE helps clinicians rule out multiple complications associated to AAD, principally the ones related to type A AAD, such as aortic root involvement, aortic regurgitation, pericardial effusion, pericardial tamponade, and abnormalities in wall motion [1, 2, 7].

Transesophageal echocardiography (TEE) has a higher sensitivity (88–99%) and specificity (80–100%) for unmasking aortic pathology, except the proximal aortic arch [1, 3, 9]. Even IMHs can be detected through the identification of wall thickening while in the absence of a false lumen and an intimal flap [3, 7]. The drawbacks of this imaging study are related to the need for proper sedation and that it cannot be carried out as fast as TTE (Figs. 6.5 and 6.6).

6.11.3 Computed Tomography

Emergency CT imaging usually is the first-line imaging option. Multidetector helical CT angiogram offers high sensitivity and specificity for the detection of AAD and AIMH, both nearing 100% [2, 3, 9]. It has the capability to rule out other

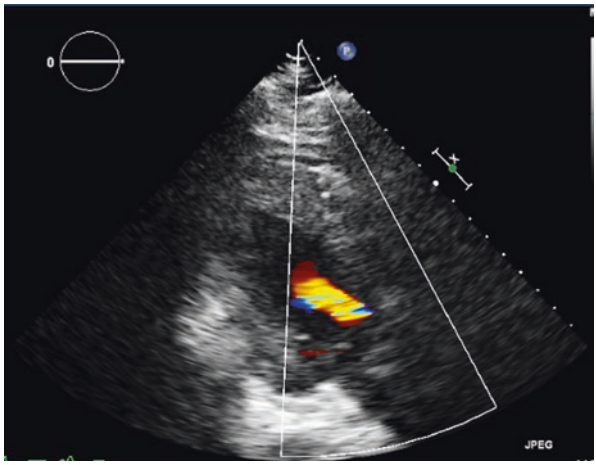

Fig. 6.5 Transthoracic echocardiogram is featuring aortic regurgitation in a patient with an acute aortic dissection

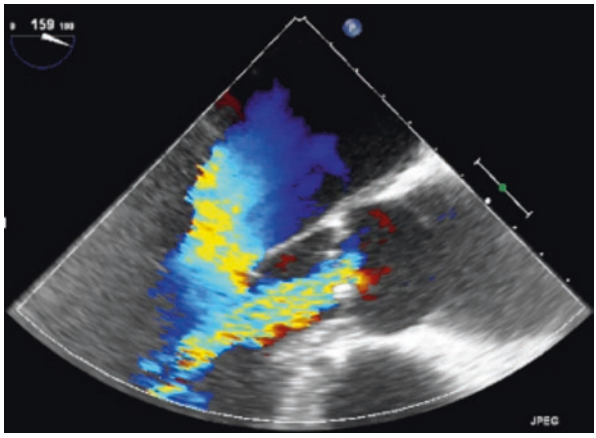

Fig. 6.6 Transesophageal echocardiogram is depicting aortic regurgitation in the same patient with an acute aortic dissection

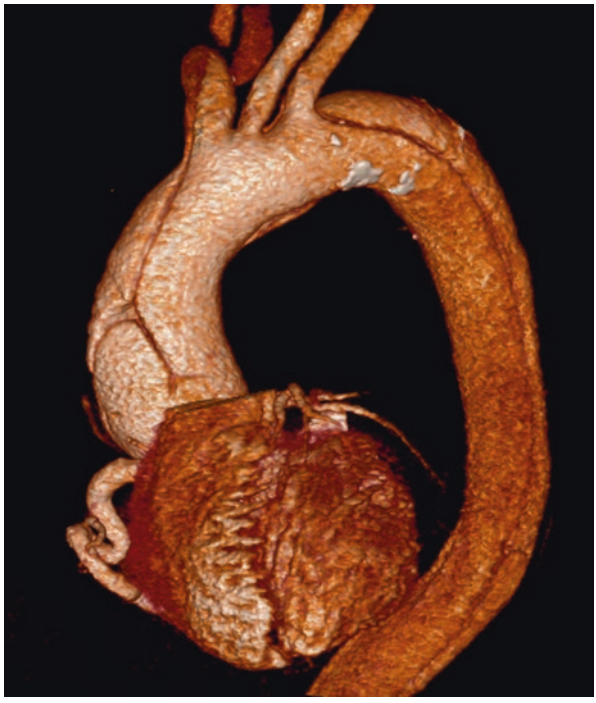

Fig. 6.7 CT angiography 3D reconstruction of a DeBakey type I dissection which starts at the aortic root and extends all the way through the ascending aorta, supra-aortic arch and supra-aortic vessels

differential diagnoses (such as lung or coronary pathologies) [1, 5, 7]. Images are acquired in a speedy fashion, which is ideal inside the ER environment or while evaluating unstable patients.

CT imaging offers high spatial resolution and isn't limited to a few windows nor by the patient's anatomical variants. Using this imaging study, CT technicians can display a 3D reconstruction that allows clinicians to better understand the patient's anatomical variants and disease burden (Figs. 6.7, 6.8, 6.9, 6.10, 6.11, and 6.12).

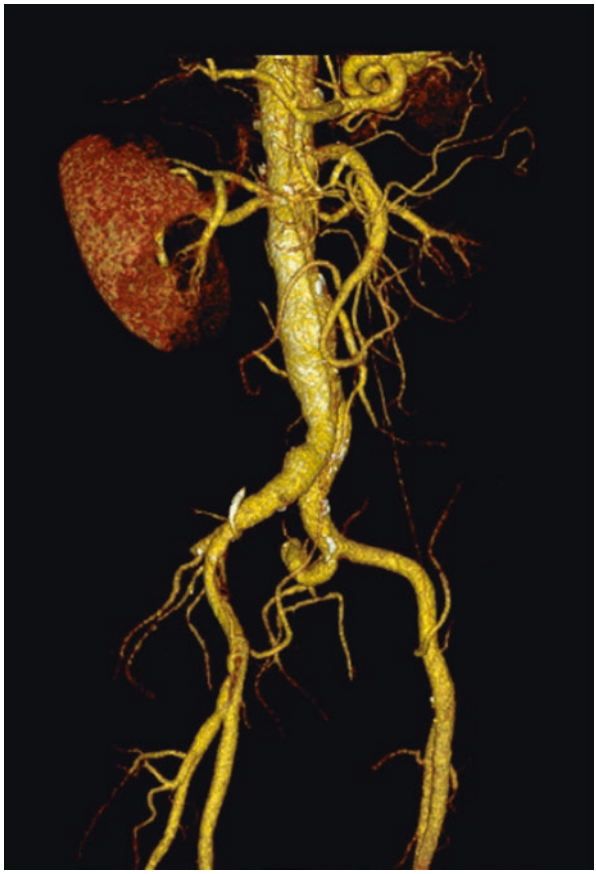

Fig. 6.8 CT angiography 3D reconstruction of a DeBakey type I dissection extending from the ascending aorta to both iliac arteries. During its trajectory along the abdominal aorta, the dissection tear excluded the left renal artery

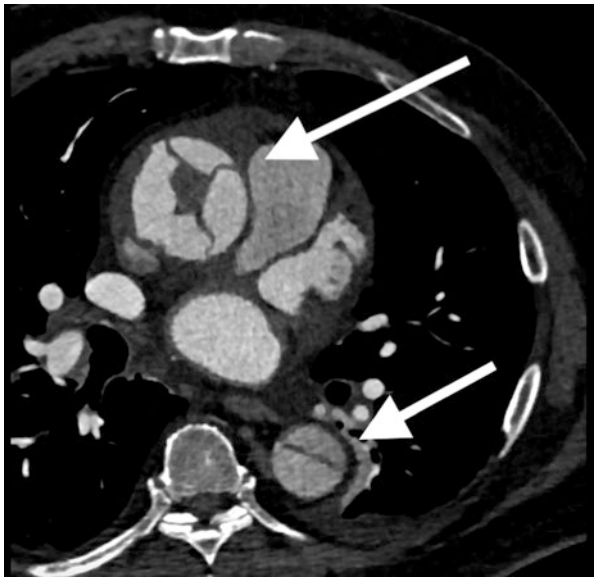

Fig. 6.9 CT angiography transverse projection of a patient with an acute aortic dissection. The tear can be seen in the thoracic ascending and descending aorta (arrows) along with its true and false lumens

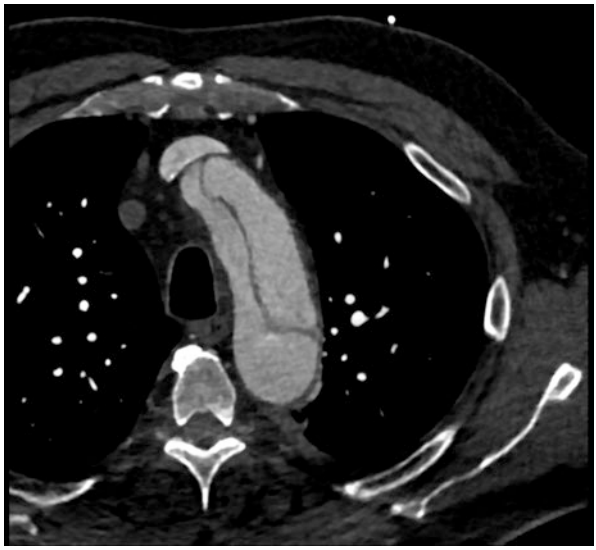

Fig. 6.10 CT angiography transverse projection of a patient with an acute aortic dissection. The arrow shows the tear extending along the aortic arch

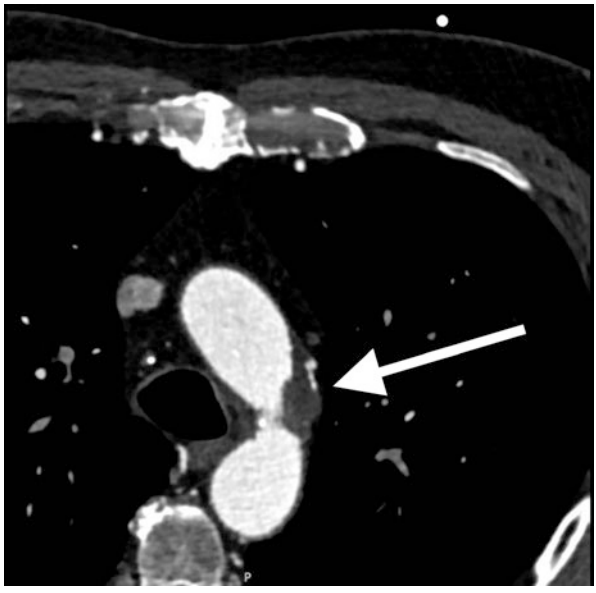

Fig. 6.11 CT angiography transverse cut in which an intramural hematoma is identified. A large hematoma (arrow) is seen at the aortic walls, along with some atherosclerotic plaque

CT scanning and image post-processing can also ascertain accurate measurements between anatomical landmarks. Computed tomography could characterize the aneurysmal aortic disease, the atherosclerotic burden, ulceration, intravascular thrombosis, the presence of flaps, dissection, calcification, or rupture. Anatomic areas of abnormal perfusion can be observed through irregular contrast distribution [2, 3] (Figs. 6.13 and 6.14).

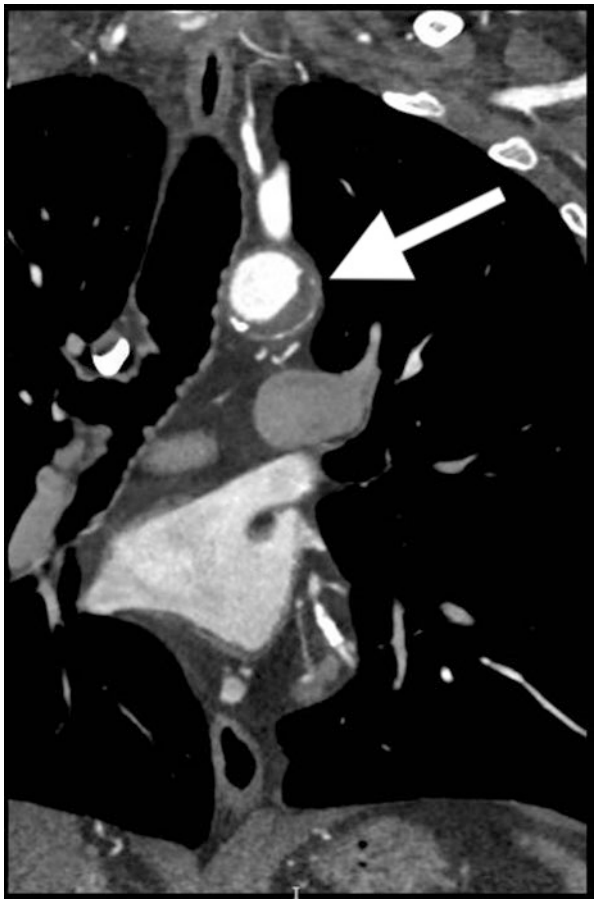

Fig. 6.12 CT angiography coronal projection of the same intramural hematoma

The downsides are that CTs are not readily available in many hospitals, they lack mobile capacities, patients are exposed to ionizing radiation (usually low doses), and to gain better imaging resolution, CT studies need IV contrast [1, 5, 7]. Iodinated contrast agents carry inherent risks such as allergic reaction and contrast nephropathy [1] (Figs. 6.15 and 6.16).

6.11.4 Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) is another highly sensitive and specific imaging procedure, both ranging between 98 and 100% [3, 7]. It shares similar advantages with CT angiography, like the ability to deliver unlimited windows, and it possesses a high spatial resolution. MRI is notably helpful in patients presenting with aortic regurgitation because it can accurately calculate regurgitating volumes,

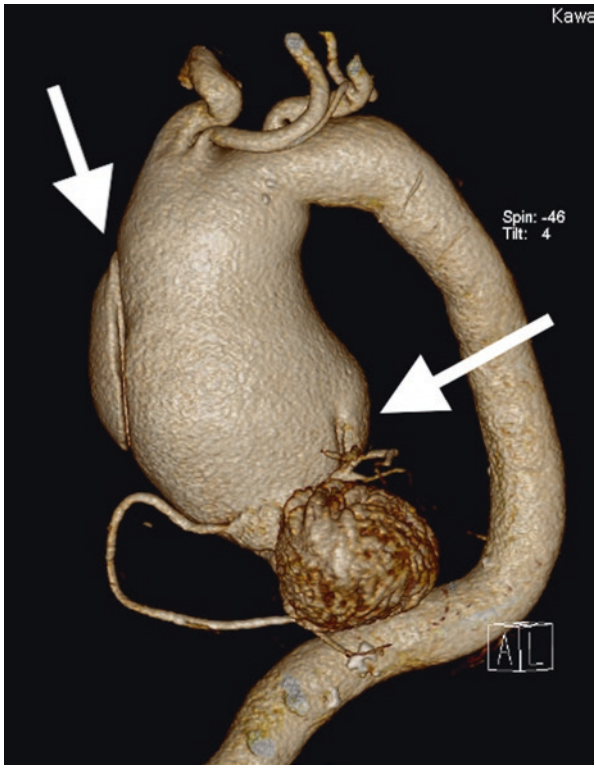

Fig. 6.13 CT angiography 3D reconstruction of an aortic aneurysm affecting the ascending aorta. An aneurysm presents a type I DeBakey Stanford A dissection with two tears (arrow)

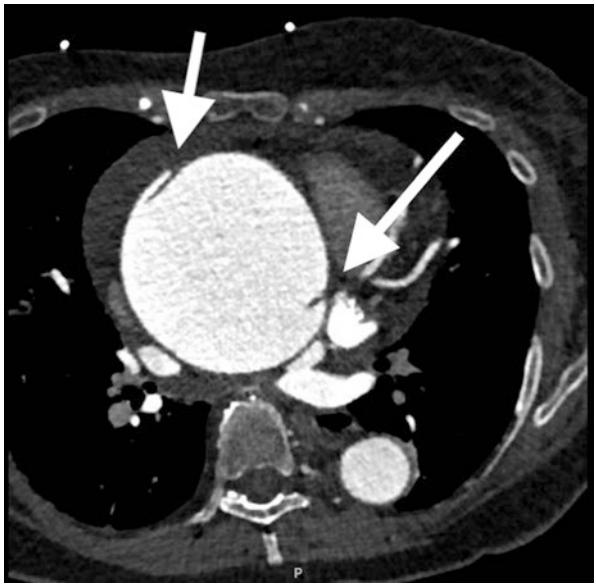

Fig. 6.14 CT angiography of the same patient presenting an aortic aneurysm with a type I DeBakey Stanford A dissection with two tears (arrows)

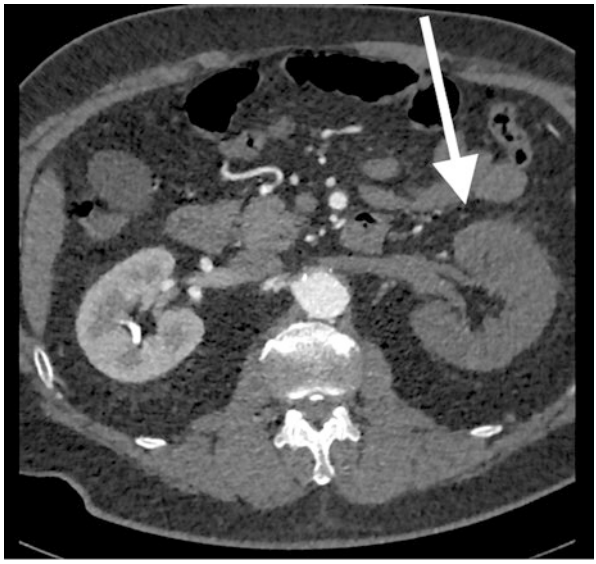

Fig. 6.15 CT angiography images showing two different reconstructions of a patient with an abdominal dissection tear. The left renal artery was adjacent to the false lumen. The lack of contrast in the left kidney is compatible with hypoperfusion

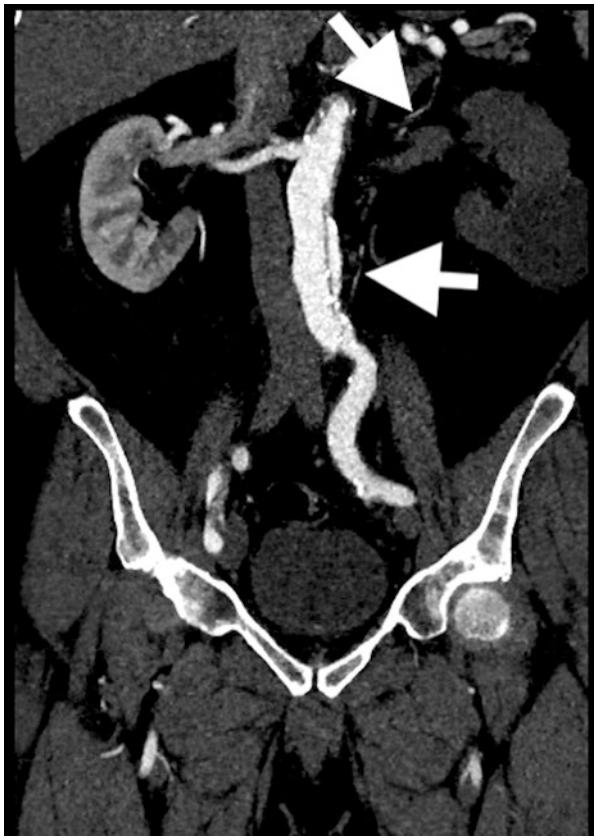

Fig. 6.16 CT angiography images showing two different reconstructions of a patient with an abdominal dissection tear. The left renal artery was adjacent to the false lumen. The lack of contrast in the left kidney is compatible with hypoperfusion

and normally no IV contrast is needed during the blood vessels evaluation. The reconstruction of 3D angiograms is also feasible using this imaging modality. An added benefit is that this imaging modality lacks the characteristic risk of radiation exposure [2].

The inconveniences it presents are its higher cost and poor availability; many hospitals are not equipped with MRI. Unstable patients are not the best candidates because the image-acquisition process tends to be time-consuming [1, 5, 7]. The prolonged duration of this process can be an issue with claustrophobic patients. Some other common contraindications are the presence of ferromagnetic implants, prosthesis, and pacemakers [3]. MRI falls short during the discrimination process of the coronary arteries and the aortic root; for these reasons it is the least used imaging study during emergencies. Information retrieved from the International Registry of Aortic Dissection reports a 1–5% usage in the ER setting, and normally patients who underwent MR imaging had a delayed diagnosis of AAD, fact that is related to increased mortality [3, 7]. Figures 6.17 and 6.18 show the MRI angiography of a patient with an acute dissection tear extending from the ascending to the descending aorta along with the aortic arch.

6.12 Treatment and Management

Aortic syndromes prompt strict blood pressure management. Normal blood pressure (BP) decreases aortic wall stress and lowers the possibility of wall rupture. Ideally, BP levels should be set below 110 mmHg systolic and 60 mmHg diastolic. The drugs of choice are intravenous beta-blockers (also helpful in patients with aortic regurgitation), and accepted choices are intravenous nitrates/vasodilators and oral calcium channel blockers. Intravenous beta-blockers (BB) not only help

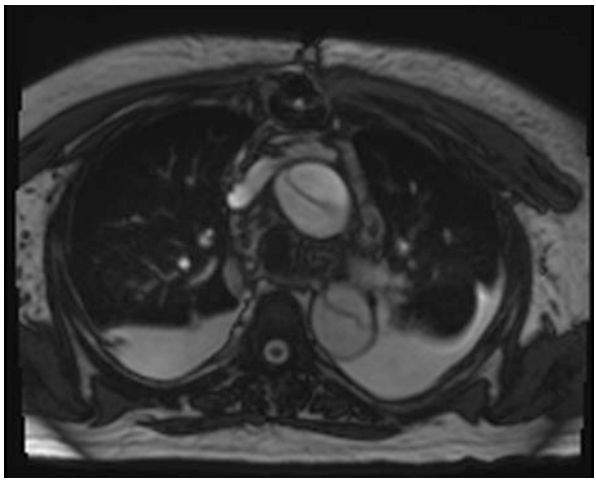

Fig. 6.17 MRI angiography of a patient with an acute dissection tear extending from the ascending to the descending aorta along with the aortic arch (arrow). Bilateral pleural effusions are observed. No contrast was needed for this MRI

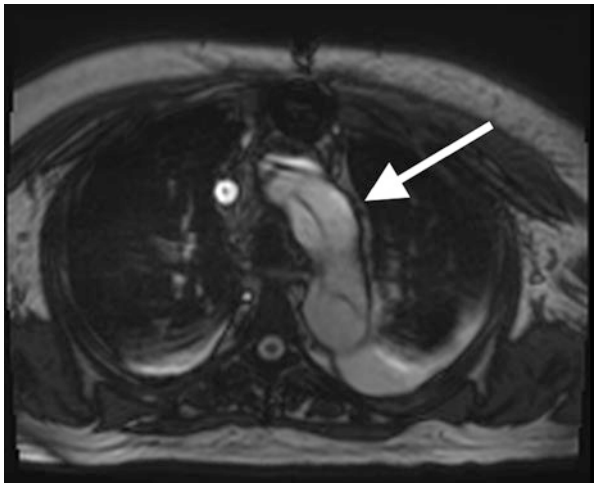

Fig. 6.18 MRI angiography of a patient with an acute dissection tear extending from the ascending to the descending aorta along with the aortic arch (arrow). Bilateral pleural effusions are observed. No contrast was needed for this MRI

lower BP, but they also offer heart rate control, which is also beneficial in lowering vascular wall stress. Usually, beta-blocking therapy is titrated to an HR goal of 60 bpm or less. ACE inhibitors or ARBs might be added to medical treatment if BBs have been initiated and systolic BP remains above 120 mmHg. Vasodilating agents should not be initiated as a first-line agent to avoid reflex tachycardia [3]. Systolic BP should be maintained between 100 and 120 mmHg, so careful monitoring is key to success [1].

Pain control is very important; strong analgesics, usually opioids, are needed. Avoid nonsteroidal anti-inflammatory drugs due to their intrinsic antiplatelet activity. Unstable patients should be stabilized and treated in an as-needed basis, inotropic support, central IV lines, and blood transfusions. Management of AAS is often surgical. All type A dissections should undergo surgical correction. Surgical treatment has shown to reduce 1-month and long-term mortality in patients with type A AD. Several factors, such as low coronary perfusion, pericardial tamponade, and stroke, have a negative impact on mortality. Regarding aortic regurgitation, a surgical team must evaluate the feasibility for the repair or replacement of the aortic valve. Grafting can be needed if the dissection extends into the supra-aortic branches [1–3].

Type A AIMH and APAUs when complicated (pericardial effusion, aortic hematomas, rapidly growing lesions) are subject to urgent medical care [2].

Most uncomplicated type B dissections, intramural hematomas, and penetrating ulcers can be subject to endovascular aortic repair. Uncomplicated AAS are those in which circulatory shock and low perfusion are absent. Thoracic endovascular aortic repair has shown lower rates of aortic remodeling and lower mortality compared to patients receiving only medical therapy [7]. This device directs blood flow through the true lumen improving distal perfusion and promoting the thrombosis of the false lumen [2, 3].

Table 6.6 summarizes key clinical aspects for the evaluation and treatment of acute aortic syndromes.

Table 6.6 Quick evaluation guide

Describe chest pain	Intense, sharp or stabbing Sudden-onset Radiation to back or abdomen
Risk factors	Smoker, history of high blood pressure Abnormal phenotype (Marfan) Recent aortic valve or aortic manipulation
Physical examination	Wide pulse pressure (>60 mmHg) Abnormal pulse (collapsing) Absent pulse (unilateral) Aortic regurgitation murmur (new/not known)
Diagnostic testing	Chest X-Ray (wide mediastinum, calcified aortic knob) Electrocardiogram (ST-elevation myocardial infarction, Left ventricular hypertrophy/overload) D-dimer (>500 ng/mL) Troponin (1/4 patients are Tn positive)
CT angiogram	Quick and with high sensibility and especificity for acute aortic syndrome Establishes the classification and extension Helps evaluate the alternate diagnosis 1. Coronary artery disease 2. Lung/pleural pathology Affected adjacent organs
Treatment	Pain management Blood pressure and heart rate control
TTE	Consider if patient's vitals are unstable

TTE transthoracic echocardiogram

6.13 Additional Clinical Practice Takeaways

- Be highly suspicious of patients presenting to the ER with acute, stabbing, and severe thoracic pain.
- Particularly young males with an abnormal phenotype or older ones with long-standing high blood pressure who present with pain and difficult control high blood pressure in the ER setting.
- Coronary risk factors may be a common denominator, and usually ACS are ruled out, but still, severe pain persists.
- Due to its high diagnostic yield and fast imaging processing, consider expediting aortic imaging, especially if patients present with hemodynamical deterioration.
- AAS, including aortic dissection, penetrating aortic ulcer, and aortic intramural hematoma, are clinically indistinguishable one from another, and their cardinal manifestation is acute onset of severe chest pain.
- Specific groups of patients tend to be at high risk for aortic pathology (Marfan syndrome, smokers, hypertension, high-speed trauma, or deceleration).

- D-dimer levels below the 500 ng/mL threshold make the diagnosis of aortic syndrome less probable; D-dimer levels below the 500 ng/mL threshold make the diagnosis of aortic syndrome less probable.
- Normal D-dimer does not exclude the possibility of AIMH biomarkers such as cardiac troponin I.
- Biomarkers such as cardiac troponin I and B-type natriuretic peptide are of special importance while assessing myocardial stress.
- Transthoracic echocardiography has a sensitivity which ranges around 77–100% for AAS type A AAD with a specificity of 93–96% and sensitivity around 31–55% for AAS.
- Transesophageal echocardiography (TEE) has a higher sensitivity (88–99%) and specificity (80–100%) for unmasking aortic pathology, except for the proximal aortic arch.
- Multidetector helical CT angiogram offers high sensitivity and specificity for the detection of AAD and AIMH, both nearing 100%.

Acknowledgments Images are courtesy of Erasmo de la Peña-Almaguer, Head of Cardiovascular Imagen at Instituto de Cardiologia y Medicina Vascular, Tec Salud, Hospital Zambrano Hellion, Escuela de Medicina y Ciencias de la Salud, Tecnologico de Monterrey.

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Chapter 7
Cardiac Tamponade in the ER

Carlos Jerjes-Sánchez and Alejandro Trevino

7.1 The Scope of the Problem

Cardiac tamponade is a condition caused by several clinical conditions which can eventually lead to cardiovascular collapse as a final event. High-clinical suspicion is paramount in order to identify these patients and provide timely treatment. In current times, with percutaneous cardiovascular interventions becoming more readily available and with early discharges being emphasized, we may see more of these patients presenting to the emergency room (ER).

7.2 Prevalence

The prevalence of cardiac tamponade varies depending on the etiology and degree of pericardial effusion. Table 7.1 lists the main etiologies of cardiac tamponade and their prevalence. In a study including 322 patients with moderate to severe pericardial effusion, the prevalence of cardiac tamponade was of 37% [1]. An older study in patients undergoing pericardiocentesis documented cardiac tamponade in 48% of the cohort; however, the sample size was small [2]. Although it varies through studies, the most common causes of an effusion resulting in tamponade are malignancy 26–44%, idiopathic 8–27%, iatrogenic 14–21%, and post-cardiac surgery 9–28%. During atrial fibrillation, a study with more than 5000 patients found an incidence close to 1%, being more frequent in patients who underwent ablation with radiofrequency when compared to cryoballoon [3].

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Table 7.1 Etiology of cardiac tamponade [1, 2, 4, 5]

Malignancy	26–44%
Acute idiopathic	8–27%
Iatrogenic effusion (post procedure)	14–21%
Post-cardiac surgery	9–28%
Acute myocardial infarction	4–10%
Uremia	4–12%
Connective tissue disease	4–12%
Viral	2–14%
Tuberculous/purulent	10–26%
Radiation induced	14%
Other causes trauma, aortic dissection, pneumopericardium, medications (anticoagulants, procainamide, hydralazine, isoniazid)	NA

Percentages from reference [2] include patients with tamponade; references [1, 4, 5] include patients who underwent pericardiocentesis with no specification about tamponade and causative etiology

7.3 High-Clinical Suspicion in the ER

There should be a high index of suspicion of cardiac tamponade in patients who have had a recent cardiac procedure, history of malignancy, chest trauma, or other clinical conditions (Table 7.1) and have elevated jugular venous pressure (JVP) on clinical examination. Suspicion should be even higher if they present with hypotension or borderline blood pressure measurements. A quick bedside echocardiogram in the ER can determine if further detailed testing is needed. If these patients are not identified promptly early on their presentation, they can decompensate quickly. We recommend early thoracentesis in the setting of atrial or ventricular collapse by echocardiography, even in the case of clinical stability patients with severe pericardial effusion.

7.4 Risk Factors

The likelihood of a pericardial effusion developing cardiac tamponade depends on several factors, for which understanding the underlying pathophysiology is of critical importance. In a normal heart, intrapericardial pressures (IPP) are lower than intracardiac pressures at baseline and have physiologic changes in response to intrathoracic and intracardiac pressures. The presence of greater than the normal fluid in the pericardial space increases the IPP, the extent to which it will do so depends on the pressure-volume relationship, which itself depends on the time frame in which

the fluid accumulated. In acute effusions resulting from cardiac injury, for example, the pericardial reserve volume is low, and small amount of fluid as low as 100–200 cc may increase IPP significantly.

In chronic effusions the pericardium has time to adapt and become more elastic, increasing the pericardial reserve volume and allowing a greater amount of fluid to accumulate before the IPP exceeds intracardiac pressures. Increased IPP results in underfilling of the right atrium, producing a decrease in ventricular dimensions and cardiac output. Progressive increases in IPP eventually lead to equalization of intrapericardial and intracardiac pressures, impairing cardiac output and resulting in cardiovascular collapse as a final event [6]. Cardiac tamponade has a progressive course which can be classified into several stages. Table 7.2 describes the events that occur in each of these four stages.

Some conditions causing pericardial effusion are more likely to evolve into cardiac tamponade than others. Table 7.3 compares conditions that are likely, less likely, and very unlikely to progress to pericardial effusion.

Table 7.2 Stages of cardiac tamponade [7, 8]

Stage	Hemodynamic/clinical effect
Preclinical	IPP equals right atrial pressure but is lower than
	left atrial pressure
	Normal JVP
	No hypotension or tachycardia
	Perfusion preserved
Initial tamponade/compensated	IPP equals left atrial pressure
	Pulsus paradoxus present <20 mmHg
	Elevated JVP
	No hypotension or tachycardia
	Mild RA, RV collapse
Moderate tamponade/compensatory mechanisms activated	IPP > 10–12 mmHg
	Elevated JVP >15 mmHg
	Signs of right chamber compression
	Tachycardia, dyspnea
	Prominent pulsus paradoxus
	Adequate perfusion
Advanced tamponade/decompensated	Sinus tachycardia and tachypnea
	JVP >20 mmHg
	Decreased stroke volume
	Hypotension with clear pulsus paradoxus
	Decreased perfusion

RA right atrium, *RV* right ventricle, *IPP* intrapericardial pressure, *JVP* jugular venous pressure

Table 7.3 Progression to cardiac tamponade based on etiology [7]

Likely to progress to pericardial effusion	Iatrogenic hemopericardium
	Postcardiotomy syndrome
	Neoplastic
	Infectious (tuberculosis, cytomegalovirus, human immunodeficiency virus, enteroviruses)
	Post-traumatic
	Renal
	Pericardial effusion from aortic dissection
	Pericardial effusion from myocardial rupture post-myocardial infarction
Less likely to progress to pericardial effusion	Autoimmune disease
	Autoreactive pericardial effusion
	Thyroid disorders
	Late/early pericarditis post-myocardial infarction
	Other etiologies (chylopericardium, cholesterol pericarditis)
Very unlikely to progress to pericardial effusion	Transudates in heart failure or pulmonary hypertension
	Transudates in last trimester of normal pregnancy

7.5 Clinical Presentation

7.5.1 Main Clinical Characteristics

- Dyspnea
- Tachypnea
- Syncope
- Tachycardia
- Hypotension
- Pulsus paradoxus
- Jugular venous distension
- Lung fields clear to auscultation
- Muffled heart sounds

7.5.2 Physical Exam

A physical exam is of great importance, given the diagnosis of cardiac tamponade is a clinical one, and imaging studies should be confirmatory. A systematic review calculated a pooled sensitivity for physical exam findings in cardiac tamponade: pulsus

paradoxus 82%, tachycardia 77%, hypotension 26%, diminished heart sounds 28%, and JVD 76% [9].

In cardiac tamponade, inspiration results in an increased filling of the right atrium and ventricle, producing septal shifting toward the left ventricle (LV) and decreasing its filling. These changes result in a decreased cardiac output, producing a drop of systolic blood pressure during inspiration manifested as pulsus paradoxus. Pulsus paradoxus is usually measured with a sphygmomanometer by inflating the brachial cuff above the systolic pressure and deflating it slowly. A note is taken when the first Korotkoff sound is heard, and as the cuff continues to deflate, the Korotkoff sounds will only be present during expiration initially; careful attention must be paid to when the Korotkoff sounds are heard both during inspiration and expiration, marking the second and final measurement.

Pulsus paradoxus is present when the difference between the first and second measurements is greater than 10 mmHg. A physiologic measurement should produce a difference of less than 6 mmHg. A value greater than 10 mmHg has a sensitivity of 98% and a specificity of 70%; if the cutoff is increased to 12 mmHg, the specificity increases to 83% [9]. Pulsus paradoxus can also be present in different pathologies listed in Table 7.4. The absence of pulsus paradoxus in the presence of cardiac tamponade may be due to several cardiac conditions in which the intracardiac pressure and flows are modified. These conditions include left ventricular (LV) or right ventricular (RV) dysfunction, LV hypertrophy, aortic regurgitation, atrial septal defect, extreme hypotension, local cardiac adhesions, and acute LV myocardial infarction [10, 11].

The acute cardiac compression triad, also known as Becks triad, consists in hypotension, JVD, and diminished heart sounds. While it is frequently mentioned when entertaining a diagnosis of cardiac tamponade, clinicians must be aware that the population initially studied included surgical patients with intrapericardial hemorrhage from cardiac trauma, myocardial rupture from myocardial infarction, and aortic or coronary rupture [12]. Medical patients commonly present with a slower accumulating effusion evolving into cardiac tamponade, in which the absence of Becks triad should not rule out the diagnosis [13].

Table 7.4 Other causes of pulsus paradoxus [10, 11]

Acute asthma
Chronic obstructive pulmonary disease exacerbation
Severe pericardial effusion
Hypovolemic shock
External cardiac compression Figure
Restrictive cardiomyopathy
Constrictive pericarditis
Tracheal compression
Tension pneumothorax
Compressive pleural effusions
Tricuspid atresia

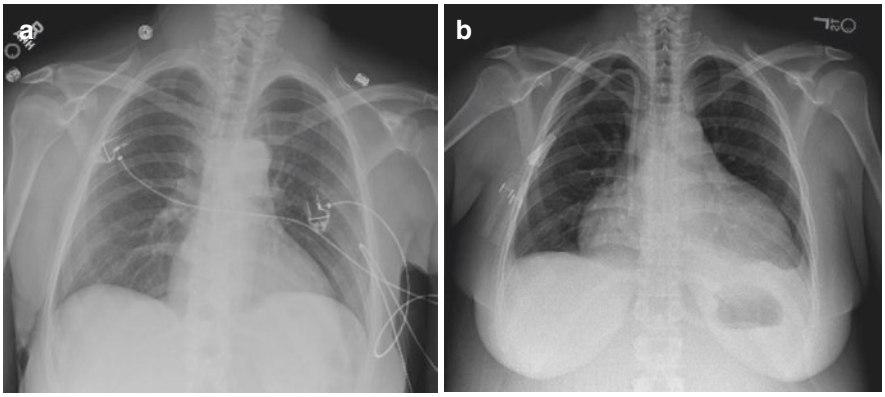

Fig. 7.1 (**a**) Baseline chest X-ray. (**b**) Chest X-ray 3 weeks after placement of dialysis catheter; notice the water bottle appearance

7.5.3 Chest X-ray

Chest X-ray can provide initial clues to the presence of a large pericardial effusion, but it is not diagnostic and does not provide information as to whether cardiac tamponade is present. Findings include an enlarged heart in a "water bottle" shape (Fig. 7.1) compared to previous (sensitivity 71%, specificity 41%), a pericardial fat stripe (sensitivity 12%, specificity 94%), and a predominant left-sided pleural effusion (sensitivity 20%, specificity 100%) [14]. A systematic review found a pooled sensitivity of 89% for cardiomegaly in the diagnosis of cardiac tamponade [9].

7.5.4 Electrocardiogram

The presence of low voltage in the ECG should raise suspicion for cardiac tamponade, as seen in a study where 61% of the patients with cardiac tamponade had low voltage but was not present in stable patients with large pericardial effusions [15]. However, other studies have shown lower sensitivities with low QRS voltage; a systematic review found a pooled sensitivity of only 42% [9].

7.5.4.1 Transthoracic Echocardiogram

The findings seen on echocardiography reflect the effects increased intrapericardial pressure has on intracardiac pressures (Fig. 7.2). They are summarized in Table 7.5.

Inferior vena cava dilatation measured during M mode greater than 2.1 cm with less 50% collapse in diameter with inspiration can be found in up to 92% of patients. The same study showed a sensitivity of 97% with a specificity of 40%, as it can

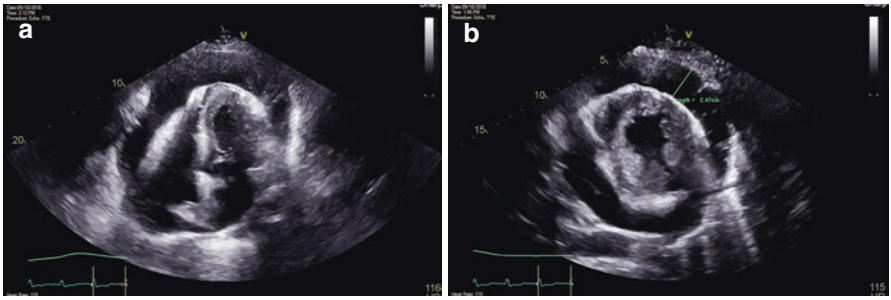

Fig. 7.2 2D echocardiogram showing a large pericardial effusion in (**a**) apical four chamber and (**b**) short axis

Table 7.5 Echocardiographic findings in cardiac tamponade

2D M-mode echocardiography	Inferior vena cava dilatation >2.1 cm with <50% collapse with inspiration
	Right atrium diastolic collapse
	Right ventricular diastolic collapse
	Increased right ventricular and decreased left ventricular dimensions with inspiration
	Septal bounce
	Swinging of the heart
Doppler	Decreased left ventricular outflow tract velocities and respiratory variation
	Decrease >30% of mitral peak E inflow velocity with inspiration
	Decrease >60% of tricuspid peak E inflow velocity with expiration
	Decrease in diastolic flow, in expiration absence of diastolic flow, diastolic flow reversal, or absence of forwarding flow
	Decrease >30% of mitral peak E inflow velocity with inspiration

be present in other conditions that increase systemic venous pressure [16]. On M mode, an increase in RV dimensions with a subsequent decrease in LV dimensions during inspiration can be observed [17].

Chamber collapse observed on 2D echocardiography is usually the result of the intrapericardial pressure being higher than the intracardiac pressure and lasts until the pressures are reversed again. Diastolic right atrial (RA) collapse is assessed in cardiac tamponade starting at the peak for the R wave. When the RA collapse lasts more than one-third of the cardiac cycle (right atrial time index >0.34; right atrial time index = # of frames with RA collapse/# of frames in duration of cardiac cycle) , it has a sensitivity of up to 94% and a specificity and positive predictive value of 100% [18, 19]. Another study showed a much lower sensitivity of 68%, a specificity of 66%, and a positive predictive value of 52% [20].

RV diastolic collapse (Fig. 7.3) is usually observed at the end of the T wave and is present when there has been a decrease of 20% in cardiac output without hypotension [21]. It can have a sensitivity of 92% and specificity and positive predictive value of 100% [22]. The severity of the cardiac tamponade is related to the length

of RV collapse during the cardiac cycle [23]. Another study showed a much lower sensitivity of 60%, specificity of 90%, and positive predictive value of 77%. The presence of collapse of both chambers had a sensitivity of 45%, specificity of 92%, and positive predictive value of 74% [20].

Hemodynamic changes to respiratory patterns can be observed in Doppler echocardiography. As a result of decreased cardiac output, there are decreased flow velocities through the left ventricular outflow tract, as well as a decrease in velocities with inspiration. Reflecting decreased LV filling, there is a decrease in mitral peak E inflow velocity during inspiration, with the lowest value being on the initial beat of inspiration (mitral peak E velocity is highest during expiration). A decrease in mitral peak E inflow velocity during inspiration of more than 30% is usually considered diagnostic (Fig. 7.4).

In the tricuspid valve, the exact opposite changes occur given the increased flow; with expiration there is a decrease of tricuspid peak E inflow velocity, with the lowest being the initial beat during expiration (tricuspid peak E velocity is highest during inspiration). A decrease in tricuspid peak E inflow velocity during expiration of

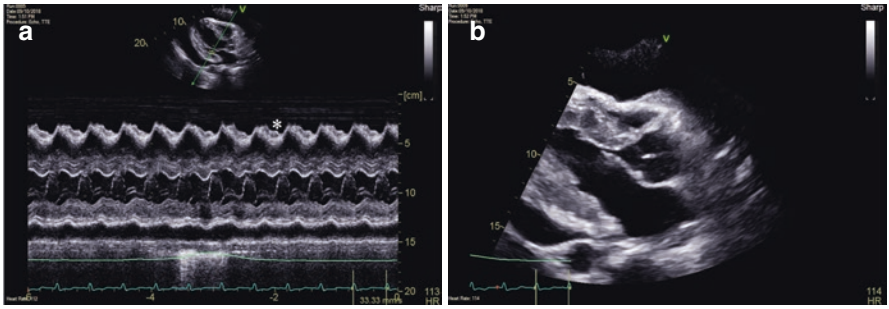

Fig. 7.3 (**a**) M mode is showing right ventricular diastolic collapse marked with an asterisk; notice the RV is nearly touching the interventricular septum during mitral valve opening. (**b**) 2D echocardiogram showing RV collapsed during diastole

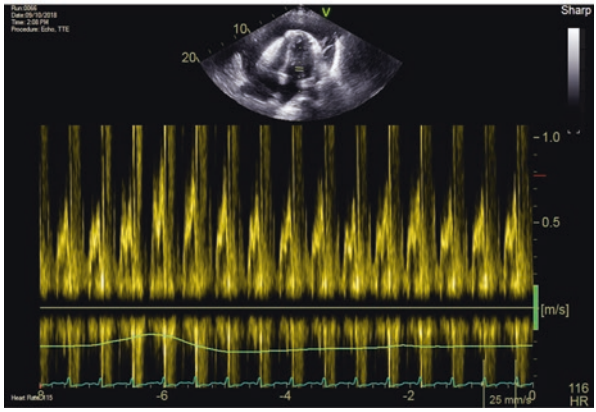

Fig. 7.4 Pulsed wave Doppler show there is a decrease in the mitral peak E inflow velocity during inspiration greater than 30% when compared to expiration

>60% (it will be a negative value) is suggestive of cardiac tamponade. Both values are calculated: (expiration-inspiration)/expiration. It is important to take into consideration that these findings by themselves do not confirm the diagnosis of cardiac tamponade and additional parameters need to be analyzed [19, 20, 24, 25].

Hepatic vein Doppler velocities also provide clues suggesting the presence of cardiac tamponade; velocities are lower in the 20–40 cm/s range. There is a predominance of systolic flow over diastolic flow; with expiration there can be the absence of diastolic flow, diastolic flow reversal, or no forward flow in advanced tamponade. The presence of hepatic flow changes has a sensitivity of 75%, specificity of 91%, and positive predictive value of 82% [19, 20, 26].

7.5.5 Computed Tomography

Computed tomography is not the initial diagnostic tool to evaluate pericardial tamponade. However it's a commonly performed test which can provide valuable information. Real-time cine cardiac CT can show similar findings as echocardiography, such as chamber collapse and septal bounce. Additionally, it can help delineate the anatomy in pericardiocentesis, identify loculated effusions, and assess the presence of compressive hematoma or calcified pericardium [27]. Findings on non-cardiac CT that can be seen in cardiac tamponade include increased diameter of the vena cava compared to the aorta and reflux of contrast into the inferior vena cava and hepatic veins [28]. However, these findings can be seen in pathologies that increase the right ventricular pressure and are not specific for cardiac tamponade.

7.5.6 Differential Diagnosis

During the initial presentation in the ER, the differential diagnosis can be wide; it includes conditions that increase right-sided pressures resulting in elevated JVP and may produce hypotension conditions which should include heart failure, pulmonary embolism, constrictive pericarditis, large pleural effusions impairing cardiac filling, mediastinal hematomas impairing cardiac filling, and advanced cirrhosis.

7.6 Treatment

7.6.1 Medical Management

If there is evidence of cardiac tamponade, medical management has a limited role in the treatment of cardiac tamponade. While a patient is awaiting pericardiocentesis, intravenous fluids are commonly given to expanding right-side chambers. However, there is

evidence that overhydration in these patients may be harmful. Fluid resuscitation with 250 ml up to 500 ml produced an increase in cardiac output, cardiac index, and systolic blood pressure; with higher intracardiac pressures, elevated heart rates, lower systolic blood pressure, and cardiac index as predictors of a >15% increase in CI as a response to fluid administration. After the 500 ml cutoff, pulmonary capillary wedge pressure, pulmonary pressure, right atrial pressure, and intrapericardial pressure continue to rise, decreasing cardiac output and resulting in pulmonary edema [29]. Therefore, if fluid administration is planned, it should be performed in a judicious manner.

7.6.2 Pericardiocentesis

The presence of pericardial effusion producing cardiac tamponade physiology usually warrants drainage of the pericardial effusion via pericardiocentesis or a surgical approach. Pericardiocentesis may be a better option in emergent cases, as it can be performed with fewer delays and can also be performed at bedside if needed. An exception is a hemopericardium secondary to myocardial rupture from myocardial infarction and secondary to type A aortic dissection, where pericardiocentesis should not delay surgical treatment. In these cases, there is a concern that performing pericardiocentesis can worsen the patient's condition by elevating blood pressure, worsening aortic tear, and increasing the gradient between the false lumen and pericardial effusion, thus increasing the size of the effusion [30]. However, in patients with type A aortic dissection, it has been shown that removal of a small amount of fluid (average fluid removal 40 cc) can help stabilize patients awaiting surgery [31]. In patients with cardiogenic shock, pericardiocentesis should be performed urgently. Patients with chest trauma, purulent pericarditis, loculated effusions, and iatrogenic effusions with uncontrollable bleeding should also generally be drained via a surgical approach. In stable patients with a diagnosis of cardiac tamponade, timing of drainage may be an element of the debate. There are scoring systems to help guide decision-making of when to perform pericardiocentesis. The European Society of Cardiology published a triage strategy to aid the timing of pericardiocentesis, where a score ≥ 6 warrants urgent pericardiocentesis and a score < 6 pericardiocentesis can be delayed for up to 12/48 hours (Fig. 7.5).

There are several approaches to perform pericardiocentesis, and the decision on which one to use should be made depending on the location of the effusion as seen on echocardiography or computed tomography. The three main approaches used are left apical, subxiphoid, and left parasternal. In general, it is recommended to perform pericardiocentesis guided by echocardiography, as it has been shown to be successful with a relatively low risk of complications [32]. Fluoroscopy has been used for many years to guide pericardiocentesis, with the subxiphoid approach being more common during this modality. It is commonly used when pericardial tamponade develops during cardiac procedures. Although not readily available in all hospitals, CT-guided pericardiocentesis can be a useful tool, especially when echocardiographic windows are suboptimal [33]. The technical aspects of pericardiocentesis are detailed in the procedures chapter.

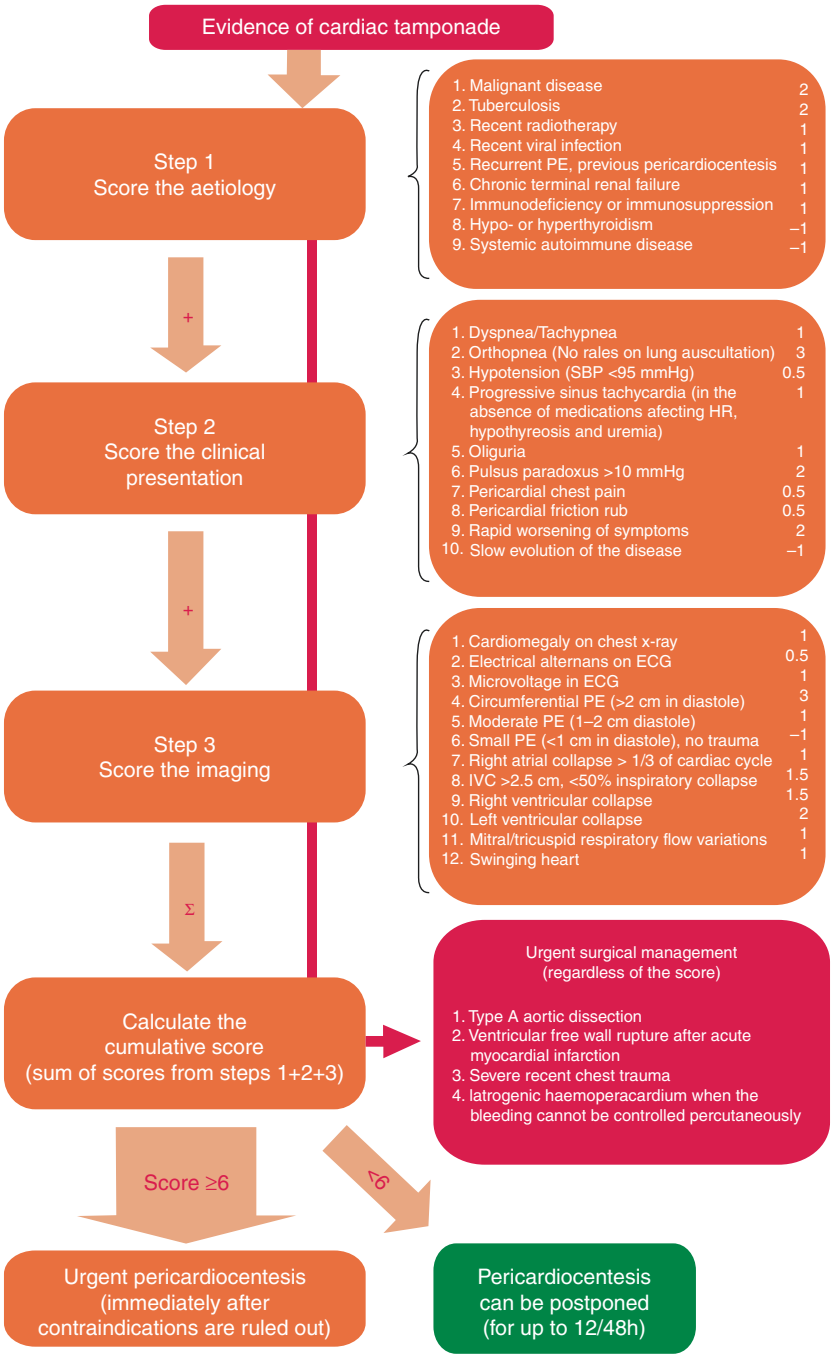

Fig. 7.5 Algorithm by the European Society of Cardiology to aid decision-making regarding the timing of pericardial drainage

Table 7.6 ESC recommendations for the diagnosis and treatment of cardiac tamponade [34]

Recommendations	COR	LOE
In a patient with clinical suspicion of cardiac tamponade, echocardiography is recommended as the first imaging technique to evaluate the size, location, and degree of hemodynamic impact of the pericardial effusion	I	C
Urgent pericardiocentesis or cardiac surgery is recommended to treat cardiac tamponade	I	C
Judicious clinical evaluation including echocardiographic findings is recommended to guide the timing of pericardiocentesis	I	C
A triage system may be considered to guide the timing of pericardiocentesis	IIb	C
Vasodilators and diuretics are not recommended in the presence of cardiac tamponade	III	C

ESC European Society of Cardiology, *COR* a class of recommendation; *LOE* level of evidence

Table 7.6 summarizes the most important recommendations on the diagnosis and treatment of cardiac tamponade, according to the ESC.

7.7 Additional Clinical Practice Takeaways

- The diagnosis of cardiac tamponade is a clinical one.
- The most common causes are malignancy, iatrogenic, and post-cardiac surgery.
- The presence of a pulsus paradoxus >10 mmHg is suggestive of cardiac tamponade.
- Echocardiographic finding suggestive of cardiac tamponade include dilated and not collapsible IVC, right chamber collapse, mitral peak E velocity during inspiration with a >30% decrease when compared to expiration, tricuspid peak E velocity during expiration with a >60% decrease when compared to inspiration, hepatic systolic flow reversal, septal flattening, and swinging of the heart.
- Pericardial drainage either by pericardiocentesis or surgical is generally the treatment; hemodynamic status and etiology guide the urgency of the procedure.

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Chapter 8
Cardiogenic Shock in the ER

Carlos Jerjes-Sánchez and Vicente Jimenez-Franco

8.1 The Scope of the Problem

Cardiogenic shock (CS) is a potentially lethal condition characterized by a low cardiac output state resulting in life-threatening end-organ hypoperfusion and hypoxia [1]. It is defined as a state in which ineffective cardiac output results in both clinical and biochemical manifestations of unsuccessful tissue perfusion (Fig. 8.1). CS shock is a high-acuity, potentially complex, and hemodynamically diverse state of end-organ hypoperfusion that is frequently associated with multisystem organ failure. Despite improving survival in recent years, patient morbidity and mortality remain high, and there are few evidence-based therapeutic interventions known to clearly improve patient outcomes. Acute myocardial infarction (MI) with left ventricular (LV) dysfunction remains the most frequent cause of CS [2].

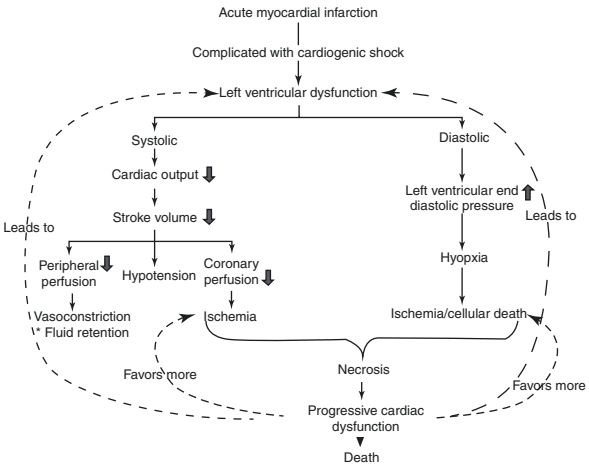

Fig. 8.1 Pathophysiology of the cardiogenic shock cascade

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Further efforts to reduce CS mortality have been directed toward improvements in mechanical circulatory support (MCS) devices. The largest randomized trial in patients with acute MI complicated by CS did not show a benefit with routine intra-aortic balloon pump (IABP) placement in addition to revascularization [2]. As a result, there has been a decrease in the use of IABPs in clinical practice and a downgrading in guideline recommendations. Recently, other percutaneous MCS devices have shown promise in the treatment of CS, but more data from randomized clinical trials are needed [2].

8.2 Prevalence

CS is the most common cause of death in patients with acute MI and has a frequency of 7–10%, translating to 40,000–50,000 of cases per year in the United States [1]. Short-term mortality in CS complicating MI is 40–60% and even more than 80% in case of ventricular septal rupture (VSR) [1]. Among patients with MI, the SHOCK trial registry reported that LV failure (78.5%) was the most common etiology of CS, followed by severe mitral regurgitation (MR) (6.9%), VSR (3.9%), right ventricular failure (2.8%), and cardiac tamponade (1.4%) [3]. Table 8.1 lists the causes of CS associated with AMI and others that are not.

8.3 Pathophysiology

The main physiopathogenic characteristic is a profound depression of myocardial contractility resulting in a potentially deleterious spiral of reduced cardiac output, low blood pressure, and further coronary ischemia, followed by additional

Table 8.1 Causes of cardiogenic shock

Associated with myocardial infarction	Unrelated to myocardial infarction
Acute coronary ischemia is directly impairing cardiac contractile function ±; additional causes listed below: Dynamic left ventricular outflow tract obstruction Acute dysrhythmia secondary to acute ischemia Acute ventricular septal defect Mitral valve papillary muscle rupture/ischemia Left ventricular free wall rupture Pericardial tamponade Type A dissection involving coronary arteries	Secondary severe left ventricular dysfunction Neurogenic "stunning" (e.g., subarachnoid hemorrhage, Takotsubo cardiomyopathy) Myocarditis Acute dysrhythmia secondary to chronic causes Hypertrophic cardiomyopathy with obstruction Decompensated dilated/restrictive cardiomyopathy End-stage valvular heart disease Cardiac contusion Myocardial dysfunction associated with prolonged cardiopulmonary bypass

CS cardiogenic shock

reductions in contractility (Fig. 8.1) [2]. This cycle may lead to death. This classic paradigm also includes compensatory, although pathological, systemic vasoconstriction that results from acute cardiac injury and ineffective stroke volume [2].

Currently, it is now well established that CS can result in both acute and subacute derangements to the entire circulatory system, including the peripheral vasculature [2]. Extremity and vital organ hypoperfusion remain a clinical hallmark. Although ineffective stroke volume is the inciting event, inadequate circulatory compensation may also contribute to shock [2].

Peripheral vasoconstriction may improve coronary and peripheral perfusion at the cost of increased afterload. Alternatively, systemic inflammation triggered by acute cardiac injury may induce pathological vasodilatation. Endothelial and inducible nitric oxide (NO) synthase may play a major role in the production of high NO levels, along with peroxynitrite, which has a negative inotropic effect and is cardiotoxic [2].

Other inflammatory mediators such as interleukins and tumor necrosis factor can also contribute to systemic vasodilation and have been associated with mortality in CS [2]. Also, bleeding and transfusions may be associated with mortality [2]. Alterations in erythrocyte NO biology of stored blood can lead to vasoconstriction, platelet aggregation, and ineffective oxygen delivery, whereas transfusion of stored blood may also contribute to inflammation [2]. Figure 8.1 shows the main pathophysiologic mechanisms in cardiogenic shock patients.

8.4 High-Clinical Suspicion in the ER

High-clinical suspicion for CS must be considered in all patients with (Table 8.1):

- Hypotension (systolic blood pressure <90 mm Hg or vasopressors required to achieve a blood pressure ≥90 mm Hg) [1]
- Signs of impaired organ perfusion as confusion or lack of alertness, loss of consciousness, oliguria, cold, clammy skin, and extremities, increased arterial lactate (>2 mmol/L) in the state of normovolemia or hypervolemia [1]

8.5 Patients at High Risk of CS

- Older age
- Female sex
- Prior MI or angina
- Type 2 diabetes
- Prior diagnosis of heart failure
- Anterior ST-elevation MI (ST-elevation MI)
- ST-elevation MI with new left bundle branch block (LBBB)
- Multivessel coronary artery disease (CAD)

Acute cardiac hemodynamic instability may result from disorders that impair the function of the myocardium, valves, conduction system, or pericardium, either in isolation or combination. CS is pragmatically defined as a state in which ineffective cardiac output caused by a primary cardiac disorder results in both clinical and biochemical manifestations of inadequate tissue perfusion [2].

The clinical presentation is typically characterized by persistent hypotension unresponsive to volume replacement and is accompanied by clinical features of end-organ hypoperfusion requiring intervention with pharmacological or mechanical support [2].

8.6 Evaluation

8.6.1 Clinical Signs of Cardiogenic Shock

- Cyanosis
- Rapid and/or faint pulses
- Jugular venous distention
- Cold extremities
- Pulmonary rales
- Respiratory distress
- Distant heart sounds
- Third and fourth heart sounds
- Decreased urine output
- Altered mental status

8.6.2 Cardiogenic Shock Definition

Although not mandated, objective hemodynamic parameters for CS can help confirm the diagnosis and enable comparison across cohorts and clinical trials [2]. Table 8.2 shows the definitions from the European Society of Cardiology clinical practice guidelines and operationalized definitions used in the SHOCK (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) and IABP-SHOCK II (Intraaortic Balloon Pump in Cardiogenic Shock II) trials [2].

Table 8.3 describes the four hemodynamic presentations of CS depending on clinical presentation, volume status, and peripheral circulation.

8.6.3 Laboratory

High-sensitivity cardiac troponins provide an idea of the extent of myocardial injury; serial measurements are useful in assessing early washout and in estimating the amount of cardiac necrosis. B-type natriuretic peptide rise is associated with

Table 8.2 Cardiogenic shock definitions from ESC and clinical trials

European Society of Cardiology HF guidelines	SBP <90 mm Hg with adequate volume and clinical *or* laboratory signs of hypoperfusion *Clinical hypoperfusion:* Cold extremities, oliguria, mental confusion, dizziness, narrow pulse pressure *Laboratory hypoperfusion:* Metabolic acidosis, elevated serum lactate, elevated serum creatinine
SHOCK trial (MI complicated by predominantly LV dysfunction)	SBP <90 mm Hg for ≥30 min *or* support to maintain SBP ≥90 mm Hg, *and* end-organ hypoperfusion (urine output <30 mL/h or cool extremities) *Hemodynamic criteria:* Cardiac index of ≤2.2 l L/min^{-1}/m^2 *and* pulmonary capillary wedge pressure ≥15 mm Hg
IABP-SHOCK II trial (acute myocardial infarction)	SBP <90 mm Hg for ≥30 min *or* catecholamines to maintain SBP >90 mm Hg and clinical pulmonary congestion *and* impaired end-organ perfusion (altered mental status, cold/clammy skin *and* extremities, urine output <30 mL/h, or lactate >2.0 mmol/L)

SBP systolic blood pressure

acute heart failure progressing to CS and mortality [6]. B-type natriuretic peptide measurements >600 pg/dL increase the high-clinical suspicion in hypotension and systemic hypoperfusion patients.

Elevated lactic acid levels are indicative of tissue hypoxia and associated with mortality in the context of CS. Peripheral oxygen demand-delivery mismatch will result in low central venous oxygen measurements [2]. Creatinine elevation and reduction in urinary output indicate acute kidney injury secondary to renal hypoperfusion. Acute ischemic or congestive liver can occur and manifests as an elevation in serum aspartate aminotransferase, alanine aminotransferase, serum bilirubin, and lactate dehydrogenase levels and sometimes accompanied by an increase in prothrombin time with a peak at 24–72 h [2].

8.6.4 Noninvasive Testing

- *Chest X-ray*: provides information on cardiac size and pulmonary congestion and also may suggest alternative pathogeneses such as aortic dissection, pericardial effusion, pneumothorax, esophageal perforation, or pulmonary embolism.
- *12-lead ECG*: diagnostic in patients with STEMI but can provide evidence for other clinical conditions, including non-ST-elevation MI (NSTEMI), pulmonary embolism, myocarditis, electrolyte imbalances, and drug toxicity.
- *Transthoracic echocardiogram*: can provide additional hemodynamic information, as hypovolemia state (right ventricle collapsed), left ventricular global hypokinesis, or akinesia, exclude mechanical complications, and help drive therapeutic decisions. When images are inadequate, a transesophageal echocardiogram should be considered.

Table 8.3 Cardiogenic shock phenotypes, hemodynamics, and practice essentials

Phenotype	Hemodynamics
Cold and dry	Cardiac index low SVR high PCWP constant
Practice essentials This phenotype has a mortality of 28% Patient with clinical history of diuretic-responsive chronic heart failure with apparent acute decompensation Patients typically present with cold sweated extremities, frequently with poor capillary refill, don't report dyspnea and have a clear lung CXR	
Cold and wet	Cardiac index <1.8 to 2.2 L-min^{-1} SVR variable, typically high PCWP high
Practice essentials Most common form of cardiogenic shock with a mortality of 51% presents in two-thirds of cases with low cardiac output and high filling pressures which cannot be fixed with volume If the patient is initially given diuretic, the preload will inevitably decrease, in so lowering the afferent renal artery perfusion and triggering a vascular response that increases afterload that leads to worsening heart failure, and if fluid is administered to correct the error, then FP increases, exacerbating the pulmonary edema	
Warm and wet	Cardiac index low Systemic vascular resistance low Pulmonary capillary wedge pressure high
Practice essentials The most common form of acute decompensated heart failure or de novo acute heart failure This subtype represents a patient who is adequately perfused and, however, does present with signs of congestion such as orthopnea/paroxysmal nocturnal dyspnea, jugular venous dilatation, congested hepatomegaly, and hepato-jugular reflux This phenotype is cytokine mediated (possibly due to ischemic tissue damage) mimicking septic shock due to consistencies in vasodilation, shock, reduced systolic heart failure, and systemic inflammation [4] Two variations exist, the vascular variation, where hypertension predominates, and the cardiac variation, where congestion predominates [5]	
Warm and dry	Cardiac index high Sistemic vascular resistance low Pulmonary capillar wedge pressure low
Practice essentials With a mortality of <3%, patient presents with no hypoperfusion or congestion This represents a shock phenotype that is not cardiogenic in origin [5]	

8.7 Treatment

8.7.1 Initial Stabilization

CS is a medical emergency and requires urgent evaluation and management. Understanding the underlying pathology will allow directed strategies to the cause.

Circulatory collapse should be treated with the following measures:

- Establish large bore peripheral intravenous (IV) access.
- Correction of bradyarrhythmia or tachyarrhythmia (may be contributing to hypotension): temporary pacing and atropine/direct current cardioversion.
- Insert a peripheral arterial line, central venous catheter and urinary catheter.
- Consider invasive hemodynamic monitoring of left heart filling pressures with a Swan-Ganz catheter for assessment of (central venous pressure) CVP and PCWP:
  - PCWP <15 mm Hg infuse 100–200 ml boluses of IV fluid to optimize left ventricular filling pressures; if signs or hemodynamic monitoring indicate low precharge [7]
  - If PCWP >15 mm Hg do not infuse IV fluid, offloading with diuretics in conjunction with inotropes [7]

8.7.2 Cardiac Support with Inotropes

Inotropic agents enhance cardiac output and vascular tone in short to medium term in patients with CS. However, all of these agents increase oxygen demand, propensity to ventricular arrhythmia, and the extension of the infarct area [6].

In case of evidence of predominant low cardiac output and preserved perfusion pressure, dobutamine is the initial therapy, starting at a dose of 2.5 μg/kg/min to restore stroke volume.

Other inotropes useful in this context are levosimendan and milrinone [2]. A vasopressor agent like norepinephrine or dopamine may be required to improve hemodynamics and limit important side effects (hypotension) compared with each agent. Table 8.4 highlights the dose for available pharmacological agents and their respective affinity for adrenergic receptors.

8.7.3 Mechanical Ventilation

Most CS patients have moderate or severe respiratory distress, so noninvasive or invasive mechanical ventilation is mandatory.

8.8 Identifying the Cause of Cardiogenic Shock

After hemodynamic resuscitation and stabilization of a patient presenting with CS, identification of the underlying cause can permit the initiation of specific pharmacological or mechanical therapies.

Table 8.4 Treatment dosage, hemodynamic effect, and mechanism of action of medication in CS

Medication	Infusion dose	Hemodynamic effect	Receptor binding
Vasopressors/inotropes			
Dopamine	0.5–2 μg/kg/min	CO ↑	Dopamine +++
	5–10 μg/kg/min	CO↑↑, SVR↑	$ß_1$ +++, dopamine ++, $α_1$ +, $ß_2$ +
	10–20 μg/kg/min	CO↑, SVR↑↑	$α_1$ +++, $ß_1$ ++, dopamine ++
Norepinephrine	0.05–0.4 μg/kg/min	CO↑↑, SVR↑	$α_1$ ++++, $ß_1$ ++, $ß_2$ +
Epinephrine	0.01–0.5 μg/kg/min		$α_1$ ++++, $ß_1$ ++++, $ß_2$+++
Phenylephrine	0.1–10 μg/kg/min	SVR↑↑	$α_1$ +++
Vasopressin	0.02–0.04 U/min	SVR↑↑, PVR ⟷	V_1 receptors in vascular smooth muscle
Inodilators			
Dobutamine	2.5–20 μg/kg/min	CO↑↑, SVR↓, PVR↓	$ß_1$ ++++, $ß_2$ ++, $α_1$ +
Isoproterenol	2.0–20 μg/min		$ß_1$ ++++, $ß_2$ +++
Milrinone	0.125–0.75 μg/kg/min	CO↑, SVR↓, PVR↓	PD-3 inhibitor
Enoximone	2–10 μg/kg/min		
Levosimendan	0.05–0.2 μg/kg/min		Myofilament Ca^{2+} sensitizer, PD-3 inhibitor

CO cardiac output, *SVR* systemic vascular resistance, *PVR* pulmonary vascular resistance, *PD-3* phosphodiesterase-3

8.8.1 Myocardial Infarction

A contemporary registry has reported that as many as 81% of patients presenting with CS had an underlying ACS, often associated with a large degree of the at-risk myocardium. MI should be the focus of initial diagnostic testing, and this testing should include an ECG within 10 min of presentation, high-sensitivity cardiac troponins, and B-type natriuretic peptide; rapid echocardiography is required to exclude mechanical complications, including papillary muscle rupture, ventricular septal defect, or free wall rupture [2]. Mechanical reperfusion should be considered in MI patients without mechanical complications and pharmacological and mechanical support with later stratification in those with some mechanical complication [2].

8.8.2 Chronic Heart Failure

Chronic HF can present in an acutely decompensated state and may account for up to 30% of CS cases. These patients have often experienced a decline in disease stability or have poor adherence to guideline-based therapies that may trigger an acute worsening of their chronic disease [2]. However, the hemodynamic phenotype and neurohormonal milieu are often strikingly different in chronic heart failure patients [2] and often have profound upregulation of vasoconstrictor

substances such as angiotensin II, endothelin-1, and norepinephrine [2]. Most of these patients should be considered to pharmacologic and mechanical support that includes intra-aortic balloon pump, TandemHeart® Percutaneous Ventricular Assist Device (pVAD)™ system (Cardiac Assist, Inc.; Pittsburgh, PA), Impella (Abiomed, Danvers, MA), and extracorporeal membrane oxygenation, as a bridge to cardiac transplant.

8.9 Other Causes of Cardiogenic Shock

8.9.1 Myocarditis

If these common causes of CS are not consistent with the presentation, then less common causes should be considered [2]. In acute myocarditis, paradoxically, the sickest patients on presentation have the best odds of recovery, particularly in younger age groups [2]. However, myocarditis is not exclusive of young population, so physicians in charge should be considered this diagnosis in cardiogenic shock elderly patients. Survival may depend on rapid recognition of the clinical syndrome and early institution of aggressive hemodynamic support [2].

8.9.2 Takotsubo Syndrome

Stress-induced cardiomyopathy is increasingly recognized, and although it often presents with mild cardiovascular compromise, it has been associated with CS and may require MCS. Patients with stress-induced cardiomyopathy typically recover [2]. However, data from the RETAKO registry that included a total of 711 patients showed 81 (11.4%) developed CS. Male sex, QTc interval prolongation, lower left ventricular ejection fraction at admission, physical triggers, and presence of "a significant" left intraventricular pressure gradient were associated with CS (C index ¼ 0.85). In-hospital complication rates, including mortality, were significantly higher in patients with CS [8], suggesting that the rapid and complete recovery is a myth in Takotsubo syndrome patients complicated with CS.

Over a median follow-up of 284 days, CS was the strongest independent predictor of long-term, all-cause mortality, cardiovascular death, and non-cardiovascular death, whereas no significant difference in the recurrence rate was observed between groups. Among patients with CS, those who received beta-blockers at hospital discharge experienced lower 1-year mortality compared with those who did not receive a beta-blocker [8].

This new evidence suggests that CS is not an uncommon complication and is associated with worse short- and long-term prognosis in Takotsubo syndrome patients. Also, CS complicating Takotsubo syndrome may constitute a marker of

underlying disease severity and could identify a masked heart failure phenotype with increased vulnerability to catecholamine-mediated myocardial stunning [8].

8.9.3 Valvular Heart Disease, Thyroid Disorders, and Pregnancy

Advanced valvular heart disease and prosthetic dysfunction, especially when previously undetected or inadequately monitored, may present as CS, although this has become less common as echocardiographic techniques and surveillance have improved [2]. Thyroid disorders, both hyperthyroidism and hypothyroidism, can also cause circulatory collapse [2]. Pregnancy-associated cardiac conditions, including both peripartum cardiomyopathy and acute coronary dissection, may present as CS. Numerous additional causes of CS have been reported, but they typically occur in <1% of patients [2].

8.10 Mechanical Support

8.10.1 Intra-aortic Balloon Counterpulsation

IABP is the most widely available MCS device. It increases coronary blood flow during diastole and decreases the afterload by lowering the systemic vascular resistance during systole [9].

CS arising from MI is the most common reason for instituting IABP therapy. Clinical trials evaluating its benefit in mortality did not show a significant difference compared with controls.

Potential complications that must be taken into account are severe limb ischemia, bleeding, balloon leak, and infection [10].

The European Society of Cardiology (ESC) guidelines for ST-elevation myocardial infarction (STEMI) suggest the use of IABP in these patients with a class of recommendation (COR) IIb and a level of evidence (LOE) B. The American Heart Association (AHA) and the American College of Cardiologists (ACC) guidelines put forward the use of IABP in these patients with a COR IIa and a LOE B.

8.10.2 TandemHeart

- This device TandemHeart® Percutaneous Ventricular Assist Device (pVAD)™ system (Cardiac Assist, Inc.; Pittsburgh, PA) provides mechanical circulatory support of up to 4 L/min of blood with a continuous flow centrifugal pump. The

oxygenized blood is aspirated from the left atrium and injected into the lower abdominal aorta or iliac arteries via a femoral artery cannula [7].
- Potential complications are perforation of the left atrium, femoral artery dissection, hematoma, bleeding, limb ischemia, infection, coagulopathy, and stroke [1].
- The AHA/ACC guidelines for management of STEMI recommend the use of alternative ventricular assist devices for patients with refractory cardiogenic shock (COR IIb LOE C) [11].

8.10.3 Mechanical Support with the Impella Device

- Consists of a family of different axial flow pumps positioned across the aortic valve to provide active support by transvalvular left ventricular assistance, expelling aspirated blood from the left ventricle into the ascending aorta.
- Three versions are currently available: Impella CP, Impella 2.5, and Impella 5.0 (Abiomed, Danvers, MA) [9].
- The ESC guidelines for STEMI suggest the use of short-term mechanical support in patients with refractory CS (COR IIb LOE C) [12].
- The ESC guidelines for STEMI suggest the use of short-term mechanical support in patients with refractory CS (COR IIb LOE C) [12].

8.10.4 Extracorporeal membrane oxygenation (ECMO)

8.10.4.1 Venoarterial ECMO

- A modified heart-lung machine that consists of a centrifugal pump, a heat exchanger, and a membrane oxygenator.
- Venous desaturated blood is aspirated from the right atrium into a centrifugal pump through a cannula inserted into the atrium via the femoral vein.
- The pump outflow is directed into a membrane oxygenator and then is guided via an outflow cannula into the descending aorta via the femoral artery [7].
- ECMO can provide hemodynamic support reducing LV preload but also has deleterious effects increasing afterload, thereby increasing oxygen demand and impending myocardial protection [7].
- Complications include bleeding, limb ischemia, renal failure, and sepsis [1].

As above, the ESC guideline for STEMI suggests the use of short-term mechanical support in patients with refractory CS (COR IIb LOE C) [12]:

- Considering LV assist device for circulatory support in patients with refractory cardiogenic shock (IIb/C).
- ECMO implantation for temporary support in CS MI patients who continue to deteriorate due to inadequate circulatory support (expert consensus).

8.11 Additional Clinical Practice Takeaways

- A cardiogenic shock potentially lethal condition characterized by low cardiac output state resulting in life-threatening end-organ hypoperfusion and hypoxia.
- Myocardial infarction with left ventricular dysfunction is the most frequent cause of cardiogenic shock.
- Mortality in cardiogenic shock complicating myocardial infarction is 40–60% and even more than 80% in case of ventricular septal rupture.
- High-sensitivity cardiac troponins provide an idea of the extent of myocardial injury in MI patients.
- MI should be the focus of initial diagnostic testing in high-clinical suspicion CS patients.
- This testing should include an ECG within 10 min of presentation, high-sensitivity cardiac troponins, and B-type natriuretic peptide.
- Rapid echocardiography is required to exclude mechanical complications, including papillary muscle rupture, ventricular septal defect, or free wall rupture.
- B-type natriuretic peptide measurements >600 pg/dL increase the high-clinical suspicion in hypotension and systemic hypoperfusion patients.
- The hemodynamic phenotype and neurohormonal milieu are often strikingly in chronic heart failure patients.
- CS is not uncommon complication and is associated with worse short- and long-term prognosis in Takotsubo syndrome patients.
- Treatment is based on directed strategies to correct the underlying cause, meanwhile maintaining organ perfusion.
- The use of mechanical support in cardiogenic shock should be considered depending on the type, center expertise, and availability of the device.

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Chapter 9
Pulmonary Embolism in the ER

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9.1 Scope of the Problem

Pulmonary embolism (PE) is the third cause of cardiovascular mortality after myocardial infarction and stroke, the leading cause of pregnancy-related maternal death in developed countries and the second cause of mortality in cancer patients [1]. PE is the third most common cause of death in patients surviving the first 24 h after traumatic injury [2]. Unfortunately, PE diagnosis can be a challenge due to a broad clinical presentation. The significant morbidity and mortality associated with this condition warrants prompt and accurate diagnosis evaluation and optimal treatment. The right ventricular function and the clinical condition drive the risk stratification, treatment, and in-hospital prognosis [3].

9.2 Prevalence

The epidemiology of PE is uncertain because it may remain asymptomatic, or its diagnosis may be an incidental finding. Among 900,000 annual venous thromboembolism (VTE) events occurring in the United States, it is estimated that more than 250,000 are diagnosed with PE in the emergency room (ER) [4]. The incidence of VTE rises sharply after age 60 for both, male and female, and PE accounts for most of this increase [5]. Of the lethal cases, 34% presented with sudden fatal PE, and 59% were deaths resulting from PE that remained undiagnosed during life [6]. The growing epidemic of obesity is another important contributor to the increasing incidence of PE.

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9.3 Thrombosis Mechanisms

Venous thrombosis is included among thrombosis models of low-pressure segment circulation. Currently, multiple clinical and molecular lines of evidence suggest a close link between the coagulation system, inflammation, and immunothrombosis [1]. Current evidence establishes a relationship among atherothrombotic risk factors, venous thrombosis, and inflammation as a trigger of thrombosis events [1] (Table 9.1).

9.4 High-Clinical Suspicion in the ER

The relevance of categorizing a patient in a high-clinical suspicion level attempt to accurate testing and is based on at least one transitory or permanent risk factors (Table 9.2), clinical findings, and expertise (Fig. 9.1) (Table 9.3).

Table 9.1 Mechanisms of venous thrombosis

Initiation	The process of coagulation starts on intravascular tissue factor (ITF)-exposing cells and on the surface of activated platelets. In the beginning, ITF-exposing cells and microparticles are exposed to coagulation factors in the vessels lumen. Platelets activated by vascular injury are recruited and adhere to the site of injury. The ITF/FVIIa complex activates coagulation factors IX to IXa and X to Xa, generating trace amounts of thrombin
Amplification	The small amount of thrombin acts as a signal for further platelet activation and aggregation. On the surface of platelets, thrombin activates FV, FVIII, and FXI
Propagation	FVIIIa forms a complex with FIXa (Xase), and FVa forms a complex with FXa (prothrombinase) on the platelet surface, accelerating the generation of FXa and thrombin, respectively. When FXa is associated with FVa, it is protected from ITF pathway inhibitor and antithrombin. In the propagation phase, a burst of thrombin is generated, which is sufficient for the clotting of soluble fibrinogen into a fibrin meshwork.
Inflammation	Interleukin-6 induces the expression of intravascular tissue factor, fibrinogen, factor VIII, and von Willebrand factor. Interleukins-6 and -8 enhancements of cytokine and chemokine levels inducing endothelial activation, endothelial cell damage, increased platelet aggregation, increased sensitivity to thrombin, and recruitment and activation of leukocytes at the vascular wall. An increased interleukin-6 level lowers the concentration of antithrombin, protein S, and thrombomodulin
Immunothrombosis	Includes innate immune mechanisms, the neutrophil extracellular genetic traps (NETs), and the immunothrombosis dysregulation. The relationship among pathogen-associated molecular patterns or damage-associated molecular patterns, monocytes, and their microvesicles express and deliver activated intravascular tissue factor to sites of pathogen exposure, which initiates the extrinsic pathway of coagulation

Transitory risk factors separate provoked from unprovoked PE. The risk of PE increases in patients older than 40 years, with double risk each subsequent decade [6]. Atherosclerotic risk factors are frequently present in unprovoked PE outpatients. Possibly, chronic or acute infections triggering immunothrombosis and inflammation are the main mechanisms in unprovoked PE older outpatients [1].

9.5 Clinical Presentation

PE presents with rapid onset and ensuing precipitous decline. The capital symptom is dyspnea at rest or induced by exertion. Clinical and physical findings are highly variable, often depending on the presence of burden thrombus, pulmonary hypertension, right ventricular dysfunction (RVD), and previous cardiopulmonary state (Table 9.3). Transitory dyspnea or tachycardia is often the clinical expression in segmental or subsegmental PE patients. In some cases, near syncope or syncope is the

Table 9.2 Major risk factors for pulmonary embolism [1, 6, 7]

Odds ratios	Molecular bases
Odds ratios >10 Fracture of lower limb (previous 3 months) Hip or knee replacement Major trauma Myocardial infarction (within previous 3 months) Previous venous thromboembolism Spinal cord injury	*Inflammation* Smoking, obesity, dysglycemia, diabetes mellitus, metabolic syndrome, dyslipidemia, ischemic heart disease, acute coronary syndromes, stroke, peripheral artery disease, hypertension, COPD, acute or chronic heart failure, respiratory failure, atrial fibrillation, connective tissue diseases (systemic lupus erythematosus, rheumatoid arthritis, etc.) renal chronic failure, nephrotic syndrome, Behcet's disease, chemotherapy, active cancer
Odds ratios 2–9 Arthroscopic knee surgery Autoimmune diseases Blood transfusion Central venous lines Chemotherapy Congestive heart or respiratory failure Erythropoiesis-stimulating agents Hormone replacement therapy (depends on formulation) In vitro fertilization Cancer (highest risk in metastatic disease) Oral contraceptive therapy Paralytic stroke Postpartum period Thrombophilia	*Secondary thrombophilia* *Coagulation cascade and platelet activation* Fracture, hip or knee replacement, major or minor surgery, major trauma, spinal cord injury, arthroscopic knee surgery, fracture, hip or knee replacement, major or minor surgery, major trauma, spinal cord injury, arthroscopic knee surgery, and cesarean section

(continued)

Table 9.2 (continued)

Odds ratios	Molecular bases
Odds ratios <2 Bed rest >3 days Diabetes mellitus Hypertension Immobility due to sitting (e.g., prolonged car or air travel) Increasing age Laparoscopic surgery (e.g., cholecystectomy) Obesity Pregnancy Varicose veins	*Molecular thrombophilia* *Acquired* Lupus anticoagulant, antiphospholipid antibody syndrome, hyperhomocysteinemia (less commonly inherited secondary to a mutation in methylenetetrahydrofolate reductase), deficiency of dysfibrinogenemia, myeloproliferative disorders such as polycythemia rubra vera, elevated levels of lipoprotein (a) Hereditary Deficiency of antithrombin III, protein C or protein S, factor V Leiden mutation, prothrombin gene mutation, primary thrombocytopenia, hypercoagulability syndromes, deficit or abnormalities of plasminogen, dysplasminogenemia, hyperprothrombinemia, deficiency of factor XII, factor VIII increase, deficiency or abnormalities of plasminogen, increase plasminogen activator inhibitor type-1, paroxysmal nocturnal hemoglobinuria
	Miscellaneous mechanisms Hypercoagulable state: age >40 years, aging, pregnancy, postpartum, secondary polycythemia Therapeutic action: hormone replacement and oral contraceptive therapy, pacemaker or implantable cardiac defibrillator leads and indwelling venous catheters Heparin-induce thrombocytopenia
	Triggers *Stasis*: prolonged car or air travel, bed-bound, computer work, or immobility related to the home or nursing home: frail elder, convalescence secondary to chronic heart failure, pulmonary or neurological diseases, cancer, degenerative osteoarthropathy, obesity *Chronic or acute infections*: periodontitis, upper or lower respiratory tract, gastrointestinal, urinary, prostate, etc.

only clinical expression in elderly low-risk or submassive PE [8]. Also, physicians should be in warning in unexplained acute exacerbation of COPD [9], in-hospital patients with community-acquired pneumonia [10], and unexplained worsening of dyspnea in chronic atrial fibrillation patients [11].

Dyspnea plus ischemic-like chest pain, near syncope or syncope, with or without hypotension are highly suggestive of submassive or massive PE. Concomitant neurologic symptoms or signs and/or back or abdominal pain suggest a paradoxical embolism secondary to patent foramen ovale in submassive PE patients. Physicians in charge should be in warning to identify subclinical strokes in the intent to avoid hemorrhagic transformation [12].

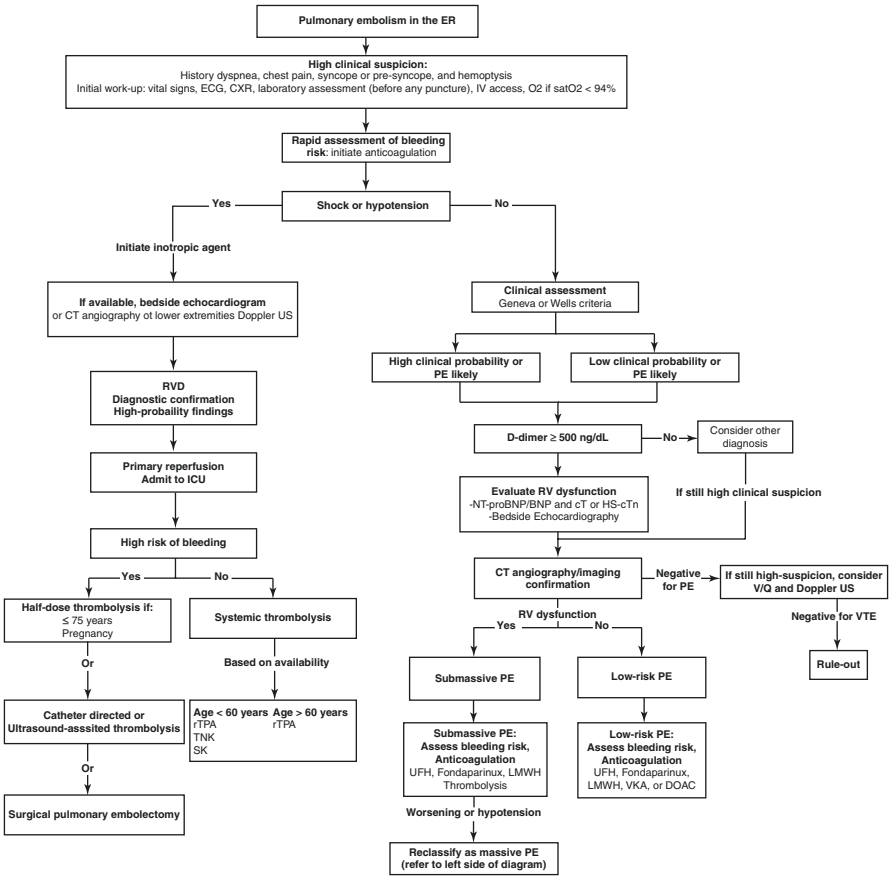

Fig. 9.1 Diagnostic algorithm for low-probability, submassive, and massive PE

Table 9.3 Main clinical characteristics of acute pulmonary embolism

Low risk	Submassive or massive
Persistent or transitory dyspnea at rest or exertion	Dyspnea at rest or exertion
Tachycardia	Ischemic-like chest pain
Tachypnea	Near syncope or syncope
Pleuritic chest pain	Tachycardia
Cough without hemoptysis	Respiratory distress
Dizziness	Hypotension
Near syncope or syncope	Oxygen desaturation
Transitory oxygen desaturation or normal	Cardiogenic shock
Normal blood pressure	Cardiac arrest

9.6 Assessment of Clinical Probability

Despite the limited sensitivity and specificity of individual symptoms, signs, and common tests, the combination of each of these findings, using clinical judgment or prediction rules, allows to classify patients with suspected PE into distinct categories of clinical or pretest probability and severity that correspond to an increasing actual prevalence of confirmed PE [6]. The pretest probability must be assessed based on validated scores, Wells or revised Geneva (Tables 9.4 and 9.5), in patients with high-clinical suspicion of low-risk PE. Both tests are simple and based on information easy to obtain [6].

Table 9.4 Wells rules

Clinical prediction rules	Original version	Simplified version
Previous PE or DVT	1.5	1
Heart rate ≥ 100 b.p.m	1.5	1
Surgery or immobilization last 4 weeks	1.5	1
Hemoptysis	1	1
Active cancer	1	1
Clinical signs of DVT	3	1
Alternative diagnosis less likely PE	2	1
The clinical probability of PE		
Three-level score		
Low	0–1	NA
Intermediate	2–6	NA
High	≥7	NA
Two-level score		
PE unlikely	0–4	0–1
PE likely	≥5	≥2

PE pulmonary embolism, *DVT* deep venous thrombosis, *BPM* beats per minute, *NA* not available

Table 9.5 Revised Geneva score

Clinical prediction rules	Original version	Simplified version
Previous PE or DVT	3	1
Heart rate	NA	NA
75–94 bpm	3	1
>95 bpm	5	2
Surgery or fracture in the last month	2	1
Hemoptysis	2	1
Active cancer	2	1
Unilateral lower limb pain	3	1
Pain on lower deep venous palpation and unilateral edema	4	1
Age >65 years	1	1
The clinical probability of PE		
Three-level score		
Low	0–3	0–1

Table 9.5 (continued)

Clinical prediction rules	Original version	Simplified version
Intermediate	4–10	2–4
High	≥11	≥5
Two-level score		
PE unlikely	0–5	0–2
PE likely	≥6	≥3

PE pulmonary embolism, *BPM* beats per minute, *NA* not applicable

9.7 D-Dimer

This biomarker reflects the coagulation system and endogenous fibrinolysis activation. D-Dimer testing should be considered in the context of clinical probability, in patients with or without clinical stability. D-Dimer is a highly sensitive test (91–97% for enzyme-linked immunofluorescence) to exclude PE (<500 ng/dL) (Fig. 9.1) [6]. A positive D-dimer (>500 ng/dL) may be useful in high-clinically suspected PE as it indicates that venous thrombosis is possible. In the setting of high-clinical suspicion and normal value D-dimer (<500 ng/dL), diagnosis tests are mandatory [6].

D-Dimer has a low to moderate specificity (43–50%) since abnormal values may be found in several clinical conditions such as cancer, trauma, inflammatory disease, and infections [6]. However, D-dimer increased in a lower proportion of community-acquired pneumonia patients and had higher levels associated with PE [10]. D-Dimer must be obtained from the first venous or puncture. We recommended the same cutoff level for the young and elderly population.

9.8 Initial Risk Stratification

A fast-track approach is the cornerstone of the initial workup. The history and physical examination can provide important clues for risk stratification. The Pulmonary Embolism Severity Index (PESI) score and its simplified (sPESI) (Table 9.6) version offer clinicians' similar prognostic accuracy with greater ease. Patients are considered candidates for the outpatient treatment of PE if their PESI score is <85 points or have sPESI 0 points. Considering that several reports have shown sPESI failure, in the setting of submassive PE [13, 14], biomarkers and/or echocardiogram is an important complement before making a decision, especially in those considered to outpatient treatment.

Clinically defining an acute PE will depend if we use the American Heart Association [15] classification or European Society of Cardiology [6] classification. However, in both RVD (Table 9.7), the hemodynamic impact on systemic and pulmonary pressure constitutes the cornerstone of risk stratification.

Pulmonary vascular obstruction >25% is frequently associated with pulmonary arterial hypertension, RVD (Table 9.7), and clinical instability, whereas pulmonary vascular obstruction <25% is often associated with clinical stability and normal right ventricular function [16].

Table 9.6 Pulmonary Embolism Severity Index

PESI score		Simplified PESI score	
Age	Age in years	Age >80 years	1
Male sex	10	History of cancer	1
History of cancer	30	History of cardiopulmonary disease	1
History of heart failure	10	Heart rate >110 bpm	1
History of chronic lung disease	10	SBP <110 mmHg	1
Heart rate >110 bpm	20	Oxygen saturation <90%	1
SBP <100 mmHg	30		
Oxygen saturation <90%	20		
Respiratory rate ≥30/min	20		
Temperature <36 °C	20		
Altered mental status	60		
Class I very low risk ≤65 II low risk 66–85 III intermediate risk 86–105 IV high risk 106–125 V very high risk >125		*Class* Low risk 0 High risk >1	

PESI pulmonary embolism severity index, *BPM* beats per minute, *SBP* systolic blood pressure

Table 9.7 Classifications of pulmonary embolism [6, 15]

American Heart Association	European Society of Cardiology
Massive: clinical instability by sustained hypotension (systolic blood pressure <90 mmHg) for at least 15 min or requiring inotropic support, not due to a cause other than PE and RVD	*High risk*: shock of hypotension, PESI class III–V or sPESI >1, signs of RV dysfunction on an imaging test and cardiac laboratory biomarkers (both positives)
Submassive: clinical stability without systemic hypotension (systolic blood pressure >90 mmHg) but either RVD or myocardial necrosis	*Intermediate* *High risk*: normal blood pressure, PESI class III–V or sPESI ≥1, signs of RV dysfunction on an imaging test and cardiac laboratory biomarkers (both positives)
Low risk: clinical stability, the absence of RVD and normal biomarkers	*Low risk*: normal blood pressure, PESI class III–V or sPESI >1, signs of RV dysfunction on an imaging test and cardiac laboratory biomarkers (either one or none positive)
	Low risk: normal blood pressure, PESI class I–II or sPESI 0, assessment of RV dysfunction and cardiac laboratory biomarkers optional, if assessed both negative

PESI pulmonary embolism severity index, *sPESI* simplified PESI, *PE* pulmonary embolism, *RVD* right ventricular dysfunction, *RV* right ventricle

Table 9.8 Physical examination findings

Low risk	Massive or submassive
Cardiac examination Normal heart sounds Tachycardia	*Cardiac examination* Tachycardia Right ventricular lift Increased P2 Third and fourth heart sound suggesting pulmonary hypertension and right ventricular dysfunction Low P2 it is a confounder and has been related with severe right ventricular dysfunction
Respiratory examination Normal lung sounds	*Respiratory examination* Normal lung sounds
Deep venous system Leg pain Warmth Swelling Homans' sign Ollow' sign	*Deep venous system* Leg pain Warmth Swelling Homans' sign Ollow' sign

9.9 Physical Examination

A careful clinical examination should be performed, with attention being paid to identify clinical stability, pulmonary hypertension, RVD, as well as deep venous thrombosis (Table 9.8). In most of the low-risk patients, the cardiopulmonary examination is normal, and it is possible to identify symptoms and signs of deep venous thrombosis. In addition, normal oxygen saturation is observed in 21% of low-risk PE patients [17].

Listening to an attenuated and low S_2 could be considered as an early sign of severe RVD. Jugular venous distension and cyanosis are infrequent specifically in patients with early onset of symptoms and early arrival to the ER. Cyanosis must be related to severe RVD and cardiogenic shock or another clinical situation (COPD, congenic heart disease) [7]. Normal blood pressure cannot exclude impending clinical instability and in-hospital poor outcome in submassive PE [18]. Deep venous thrombosis complicated with severe edema, warm, swelling, and pain is infrequent in submassive and massive PE patients.

9.10 Work up

9.10.1 Chest X-Ray

The analysis must focus on the pulmonary artery circulation. The study could be normal in low-risk PE (segmental or subsegmental) and, however, always is abnormal in lobar, submassive, and massive PE (Fig. 9.2) (Table 9.9). Main pulmonary

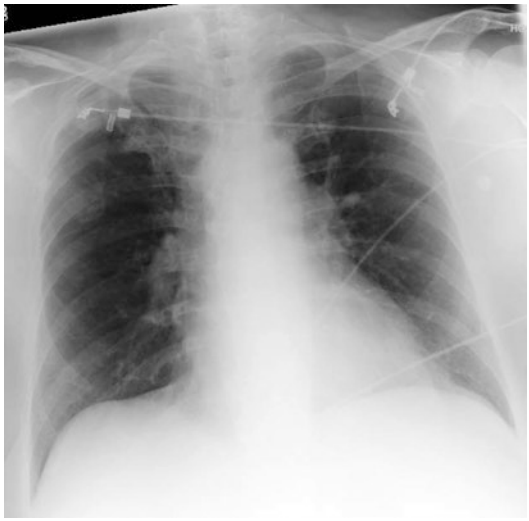

Fig. 9.2 A female patient with submassive pulmonary embolism. Chest X-Ray showing bilateral Westermark sign and right main artery dilatation with cutoff

Table 9.9 Chest X-ray in pulmonary embolism

Findings	Low risk	Submassive	Massive
Normal heart size and pulmonary arterial circulation[a]	✓		
Hampton sign	✓		
Fleischner lines			
Significative or small right or left pleural effusion	✓		
Westermark sign	✓	✓	✓
Left or right or both pulmonary artery cutoff	✓	✓	✓
Left or right or both pulmonary artery dilatation	✓	✓	✓
Main pulmonary artery dilatation		✓	✓
Right ventricular dilatation		✓	✓
Elevated right diaphragm		✓	✓

[a]Segmental or subsegmental thrombus

artery dilatation and right ventricular dilatation is infrequent, mainly in those who early arrival after onset symptoms. Bedside chest X-ray is a challenge to identify classic signs in clinical instability PE patients, however, allows to excluding other clinical situations mimicking PE (acute pulmonary edema, COPD exacerbation, cardiac tamponade, extensive pneumothorax, etc.)

9.10.2 Right Ventricular Dysfunction Multimodal Risk Stratification

We suggest a multimodal approach to identify RVD (Fig. 9.1) through clinical findings, ECG, biomarkers, and echocardiogram at the time of screening (Table 9.10).

The best stratification approach will be depending on experience, expertise, and available technology in each center.

9.10.3 Electrocardiogram

In the stratification approach, this accessible tool provides important findings to identify severe right ventricular pressure overload, ischemia, or infarction (Table 9.11). A normal electrocardiogram (ECG) is unlikely in submassive or massive PE. ECG is not a test to rule out PE. However, it is helpful in predicting

Table 9.10 Biomarkers of right ventricle dysfunction

Modality	Findings
Clinical	Dyspnea plus ischemic-like chest pain or near syncope or syncope, transitory or sustained hypotension, increased P2, third and fourth right heart sound, oxygen saturation <90%
ECG	Right axis deviation, S1Q3T3, aVR ST elevation, V1 qR and ST elevation, anteroseptal ST elevation or depression or anteroseptal T-wave inversion, new complete or incomplete right bundle-branch block, new-onset atrial fibrillation or flutter
Biomarkers	Elevation of BNP >100 pg/mL or elevation of N-terminal pro-BNP >300 pg/mL and elevation of high-sensitive troponin assays with a coefficient of variance of <10% at the 99th percentile value
Echocardiography	RV dilation (apical four-chamber RV diameter divided by LV diameter >0.9) RV systolic dysfunction RV dilation (four-chamber RV diameter divided by LV diameter >0.9), RV hypokinesis
CT scan	RV dilatation, RV/LV dimension ratios, ventricular and atrial septum shifting to the left side

BNP B-type natriuretic peptide, *RV* right ventricle, *LV* left ventricle

Table 9.11 Electrocardiogram in pulmonary embolism

Findings	Low risk	Submassive	Massive
Normal	✓		
ST unspecific changes	✓		
Normal axis	✓		
QRS axis deviation >90° or indeterminate axis		✓	✓
S1Q3T3		✓	✓
Q wave and T inversion (III and aVF) but not in II		✓	✓
aVR ST elevation		✓	✓
V1 qR and ST elevation		✓	✓
ST elevation inferior or anteroseptal		✓	✓
ST depression inferior or anteroseptal		✓	✓
V1 to V4 anteroseptal T-wave inversion		✓	✓
Complete or incomplete right bundle-branch block		✓	✓
Atrial fibrillation or flutter		✓	✓
Low-voltage in the limbs leads			✓

Table 9.12 Electrocardiogram related to in-hospital adverse events

Outcomes	ECG findings	OR	95% CI	p-value
In-hospital mortality	qR in V1	4.72	2.54–8.78	<0.001
	ST elevation in V1	4.27	2.73–6.66	<0.001
	Right ventricular strain	4.13	1.22–14.0	0.023
	Complete right bundle-branch block	3.90	2.46–6.29	<0.001
	S1Q3T3	3.38	2.46–4–66	<0.001
	QRS axis deviation >90°	3.24	1.86–5.64	<0.001
	ST elevation in DIII	3.08	1.65–5.81	<0.001
	ST depression in V1–V6	2.50	1.43–4.36	
Adjusted in-hospital mortality	Advanced right bundle-branch block	5.790	2.47–13.6	<0.001
30 days mortality	T peak – Tend interval	12.9	3.05–54.7	0.001
	RV transmural ischemic pattern	4.22	1.14–15.6	0.031
	RV subendocardial ischemia plus RV transmural ischemia	4.02	1.13–14.3	0.032
	ST elevation in V1	3.23	1.71–6.11	<0.001
	ST depression DI and DIII or V4–V6	2.52	1.30–4.90	0.006
	Atrial fibrillation	2.47	1.18–5.17	0.01
	St elevation DI and DIII or V4–V6	2.03	1.06–3.90	0.03
	Negative T waves	6.1	1.3–29.1	NR

ECG electrocardiogram, *OR* odds ratio, *CI* confidence interval, *RV*, right ventricle

adverse clinical outcomes in confirmed PE (Table 9.12) [19]. Although tachycardia is a classical electrocardiogram finding, bradycardia could be identified in patients with primary or secondary conduction system disease [20]. The dynamic ST abnormalities on ECG mimicking an acute coronary syndrome (Fig. 9.3).

9.10.4 Transthoracic and Transesophageal Echocardiogram

In the setting of clinical instability, transthoracic echocardiography (TTE) can be performed to establish or excluded rapidly bedside RVD (Figs. 9.4 and 9.5). In addition, excluded alternative diagnosis mimicking PE as acute myocardial infarction, aortic dissection, pericardial tamponade, etc. In those with poor acoustic window, transesophageal echocardiography (TEE) allows a better right ventricular examination, and eventually thrombus in the main pulmonary artery, and proximal branches can be found. Table 9.13 shows the echocardiographic findings in the broad clinical spectrum of PE.

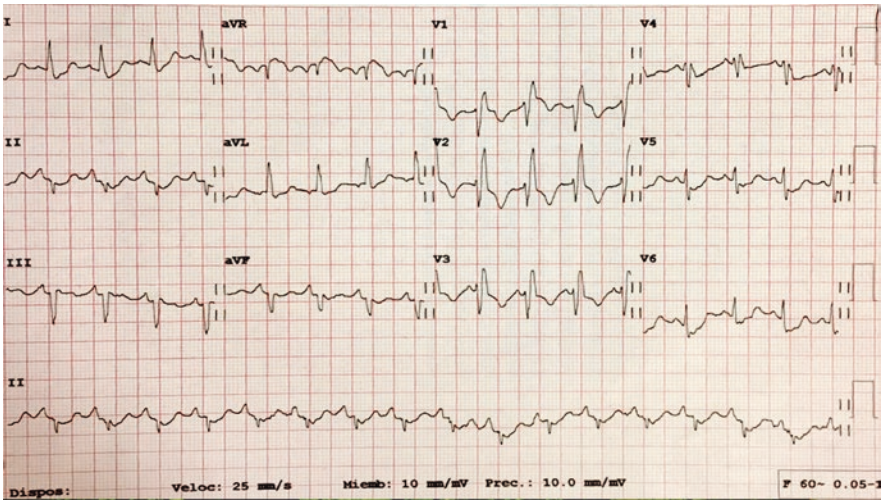

Fig. 9.3 A female patient with massive PE. ECG showing QRS axis deviation <30°, aVR ST elevation, incomplete right bundle-branch block, and V1 ST elevation, as well as ST depression

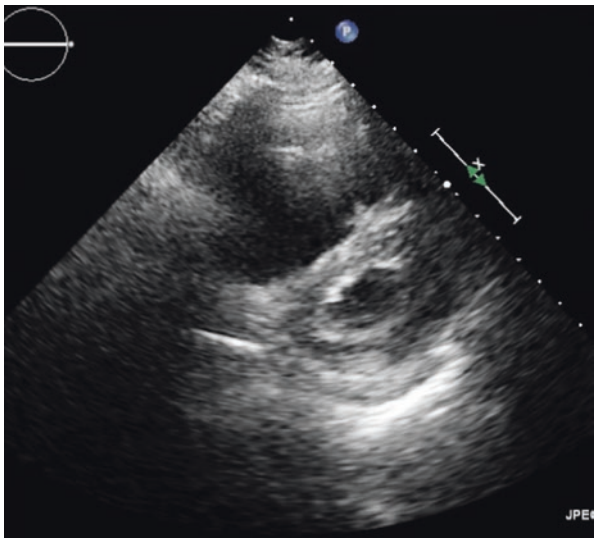

Fig. 9.4 A female patient with massive PE. Transthoracic echocardiogram showing right ventricular dilatation

TTE has more sensitivity to identify patent foramen ovale in submassive PE patients [12]. TTE/TEE findings plus clinical and plasmatic measurement biomarkers of RVD are enough to start thrombolysis in severe massive PE. Systolic pulmonary artery pressure >60 mmHg suggests chronic pulmonary hypertension.

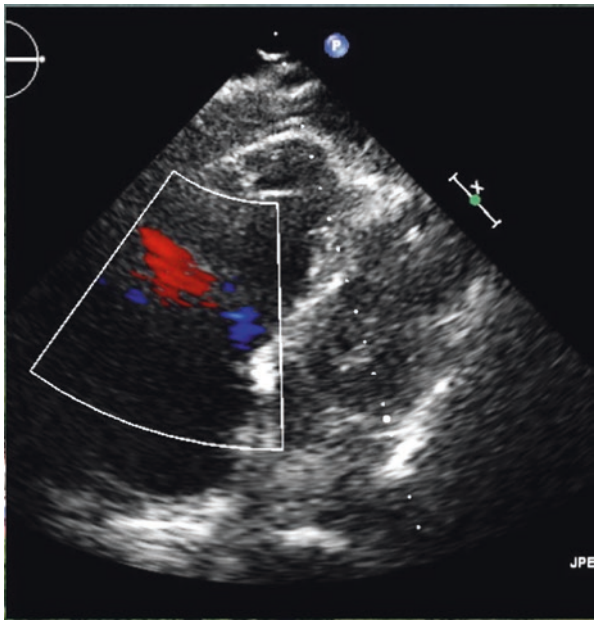

Fig. 9.5 A female patient with massive PE. Transthoracic echocardiogram showing right ventricular dilatation and McConnell's sign

Table 9.13 Echocardiographic findings in pulmonary embolism

Qualitative evaluation	**Low risk**	**Submassive**	**Massive**
Normal right ventricle	✓		
Right ventricular wall	5 mm	5 mm	5 mm
Paradoxical interventricular systolic septum motion		✓	✓
Flattened interventricular septum		✓	✓
Right atrium dilatation		✓	✓
Right ventricular dilatation		✓	✓
Four-apical chamber view RV/LV change ratio	<1:1	2:1	>2:1
Regional right ventricular hypokinesis		✓	✓
McConnell's sign		✓	✓
Patent foramen oval		✓	✓
Thrombus in-transit		✓	✓
Global right ventricular hypokinesis			✓
Quantitative evaluation			
RV/LV end-diastolic dimension ratio		✓	✓
Parasternal long axis view	<0.6	>0.6	>0.6
Four-chamber view	<0.9	>0.9	>0.9
Tricuspid regurgitation jet velocity	<2.6 m/s	>2.6 m/s	>2.6 m/s
Systolic pulmonary artery pressure	<50 mmHg	>50 mmHg	>50 mmHg
TAPSE	>17 mm	<17 mm	<17 mm

RV right ventricle, *LV* left ventricle, *TAPSE* tricuspid annular plane systolic excursion

9.10.5 Limitations of Transthoracic and Transesophageal Echocardiography

9.10.5.1 Transthoracic Echocardiogram

- Poor acoustic window
- Not available in the ER

9.10.5.2 Transesophageal Echocardiogram

- Expertise in the setting of severe clinical instability is mandatory
- Not available in the ER

9.10.6 Cardiac Computed Tomography

This imaging test has prognostic utility to establish signs of RVD, such as RV dilatation. RV/LV dimension ratios, ventricular and atrial septum shifting to the left side, and inferior vena cava diameter. In addition, it is possible identify severe right ventricular dilatation and septal deviation, also detect thrombus occluding right or left main, segmental or subsegmental pulmonary arteries.

9.10.7 Biomarkers

Bedside cardiac biomarkers establish RVD, ischemia, or type 2 myocardial infarction (Table 9.14). B-type natriuretic peptide (BNP) plasma measurements >600 pg/dL are observed in the setting of massive PE complicated with cardiogenic shock or in the late stage of RVD. Amounts around 400 pg/dL are frequent in the early stage of submassive or massive PE.

Considering that the half-life of BNP is 23 min, therefore approximately 2 h are required to reflect changes in the setting of the acute left of RVD. Physicians in charge should be aware of this 2-hour lag period before the onset of BNP to avoid underdiagnosing ventricular dysfunction [21].

Abnormal values of high-sensitive troponin assays establish right ventricular ischemia or necrosis. Troponin T concentrations >14 pg/mL had a negative predictive value of 98% about a complicated clinical course [22]. Also, abnormal measurements of BNP and high-sensitive troponin assays are closely related with an increase rate of in-hospital mortality and adverse events.

9.11 Diagnosis Approach

9.11.1 Chest Computed Tomography

Contrast-enhanced chest CT is the predominant diagnostic imaging technique to establish PE diagnosis by a thrombus in the pulmonary circulation (Fig. 9.6) (Table 9.15). The enhanced resolution of newer multi-detector CT scanners has increased the detection rate of subsegmental PE [23]. Negative chest CT has a high (99.1–99.4%) negative predict value to exclude PE in the assessment of high-clinical suspicion patients (Fig. 9.1). In the setting of high-clinical suspicion and negative chest CT, a multimodal approach including ventilation-perfusion lung scan and/or venous ultrasound increase facilitates making a clinical decision. Chest CT appears to be at least as accurate as invasive contrast pulmonary angiography.

Table 9.14 B-type natriuretic peptide and high-sensitivity troponin assays

Findings	Low risk	Submassive	Massive
BNP	<100 pg/dL	>100 pg/dL	>100 pg/dL
N-terminal pro-BNP	<300 pg/dL	>300 pg/dL	>300 pg/dL
High-sensitive troponin assays	At least one value above the 99th percentile upper reference limit		

BNP B-type natriuretic peptide

Table 9.15 Chest CT and ventilation-perfusion lung scan findings

Chest CT	**Low risk**	**Submassive**	**Massive**
Subsegmental or segmental artery	✓		
Lobar artery	✓		
Right or left artery		✓	✓
Both right and left artery		✓	✓
Main pulmonary artery			✓
Saddle thrombus			✓
V/Q lung scan			
Two subsegmental defects	✓		
<segmental defects	✓		
<8 segmental defects	✓	✓	
≥8 segmental defects		✓	✓
Vascular pulmonary obstruction <25%	✓		
Vascular pulmonary obstruction >25%	✓	✓	✓

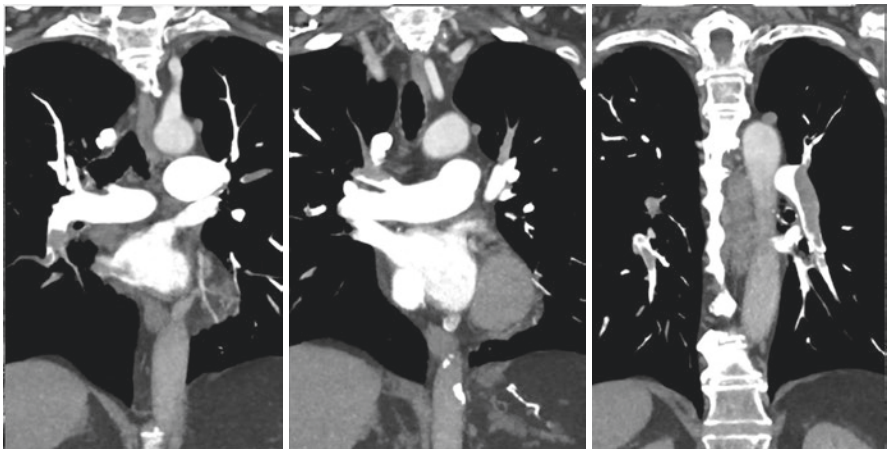

Fig. 9.6 A female patient with massive PE. Chest computed tomography showing bilateral thrombus in the pulmonary circulation

9.11.2 Ventilation-Perfusion Lung Scanning

The diagnostic requires at least one segmental or two subsegmental defects (Table 9.15). The purpose of the ventilation-perfusion scan is to increase specificity. In acute PE, ventilation is expected to be normal in hypoperfused segments, the so-called mismatch. Should be used in outpatients with low clinical probability and a normal chest X-ray is an important option in special populations as children, female, young, pregnant, history of contrast medium-induced anaphylaxis, severe renal failure, and history of with myeloma or paraproteinemia [7].

9.11.3 Laboratory Evaluation

In high-clinical suspicion, PE patients should focus on the use of D-dimer, BNP, and high-sensitive troponin. However, basal creatinine clearance, hemoglobin, and platelet count measurements identify high-risk patients to bleeding complications and a potential heparin-induced thrombocytopenia. Hyperglycemia and leukocytosis are linked to poor in-hospital outcome.

9.12 Treatment in the ER

The clinical condition, RVD, and risk for major bleeding complications drive the treatment choice [3]. There is an association between early anticoagulation and reduced mortality for patients with acute PE [24].

There is no bleeding risk score validated in PE. Variables related to major bleeding complications are elderly, female gender, low body mass index, and short size [25]. Parenteral or oral anticoagulation is the foundation of the treatment in low-risk PE patients (Table 9.16) and systemic thrombolysis in massive PE.

Non-vitamin K antagonist oral anticoagulants facilitated outpatient treatment; however, current evidence suggesting caution in PE associated with RVD [13].

Unfractionated heparin is recommended in >75 years with high risk of bleeding complication, renal failure, and morbid obesity low-risk PE patients (Table 9.17). Weight-adjusted unfractionated heparin regimen is recommended in impeding clinical instability submassive PE and as adjunctive treatment in massive PE [26] (Table 9.17).

Thrombolysis is recommended (without major risk bleeding) in clinical suspicion of impending instability, increased respiratory rate [27], and normal blood pressure in lower limits [18] submassive PE patients. If physicians in charge decide to use the "wait-and-see approach" [6], in the event that thrombolysis is needed, unfractionated heparin is the option to avoid crossover heparins. Tenecteplase and alteplase are an option in <65 years and half-dose alteplase in >65 years PE patients [3, 28]. The major and relative contraindications to use systemic thrombolysis are shown in Table 9.18. Low-dose alteplase is safety and efficacy in the catheter- or ultrasound-directed thrombolysis [29] (Table 9.19). The European Society of Cardiology, American Heart Association, and American College of Cardiology recommendations for anticoagulation and thrombolysis are shown in Tables 9.20 and 9.21.

Table 9.16 Parenteral and oral anticoagulation in low-risk pulmonary embolism

Drug	Dosage	Interval
Enoxaparin	1.0 mg/kg or 1.5 mg/kg	BID or OD
Tinzaparin	175 U/kg	OD
Dalteparin	100 IU/kg or 200 IU/kg (cancer patients)	OD or BID
Nadroparin	86 IU/kg or 171 IU/kg	OD or BID
Fondaparinux	5 mg (body weight <50 kg) 7.5 mg (body weight 50–100 kg) 10 mg (body weight >100 kg)	OD
Apixaban	10 mg 5 mg or 2.5 mg	BID for 7 days BID
Rivaroxaban	15 mg 20 mg or 15 mg	BID for 21 days OD

Table 9.17 aPTT- and weight-adjusted unfractionated heparin regimens

aPTT adjusted	**Regimens**
<35 s (<1.2 times control)	80 U/kg bolus increase infusion rate by 4 UI/kg/h
35–45 s (1.2–1.5 times control)	40 U/kg bolus increase infusion rate by 2 U/kg/h
46–70 s (1.5–2.3 times control)	No change
71–90 s (2.3–3.0 times control)	Reduce infusion rate by 2 U/kg/h
>90 s (>3.0 times control)	Stop infusion for 1 h, and then reduce infusion rate by 3 U/kg/h
Weight adjusted A bolus of 60 U/kg (maximum 4000 U)	Constant heparin infusion (12 U/kg/h, maximum 1000 U/h) adjusted to maintain an aPTT of 50–70 s for 24–48 h

aPTT activated partial thromboplastin time, *U* units

Table 9.18 Major and relative contraindications to use systemic thrombolysis [6]

Relative	Major
The transient ischemic attack in the preceding 6 months Oral anticoagulant therapy Pregnancy or within 1 week postpartum Non-compressible puncture site Traumatic resuscitation Refractory hypertension (systolic blood pressure >180 mmHg) Advanced liver disease Infective endocarditis Active peptide ulcer	Hemorrhagic stroke or stroke of unknown origin at any time Ischemic stroke in the preceding 6 months Central nervous system damage or neoplasms Recent major trauma/surgery/head injury in the preceding 3 weeks Gastrointestinal bleeding within the last month Known bleeding risk

Table 9.19 Thrombolytic regimens

Medication	Regimens	
FDA approved		
Alteplase	100 mg in 2-hour infusion	
FDA not approved		
Streptokinase	1,500,000 IU in 1 or 2 hours infusion	
Alteplase	20 mg bolus followed 80 mg in 1-hour infusion	
Alteplase	10 mg as a loading dose over 10 min followed by 40 mg over 2 h or 50 mg over 1 h infusion	
Tenecteplase	*Weight (kg)*	*Dose (mg)*
	<60	30
	60–70	35
	70–80	40
	80–90	45
	>90	50
Catheter-directed thrombolysis with alteplase	20 mg	
Ultrasound-directed thrombolysis with alteplase	17.2 mg to 35.1 mg in 14 h to 33.2 h infusion or 4 mg in 2 or 4 h	

FDA Food and Drug Administration, *IU* international units

Table 9.20 European Society of Cardiology recommendations [6]

High-risk PE	COR	LOE
It is recommended that intravenous anticoagulation with UFH be initiated without delay in patients with high-risk PE	I	C
Thrombolytic therapy is recommended	I	B
Surgical pulmonary embolectomy is recommended for patients in whom thrombolysis is contraindicated or has failed	I	C
Percutaneous catheter-directed treatment should be considered as an alternative to surgical pulmonary embolectomy for patients in whom full-dose systemic thrombolysis is contraindicated or has failed	IIa	C
Intermediate or low risk		
Initiation of parenteral anticoagulation is recommended without delay in patients with high or intermediate clinical probability of PE while diagnostic workup is in progress	I	C
LMWH or fondaparinux is the recommended form of acute-phase parenteral anticoagulation for most patients	I	A
In parallel to parenteral anticoagulation, treatment with a VKA is recommended, targeting an INR of 2.5 (range 2.0–3.0)	I	B
As an alternative to the combination of parenteral anticoagulation with VKA, anticoagulation with rivaroxaban 15 mg twice daily for 3 weeks, followed by 20 mg once daily is recommended	I	B
As an alternative to the combination of parenteral anticoagulation with VKA, anticoagulation with apixaban 10 mg twice daily for 7 days, followed by 5 mg twice daily is recommended	I	B
As an alternative to VKA treatment, administration of dabigatran 150 mg twice daily or 110 mg twice daily for patients >80 years of age or those under concomitant verapamil treatment is recommended following acute-phase parenteral anticoagulation	I	B
As an alternative to VKA treatment, administration of edoxaban is recommended following acute-phase parenteral anticoagulation	I	B
New oral anticoagulants are not recommended in patients with severe renal impairment (creatinine clearance <30 mL/min for rivaroxaban, dabigatran, and edoxaban and < 25 mL/min for apixaban)	III	A
Reperfusion treatment		
Routine use of primary systemic thrombolysis is not recommended in patients not suffering from shock or hypotension	III	B
Close monitoring is recommended in patients with intermediate-high-risk PE to permit early detection of hemodynamic decompensation and timely initiation of rescue reperfusion therapy	I	B
Thrombolytic therapy should be considered for patients with intermediate-high-risk PE and clinical signs of hemodynamic decompensation	IIa	B
Surgical pulmonary embolectomy may be considered in intermediate-high-risk patients if the anticipated risk of bleeding under thrombolytic treatment is high	IIb	C
Percutaneous catheter-directed treatment may be considered in intermediate-high-risk patients if the anticipated risk of bleeding under thrombolytic treatment is high	IIb	B

PE pulmonary embolism, *COR* class of recommendation, *LOE* level of evidence, *UFH* unfractioned heparin, *LMWH* low molecular weight heparin, *VKA* vitamin K antagonists

Table 9.21 American Heart Association and American College of Cardiology recommendations [15]

Initial anticoagulation	COR	LOE
Therapeutic anticoagulation with subcutaneous LMWH, intravenous or subcutaneous UFH with monitoring, unmonitored weight-based subcutaneous UFH, or subcutaneous fondaparinux should be given to patients with objectively confirmed PE and no contraindications to anticoagulation	I	A
Therapeutic anticoagulation during the diagnostic workup should be given to patients with intermediate or high clinical probability of PE and no contraindications to anticoagulation	I	C
Fibrinolysis		
Fibrinolysis is reasonable for patients with massive acute PE and an acceptable risk of bleeding complications	IIa	B
Fibrinolysis may be considered for patients with submassive acute PE judged to have clinical evidence of adverse prognosis (new hemodynamic instability, worsening respiratory insufficiency, severe RV dysfunction, or major myocardial necrosis) and low risk of bleeding complications	IIb	C
Fibrinolysis is not recommended for patients with low-risk PE	III	B
Fibrinolysis is not recommended for patients with submassive acute PE with minor RV dysfunction, minor myocardial necrosis, and no clinical worsening	III	B
Fibrinolysis is not recommended for undifferentiated cardiac arrest	III	B
Catheter embolectomy		
Depending on local expertise, either catheter embolectomy and fragmentation or surgical embolectomy is reasonable for patients with massive PE and contraindications to fibrinolysis	IIa	C
Catheter embolectomy and fragmentation or surgical embolectomy is reasonable for patients with massive PE who remain unstable after receiving fibrinolysis	IIa	C
For patients with massive PE who cannot receive fibrinolysis or who remain unstable after fibrinolysis, it is reasonable to consider a transfer to an institution experienced in either catheter embolectomy or surgical embolectomy if these procedures are not available locally and safe transfer can be achieved	IIa	C
Either catheter embolectomy or surgical embolectomy may be considered for patients with submassive acute PE judged to have clinical evidence of adverse prognosis (new hemodynamic instability, worsening respiratory failure, severe RV dysfunction, or major myocardial necrosis)	IIb	C
Catheter embolectomy and surgical thrombectomy are not recommended for patients with low-risk PE or submassive acute PE with minor RV dysfunction, minor myocardial necrosis, and no clinical worsening	III	C
Endovascular thrombolysis and surgical venous thrombectomy		
CDT or PCDT should be given to patients with IFDVT associated with limb-threatening circulatory compromise (i.e., phlegmasia cerulea dolens)	I	C
Patients with IFDVT at centers that lack endovascular thrombolysis should be considered for transfer to a center with this expertise if indications for endovascular thrombolysis are present	I	C
CDT or PCDT is reasonable for patients with IFDVT associated with rapid thrombus extension despite anticoagulation and/or symptomatic deterioration from the IFDVT despite anticoagulation	IIa	B

(continued)

Table 9.21 (continued)

Initial anticoagulation	COR	LOE
CDT or PCDT is reasonable as first-line treatment of patients with acute IFDVT to prevent PTS in selected patients at low risk of bleeding complications	IIa	B
Surgical venous thrombectomy by experienced surgeons may be considered in patients with IFDVT	IIb	B
Systemic fibrinolysis should not be given routinely to patients with IFDVT	III	A
CDT or PCDT should not be given to most patients with chronic DVT symptoms (>21 days) or patients who are at high risk for bleeding complications	III	B

COR a class of recommendation, *LOE* level of evidence, *LMWH* low molecular weight heparin, *UFH* unfractionated heparin, *PE* pulmonary embolism, *RV* right ventricle, *CDT* catheter-directed thrombolysis, *PCDT* pharmaco-mechanical catheter-directed thrombolysis, *IFDVT* iliofemoral deep venous thrombosis

Table 9.22 Differential diagnosis

Diseases	Low risk	Submassive	Massive
Physical deconditioning	✓		
Anxiety	✓		
Hyperreactivity	✓		
Asthma	✓		
Bronchial acute infection	✓		
Pneumonia	✓		
Pulmonary fibrosis	✓	✓	
COPD exacerbation	✓	✓	
Non-cardiogenic pulmonary edema		✓	✓
Heart failure	✓	✓	✓
Cardiac prosthetic valvular dysfunction	✓	✓	✓
Acute coronary syndromes	✓	✓	✓
Pericardial effusion	✓	✓	
Cardiac tamponade		✓	✓
New onset atrial fibrillation or flutter		✓	✓
Acute aortic syndromes		✓	✓

COPD chronic obstructive pulmonary disease

9.13 Differential Diagnosis

In the setting of high-clinical suspicion PE, the differential diagnosis depends on clinical stability or instability (Table 9.22). PE must be excluded through diagnostic workup. However, we need to considerer other cardiovascular and pulmonary frequent clinical conditions.

9.14 Additional Clinical Practice Takeaway

- PE is frequently seen in unexplained acute exacerbation of COPD [9], in patients with community-acquired pneumonia [10], and in those with unexplained worsening of dyspnea and chronic atrial fibrillation [11].
- In new-onset paroxysmal atrial fibrillation and right ventricular strain on ECG, PE must be suspected.
- PE must be excluded in patients older than 70 years and in patients presenting syncope with or without an alternative explanation [8].
- PE should be considered, in patients with a previous history of heart failure with or without preserved ejection fraction or chronic lung diseases and unexplained acute exacerbation.
- There is an increased in mortality in ER patients who did not receive heparin until after hospital admission compared with patients who received heparin in the ER [30].
- Patients who suffer unprovoked PE have an increased risk of future recurrence.
- Central venous access must be guided by echocardiography, to avoid multiple punctures increasing potential bleeding complications.
- Unfractionated heparin is preferred over LMWH in patients with a high probability for surgical interventions and in unstable patients. This avoids the increase of risk if the patient requires thrombolysis thereafter.
- Avoid fluid overload in hypotensive patients, since it could precipitate or worsen RVD.
- Streptokinase could induce severe hypotension, typically at the 30-minute mark or after 30 min of ongoing infusion, monitor accordingly.

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Chapter 10
Hypertensive Crisis in the ER

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10.1 The Scope of the Problem

Hypertension is an increasingly prevalent chronic illness. The condition may present as a hypertensive crisis, and this entity may be further categorized as either hypertensive emergency or urgency. As the presentation is quite variable and is dependent upon the specific end-organ injury, a thorough history-taking and physical examination are necessary. Once the underlying pathology is known, a target blood pressure can be determined and a specific therapeutic agent selected. In hypertensive emergencies, the therapeutic goal is to protect the remaining end-organ function, reduce the risk of complications, and thereby improve patient outcomes, whereas in a hypertensive urgency, outpatient blood pressure control is recommended with oral hypertensives in a maximum of 48 h [1, 2]. On the other hand, hypertensive urgency prompts for a gradual (not immediate) control of the blood pressure [3, 4].

10.2 Prevalence

Hypertension affects nearly 30% of the population over 20 years of age. The World Health Organization (WHO) has estimated that by the year 2025, the number of individuals with hypertension will have risen to 1 billion or greater, and that at least 1% of these patients will experience an acute hypertensive episode requiring hospitalization [4].

10.3 Classification and Main Characteristics

The 2017 Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults defined hypertensive crisis as a systolic blood pressure (SBP) level ≥180 mmHg and/or a diastolic blood pressure (DBP)

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Table 10.1 Classification of hypertensive crisis

Hypertensive urgency	Blood pressure ≥180/110 mmHg without end-organ damage
Hypertensive emergency	Blood pressure ≥180/120 mmHg with new or worsening end-organ damage

level ≥120 mmHg. Hypertensive crisis is further divided into two categories based upon the evidence of target-organ damage. If end-organ damage is present, the condition is classified as hypertensive emergency [1]. The classification of hypertensive crisis is shown in Table 10.1.

The severe increase in blood pressure (BP) in hypertensive urgency is not associated with end-organ damage. However, non-life-threatening symptoms such as anxiety, headache, epistaxis, palpitations, or mild dyspnea may be present. BP in this case does not require urgent control and most of the time can be lowered over the course of several hours or days.

Hypertensive emergency, on the other hand, is associated with new or progressive end-organ damage. This is a true emergency requiring immediate BP control in minutes to hours.

10.4 Precipitant Factors

- Progression of essential hypertension and/or renovascular disease
- Stop of drugs to hypertension treatment
- Poor adherence to treatment
- Endocrine conditions (pheochromocytoma, Cushing syndrome)
- Sympathomimetics (cocaine, amphetamines)
- Cerebral injury

10.5 Clinical Presentation

Chronic hypertension is the most common precipitating factor in a hypertensive emergency, and the presentation is directly related to the organ affected. It can cause neurological damage (encephalopathy, hemorrhagic or ischemic stroke, or papilledema), cardiac damage (unstable coronary artery disease, heart failure, pulmonary edema, or aortic dissection), renal damage (proteinuria, hematuria, acute renal failure), scleroderma renal crisis, microangiopathic hemolytic anemia, and preeclampsia or eclampsia. Table 10.2 enlists the different manifestations of end-organ damage associated with hypertensive emergency.

Table 10.2 End-organ damage associated with hypertensive emergency

End organ	Damage type
Brain	Seizure, transient ischemic attack, cerebral infarction, intracerebral or subarachnoid bleed, hypertensive encephalopathy, posterior reversible leukoencephalopathy
Heart	Acute pulmonary edema, acute heart failure, unstable coronary artery disease
Blood vessels	Acute aortic dissection, microangiopathic hemolytic anemia
Kidney	Acute kidney injury
Retina	Papilledema, hemorrhages, retinal edema
Uterus	Eclampsia

10.6 Physical Examination

Clinical assessment for end-organ damage in patients with hypertensive crisis becomes the best approach to this disease. Table 10.3 gives a detailed description of the symptoms and signs that should be assessed during the history and physical examination of a patient presenting to the ER with severely elevated BP. We recommend in all patients a careful retina exploration to identify papilledema, hemorrhages, or retinal edema. Table 10.4 shows other clinical elements to suspect uncontrol hypertension.

10.7 Workup in the Emergency Room

Every patient presenting to the emergency room (ER) with a systolic blood pressure (SBP) ≥180 mmHg and/or diastolic blood pressure (DBP) ≥120 mmHg, with or without symptoms of end-organ damage, must be considered for workup of this pathology (Fig. 10.1) [5].

10.7.1 Laboratory Evaluation

The laboratory evaluation of a patient with a hypertensive urgency or emergency should focus on the analysis of renal function to exclude chronic renal disease or an acute renal failure as expression of renal damage. B-type natriuretic peptide and high-sensitivity cardiac T or I troponin abnormal measurements could stablish a subclinical end-organ damage in hypertensive urgency patients.

Table 10.3 Clinical workup and assessment based on organs

Organ	Ask for	Assessment	Additional workup
Brain	Headache, agitation, anxiety, mental status change/ delirium/stupor, seizures, history of prior stroke, and/or cerebral aneurysms	Head injury, decrease in cognition	Brain CT or MRI without contrast
Eyes	Visual disturbances	Ptosis, funduscopic (flame hemorrhages, exudates and papilledema), vision exam	–
Face	Diaphoresis	Facial weakness/paresis	–
Mouth	Active use medications, alcohol use, illicit drug use, antihypertensive use/ compliance, recent diet	Dysarthria	–
Neck	Dysphagia	Carotid bruits, JVD, spinal cord injury	–
Aorta	"Tearing" chest or abdominal pain radiating to the back; recent major vascular surgery	Comparative BP measurements in the contralateral arm and lower extremities	Chest radiograph, chest/abdominal CT with contrast
Heart	Chest discomfort/pressure, referred jaw and/or left arm discomfort, nausea/emesis/ epigastric discomfort, palpitations, history of or known existing CHF and/or CAD	Tachycardia, cardiac enlargement by palpation of the precordium, gallop on cardiac auscultation, new cardiac murmurs in particular mitral regurgitation, new friction rub	ECG, cardiac enzymes, brain natriuretic peptide, ECHO
Lungs	Shortness of breath, cough with production of pinkish phlegm	Pulmonary rales	Chest radiograph
Kidneys	Anuria/oliguria, history of pre-existing kidney disease and/or scleroderma	Renal artery bruits	Complete electrolyte profile, BUN, serum creatinine, CBC and coagulation studies, urinalysis, renal ultrasound with Doppler assessment
Bladder	Bladder discomfort/ distension, polyuria/oliguria/ dysuria, urinary stream with hesitancy	Bladder outlet obstruction	Urine drug screen, bladder scan/ ultrasound, bladder straight cath
Extremities	Weakness/numbness/tingling	Focal neurologic deficits, arm pronator drift, edema/ anasarca	Brain imaging (CT or MRI)

CT computed tomography, *MRI* magnetic resonance imaging, *JVD* jugular venous distention, *BP* blood pressure, *CHF* congestive heart failure, *CAD* coronary artery disease, *ECG* electrocardiogram, *ECHO* echocardiogram, *BUN* blood urea nitrogen, *CBC* complete blood count

Table 10.4 Clinically available clues indicating indicate poorly controlled hypertension

Eyes – retinopathy	Arteriolar narrowing, arteriovenous thickening Focal and general arteriolar narrowing, arteriolar silver wiring Hemorrhages, exudates, cotton-wool spots, papilledema, and/or microaneurysms
Heart	Laterally displaced and/or enlarged point of maximal impulse S4 gallop Other signs of heart failure (jugular venous pressure, edema, and rales)
Electrocardiogram	Voltage criteria for left ventricular hypertrophy Inverted or biphasic P wave in precordial lead V1
Renal	Clinical evidence of volume overload (jugular venous pressure, edema, crackles) Creatinine level increased and proteinuria

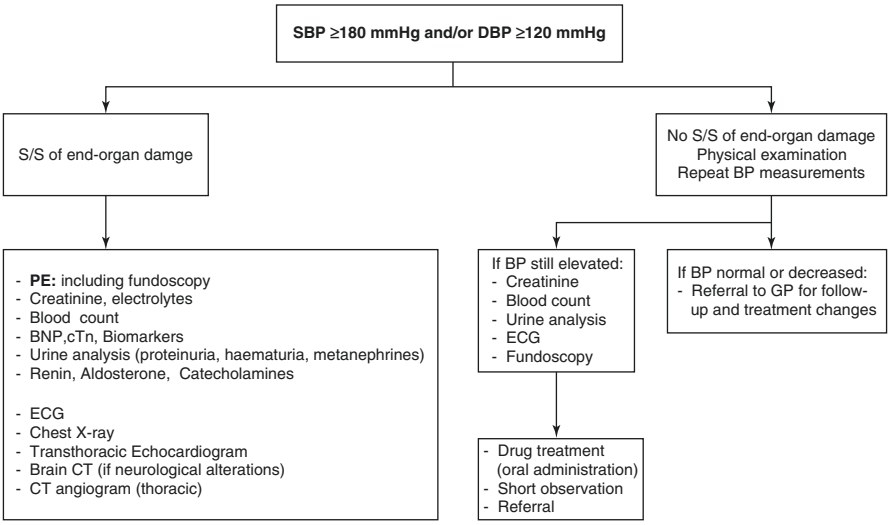

Fig. 10.1 Hypertensive crisis workup

10.7.2 Electrocardiogram

One of the most commonly used tools in the diagnostic workup in a hypertensive crisis is the electrocardiogram. This might reveal evidence of myocardial ischemia or infarction, typically T wave inversion and, in more severe cases, ST segment displacement. These changes mirror cardiac injury and indicate a hypertensive emergency and therefore prompt medical intervention, as well as evidence of left ventricular hypertrophy due to chronic hypertension.

10.7.3 Chest X-ray

A chest radiograph should be obtained to evaluate for pulmonary vascular congestion, cardiomegaly, as well as a widened mediastinum, which could suggest an aortic dissection. In most cases, however, the chest x-ray is unremarkable.

10.7.4 Additional Imaging Studies

Computed tomography (CT) or magnetic resonance imaging (MRI) of the brain (if head injury, neurologic symptoms, hypertensive retinopathy, nausea, or vomiting are present). Contrast-enhanced CT or MRI of the chest or transesophageal echocardiography (if aortic dissection is suspected, although rapid blood pressure lowering need not be delayed in such patients while awaiting the results of imaging).

Echocardiography is considered a second-line study in the evaluation of hypertensive patients, and its findings usually represent data of a remodeled heart [6]. The most common findings are those due to a longstanding hypertensive state. Valuable data that can be obtained includes the following:

- Left ventricular hypertrophy based on left ventricular mass
- Myocardial strain can detect subclinical organ damage earlier as depressions of global longitudinal left ventricular systolic strain and global systolic strain rate during hypertensive crisis
- Altered left ventricular diastolic function that can be assessed with mitral inflow velocity and mitral annular velocity
- Left ventricular systolic function to measure ejection fraction and abnormal segmental movement

10.8 Blood Pressure Control and Goals

BP should be readily controlled in the case of a hypertensive emergency. There are specific goals based on the timing and onset of treatment, as shown in Table 10.5. The main objective is to ensure control of end-organ damage.

In the case of a hypertensive urgency, blood pressure can be gradually normalized, as it does not involve an end-organ damage. There is no indication for immediate reduction of blood pressure in the emergency department or hospitalization [7].

The classes of antihypertensives that can be employed to control hypertensive crisis, their doses, and effects on preload, afterload, and cardiac output are listed in Table 10.6.

Table 10.7 summarizes the most relevant points from the ACC/AHA guidelines for hypertensive crises

Table 10.5 Blood pressure goals for hypertensive emergency

Goal time	BP target
First hour	Reduce mean arterial pressure by 25% (while maintaining goal diastolic blood pressure ≥100 mmHg)
Hours 2–6	Systolic blood pressure 160 mmHg and/or diastolic blood pressure 100–110 mmHg
Hours 6–24	Maintain goal for 2–6 h during first 24 h
Hours 24–48	Outpatient blood pressure goals according to the 2017 Guidelines for Management of High Blood Pressure in Adults

Table 10.6 IV drugs and dosing for hypertensive emergencies

Medication	Dosing range	Onset	Duration
Beta-blockers (preload ↔, afterload ↔ / ↓, CO ↓)			
Esmolol	IV 25–300 mcg/kg/min (bolus of 500 mcg/kg not often required, given short onset) Titrate by 25 mcg/kg/min q3–5 min	1–2 min	10–20 min
Labetalol	IV bolus: 20 mg; may repeat escalating doses of 20–80 mg q5 10 min PRN IV 0.5–10 mg/min Titrate by 1–2 mg/min q2hr, given the agent's longer half-life, and consider dose reduction after BP control is achieved	2–5 min, peak 15 min	2–6 h up to 18 h
Metoprolol	IV bolus: 5–15 mg q5–15 min PRN	5–20 min	2–6 h
Vasodilators (preload ↔ / ↓, afterload ↔ / ↓, CO ↔ / ↑)			
Hydralazine	IV bolus: 10–20 mg IM: 10–40 mg q30min PRN	IV: 10 min IM: 20 min	IV: 1–4 h IM: 2–6 h
Nitroglycerin	IV 5–200 mcg/min Titrate by 5–25 mcg/min q5–10 min	2–5 min	5–10 min
Sodium nitroprusside	IV 0.25–10 mcg/kg/min Titrate by 0.1–0.2 mcg/kg/min q5min	Seconds	1–2 min
Calcium channel blockers (preload ↔, afterload ↓, CO ↑)			
Clevidipine	IV 1–6 mg/h Titrate by 1–2 mg/h q90s; max 32 mg/h	1–4 min	5–15 min
Nicardipine	IV 5–15 mg/h Titrate by 2.5 mg/h q5–10 min	5–10 min	2–6 h
ACEI (preload ↓, afterload ↓, CO ↑)			
Enalaprilat	IV bolus: 1.25 mg q6hr Titrate no more than q12–24 h; Max dose: 5 mg q6hr	15–30 min	12–24 h
Alpha-antagonist (preload ↔ / ↓, afterload ↓, CO ↑)			
Phentolamine	IV bolus: 1–5 mg PRN; max 15 mg	Seconds	15 min
D1 receptor antagonists (preload ↔ / ↓, afterload ↓, CO ↑)			
Fenoldopam	IV 0.03–1.6 mcg/kg/min Titrate by 0.05–1 mcg/kg/min q15min	10–15 min	10–15 min

IV intravenous, *CO* cardiac output, *BP* blood pressure, *IM* intramuscular, *ACEI* angiotensin converting enzyme inhibitor

Table 10.7 Recommendations for Hypertensive Crises and Emergencies (2017 ACC/AHA) [1]

I B – NR	In adults with a hypertensive emergency, admission to an intensive care unit is recommended for continuous monitoring of BP and target-organ damage and for parenteral administration of an appropriate agent
I C – EO	For adults with a compelling condition (aortic dissection, severe preeclampsia or eclampsia, or pheochromocytoma crisis), SBP should be reduced to less than 140 mmHg during the first hour and to less than 120 mmHg in aortic dissection
I C – EO	For adults without a compelling condition, SBP should be reduced by no more than 25% within the first hour; then, if stable, to 160/100 mmHg within the next 2 to 6 h; and then cautiously to normal during the following 24–48 h

NR no recommendation, *EO* expert opinion

10.9 Additional Clinical Practice Takeaways

- The first step is an appropriate assessment of the presence (emergency) or absence (urgency) of end-organ damage, which is crucial for appropriate management.
- To reach a diagnosis, a complete history, physical examination, basic laboratory tests, and an electrocardiogram are necessary.
- In hypertensive emergency, reduce SBP by ≤25% in 1 h for the next 2–6 h, target 160/100 mmHg; and for the next 24–48 h, cautiously reduce blood pressure to normal.
- A hypertensive urgency can be treated as an outpatient with oral antihypertensive drugs, while a hypertensive emergency prompts tailored therapy, based on IV drugs and requiring observation seen in an inpatient setting. There's a wide array of medications, but specific end-organ involvement and patient comorbidities guide the appropriate therapy.
- In hypertensive urgency, there is no indication for immediate reduction of blood pressure in emergency department or hospitalization.

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Chapter 11
Tachyarrhythmias in the ER

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11.1 The Scope of the Problem

Cardiac arrhythmia is one of the most frequent cardiovascular causes of visit in the emergency room (ER). These patients require an accurate initial assessment and risk stratification because of the broad clinical and prognostic spectrum of the different types of dysrhythmias. The cardiac tachyarrhythmias are divided into two categories, narrow QRS complex tachycardia and wide QRS complex tachycardia. The first step in assessment in the ER is to discern between stable and unstable patients, depending on vital signs, mental status, and symptoms. This classification will give the attending physician an idea of the probable diagnosis and the urgency of treatment. The electrocardiogram (ECG) continues to be the cornerstone of the diagnosis, and its meticulous analysis provides important information. An additional benefit is accessibility and feasibility to obtain an ECG bedside. Tachyarrhythmias could be secondary to other cardiac and metabolic causes that should be considered during the initial approach. Some type of arrhythmias can be a challenge due to a complex pathophysiology mechanism and could require a multidisciplinary evaluation.

11.2 Prevalence

Cardiac arrhythmias are a common consultation in the ER and their prevalence can be divided according to the type of arrhythmia. Atrial fibrillation (AF), the most common cardiac dysrhythmia, has an estimated prevalence of 0.5–1% in the general population, and it accounts for 0.5% of all ER visits [1]. Palpitations were the chief complaint in an estimated 684,000 visits, representing a national prevalence of 5.8 per 1000 ER visits in the United States (0.58%; 95% CI 0.52-% to 0.64%). Supraventricular tachycardia (SVT) affects approximately 570,000 people in the United States alone and accounts for roughly 50,000 ER visits annually [2], with a prevalence in the general population of 2.29 per 1000 persons. There are

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approximately 89,000 new cases per year and 570,000 persons with paroxysmal SVT [3]. Ventricular tachycardia (VT) and ventricular fibrillation (VF) are the causes of approximately 300,000 deaths per year in the United States with an incidence of 53 per 100,000 people over 1 year [4].

11.3 High-Clinical Suspicion in the ER

Patients presenting in the ER, regardless of age and gender, with palpitations, chest pain, dyspnea, near- or syncope, and new or heart failure history, have a high probability of having some type of cardiac arrhythmia or another serious condition that threatens ventricular function or life as myocardial infarction, pulmonary embolism, etc., so an ECG must be done in the first 10 min after arrival to the ER. Physicians in the ER should be alerting to identify a primary or secondary tachyarrhythmia.

11.4 Risk Factors

Clinical features that are related to high-clinical suspicion are the following:

- Past medical history of:
  - Atrial fibrillation
  - Supraventricular tachycardia episode
  - Preexcitation syndrome (e.g., Wolff-Parkinson-White)
  - Cardiomyopathies
  - Extent ischemic heart disease
  - Sudden cardiac death episode
  - Unexplained syncope
  - Diseases inducing electrolyte imbalances
- Alcohol abuse
- Drug abuse
- Use of herbal medication with unknown effect
- Drugs that prolong QT interval
- Use of drugs that alter potassium or magnesium levels
- The family history of sudden cardiac death

Table 11.1 lists possible cardiovascular, pulmonary, and metabolic causes of tachyarrhythmias.

11.5 Clinical Presentation

Clinical presentation and physical findings of cardiac arrhythmias are highly variable, depending on the cause of the tachyarrhythmia, underlying mechanism, and heart rate. The spectrum varies from a light palpitation to sudden cardiac death that

Table 11.1 Frequent causes of tachyarrhythmias in the ER

System	Clinical conditions
Cardiovascular	Acute coronary syndrome Myocarditis Pulmonary embolism New-onset or chronic exacerbation AF or flutter Cardiac tamponade Acute aortic syndromes Long QT syndrome Hypertensive emergencies or urgencies
Pulmonary	COPD exacerbation Pulmonary embolism Chronic lung diseases
Metabolic	Chronic kidney disease exacerbation Hyper- or hypothyroidism Hypomagnesemia Hyper- or hypopotassemia

AF atrial fibrillation, *COPD* chronic obstructive pulmonary disease

arrives in cardiac arrest. Palpitation is the most frequent main complaint, followed by chest pain [5].

11.6 Main Clinical Characteristics

- Dyspnea
- Palpitations
- Chest pain
- Nausea
- Syncope
- Lightheadedness
- Diaphoresis
- Polyuria
- Fatigue
- Weakness
- Dizziness
- Cognitive impairment

11.7 Physical Examination

11.7.1 Clinical Stability

An extent clinical examination should be performed, with attention to vital signs, heart sounds, lung sounds, pulse examination, and oxygen saturation trying to rule out any cardiovascular cause of arrhythmias that require further evaluation and treatment, such as acute coronary syndrome, pulmonary embolism, cardiac tamponade,

etc. Physicians in charge should be aware of those patients with impending clinical instability, especially when vital signs are borderline.

11.7.2 Clinical Instability

The most important clinical aspect and the first step in the clinical assessment in the ER is the evaluation of hemodynamic stability depending on the following indicators [6]:

- Hypotension (systolic blood pressure <90 mmHg)
- Systemic hypoperfusion
- Altered mental status
- Respiratory distress
- Chest pain with ischemic characteristics
- Oxygen saturation <90%
- Very rapid ventricular rate (>200 beats/min)

11.7.3 Chest X-ray

A chest X-ray is not required for the diagnostic assessment of patients with arrhythmia unless another cardiac or pulmonary cause is highly suspected. In patients with heart failure history or with comorbidities, a chest X-ray is mandatory.

11.7.4 Electrocardiogram

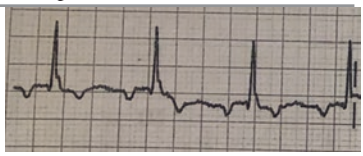
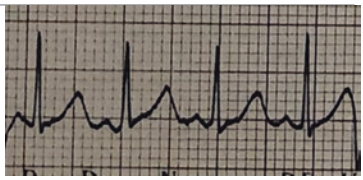
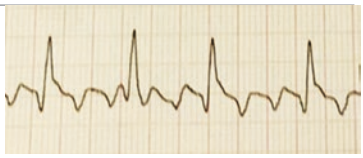
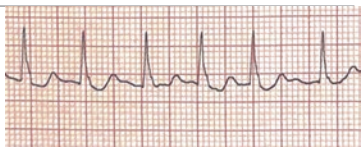
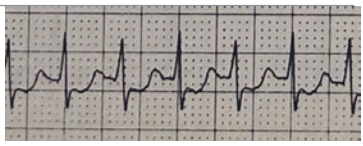
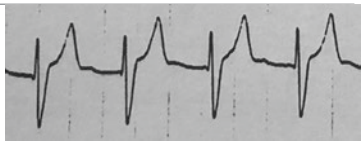
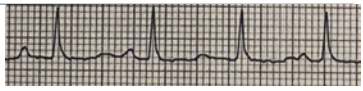
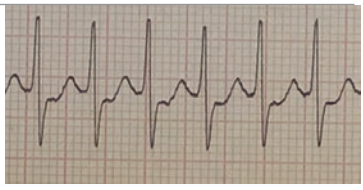
The ECG is the most important diagnostic tool and is mandatorily performed as the first step in the emergency attention care.

Tachyarrhythmias are initially classified as having a wide or narrow QRS complex, the cutoff point being 120 ms. This allows for narrowing down of diagnosis and treatment. Wide QRS tachycardias can be VT, SVT conducting with bundle branch block aberration, or SVT conducting with an accessory pathway, with a proportion of 80%, 15%, and 5%, respectively [5].

Another parameter that is useful in the ECG interpretation and classification of tachyarrhythmias is RP interval. The RP interval starts in the R wave and finishes in the P wave of the next heartbeat. A short RP interval is defined as being shorter than half the RR interval. Long RP is defined as RP > PR [5]. A very short RP interval (<70 ms) indicates typical AVNRT, atrial tachycardia, or focal junctional tachycardia. RP > 70 ms but still shorter than the RR interval indicates orthodromic AVRT, atypical AVNRT, atrial tachycardia, or non-paroxysmal junctional tachycardia. Along RP interval is possible in atrial tachycardia, AVRT, and atypical AVNRT.

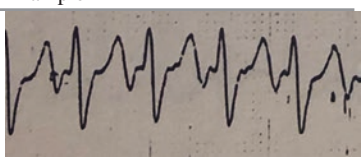
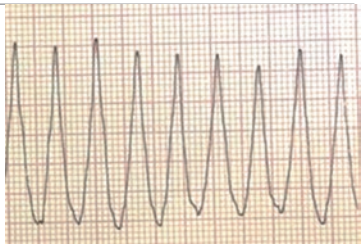
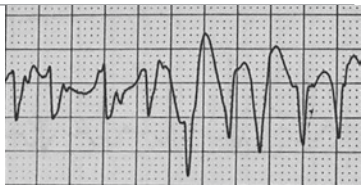
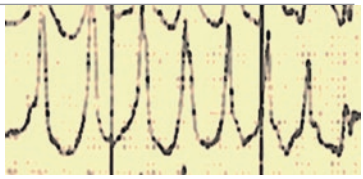
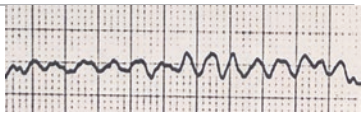
The ECG findings for each specific tachyarrhythmia are listed in Table 11.2.

Table 11.2 ECG findings in the principal arrhythmias [3, 7, 8]

Tachyarrhythmia	ECG characteristics	Example
Atrial reentrant tachycardia	Narrow QRS, regular, heart rate >100 bpm. P wave non-sinus buried in the QRS complex or T waves. Negative P waves in the inferior leads	
Focal atrial tachycardia	Narrow QRS, P wave inscribed before QRS complex with different form that of the sinus rhythm. Usually with negative P waves in inferior leads. Long RP interval. Heart rate 150–200 bpm	
Atrial flutter	Narrow QRS, regular or irregular depending on conduction, heart rate 75–175 bpm, recurrent regular sawtooth flutter waves (F wave) with lack of isoelectric interval between F waves	
Atrial fibrillation	Narrow QRS, grossly irregular, heart rate 100–160 bpm, no P waves with baseline undulation (f wave)	
AV nodal reentrant tachycardia	Narrow-QRS, regular, P waves inscribed at the end of the QRS complex, seen best in inferior leads or like pseudo r' in V1. Short RP interval. Heart rate 180–200 bpm	
Focal junctional tachycardia	Narrow QRS, regular, heart rate 100–180 bpm, P wave inverted present just before, hidden during or after QRS. Short RP interval	
Multifocal atrial tachycardia	Narrow QRS, irregular, heart rate >100 bpm, P waves with at least three different morphologies separated by isoelectric intervals variable RP and PR intervals	
Orthodromic AV reentrant tachycardia	Narrow QRS, P waves in ST-segment after QRS complex. Short RP interval. Functional bundle branch block usually associated with an accessory pathway ipsilateral to the blocked bundle, ST-segment depression. Heart rate 150–250 bpm	

(continued)

Table 11.2 (continued)

Tachyarrhythmia	ECG characteristics	Example
Antidromic AV reentrant tachycardia	Wide QRS when preexcited, P waves inscribed within the ST-T segment, long RP interval. Heart rate 150–200 bpm	
Ventricular tachycardia	Wide-QRS, monomorphic, heart rate >100 bpm (cycle length <600 ms), stable single QRS morphology from beat to beat. AV dissociation	
Polymorphic VT	Wide-QRS, polymorphic, changing or multiform QRS morphology from beat to beat	
Torsade de pointes	Wide-QRS, polymorphic, waxing and waning QRS amplitude, twisting of the points, long-short initiating sequence with a long coupling interval to the first VT beat	
Ventricular fibrillation	Wide-QRS, rapid, grossly irregular electrical activity, ventricular rate >300 bpm (cycle length <200 ms)	

BPM beats per minute, *AV* atrioventricular, *VT* ventricular tachycardia

11.8 Diagnostic Approach

As seen before, the diagnostic approach starts with ECG findings, which will give the physicians the principal clues to arrive at an accurate diagnosis and initial treatment. Figure 11.1 shows a diagnostic approach of tachyarrhythmias.

In wide QRS tachyarrhythmia, the principal challenge of the diagnostic approach is differentiating VT from SVT. Brugada, Vereckei, Wellens, and Kindall are exam-

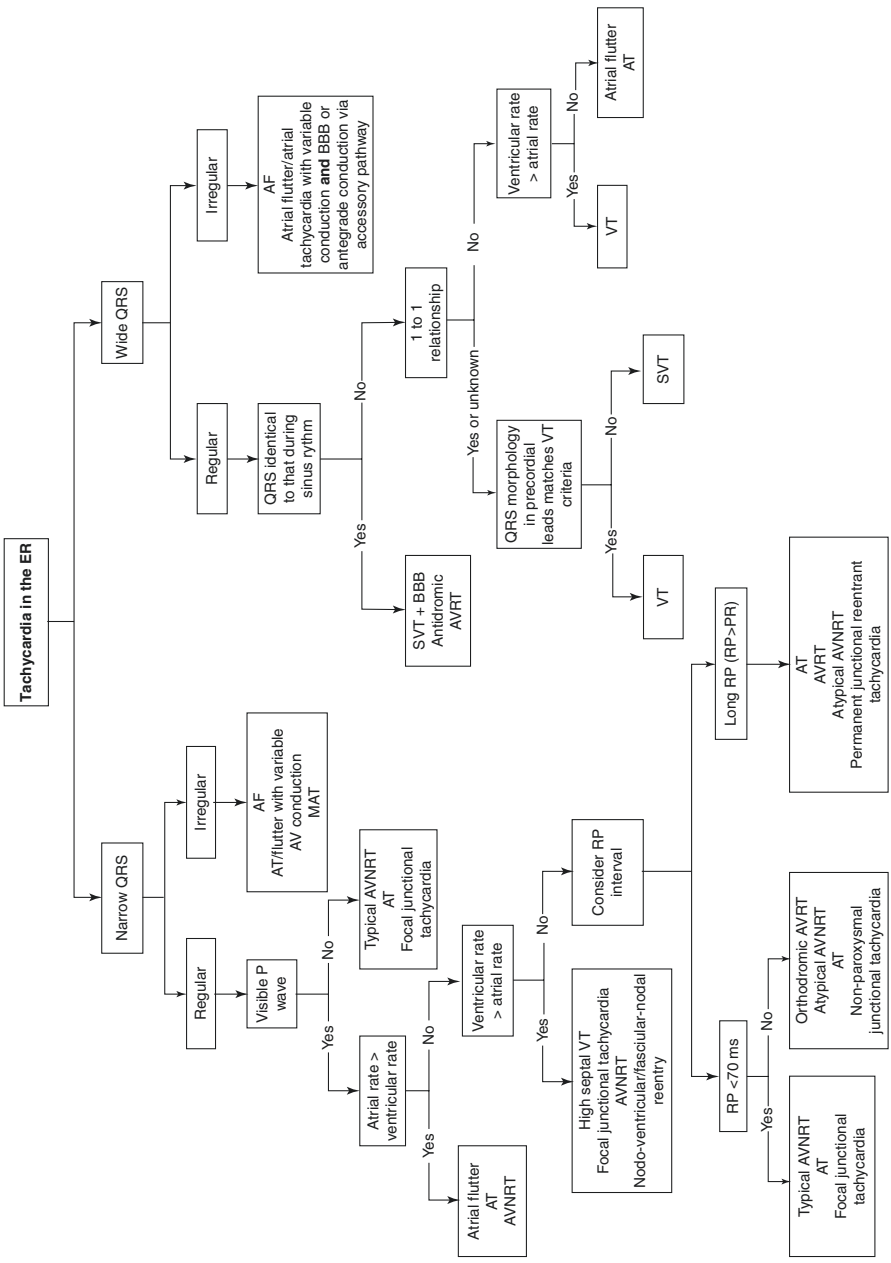


Fig. 11.1 Diagnostic approach of tachyarrhythmias

Table 11.3 Electrocardiographic characteristic of supraventricular and ventricular tachycardia [5–7, 9]

Criteria	Variables	SVT	VT
Brugada algorithm	The absence of an RS complex in all precordial leads		✓
	R to S interval >100 ms in one precordial lead		✓
	AV dissociation		✓
	Morphology criteria for VT presented both V1-V2 and V6 If RBBB morphology: Monophasic R or qR in V1 R taller than R' rS in V6 If LBBB morphology: Initial R >40 ms Slurred or notched S in V1 or V2 Beginning Q or QS in V6		✓
Vereckei algorithm	Presence of an initial R wave in QRS complex in aVR		✓
	Initial R or Q wave >40 ms in aVR		✓
	Presence of a notch on the descending limb at the onset of a predominantly negative QRS		✓
	Vinitial/Vterminal ≥1		✓
Wellens algorithm	AV dissociation		✓
	QRS width >140 ms		✓
	Left axis deviation > −30°		✓
	If RBBB morphology:		
	Monophasic or biphasic QRS in V1	✓	
	R-to-S ratio of <1 in V6		✓
	If LBBB morphology:		
	S in V1-V2		✓
Lead II R wave peak time criterion	Time to intrinsicoid deflection in lead II (interval from QRS onset to peak of the first wave ≥50		✓
Kindall criteria	R >30 ms in V1 or V2		✓
	Any Q in V6		✓
	>60 ms to S wave nadir in V1 or V2		✓
	Notched downstroke S wave in V1 or V2		✓
Other characteristics	Onset with premature P wave	✓	
	RP interval <100 ms	✓	
	QRS complexes in precordial leads all positive or negatives (concordant)		✓
	QRS in tachycardia that is identical to sinus rhythm	✓	

AV atrioventricular, *VT* ventricular tachycardia, *RBBB* right bundle branch block, *LBBB* left bundle branch block

ples of available algorithms useful in the decision-making of initial treatment. The algorithms are presented in Table 11.3.

11.9 Transthoracic and Transesophageal Echocardiogram

A transthoracic echocardiogram is not required in the diagnostic assessment of patients with arrhythmia unless another cardiac or pulmonary cause is highly suspected (e.g., pulmonary embolism, ACS, or arrhythmogenic right ventricular dysplasia).

The only role transesophageal echocardiogram has in arrhythmias approach is the assessment of thrombi presence in the left atrium appendage if the cardioversion will be performed in patients with AF >72 h duration and unknown time since initial symptoms.

11.10 Cardiac Computed Tomography

A cardiac computed tomography (CT) is not required for the diagnostic assessment of patients with arrhythmia unless another cardiac or pulmonary cause is highly suspected (e.g., pulmonary embolism or aortic dissection, arrhythmogenic right ventricular dysplasia).

Table 11.4 Differential diagnosis of tachyarrhythmias [3, 5, 6, 10]

QRS duration	Regular rhythm	Irregular rhythm
Narrow QRS (<20 ms)	Physiological sinus tachycardia Inappropriate sinus tachycardia Sinus nodal reentrant tachycardia Focal atrial tachycardia Atrial flutter Atrial fibrillation with a very fast ventricular response AV nodal reentrant tachycardia Non-paroxysmal or focal junctional tachycardia Orthodromic AV reentrant tachycardia Idiopathic ventricular tachycardia (especially high septal VT)	Atrial fibrillation Atrial focal tachycardia or atrial flutter with varying AV block Multifocal atrial tachycardia
Wide QRS (>120 ms)	Antidromic AV reentrant tachycardia Any regular atrial or junctional reentrant tachycardia with aberration/bundle branch block or preexcitation/bystander accessory pathway Ventricular tachycardia/flutter Paced rhythm	Atrial fibrillation or atrial tachycardia with varying block conducted with aberration Antidromic AV reentrant tachycardia with a variable VA conduction Preexcited AF Polymorphic VT Torsade de pointes Ventricular fibrillation Artifact

AV atrioventricular, *VT* ventricular tachycardia, *VA* ventriculoatrial, *AF* atrial fibrillation

11.11 Differential Diagnosis

Tachyarrhythmias are a broad category of disease and ECG expression. ECG findings allow for the initial differentiation between the diverse types of arrhythmias. The first step to identify auricular or ventricular etiology is to establish if the tachycardia has a narrow or wide QRS complex. Table 11.4 shows tachyarrhythmias with narrow or wide QRS complex.

11.12 Laboratory Evaluation

The laboratory workup is related primarily to find electrolyte imbalance and rule out the differential diagnosis causes of arrhythmias. The laboratory tests are listed below:

- Chemistry profile
- Electrolytes
- Troponin
- D-dimer
- B-type natriuretic peptide
- Toxicologic test
- Thyroid profile

11.13 Treatment

The treatment of tachyarrhythmias is based on the type, duration, and stability of the patient (see Fig. 11.2 acute treatment algorithm).

It is important to remember that initial treatment includes continuous ECG monitoring, vital signs, and oximetry and must be performed in a facility that can provide a complete cardiac resuscitation.

The Vaughan Williams classification divides antiarrhythmic drugs by membrane effect in the conduction heart system in four different classes listed in Table 11.5.

In SVT with hemodynamic stability, the initial management in ER is vagal maneuvers that consist in [6]:

- *Carotid sinus massage*: massage only one side at a time for 20 s and change of side if you need to repeat the procedure. Recommendation: always listen for bruit before the start, and do not massage if it is present.
- *Valsalva maneuver***:** request the patient to hold breath and strain against closed glottis while tightening abdominal wall muscles for >20 s. The vagal tone increases during release phase after holding breath.
- *Diving reflex***:** place bag of ice and water on the face for 15–30 s.

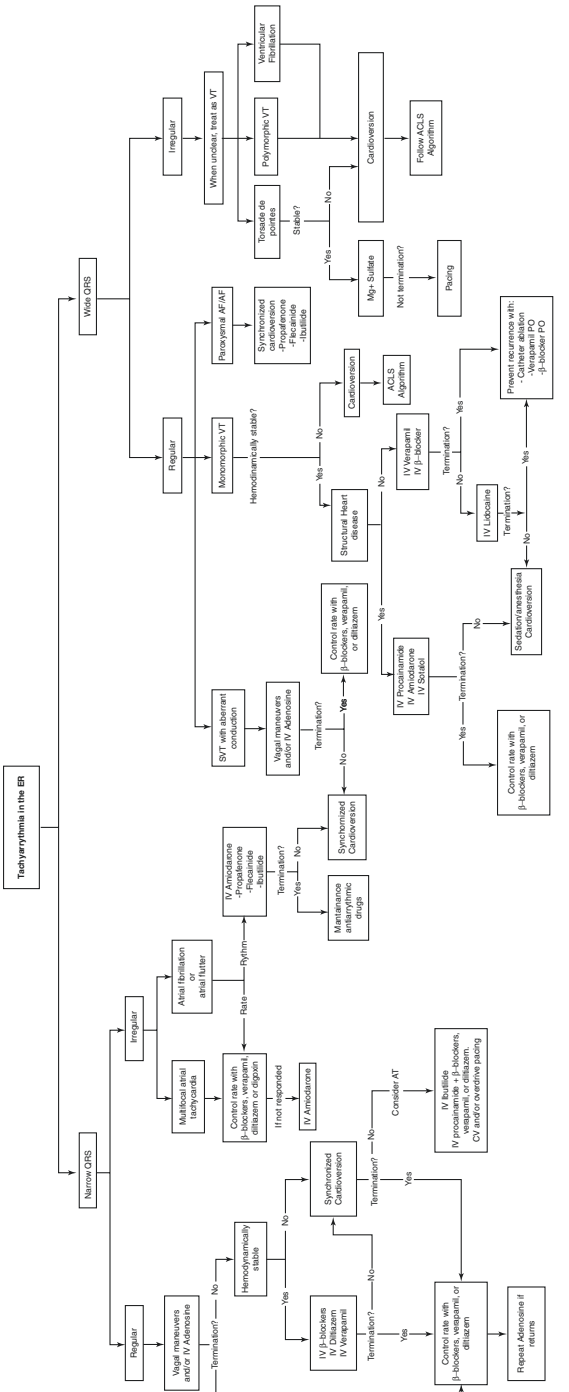


Fig. 11.2 Treatment algorithm for tachyarrhythmias

Table 11.5 Vaughan Williams classification [11]

Class	Mechanism of action	Drugs
Ia	Na^+ channel block; intermediate kinetics K^+ channel block	Quinidine Procainamide Disopyramide
Ib	Na^+ channel block; rapid kinetics	Lidocaine Tocainide Mexiletine
Ic	Na^+ channel block; slow kinetics	Flecainide Propafenone Moricizine
II	Beta-adrenergic receptor inhibition	Propranolol Metoprolol Sotalol
III	K^+ channel block; slow Na^+ channel facilitator	Amiodarone Dronedarone Sotalol Ibutilide
IV	Ca^{2+} channel block	Verapamil Diltiazem

If vagal maneuvers are not effective or preferred, the first choice of antiarrhythmic drug is adenosine, followed by verapamil, diltiazem, and beta-blockers as second-line antiarrhythmic drugs [3, 5].

In SVT with hemodynamic instability, synchronized cardioversion is the treatment of choice [3, 5]. The initial recommended doses are the following [12]:

- Narrow regular: 50–100 joules
- Narrow irregular: 120–200 joules
- Wide regular: 100 joules

If the rhythm is not recovered, the second shock must be 200 joules in biphasic defibrillator or equivalent to 360 joules monophasic defibrillator [12]. We recommend in situations that endanger life or in clinical conditions that require a rapid restoration (pregnant, abnormal ejection fraction, ACS, etc.) of sinus rhythm a discharge with the greatest energy available.

Some specific arrhythmias have different acute treatment options that must be considered in the initial approach of the patients with this diagnosis. The specific treatment of those is described in Tables 11.6 and 11.7.

In hemodynamically stable VT, the treatment recommended is amiodarone, flecainide, procainamide, or beta-blockers trying to terminate the arrhythmia [4, 5, 13].

In VT with hemodynamic instability, cardioversion with 200 joules biphasic or 360 joules monophasic equivalent no synchronized is the gold standard of care, and advanced vital life support must is instituted with a multidisciplinary approach [12].

Table 11.6 Acute therapeutic approach to auricular and ventricular arrhythmias

Focal atrial tachycardia	
First-line	Hemodynamically stable: IV beta-blocker, IV diltiazem, or IV verapamil Hemodynamically unstable: synchronized cardioversion
Second-line	Stable patients: IV adenosine, IV flecainide, IV propafenone, IV amiodarone, IV ibutilide Synchronized cardioversion
Atrial flutter	
First-line treatment	*Hemodynamically stable* Rhythm control: synchronized cardioversion, PO dofetilide, IV ibutilide, rapid atrial pacing Rate control: IV beta-blocker, IV diltiazem, IV verapamil *Hemodynamically unstable* Rhythm control: synchronized cardioversion Rate control: IV amiodarone
Second-line treatment	Rate control in stable patients: IV amiodarone
Atrial fibrillation	
First-line treatment	*Hemodynamically stable* Rhythm control: <48 h: synchronized cardioversion. IV ibutilide, IV amiodarone >48 h or unknown duration: anticoagulation for 3 weeks or TEE before cardioversion Rate control: IV beta-blocker, IV diltiazem, IV verapamil *Hemodynamically unstable* Rhythm control: synchronized cardioversion (anticoagulation with heparin or NOAC)
Second-line treatment	Rhythm control in stable patients: PO flecainide, PO propafenone, PO amiodarone Rate control in stable patients: IV digoxin or IV amiodarone
AV nodal reentrant tachycardia	
First-line treatment	Stable patients: vagal maneuvers and/or IV adenosine Unstable patients: synchronized cardioversion
Second-line treatment	Stable patients: IV/PO beta-blocker, IV/PO diltiazem, IV/PO verapamil, IV amiodarone Synchronized cardioversion
Focal junctional tachycardia	
First-line	IV beta-blocker (preferred propranolol) with or without procainamide
Second-line	IV diltiazem, IV procainamide, IV verapamil
Multifocal atrial tachycardia	
First-line	IV beta-blocker (preferred metoprolol)
Second-line	IV verapamil, IV diltiazem
Orthodromic AV reentrant tachycardia	
First-line	Stable patients: vagal maneuvers and/or IV adenosine Unstable patients: synchronized cardioversion
Second-line	Stable patients: IV beta-blocker, IV diltiazem, IV verapamil Synchronized cardioversion

(continued)

Table 11.6 (continued)

Monomorphic ventricular tachycardia	
First-line	*Hemodynamically stable* SHD: cardioversion, IV procainamide, IV amiodarone, IV sotalol No SHD: IV verapamil, IV beta-blocker
Second-line	Stable patients: cardioversion, catheter ablation
Torsade de pointes	
First-line	Hemodynamically stable: magnesium sulfate Hemodynamically unstable: cardioversion
Second-line	Stable patients: mexiletine If it depends on low heart rate: atropine, isoproterenol, transient pacemaker, atrial rapid pacing

Table 11.7 Antiarrhythmic drugs for the treatment of tachyarrhythmias [3, 5, 6, 8, 13]

Drug	Initial dose	Subsequent or maintenance dose
Class Ib antiarrhythmics		
Lidocaine	1 mg/kg IV over 1 min	0.5 mg/kg IV every 5–10 min if not effective, up to 300 mg in 1 h period. 1–4 mg/min IV infusion
Mexiletine	Loading dose: 400 mg PO	Maintenance dose: 200 mg PO TID
Adverse effects: bradycardia, hypotension, rash, euphoria, tinnitus, drowsiness; mexiletine also can present with tremor, dysarthria, and dizziness		
Class Ic antiarrhythmics		
Flecainide	1.5–2 mg/kg IV over 10 min	–
	200–300 mg PO	150 mg PO every 12 h
Propafenone	1.5–2 mg/kg IV over 10 min	–
	150 mg PO every 8 h (immediate release) 225 mg PO every 12 h (extended release)	300 mg PO every 8 h (immediate release); 425 mg PO every 12 h (extended release)
Adverse effects: atrial flutter with 1:1 AV conduction, QT prolongation, torsade de pointes, worsening HF, bradycardia (PR and QRS should be monitored)		
Beta-blockers (Class II)		
Esmolol	500 mcg/kg IV bolus over 1 min	50–300 mcg/kg/min infusion, with boluses between each dosing increase
Metoprolol tartrate	2.5–5.0 mg IV bolus over 2 min	2.5–5.0 mg IV additional bolus in 10 min if not effective
	25 mg PO QD	Up to three doses 200 mg PO QD
Metoprolol succinate (long-acting)	50 mg PO QD	400 mg PO QD
Nadolol	40 mg PO QD	320 mg PO QD (reduce in renal impairment)
Propranolol	1 mg IV over 1 min	1 mg IV additional dose at 2 min intervals if not effective; up to three doses
	30–60 mg PO daily divided or a single dose (long-acting formulation)	40–160 mg PO daily divided or a single dose (long-acting formulation)

Table 11.7 (continued)

Drug	Initial dose	Subsequent or maintenance dose
Atenolol	25–50 mg PO QD	100 mg PO QD (reduce dose in renal impairment)
Sotalol	40–80 mg PO every 12 h (CrCL >60 mL/min), or every 24 h (CrCl 40–60 mL/min)	160 mg PO every 12 h (if QTc >500 ms reduce dose or discontinue)
Adverse effects: hypotension, worsening HF, bradycardia, bronchospasm Sotalol: QT prolongation, torsades de pointes, bradycardia, bronchospasm; contraindicated if QTc interval >450 ms (QT interval follow-up 2–4 h post-dose is required for first five doses)		
Class III antiarrhythmics		
Amiodarone	150 mg IV over 10 min	1 mg/min (360 mg) IV infusion over next 6 h; then 0.5 mg/min (540 mg) IV over 18 h
	Loading dose: 400–600 mg PO QD in divided doses for 2–4 wks	Maintenance dose: 100–200 mg PO QD
Droneradone	–	400 mg PO BID
Ibutilide	>60 kg: 1 mg over 10 min <60 kg: 0.01 mg/kg	1 mg once if not effective within 10 min
Dofetilide	500 mcg PO every 12 h (CrCl >60 mL/min) 250 mcg PO every 12 h (CrCl 40–60 mL/min) 125 mg PO every 12 h (CrCl 20–40 mL/min)	Repeat ECG 2–3 h after first dose, if QTc increased by >15% compared with baseline or QTc >500 ms (>550 ms if ventricular conduction abnormalities), reduce 50% subsequent dose. After 2nd dose if QTc >500 ms (>550 ms if ventricular conduction abnormalities) should be discontinued
Vernakalant	3 mg/kg IV over 10 min	2 mg/kg IV over 10 min if not effective
Amiodarone adverse effects: hypotension, bradycardia, phlebitis, QT prolongation, torsade de pointes (rare), increased INR, constipation hypothyroidism, hyperthyroidism, pulmonary fibrosis, hepatic toxicity, neuritis, corneal deposits, peripheral neuropathy, photosensitivity, adult respiratory distress syndrome after cardiac or non-cardiac surgery (rare) Droneradone/ibutilide/dofetilide**:** QT prolongation, torsades de pointes dronedarone is contraindicated in acute HF and CrCl <30 mL/min Ibutilide/dofetilide are contraindicated in patients with QTc >440 ms or 500 ms and ventricular conduction abnormalities QT interval follow-up 2–4 h post-dose is required (first five doses) Vernakalant should be avoided in severe AS, ACS within 30 days, or hypotension		
Non-dihydropyridine calcium channel antagonist		
Diltiazem	0.25 mg/kg IV bolus over 2 min	5–10 mg/h infusion; up to 15 mg/h
	120 mg PO daily divided or a single dose (long-acting formulation)	360 mg PO daily divided or a single dose (long-acting formulation)

(continued)

Table 11.7 (continued)

Drug	Initial dose	Subsequent or maintenance dose
Verapamil	5–10 mg (0.075–0.15 mg/kg) IV bolus over 2 min	10 mg (0.15 mg/kg) 30 min after first dose if not effective; then 0.005 mg/kg/min IV infusion
	120 mg PO daily in a divided or single dose (long-acting formulation)	480 mg PO daily divided or a single dose (long-acting formulation)
Adverse effects: hypotension, worsening HF in patients with pre-existing ventricular dysfunction, bradycardia, abnormal liver function studies, pulmonary edema in patients with HCM (verapamil)		
Cardiac glycoside		
Digoxin	0.25–0.5 mg IV bolus	0.25 mg IV bolus additional dose if not effective, up to maximum dose of 1.0 mg IV over 24 h. Maintenance dose 2.4–3.6 mcg/kg/d IV
	Loading dose: 0.5 mg PO with additional dose at 6–8 h intervals until adequate effect (maximum 8–12 mcg/kg over 24 h)	0.25 mg PO QD Maintenance: 0.125–0.25 mg PO QD
Adverse effects: anorexia, nausea, vomiting, visual changes, and cardiac arrhythmias if digoxin toxicity		
Nucleoside		
Adenosine	6 mg IV bolus rapid infusion followed by a saline flush	12 mg IV bolus rapid infusion if not effective in 1 min
Adverse effects: transient AV block, chest pain, hypotension, dyspnea, AF in the presence of preexcitation		
Other antiarrhythmics		
Magnesium sulfate	2 g IV over 2 min	1–2 g/h IV infusion
Adverse effects: flushing, sweating, hypotension, hypothermia, respiratory depression		

AV atrioventricular, *AF* atrial fibrillation, *IV* intravenous, *PO* oral, *QD* once daily, *HCM* hypertrophic cardiomyopathy, *BID* twice daily, *INR* international normalized ratio, *TID* three doses daily, *AS* aortic stenosis, *ACS* acute coronary syndrome, *HF* heart failure, *CrCl* creatinine clearance
The main recommendations from ventricular and auricular arrhythmias are shown in Table 11.8.

Table 11.8 Current international guideline recommendations [3, 5, 8, 13]

AHA/ACC Guidelines	COR	LOE
Ventricular arrhythmias		
CPR should be performed in patients in cardiac arrest according to published basic and advanced cardiovascular life support algorithms	I	A
Patients presenting with VA with hemodynamic instability should undergo direct current cardioversion	I	A
In patients with hemodynamically unstable VA that persist or recur after a maximal energy shock, intravenous amiodarone should be administrated to attempt to achieve a stable rhythm after further defibrillation	I	A
Patients with wide-QRS tachycardia should be presumed to have VT if the diagnosis is unclear	I	C-EO
In patients with hemodynamically stable VT, administration of intravenous procainamide can be useful to attempt to terminate VT	IIa	A
In patients with polymorphic VT due to myocardial ischemia, intravenous beta-blockers can be useful	IIa	B-R
In patients with hemodynamically stable VT, administration of intravenous amiodarone or sotalol may be considered to attempt to terminate VT	IIb	B-R
In patients with a wide QRS complex tachycardia of unknown origin, calcium channel blockers (e.g., verapamil and diltiazem) are potentially harmful	III	C-LD
Supraventricular arrhythmias		
Vagal maneuvers are recommended for acute treatment in patients with regular SVT	I	B-R
Adenosine is recommended for acute treatment in patients with regular SVT	I	B-R
Synchronized cardioversion is recommended for acute treatment in patients with hemodynamically unstable SVT when vagal maneuver or adenosine is ineffective or not feasible	I	B-NR
Synchronized cardioversion is recommended for acute treatment in patients with hemodynamically stable patients SVT when pharmacological therapy is ineffective or contraindicated	I	B-NR
Intravenous diltiazem or verapamil can be effective for acute treatment in patients with hemodynamically stable SVT	IIa	B-R
Intravenous beta-blockers are reasonable for acute treatment in patients with hemodynamically stable SVT	IIa	C-LD
Oral beta-blockers, diltiazem, or verapamil is useful for ongoing management in patients with symptomatic SVT who do not have ventricular preexcitation during sinus rhythm	I	B-R
EP study with the option of ablation is useful for the diagnosis and potential treatment of SVT	I	B-NR
Flecainide or propafenone is reasonable for ongoing management in patients without structural heart disease or ischemic heart disease who have symptomatic SVT and are not candidates for or prefer not to undergo catheter ablation	IIa	B-R
Sotalol may be reasonable for ongoing management in patients with symptomatic SVT who are not candidates for or prefer not to undergo catheter ablation	IIb	B-R
Dofetilide may be reasonable for ongoing management in patients with symptomatic SVT who are not candidates for, or prefer not to undergo, catheter ablation and in whom beta-blockers, diltiazem, flecainide, propafenone, or verapamil is ineffective or contraindicated	IIb	B-R

(continued)

Table 11.8 (continued)

AHA/ACC Guidelines	COR	LOE
Oral amiodarone may be considered for ongoing management in patients with symptomatic SVT who are not candidates for, or prefer not to undergo, catheter ablation and in whom beta-blockers, diltiazem, dofetilide, flecainide, propafenone, sotalol, or verapamil is ineffective or contraindicated	IIb	C-LD
Oral digoxin may be reasonable for ongoing management in patients with symptomatic SVT without preexcitation who are not candidates for or prefer not to undergo catheter ablation	IIb	C-LD
Atrial fibrillation and flutter		
Control ventricular rate using a beta-blocker or non-dihydropyridine calcium channel antagonist for paroxysmal, persistent, or permanent AF	I	B
IV beta-blocker or non-dihydropyridine calcium channel blocker is recommended to slow ventricular heart rate in the acute setting in patients without preexcitation. In hemodynamically unstable patients, electrical cardioversion is indicated	I	B
A heart rate control (resting heart rate <80 bpm) strategy is reasonable for symptomatic management of AF	IIa	B
IV amiodarone can be useful for rate control in critically ill patients without preexcitation	IIa	B
With preexcitation and AF, digoxin, non-dihydropyridine calcium channel antagonists, or amiodarone should not be administered	III	B
With AF or atrial flutter for ≥48 h or unknown duration, anticoagulation with warfarin for at least 3 weeks before and 4 weeks after cardioversion	I	C
With AF or atrial flutter for >48 h or unknown duration, requiring immediate cardioversion, use anticoagulation as soon as possible and continue for at least 4 weeks	I	C
With AF or atrial flutter <48 h and high stroke risk, IV heparin or LMWH, or factor Xa or direct thrombin inhibitor, is recommended before or immediately after cardioversion, followed by long-term anticoagulation	I	C
With AF or atrial flutter for ≥48 h or unknown duration and no anticoagulation for preceding 3 weeks, it is reasonable to perform TEE before cardioversion and then cardiovert if no LA thrombus is identified, provided anticoagulation is achieved before TEE and maintained after cardioversion for at least 4 weeks	IIa	B
With AF or atrial flutter ≥48 h or unknown duration, anticoagulation with dabigatran, rivaroxaban, or apixaban is reasonable for ≥3 weeks before and 4 weeks after cardioversion	IIa	C
With AF or atrial flutter <48 h and low thromboembolic risk, IV heparin, LMWH, a new oral anticoagulant, or no antithrombotic, may be considered for cardioversion	IIb	C
Cardioversion is recommended for AF or atrial flutter to restore sinus rhythm. If unsuccessful, cardioversion attempts may be repeated	I	B
Cardioversion is recommended for AF or atrial flutter with RVR that does not respond to pharmacological therapies	I	C
Cardioversion is recommended for AF or atrial flutter and preexcitation with hemodynamic instability	I	C
Flecainide, dofetilide, propafenone, and IV ibutilide are useful for cardioversion of AF or atrial flutter, provided contraindications to the selected drug are absent	I	A

Table 11.8 (continued)

AHA/ACC Guidelines	COR	LOE
Amiodarone is reasonable for pharmacological cardioversion of AF	IIa	A
Warfarin recommended for mechanical heart valves and target INR intensity based on type and location of the prosthesis	I	B
With a prior stroke, TIA, or CHA2DS2-VASc score ≥2, oral anticoagulation with warfarin is recommended	I	A
With a prior stroke, TIA, or CHA2DS2-VASc score ≥2, oral anticoagulation with dabigatran, rivaroxaban or apixaban is recommended	I	B
With nonvalvular AF and a CHA2DS2-VASc score of 0, it is reasonable to omit antithrombotic therapy	IIa	B
With nonvalvular AF and a CHA2DS2-VASc score of 1, no antithrombotic therapy or treatment with oral anticoagulant or aspirin may be considered	IIb	C
For atrial flutter, antithrombotic therapy is recommended as for AF	I	C
European heart rhythm association/ESC guidelines		
Ventricular tachycardias		
Direct current cardioversion is recommended for patients presenting with sustained VT and hemodynamic instability	I	C
In patients presenting with sustained hemodynamically tolerated VT in the absence of structural heart disease (e.g., idiopathic RVOT), IV flecainide or a conventional beta-blocker, verapamil, or amiodarone may be considered	IIb	C
Urgent catheter ablation is recommended in patients with scar-related heart disease presenting with incessant VT or electrical storm	I	B
Supraventricular tachycardia		
Hemodynamically unstable SVT synchronized electrical cardioversion is recommended	1	–
Hemodynamically stable SVT		
Vagal maneuvers, preferably in the supine position, or adenosine is recommended	1	–
IV diltiazem or verapamil may be considered	2	–
IV beta-blockers may be considered	2	–
Atrial flutter		
Synchronized DC cardioversion is recommended for hemodynamically unstable patients with macro-reentrant tachycardia	1	–
IV anticoagulation may be considered in case emergency cardioversion is necessary. Continued for 4 weeks after sinus rhythm is established	2	–
IV beta-blockers, diltiazem, or verapamil is recommended for acute rate control who are hemodynamically stable	1	–
IV ibutilide or dofetilide, under close monitoring due to proarrhythmic risk, is recommended to cardiovert atrial flutter	1	–
Amiodarone may be considered to control ventricular rate in the acute setting	2	–
Class Ic antiarrhythmic drugs should not be used in the absence of AV blocking agents because of the risk of slowing atrial rate and leading to 1:1 AV conduction	3	–

(continued)

Table 11.8 (continued)

AHA/ACC Guidelines	COR	LOE
Focal junctional tachycardia		
IV propranolol with or without procainamide, verapamil, or flecainide may be considered for acute therapy	1	–
AVRT		
Adenosine is recommended for cardioversion to sinus rhythm but should be used with caution because it may precipitate AF with a rapid ventricular rate and even ventricular fibrillation	1	–
Atrial fibrillation		
Beta-blockers, digoxin, diltiazem, or verapamil is recommended to control heart rate in AF patients with LVEF ≥40%	I	B
Beta-blockers and/or digoxin is commanded for controlling heart rate in AF patients with LVEF <40%	I	B
In patients with hemodynamic instability or severely depressed LVEF, amiodarone may be considered for acute control of heart rate	IIb	B
In patients with permanent AF (i.e., where no attempt to restore sinus rhythm is planned), antiarrhythmic drugs should not routinely be used for rate control	III	A
A resting heart rate of <110 bpm should be considered as the initial heart rate target for rate control therapy	IIa	B
Rhythm rather than rate control strategies should be considered as the preferred management in preexcited AF and AF during pregnancy	IIa	C
Rhythm control therapy is indicated for symptom improvement in patients with AF	I	B
With the exception of AF associated with hemodynamic instability, the choice between electrical and pharmacological cardioversion should be guided by patient and physician preferences	IIa	C
Electrical cardioversion of AF is recommended in patients with acute hemodynamic instability to restore cardiac output	I	B
Cardioversion of AF (either electrical or pharmacological) is recommended in symptomatic patients with persistent or long-standing persistent AF as part of rhythm control therapy	I	B
Pre-treatment with amiodarone, flecainide, ibutilide, or propafenone should be considered to enhance the success of electrical cardioversion and prevent recurrent AF	IIa	B
In patients with no history of ischemic or structural heart disease, flecainide, propafenone, or vernakalant is recommended for pharmacological cardioversion of new-onset AF	I	A
In patients with ischaemic and/or structural heart disease, amiodarone is recommended for cardioversion of AF	I	A
Vernakalant may be considered as an alternative to amiodarone for pharmacological conversion of AF in patients without hypotension, severe heart failure, or severe structural heart disease (especially aortic stenosis)	IIb	B
Anticoagulation with heparin or a NOAC should be initiated as soon as possible before every cardioversion of AF or atrial flutter	IIa	B
For cardioversion of AF/atrial flutter, effective anticoagulation is recommended for a minimum of 3 weeks before cardioversion	I	B

Table 11.8 (continued)

AHA/ACC Guidelines	COR	LOE
Transesophageal echocardiography (TOE) is recommended to exclude cardiac thrombus as an alternative to preprocedural anticoagulation when early cardioversion is planned	I	B
Early cardioversion can be performed without TOE in patients with a definite duration of AF <48 h	IIa	B

COR class of recommendation, *LOE* level of evidence, *AF* atrial fibrillation, *TIA* transient ischemic attack, *IV* intravenous, *RVR* rapid ventricular rate
Scientific rationale of recommendations of EHRA consensus document on the management of SVT: 1, recommended/indicated (scientific evidence that a treatment or procedure is beneficial and effective; requires at least one randomized trial or is supported by strong observational evidence and authors consensus); 2, may be used or recommended (general agreement and/or scientific evidence favor the usefulness/efficacy of a treatment or procedure; may be supported by randomized trials that are, however, based on small number of patients to allow a green heart recommendation); 3, should not be used or recommended (scientific evidence or general agreement not to use or recommend a treatment or procedure)

11.14 Additional Clinical Practice Takeaway

- In patients with tachyarrhythmia in whom it is not possible to distinguish between SVT from VT, treat it as VT.
- Patients with tachyarrhythmia are mandatory to realize clinical workup to rule out primary cardiovascular or metabolic disease.
- Physicians in ED must be used to recognize ECG-specific features of more prevalent tachyarrhythmias and the initial treatment.
- Physicians in the ER should be alerting to identify a primary or secondary tachyarrhythmia.
- Physicians in charge should be aware of those patients with impending clinical instability, especially when vital signs are borderline.
- Physicians in charge should be aware of those patients with tachyarrhythmia and impending clinical instability, especially when vital signs are borderline.
- Adenosine is the first-line antiarrhythmic drug for SVT, but the effectiveness depends on the correct IV infusion followed by a saline flush. If the ECG have not any change, the drug does not reach the heart in the active form and must be repeated with adjusting in the infusion technique.
- Electric cardioversion is an effective and safe therapeutic strategy that must be used in non-responders to pharmacological cardioversion in stable patients without concern of how dramatic looks like.

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Chapter 12
Bradyarrhythmia in the ER

Carlos Jerjes-Sánchez, Jose Gildardo Paredes-Vázquez, Mariana Vanoye Tamez, David Rodríguez, Raul del Toro-Mijares, and Mauricio Vázquez Guajardo

12.1 The Scope of the Problem

Bradyarrhythmias are defined by a heart rate below 60 beats per minute (bpm) and are not always a pathologic condition with life-threatening aspects. They are caused by an abnormal function at any point in the conduction system of the heart. They are a less frequent variant of cardiac arrhythmias presenting to the emergency room (ER) than tachyarrhythmias but require the same meticulous assessment and risk stratification, because of their broad clinical and prognostic spectrum. The first step in the clinical assessment must be the determination of hemodynamic stability or instability, depending on vital signs, mental status, and other symptoms. This will establish the initial management of the patient. The electrocardiogram (ECG) is the gold standard for the diagnosis and should be performed in the first 10 minutes of admission to the ER. It can be performed at the bedside of the patient, and its thorough analysis provides important information for clinical decision-making. On the other hand, it is important that other cardiac and metabolic causes of the bradyarrhythmia should be considered during the initial approach, as their recognition and treatment would resolve the acute event.

12.2 Prevalence

A bradyarrhythmia is an uncommon complaint in the ER. Unfortunately, no clinical records are available with accurate information about their real prevalence in ER. This condition can be divided according to its etiology. The primary causes are due to an intrinsic defect in the conduction system, whereas the secondary causes include extrinsic alterations of the conduction system. One study found that only 15% of unstable patients with bradyarrhythmia that presents to the ER are due to a primary defect in the conduction system. On the other hand, secondary causes are more common and account for about 85% of cases. Acute myocardial infarction

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is the most common secondary cause of bradyarrhythmia (40% of cases) and has been reported as responsible for up to 25% of hemodynamically unstable patients at ER. The most common drug cause of bradyarrhythmia is an overdose of beta-adrenergic blockers.

12.3 High-Clinical Suspicion in the ER

Any patient that presents at ER with palpitations, chest pain, dizziness, lightheadedness, dyspnea, or syncope has a high probability of having a bradyarrhythmia, and an ECG must be done within the first 10 minutes from admission to the ER. It can also present as shortness of breath, exercise intolerance, or fatigue.

12.4 Risk Factors

The clinical features related to the presence of bradycardia are the following:

- Past medical history of:
  - Atrial fibrillation
  - Cardiomyopathies
  - Structural heart disease
  - Ischemic heart disease
  - Sudden cardiac death episode
  - Unexplained syncope
  - Metabolic diseases with electrolyte abnormalities
  - Sleep disorders (i.e., sleep apnea)
- Alcohol abuse
- Drug abuse
- Use of herbal medication with unknown effect
- Use of potassium or magnesium modifying drugs
- Use of beta-blockers, digoxin, calcium channel blockers, or other medications that inhibit AV node or sinus node
- The family history of sudden cardiac death

12.5 Clinical Presentation

Clinical presentation and physical findings of bradyarrhythmias are highly variable, depending on the type and the heart rate. The spectrum varies from light dizziness to syncope with subsequent hypoperfusion, organ failure, and cardiac arrest. Dizziness and weakness are the most frequent complaint. However, these symptoms usually are not enough to make the patient go to the ER. The main symptom that makes the patients attend the ER is syncope [1].

Main clinical characteristics [2, 3]:

- Syncope
- Fatigue
- Weakness
- Dizziness
- Cognitive impairment
- Dyspnea
- Palpitations
- Chest pain
- Nausea
- Lightheadedness
- Diaphoresis

Bradycardias can be broadly divided into two main categories: nodal sinus dysfunction (SND) and atrioventricular (AV) block. The clinical presentation will be determined by the primary or secondary cause of the bradycardia (see Table 12.1), associated comorbidities, baseline medication, ventricular rate, and blood pressure compensation. The prognosis is related with the reversibility and the severity of the primary bradycardia cause. The ventricular rate is related to the presence of junctional of ventricular rhythm that reaches the depolarization threshold in these tissues.

The most common causes of reversible bradycardia are [3]:

- Myocardial infarction
- Athletic training
- Drug toxicity
  - Beta-blockers, non-dihydropyridine calcium channel blockers, digoxin, antiarrhythmic drugs, lithium, methyldopa, risperidone, cisplatin, interferon
- Toxin overdose (i.e., toluene, organophosphates, tetrodotoxin, cocaine)
- Electrolytes imbalance
- Hypothyroidism
- Hypothermia
- Hypercarbia
- Acidosis
- Sleep apnea
- Hypovolemic shock
- Guillain-Barre syndrome

12.6 Physical Examination

12.6.1 Clinical Instability

The first step in the clinical approach in ER is the evaluation of hemodynamic stability depending on the following indicators [3]:

- Hypotension (systolic blood pressure < 90 mmHg)
- Systemic hypoperfusion

Table 12.1 Main conditions associated with bradyarrhythmia [3, 4]

System	Clinical conditions
Cardiovascular	Acute coronary syndrome
	Nonischemic cardiomyopathy
	Degenerative fibrosis of conductive system
	New-onset AF associated with system conductive disorders
	Myocarditis
	Infectious endocarditis
	Cardiac amyloidosis
	Post-valvular surgery, catheterization, or septal myomectomy
Infection/ inflammation	Chagas disease
	Lyme disease
	Diphtheria
	Meningitis
	Intracranial tumors
	Sarcoidosis
	Toxoplasmosis
Infiltrative disorders	Systemic amyloidosis
	Hemochromatosis
	Lymphoma
Rheumatic disorders	Rheumatoid arthritis
	Scleroderma
	Systemic lupus erythematosus
Severe metabolic disorders	Metabolic acidosis
	Hyperkalemia
	Hypokalemia
	Hypothermia
	Hypothyroidism
	Adrenal disease
	Hypoxia
Vagotonic – -associated with increased vagal tone	Sleep apnea
	High-level athletic conditioning
	Neurocardiogenic syncope

- Altered mental status
- Acute congestive heart failure
- Ischemic chest pain
- Shock

12.6.2 Clinical Stability

An extended clinical examination should be performed, with special attention to vital signs, heart and lung auscultation, and pulse examination. The ER physicians must have a high clinical suspicion of any other cardiovascular cause of bradycardia

that requires further evaluation and treatment (e.g., acute coronary syndrome, severe hypoxemia, etc.).

12.7 Diagnosis Approach

The diagnostic approach of bradyarrhythmias is focused on the early diagnosis of the cause and the recognition of those etiologies that require immediate treatment.

The cornerstone of the diagnosis is the ECG. It must be performed in the first 10 minutes after patient's arrival to the ER, and it is the best tool to differentiate the different types of bradyarrhythmia.

The primary evaluation of the patient includes vital signs, medical history (emphasizing in medication use), complete physical exam, and laboratory test needed to rule out other cardiovascular or metabolic causes, like acute coronary syndrome and severe heart failure, which can be life-threatening.

After the acute management in the ER, the diagnostic approach to determine the specific cause of the bradyarrhythmia and to establish the chronic management can also be performed at the ER or continued as an outpatient depending on the circumstances and symptoms of the patient (see Fig. 12.1).

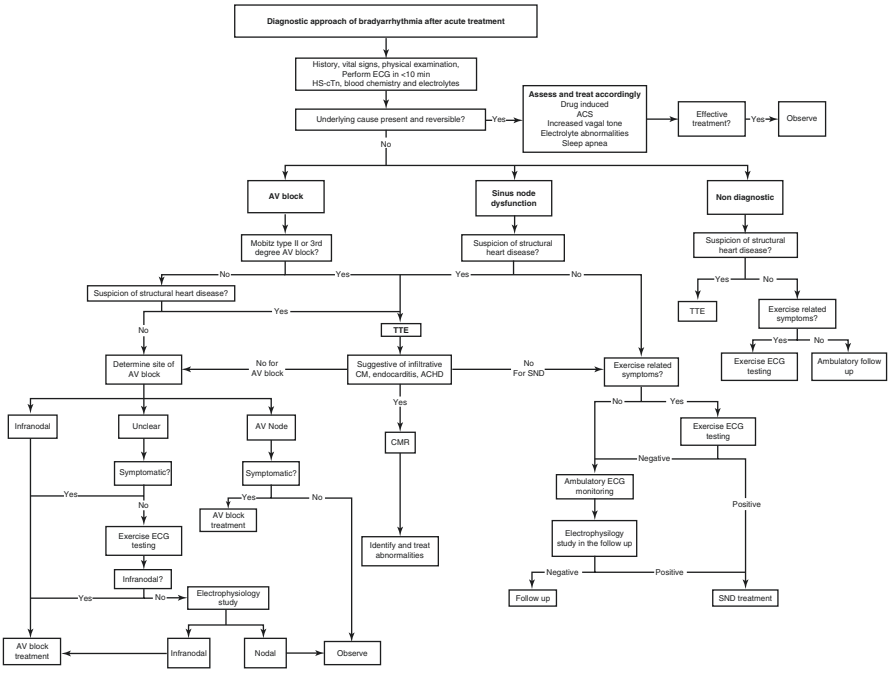


Fig. 12.1 Diagnostic approach of bradyarrhythmias after acute treatment. ECG electrocardiogram, HS-cTn high-sensitive cardiac troponin, ACS acute coronary syndromes, AV atrioventricular, TTE transthoracic echocardiogram, CM cardiomyopathy, ACHD adult congenital heart disease, SND sinus node dysfunction

12.8 Electrocardiogram

The ECG is the most important diagnostic tool and is the mandatory first step in emergency attention care.

The first step in the ECG interpretation is recognizing the presence or absence of normal atrial activity and AV conduction. This is determined by the presence of a p wave, ventricular depolarization (QRS complex) after every atrial depolarization, and normal duration between atrial and ventricular depolarization (PR interval).

The electrocardiographic findings presented in the different types of bradyarrhythmias are described in Table 12.2.

12.9 Imaging

12.9.1 Chest X-ray

A chest-X-ray is not required for the diagnostic assessment of patients with arrhythmia unless another cardiac or pulmonary cause is highly suspected. In patients with heart failure history or with comorbidities, a chest X-ray is mandatory.

12.9.2 Transthoracic and Transesophageal Echocardiogram

A transthoracic echocardiogram is required primarily to rule out structural heart diseases like cardiomyopathies, endocarditis, and adult congenital heart diseases. Transesophageal echocardiography is indicated only in patients with high clinical suspicion of infective endocarditis but is not a routinary recommendation [3].

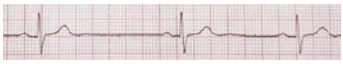
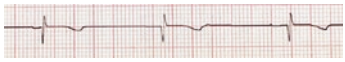
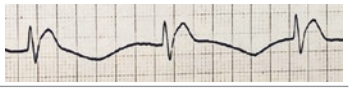
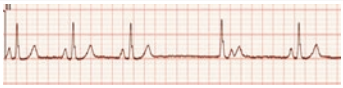
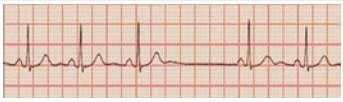
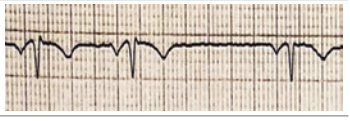
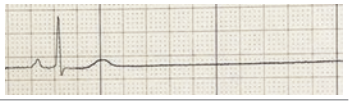
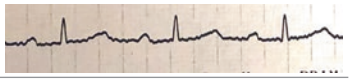
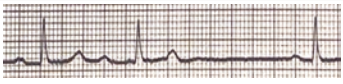
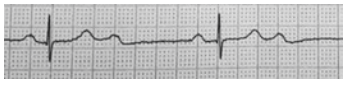
12.9.3 Cardiac Computed Tomography

Cardiac computed tomography is not required for the diagnostic assessment of patients with arrhythmia unless another cardiac or pulmonary cause is highly suspected (e.g., pulmonary embolism or aortic dissection).

12.10 Laboratory Evaluation

The laboratory workup is oriented toward the identification of electrolytic abnormalities and to ruling out other possible and potentially life-threatening causes of bradycardia like acute myocardial infarction. The laboratory tests are listed below:

Table 12.2 Electrocardiogram findings in the principal bradyarrhythmias [1]

Bradyarrhythmia	Electrocardiogram characteristics	Example
Sinus bradycardia	P wave positive in leads I, II, and III, atrioventricular conduction = 1:1, normal PR interval, heart rate <60 bpm	
Junctional rhythm	Absence of normal P wave, rare retrograde P wave inverted and adjacent to QRS complex, narrow QRS complex, regular rate, HR 40–60 bpm	
Idioventricular rhythm	Widened QRS complex, regularly QRS complexes, no P waves, HR 30–50 bpm	
Sinoatrial exit block second-degree type I Wenckebach	P-P interval progressively shortens before pause, duration of the pause is less than two P-P intervals	
Sinoatrial exit block second-degree type II	The absence of normally expected P wave. The interval without P waves is equal approximately two, three, or four times the normal P-P interval	
Sinus pause	The absence of P wave >3 s after a normal sinus complex, no multiple of the P-P interval	
Sinus arrest	The absence of P wave after a normal sinus complex, no multiple of the P-P interval	
Tachy-bradycardia syndrome	Sinus bradycardia, ectopic atrial bradycardia, or sinus pause alternating with abnormal atrial tachycardia, atrial flutter or AF	
1st grade AV block	Consistent P wave to QRS complex relationship, fix PR interval > 200 ms	
2nd grade AV block type I Wenckebach	Progressive prolongation of PR interval until an atrial impulse is completely blocked: a P wave without accompanying QRS complex. After non-conducted beat, cycle repeats	
2nd grade AV block type 2 Möbitz type II	Fix PR interval > 200 ms, P wave associated with a QRS complex until a P wave is not accompanied by QRS complex	
3rd grade AV block (complete)	AV dissociation (P wave not associated with QRS complex, atrial rate greater than ventricular rate. P wave defluxion during QRS	

- Chemistry profile
- Electrolytes
- High-sensitive troponin I
- D-dimer
- Type B brian natriuretic peptide
- Toxicologic test
- Thyroid profile

12.11 Differential Diagnosis

Differential diagnoses among bradyarrhythmia are the following:

- Sinus node dysfunction
  - Sinus bradycardia
  - Tachycardia-bradycardia syndrome
  - Sinoatrial (SA) exit block
    - First-degree SA block
    - Second-degree type I SA block
    - Second-degree type II SA block
    - Third-degree SA block
  - Sinus pauses
  - Sinus arrest
- AV block
  - 1st grade AV block
  - 2nd grade AV block type I
  - 2nd grade AV block type 2
  - 3rd grade AV block (complete)

Sinus bradycardia is a normal sinus depolarization with a heart rate < 60 bpm that reaches the atrial tissue with no interference. It is the most common clinical presentation of bradycardia secondary to drugs and has an excellent response to the acute treatment.

Tachycardia-bradycardia syndrome is an intermittent cause of bradyarrhythmias included in the spectrum of sinus node dysfunction. It is characterized by sinus bradycardia, ectopic atrial bradycardia, or sinus pause alternating with periods of abnormal atrial tachycardia, atrial flutter, or atrial fibrillation. It is usually presented in older patients with ischemic or inflammatory causes of cardiac insult.

SA exit blocks are included in the sinus node dysfunction classification. In these cases, the impulse is generated by the sinus node, but there is a block in the conduction between the sinus node and atrial tissue. This explains why the main ECG findings are multiple P-P intervals, "group-beating" of atrial depolarizations, and

sinus pauses. The block degrees are described in the same fashion that it is in AV block. The definitive diagnostic test is an electrophysiological study. This bradyarrhythmia arises from myocardial disease and drug toxicity and less frequently due to vagal stimulation.

Sinus arrest pause occurs when sinus node depolarization happens more than 3 seconds after the last atrial depolarization. It is secondary to the failure of nodal sinus discharge that results in the absence of atrial depolarization and periods of ventricular asystole or escape rhythm. P-P intervals are not multiple of the P-P interval without the bradycardia. The clinical scenarios are the same as those seen in SA blocks.

Sinus arrest has the same pathophysiology as the sinus pause, but with no evidence of sinus node depolarization during the period of bradyarrhythmia. It is related to atrial infarction and inflammatory disorders [1, 3, 4].

12.12 Treatment

The acute treatment of bradyarrhythmias in ER is based on the hemodynamic stability of the patient (see Fig. 12.2).

The initial treatment includes continuous ECG monitoring, vital signs, and oximetry and must be performed in a facility that can provide a complete cardiac resuscitation.

In unstable patients, the first-line therapy is atropine 0.5 mg IV with possible subsequent doses every 3–5 minutes until symptoms resolved.

In patients with clinical stability, the goal of the initial management is monitoring the bradycardia until it is resolved and concomitantly identifying the possible cause of the arrhythmia.

It is important to keep in mind the possibility of drug toxicity because the treatment can be more efficient with the specific antidote. The main medications related to bradycardia that have specific medical therapy are [3]:

- Non-dihydropyridine calcium channel blockers: treat with 10% calcium chloride 1–2 grams IV every 10–20 minutes or an infusion of 0.2–0.4 mL/kg/h. Another option is 10% calcium gluconate 3–6 grams IV every 10–20 minutes or an infusion of 0.6–1.2 mL/kg/h.
- Beta-blockers: treat with glucagon 3–10 mg IV with an infusion of 3–5 mg/h. If the bradycardia persists and the symptoms are moderate to severe, insulin 1 unit/kg IV bolus followed by an infusion of 0.5 units/kg/h is indicated.
- Digoxin: treat with specific digoxin antibody fragment one vial IV over 30 minutes with possible extra dose, depending on the amount ingested (that every vial binds 0.5 mg of digoxin).

In patients with severe symptoms and AV block, it is important to recognize three conditions that identify bronchodilator drugs, aminophylline, and theophylline, as a treatment of choice to abolish bradycardia symptoms and clinical instability [3].

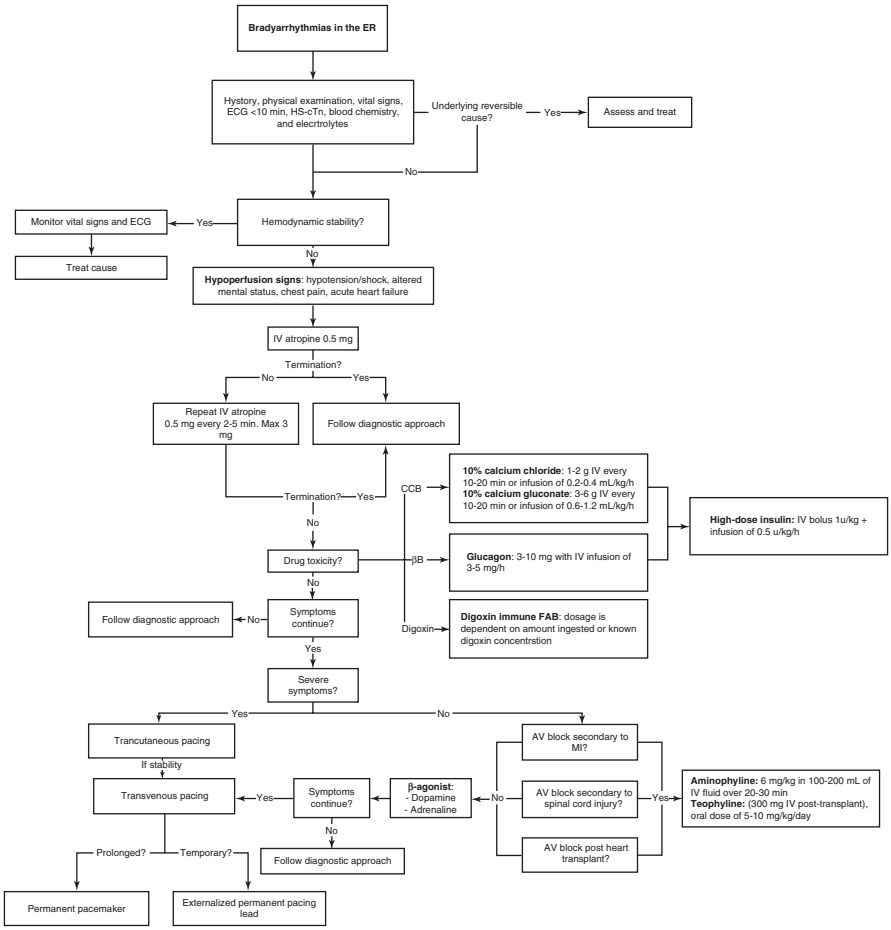


Fig. 12.2 Treatment approach of bradyarrhythmias. ECG electrocardiogram, HS-cTn high-sensitivity cardiac troponin

- Myocardial infarction and AV block
  - Aminophylline 250 mg IV in bolus
- Spinal cord injury
  - Aminophylline 6 mg/kg in 100–200 mL of IV fluid over 20–30 minutes
  - Theophylline 5–10 mg/kg/day per oral titrated to effect
- Post-heart transplant
  - Aminophylline 6 mg/kg in 100–200 mL of IV fluid over 20–30 minutes
  - Theophylline 300 mg IV followed by an oral dose of 5–10 mg/kg/day titrated to effect

In patients with unstable bradycardia unresponsive to atropine, drug antidote, or specific treatment for specific clinical conditions, the next step is beta-agonist therapy with epinephrine or dopamine with dose titration based on stability and symptoms.

If the beta-agonist is not enough to solve the bradyarrhythmia and its symptoms, the last step in the acute treatment is pacing therapy.

The pacing therapy has different modalities [2, 3]:

- Transcutaneous pacing
  - Preferred in unstable patients with severe symptoms and not time for different pacing modalities
- Transvenous pacing
  - Preferred in unstable patients with moderate symptoms that can tolerate the procedure of implantation.
  - This modality is mandatory when the patient with transcutaneous pacing is stable and the symptoms resolved, but the pacing is still needed for an undetermined duration.
- Externalized permanent pacing lead
  - Used in patients with transvenous pacing that need prolonged pacing or permanent pacing, and the permanent pacemaker implantation is not feasible.
- Permanent pacemaker implantation
  - In patients with an irreversible cause of bradycardia and the clinical condition permit the implantation procedure

Specific recommendations in different clinical conditions of American and European guidelines are presented in Table 12.3.

12.13 Additional Clinical Practice Takeaway

- The atropine in the context of acute myocardial infarction must be used with caution because of the rise in the oxygen demand that atropine produces.
- The transcutaneous pacing is the treatment of choice in patients that the transvenous pacing delays the prompt therapy.
- Digoxin is not a drug that can be removed from the blood patient with hemodialysis.
- The further diagnostic approach with imagen studies is not indicated in the acute management in the ED.
- Atropine is the gold standard medical therapy in symptomatic bradyarrhythmia.
- High-degree AV block as chronic condition must be treated with permanent pacemaker independently of the presence of symptoms.
- Consider invasive or noninvasive mechanical ventilation in patients with bradyarrhythmia, respiratory distress, and severe hypoxemia (oxygen saturation < 90%).

Table 12.3 Current international guideline recommendations [3, 5]

European guidelines	COR	LOE
Persistent bradycardia		
Sinus node disease: pacing is indicated when symptoms can clearly be attributed to bradycardia	I	B
Sinus node disease: pacing may be indicated when symptoms are likely to be due to bradycardia, even if the evidence is not conclusive	IIb	C
Sinus node disease: pacing is not indicated in patients with sinus bradycardia, which is asymptomatic or due to reversible causes	III	C
Acquired AV block: pacing is indicated in patients with third- or second-degree type 2 ABV block irrespective of symptoms	I	C
Acquired AV block: pacing should be considered in patients with second-degree type 1 AV block which causes symptoms or is found to be located at intra- or infra-His levels at EPS	IIa	C
Acquired AV block: pacing is not indicated in patients with AV block which is due to reversible causes	III	C
Intermittent documented bradycardia		
Sinus node disease (including brady-tachy form): pacing is indicated in patients affected by sinus node disease who have the documentation of symptomatic bradycardia due to sinus arrest or sinus-atrial block	I	B
Intermittent/paroxysmal AV block (including AF with slow ventricular conduction): pacing is indicated in patients with intermittent/paroxysmal intrinsic third- or second-degree AV block	I	C
Reflex asystolic syncope: pacing should be considered in patients ≥40 years with syncopes and documented symptomatic pause/s due to sinus arrest or AV block or the combination of the two	IIa	B
Asymptomatic pauses (sinus arrest or AV block): pacing should be considered in patients with a history of syncope and documentation of asymptomatic pauses >6 s due to sinus arrest, sinus-atrial block or AV block	IIa	C
Pacing is not indicated in reversible causes of bradycardia	III	C
AHA/ACC guidelines		
In patients with newly identified LBBB, second-degree Mobitz type II atrioventricular block, high-grade atrioventricular block, or third-degree atrioventricular block with or without apparent structural heart disease or coronary artery disease, transthoracic echocardiography is recommended	I	B-NR
In patients with documented or suspected bradycardia or conduction disorder during sleep, screening for symptoms of sleep apnea syndrome is recommended with subsequent confirmatory testing directed by clinical suspicion	I	B-NR
In patients with sleep-related bradycardia or conduction disorder and documented obstructive sleep apnea, treatment directed specifically at the sleep apnea (e.g., continuous positive airway pressure and weight loss) is recommended	I	B-NR
In patients with SND associated with symptoms or hemodynamic compromise, atropine is reasonable to increase sinus rate	IIa	C-LD
In patients with SND associated with symptoms or hemodynamic compromise who are at low likelihood of coronary ischemia, isoproterenol, dopamine, dobutamine, or epinephrine may be considered to increase heart rate and improve symptoms	IIb	C-LD
In patients who have undergone heart transplant without evidence for autonomic reinnervation, atropine should not be used to treat sinus bradycardia.	III	C-LD

Table 12.3 (continued)

European guidelines	COR	LOE
In patients with bradycardia associated with symptoms or hemodynamic compromise because of calcium channel blocker overdose, intravenous calcium is reasonable to increase heart rate and improve symptoms.	IIa	C-LD
In patients with bradycardia associated with symptoms or hemodynamic compromise because of beta-blocker or calcium channel blocker overdose, glucagon is reasonable to increase heart rate and improve symptoms	IIa	C-LD
In patients with bradycardia associated with symptoms or hemodynamic compromise because of beta-blocker or calcium channel blocker overdose, high-dose insulin therapy is reasonable to increase heart rate and improve symptoms	IIa	C-LD
In patients with bradycardia associated with symptoms or hemodynamic compromise in the setting of digoxin toxicity, digoxin Fab antibody fragment is reasonable to increase heart rate and improve symptoms	IIa	C-LD
In patients with bradycardia associated with symptoms or hemodynamic compromise attributable to digoxin toxicity, dialysis is not recommended for removal of digoxin	III	C-LD
In post-heart transplant patients, aminophylline or theophylline is reasonable to increase heart rate if clinically indicated	IIa	C-LD
In patients with SND associated with symptoms or hemodynamic compromise in the setting of acute spinal cord injury, aminophylline or theophylline is reasonable to increase heart rate and improve symptoms	IIa	C-LD
In patients with persistent hemodynamically unstable SND refractory to medical therapy, temporary transvenous pacing is reasonable to increase heart rate and improve symptoms until a PPM is placed or the bradycardia resolves	IIa	C-LD
In patients with SND with severe symptoms or hemodynamic compromise, temporary transcutaneous pacing may be considered to increase heart rate and improve symptoms until a temporary transvenous or PPM is placed or the bradycardia resolves	IIb	C-LD
In patients with symptoms that are directly attributable to SND, permanent pacing is indicated to increase heart rate and improve symptoms	I	C-LD
In patients who develop symptomatic sinus bradycardia as a consequence of guideline-directed management and therapy for which there is no alternative treatment and continued treatment is clinically necessary, permanent pacing is recommended to increase heart rate and improve symptoms	I	C-EO
For patients with tachy-brady syndrome and symptoms attributable to bradycardia, permanent pacing is reasonable to increase heart rate and reduce symptoms attributable to hypoperfusion	IIa	C-EO
Patients with transient or reversible causes of atrioventricular blocks, such as Lyme carditis or drug toxicity, should have medical therapy and supportive care, including temporary transvenous pacing if necessary, before determination of the need for permanent pacing	I	B-NR
In selected patients with symptomatic second-degree or third-degree atrioventricular block who are on chronic stable doses of medically necessary antiarrhythmic or beta-blocker therapy, it is reasonable to proceed to permanent pacing without further observation for drug washout or reversibility	IIa	B-NR

(continued)

Table 12.3 (continued)

European guidelines	COR	LOE
For patients with second-degree or third-degree atrioventricular block believed to be at the atrioventricular nodal level associated with symptoms or hemodynamic compromise, atropine is reasonable to improve atrioventricular conduction, increase ventricular rate, and improve symptoms	IIa	C-LD
For patients with second-degree or third-degree atrioventricular block associated with symptoms or hemodynamic compromise and who have a low likelihood for coronary ischemia, beta-adrenergic agonists, such as isoproterenol, dopamine, dobutamine, or epinephrine, may be considered to improve atrioventricular conduction, increase ventricular rate, and improve symptoms	IIb	B-NR
For patients with second-degree or third-degree atrioventricular block associated with symptoms or hemodynamic compromise in the setting of acute inferior MI, intravenous aminophylline may be considered to improve atrioventricular conduction, increase ventricular rate, and improve symptoms	IIb	C-LD
For patients with second-degree or third-degree atrioventricular block associated with symptoms or hemodynamic compromise that is refractory to medical therapy, temporary transvenous pacing is reasonable to increase heart rate and improve symptoms	IIa	B-NR
For patients who require prolonged temporary transvenous pacing, it is reasonable to choose an externalized permanent active fixation lead over a standard passive fixation temporary pacing lead	IIa	B-NR
For patients with second-degree or third-degree atrioventricular block and hemodynamic compromise refractory to antibradycardic medical therapy, temporary transcutaneous pacing may be considered until a temporary transvenous or PPM is placed or the bradyarrhythmia resolves	IIb	B-R
In patients with a first-degree atrioventricular block or second-degree Mobitz type I (Wenckebach) or 2:1 atrioventricular block which is believed to be at the level of the atrioventricular node, with symptoms that do not temporally correspond to the atrioventricular block, permanent pacing should not be performed	III	C-LD
In patients with symptomatic atrioventricular block attributable to a known reversible cause in whom the atrioventricular block does not resolve despite treatment of the underlying cause, permanent pacing is recommended	I	C-LD
In patients with acquired second-degree Mobitz type II atrioventricular block, high-grade atrioventricular block, or third-degree atrioventricular block not attributable to reversible or physiologic causes, permanent pacing is recommended regardless of symptoms	I	B-NR
In patients with permanent AF and symptomatic bradycardia, permanent pacing is recommended	I	C-LD

COR class of recommendation, *LOE* level of evidence

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Chapter 13
Acute Left Heart Failure in the ER

Carlos Jerjes-Sánchez and Mauricio Vázquez Guajardo

13.1 The Scope of the Problem

Acute heart failure (AHF) represents a significant and growing burden to health care. It can be defined as new onset or worsening heart failure (HF) signs and symptoms requiring urgent therapy [1–3]. AHF is the main cause of hospital admission in individuals aged 65 or more and accounts for nearly 70% of the total healthcare expenditure for heart failure [2]. Management of AHF syndromes is challenging given the heterogeneity of the patient population, the absence of a universally accepted definition, incomplete understanding of its pathophysiology, and lack of robust evidence-based guidelines [1, 4]. In contrast to the major achievements in the treatment of chronic heart failure (CHF) over the past decades, which lead to marked improvement in long-term survival, patients hospitalized for AHF continue to experience stubbornly poor outcomes in both the short and long term.

Patients hospitalized with HF have a higher in-hospital and post-discharge mortality as well as an increased rate of re-hospitalizations [5]. Emergency providers play a significant role in the management of patients with AHF, and it is crucial that physicians involved in early management understand the latest developments in diagnostic testing, therapeutics, and alternatives to hospitalization [6]. It is noteworthy that few settings other than the emergency room (ER) can offer open access to treatment or provide the level of care required to manage the acute phase of decompensation [7].

13.2 Prevalence

With a prevalence of over 5 million Americans and 15 million Europeans and an estimated yearly incidence of 550,000, the burden of HF is tremendous although HF is largely a condition defined by its chronicity, virtually all patients experience, at

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some point, acute symptoms that trigger a visit to the ER [4, 7, 8]. The prevalence of HF depends on the definition applied but is approximately 1–2% of the adult population in developed countries, rising to ≥10% among people 70 years of age [9].

Among people >65 years of age presenting to primary care with breathlessness on exertion, one in six will have unrecognized HF (mainly HF with preserved ejection fraction). The lifetime risk of HF at age 55 years is 33% for men and 28% for women [9]. The proportion of patients with HF with preserved ejection fraction (HFpEF) ranges from 22 to 73%, depending on the definition applied, the clinical setting (primary care, hospital clinic, hospital admission), age and sex of the studied population, previous myocardial infarction, and the year of publication [9].

Data on temporal trends based on hospitalized patients suggest that the incidence of HF may be decreasing, more for HF reduced ejection fraction (HFrEF) than for HFpEF. HFpEF and HFrEF seem to have different epidemiological and etiological profiles [9]. Compared with HFrEF, patients with HFpEF are older, more often women, and more commonly have a history of hypertension and atrial fibrillation, while a history of myocardial infarction is less common [9]. The characteristics of patients with HF mid-range ejection fraction (HFmrEF) are between those with HFrEF and HFpEF, but further studies are needed to characterize this population [9] better.

13.3 Pathophysiology

AHF was historically described as the heart pump failing, causing downstream hypoperfusion and upstream congestion. However, the pathophysiology of AHF is complex and poorly understood in the clinical setting. Figure 13.1 shows the four main pathophysiological mechanisms [10, 11].

13.3.1 Venous Congestion

It is caused by two main mechanisms: fluid retention and fluid redistribution. With regard to fluid retention, cardiac dysfunction leads to a low cardiac output that, in turn, activates the renin-angiotensin-vasopressin-aldosterone system, causing Na^+ and water retention in the kidneys and thus peripheral and pulmonary congestion. On the other hand, fluid redistribution results from venous constriction and arterial vasoconstriction, thus increasing the preload and afterload, respectively, both leading to increased left ventricular (LV) pressures, increased pressures in pulmonary capillaries, and pulmonary and systemic congestion [2, 10–12].

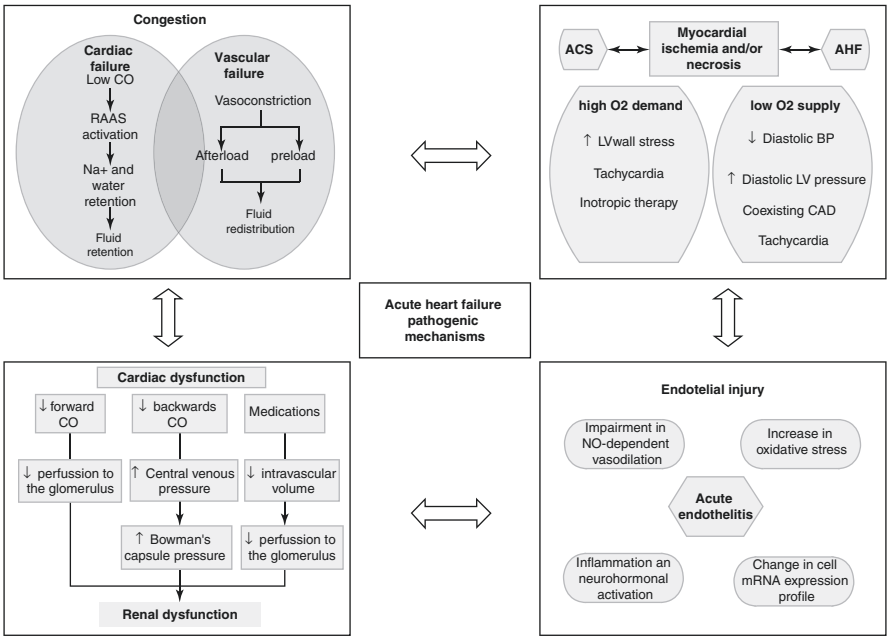

Fig. 13.1 Acute heart failure pathogenic mechanisms. CO cardiac output, RAAS renin-angiotensin-aldosterone-system, LV left ventricle, ACS acute coronary syndrome, AHF acute heart failure, BP blood pressure, CAD coronary artery disease

13.3.2 Myocardial Necrosis and Renal Dysfunction

Both can be the cause of AHF or the consequence of it, which contributes to the further deterioration of the syndrome. In the setting of extensive acute ischemia or myocardial necrosis, ST- or non-ST myocardial infarction (MI) are frequent causes of AHF. At the same time, AHF itself leads to myocardial ischemia through both a decrease in myocardial O_2 supply and an increase in myocardial O_2 demand. O_2 supply may be impaired due to poor coronary perfusion (tachycardia, low diastolic blood pressure, high diastolic LV pressure, coexisting coronary artery disease), and O_2 demand may be high due to high LV wall stress, tachycardia, and inotropic therapy. On the other hand, renal dysfunction is a prevalent abnormality in AHF because there is a close interdependence of the heart and kidneys. Intrinsic renal disease in HF is common, particularly in diabetes, hypertension, and extensive coronary disease, which can precipitate an episode of AHF. Furthermore, if a patient is admitted due to AHF, worsening renal function occurs in 20%–30% of patients during hospitalization [2, 10–12].

13.3.3 Endothelial Dysfunction

It is characterized by severe impairment in endothelial nitric oxide-dependent vasodilatation that can influence myocardial function, hemodynamics, and coronary and renal circulation. Furthermore, recent evidence has shown that an increase in venous arm pressure in healthy individuals can alter endothelial cell mRNA expression profiles and increase inflammation and neurohormonal activation [2, 10–12].

13.4 Definition

AHF refers to the rapid onset or worsening of symptoms and/or signs of HF. It is a life-threatening medical condition requiring urgent evaluation and treatment, typically leading to urgent hospital admission [9].

AHF may present as a first occurrence (de novo) or, more frequently, because of acute decompensation of chronic HF and may be caused by primary cardiac dysfunction or precipitated by extrinsic factors, often in patients with CHF [9]. Acute myocardial dysfunction (ischemic, inflammatory, or toxic), acute valve insufficiency, and pericardial tamponade are among the most frequent acute primary cardiac causes of AHF [9]. Decompensation of chronic HF can occur without known precipitant factors but more often with one or more factors, such as infection, uncontrolled hypertension, rhythm disturbances, or nonadherence with drugs/diet [9].

13.5 High Clinical Suspicion

High clinical suspicion for AHF must be considered in patients with or without a prior history of HF presenting with dyspnea, orthopnea, and/or fluid congestion with no fever. The dyspnea can be transitory or progressive, at rest or exertion, and with or without respiratory distress. In elderly populations presenting with the first episode of AHF, we must exclude extensive critical coronary artery disease, myocarditis, and aortic valve disease.

13.6 Risk Factors and Prevention

Several cardiovascular and non-cardiovascular disorders may cause a rapid development or deterioration of signs and symptoms of HF leading to hospitalization (see Table 13.1) [13]. Primary prevention of AHF concerns the early diagnosis and treatment of the causes of heart failure, mainly the cardiovascular risk factors like ischemic heart disease, cardiac valvular disease, hypertension, chemotherapy, and radiotherapy. Secondary prevention concerns the prevention of CHF that leads to AHF episodes requiring hospitalization. This is particularly important given that the greater the number of hospital admissions the worse patient survival [8, 13].

Table 13.1 Causes and precipitating factors of acute heart failure [13]

Cardiovascular	Non- and ST-elevation myocardial infarction, arrhythmias uncontrolled hypertension or hypertensive urgency/emergencies, myocarditis, acute mitral or aortic regurgitation, aortic dissection, aortic stenosis, abnormal coronary microcirculation, prosthetic valve thrombosis, cardiogenic shock
Non-cardiovascular	Sepsis, infections (bacterias, spirochetes, fungi, protozoa, parasites, rickettsia, viruses) and febrile states associated with reduced ejection fraction, renal dysfunction, anemia, hyperthyroidism, hypothyroidism, strenuous exercise, emotional stress (Takotsubo syndrome), preeclampsia, peripartum myocarditis, high-output states, fluid overload
Patient-related or toxic damage	Poor compliance, diet transgression, non-cardiac major surgery associated with abnormal ejection fraction or critical and extensive coronary artery disease, NSAID, cocaine, amphetamine, anabolic steroids, thiazolidinediones, ß-blockers), alcohol abuse, copper, iron, lead, cobalt, chemotherapy, radiotherapy

NSAID Nonsteroidal anti-inflammatory drug

13.7 Clinical Profile

There are important demographic details to highlight in regard to the patient's background [8, 13, 14].

- Patients are predominantly male.
- Mean age at presentation >70 years.
- 66–75% of patients have a previous history of HF and present with decompensation.
- High burden of comorbid diseases like diabetes, hypertension, myocardial infarction, coronary artery disease, diabetes, atrial fibrillation, and COPD.

13.8 Clinical Presentation

HF patients may present to the ER with varying clinical scenarios, each associated with specific clinical characteristics. The ER physician must determine the etiology of symptoms in patients with suspected HF based on the initial history, physical examination, diagnostic studies, and response to empiric therapy [5]. Symptoms are often nonspecific and therefore do not help discriminate between HF and other problems [9]. Dyspnea is the most common presenting symptom and is the most sensitive. However, it is not an entirely specific indicator of congestion. Other symptoms include orthopnea, paroxysmal nocturnal dyspnea, bendopnea, cough, fatigue, abdominal bloating, anorexia, and weight change (see Table 13.2) [14]. Also, asthenia and adynamia could be the clinical presentation in the elderly population.

Symptoms and signs of HF due to fluid retention may resolve quickly with diuretic therapy. Signs, such as elevated jugular venous pressure and displacement of the apical impulse, may be more specific but are harder to detect and have poor reproducibility [9]. Symptoms and signs may be particularly difficult to identify and interpret in obese individuals, in the elderly, and in patients with COPD. Younger patients with HF often have a different etiology, clinical presentation, and outcome compared with older patients [9].

Table 13.2 Diagnostic accuracy of history, physical exam, chest X-ray, and ECG findings in the AHF patient [6, 14]

	Sensitivity %	Specificity %
History		
Orthopnea	50	77
Paroxysmal nocturnal dyspnea	41	84
Cough	36	61
Fatigue and weight gain	31	70
Edema	51	76
Physical exam		
Jugular venous distention	39	78
Hepatojugular reflux	24	96
Third heart sound	33	99
Pulmonary crepitations	60	78
Peripheral edema	51	76
Chest X-ray		
Pulmonary venous congestion	54	96
Interstitial edema	74	97
Alveolar edema	6	99
Cardiomegaly	74	78
Pleural effusion	26	92
Pneumonia	4	92
Hyperinflation	3	92
Electrocardiogram		
Atrial fibrillation	26	93
New T-wave changes	24	92
Any abnormal finding	50	78
ST elevation	5	97
ST depression	11	94

13.9 Physical Examination

The main purpose of this examination is to assess the underlying hemodynamic state of the patient based on its blood pressure (BP), volume status (wet/dry), and perfusion status (warm/cold) [2, 15].

Systolic blood pressure is a particularly useful way to classify patients at presentation because it gives prognostic information as well as it guides therapeutic decisions.

- Hypertensive AHF represents 50% or more of AHF cases and is more likely to be elderly and female and to have HFpEF. The symptoms develop abruptly and usually involve pulmonary congestion. The mortality rates are significantly lower, with in-hospital mortality ranging from 1 to 7% to 2.5% and post-discharge 2–3-month mortality from 5.4% to 6% [2].

- Normotensive AHF represents 40% or more of the cases and usually has acute decompensated HFrEF. The symptoms develop gradually and involve significant systemic congestion. In-hospital mortality ranges between 8% and 10% [2].
- Hypotensive AHF represents only 8% of the cases. Many of them have advanced or end-stage heart failure and present with low cardiac output, tissue hypoperfusion, or cardiogenic shock. In-hospital mortality ranges from 15% to 30% in the case of cardiogenic shock [2].

The volume status assessment gives the examiner an idea of the underlying pulmonary capillary wedge pressure (PCWP) of the patient and ventricular filling pressures. Objectively, with a PCWP ≥22 mmHg, the patient is said to be wet; otherwise, the patient is considered dry. The signs associated with elevated ventricular filling pressures and their evaluation are the following [2, 14–16]:

- Jugular venous distention (JVD): jugular venous pressure (JVP) ≥ 10 cm H_2O.
- Orthopnea.
- Hepatojugular reflux: an increase in JVP >3 cm sustained during 10 seconds of continuous pressure on the abdomen, with an abrupt fall after the pressure is released.
- Bendopnea: patients with HF that experience shortness of breath while bending forward when putting on shoes or tying them up.
- The square-wave response in blood pressure during Valsalva maneuver occurs when the BP rises during the strain phase and remains elevated throughout the strain, instead of dropping as seen in patients without HF. However, this test is rarely done in the ER context.

It is noteworthy that of the signs enlisted above, JVD and orthopnea are the most useful in the identification of high PCWP and proper evaluation has important prognostic value. There are practical tips when assessing JVP [15]:

- Start by assessing the patient sitting upright to exclude a very high JVP.
- Assess the JVP at various angles: supine, at 30°, 45°, sitting, and standing.
- Use only one pillow slightly tipping the chin upward to extend the neck and improve the visibility of the waveform.
- Apply pressure with your finger 1–2 inches below the impulse. If the pulsation disappears, it was the jugular vein; if it persists, it was the carotid artery.
- With a flashlight, look for a waveform/pulsation rather than actual venous structure.
- Explore both sides of the neck. The waveform may be seen better on either the right or the left side.

On the other hand, the evaluation of tissue perfusion orients the physician toward the cardiac index of the patient. Objectively when the cardiac index is ≤2.2 l/min/m^2, the patient is said to be cold; otherwise, the patient is classified as warm [14,

15]. However, the perfusion assessment is more difficult, given the fewer reliable findings to determine a low cardiac index. Such findings include [2, 14, 15]:

- Narrow pulse pressure
- Long capillary refill time
- Cold extremities
- Oliguria
- Dizziness or mental confusion

13.10 Classification

Characterizing the profile of the patient constitutes a key element for therapeutic decision-making. In HF the patients can be classified according to clinical characteristics, precipitating factors, physical examination findings, and ejection fraction [9].

Classifying patients by systolic blood pressure (SBP) at presentation (hypertensive, normotensive, or hypotensive) is a strong predictor of outcome, particularly mortality, while it also guides the initial therapeutic decisions (i.e., inotropes vasopressors in hypotensive AHF or vasodilators in hypertensive AHF) [2, 9].

Another approach is to classify patients according to the presence of the following precipitants/causes leading to decompensation, which need to be treated/corrected urgently: ACS, hypertensive emergency, rapid arrhythmias or severe bradycardia/conduction disturbance, acute mechanical cause underlying AHF, or submassive or massive pulmonary embolism [9].

Bedside physical examination can help classify patients based on symptoms/signs of congestion ("wet" vs. "dry" if present vs. absent) and/or peripheral hypoperfusion ("cold" vs. "warm" if present vs. absent) [9]. The combination of these options identifies four groups: (a) warm and wet (well perfused and congested) most commonly present; (b) cold and wet (hypoperfused and congested); (c) cold and dry (hypoperfused without congestion); and (d) warm and dry (compensated, well perfused without congestion). This classification may be helpful to guide therapy in the initial phase and carries prognostic information [9].

Historically the measurement of LVEF has been used to differentiate the wide range of patients with HF. This classification is important in the AHF setting because of their different underlying etiologies, demographics, and comorbidities, as well as different long-term oral medications [9]. Patients that present with normal LVEF ($\geq$ 50%) are classified as HFpEF, whereas those with reduced LVEF (< 40%) as HFrEF. Patients with LVEF in the range of 40–49% represent a gray area, which we now define as HFmrEF [9].

Patients with HF complicating no- or ST-elevation MI can be classified according to Killip and Kimball into Class I, no clinical signs of HF; Class II, HF with rales and S3 gallop; Class III, with frank acute pulmonary edema; and Class IV, cardiogenic shock and hypotension (SBP < 90 mmHg) and evidence of peripheral vasoconstriction such as oliguria, cyanosis, and diaphoresis [9].

In practice the most useful classifications are those based on a clinical presentation at admission, allowing clinicians to identify patients at high risk of complications and to direct management at specific targets, which creates a pathway for personalized care in the AHF setting [9].

13.11 Workup

13.11.1 Chest X-Ray

This noninvasive test is a low-cost, easily obtainable study that should be routinely used in all acutely dyspneic patients with suspected HF. The classic radiographic features of AHF appear with variable frequency in the chest X-ray and are the most specific findings of any workup study in AHF but lack sensitivity (see Table 13.2). They consist of [17]:

- Pulmonary venous cephalization that typically occurs when the PCWP is >10–15 mmHg.
- Normal cardiac size or moderate cardiomegaly could suggest HFpEF.
- Cardiomegaly that may or may not be present depending on the etiology.
- Interstitial edema, characterized by peripheral septal Kerley B lines (short 2 cm lines that appear on the periphery and run to the pleura due to thickening of the interlobular septa when the PCWP is >20 mmHg).
- Alveolar edema presented as a "bat wing opacity" associated with a PCWP >25 mmHg.
- Small or large pleural effusion that suggests subacute or chronic HF stage.

However, the absence of these findings cannot rule out AHF, as up to 20% of patients with AHF will have no congestion on their ER chest X-ray (see Table 13.2) [14]. Furthermore, pulmonary edema may present with atypical features like unilateral and lobar pulmonary edema in patients with pre-existing COPD and minimal edema during the transition of interstitial edema into alveolar edema. Therefore, physicians in the ED should be cautious, particularly when excluding AHF in asymptomatic patient based on radiographic findings alone [6].

13.11.2 Electrocardiogram

The electrocardiogram, technically speaking, does not aid in the diagnosis but may suggest a specific cause or precipitant of AHF (see Table 13.2) [6]. CAD is one of the most common underlying AHF etiologies; therefore, an early ECG should always be obtained in a patient with AHF, in search of rhythm abnormalities and ST changes. Furthermore, CHF is associated with an increased incidence of ventricular and supraventricular arrhythmias, particularly atrial fibrillation and flutter [6, 18].

13.11.3 Echocardiography and Point- of-Care Ultrasonography (PoC US)

Echocardiography is integral to the diagnosis of AHF (see Fig. 13.2). If formal echocardiography is not available rapidly, focused cardiac ultrasound can be performed by the ER personnel [5]. Information obtained in a routine echocardiogram include [19]:

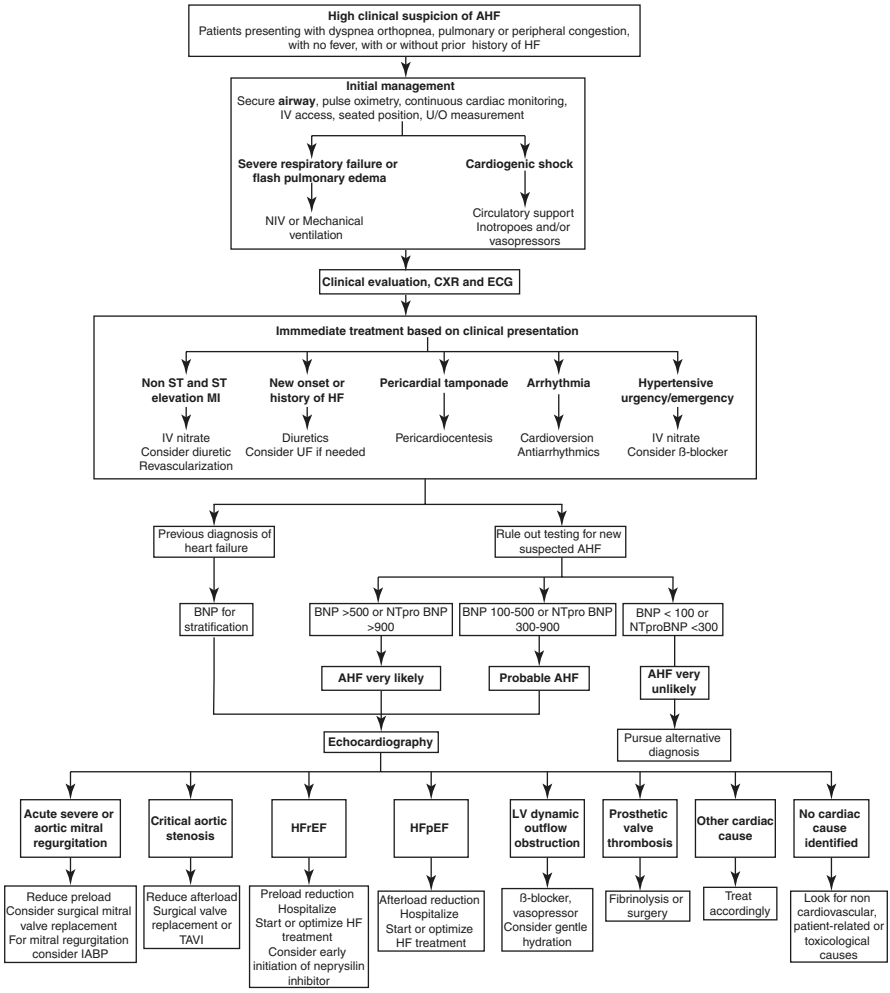

Fig. 13.2 Initial management of acute heart failure. AHF acute heart failure, NIV noninvasive ventilation, U/O urine output, CXR chest X-ray, ECG electrocardiogram, MI myocardial infarction, UF ultrafiltration, BNP B-type natriuretic peptide, IABP intra-aortic balloon pump, HFrEF heart failure with reduced ejection fraction, HFpEF heart failure with preserved ejection fraction, LV left ventricle

- Systolic function of the left and right ventricle (ejection fraction)
- Evaluation of valve function
- Evaluation of wall motion abnormalities (that suggest ischemia)
- Evaluation of pericardial effusion
- Evaluation of inferior vena cava, which is an estimate of right atrial pressure
- Cardiac structural disorders
- Identifies causes that mimic left heart failure (cardiac tamponade, pulmonary embolism)

The diagnosis of HFpEF is more challenging than the diagnosis of HFrEF. Patients with HFpEF generally do not have a dilated LV but, instead, often have an increase in LV wall thickness and/or increased left atrial size as a sign of increased filling pressures. Most have additional "evidence" of impaired LV filling or suction capacity, also classified as diastolic dysfunction, which is generally accepted as the likely cause of HF in these patients (hence the term "diastolic HF"). However, most patients with HFrEF (previously referred to as "systolic HF") also have diastolic dysfunction, and subtle abnormalities of systolic function have been shown in patients with HFpEF. Hence the preference for stating preserved or reduced LVEF over preserved or reduced "systolic function" [9].

Current clinical guidelines recommend immediate echocardiography in patients with hemodynamic instability (particularly in cardiogenic shock) and in patients suspected of acute life-threatening structural or functional cardiac abnormalities (mechanical complications, acute valvular regurgitation, aortic dissection). Early echocardiography (preferably within 48 hours from admission) should be considered in all patients with de novo AHF and those with unknown cardiac function [9].

Point-of-care ultrasonography, while not a substitute for comprehensive echocardiography, has been proposed as a valuable tool in determining the etiology of dyspnea, providing an assessment of the volume status and the left ventricular function and looking for signs of pericardial effusion [6].

- Inferior vena cava (IVC) diameter and its degree of change with respiratory variation can be used to assess the volume status. The IVC collapse index value ((IVC diameter during expiration - IVC diameter inspiration)/(IVC diameter during expiration)) in AHF with volume overload is closer to 1 compared to patients without HF where it is typically between 0.25 and 0.75. Consider that the volume overload dilates the IVC preventing the diameter change during the respiratory cycle.
- Sonographic B lines (lung comets or comet tail artifacts) that represent thickened interstitial or fluid-filled alveoli can be used to assess lung congestion.
- PoC US has been shown to be more accurate than auscultation or chest radiography for the detection of pleural effusion, consolidation, and alveolar interstitial syndrome in the critical care setting.

13.12 Laboratory Evaluation

13.12.1 Biomarkers

Natriuretic peptides, B-type natriuretic peptide (BNP) and its prohormone N-terminal (NT) proBNP, are released by the myocardium in the setting of myocardial pressure or volume stress [20–22]. The predominant hormonal effects of BNP are vasodilatation and natriuresis, as well as antagonizing aldosterone and endothelin. In a clinical setting, these peptides have demonstrated diagnostic and prognostic utility in AHF and are now the most established AHF diagnostic biomarkers.

- The BNP cutoff value of <100 pg/mL and NT-proBNP <300 pg/mL, with a sensitivity, specificity, negative predictive value, and positive predictive value of 90%, 76%, 79%, and 89%, respectively, have proven to be highly useful in excluding HF, particularly when the etiology of dyspnea is unclear [7].
- Above these levels, there is considerable overlap in BNP and NT-proBNP levels in patients with and without HF, which makes the test less accurate, and results should be interpreted with caution.

It is important to clarify that abnormal BNP and NT-proBNP measurements do not automatically confirm the diagnosis of left HF since these biomarkers of ventricular dysfunction are also expressed by conditions that induce dysfunction or right ventricular failure [6]. In some patient populations, unexpectedly low levels of BNP (< 100 pg/ml) can be detected, like in end-stage HF, flash pulmonary edema (onset 1 hour), acute pulmonary edema secondary to papillary muscle rupture with mitral regurgitation (onset <2 hours), massive pulmonary embolism (onset 1 hour) right-sided AHF, and right ventricular myocarditis secondary to systemic lupus erythematosus [23]. The main mechanism is that the half-life of BNP is 23 minutes. Therefore, it is expected that approximately 2 hours are required to reflect changes due to left or right dysfunction fully; however, the mechanism in the case of right ventricular myocarditis is unknown. Furthermore, patients with HFpEF have a smaller left ventricular radius and thicker walls compared with HFrEF resulting in proportionally lower NP levels for similar degrees of AHF, suggesting different diagnostic thresholds are needed depending on whether left ventricular ejection fraction is preserved or reduced [6].

Measurement of high-sensitivity troponin T or I is useful for detection of ACS as the underlying cause of AHF. However, elevated concentrations of circulating cardiac troponins are detected in the vast majority of patients with AHF, often without obvious myocardial ischemia or an acute coronary event, suggesting ongoing myocyte injury or necrosis in these patients; elevated troponins are useful for

risk stratification and decision-making [9]. Recent evidence has shown that HsTnT ≤99th percentile upper reference limit can be used as a marker of low-risk CV mortality even with high BNP levels [24].

13.12.2 Important Laboratory Tests at Presentation

Upon admission, patients with clinical suspicion of AHF should receive the following laboratory assessment: blood urea nitrogen, creatinine, electrolytes, liver function tests, stimulating thyroid hormone, glucose, complete blood count, and D-dimer (see Table 13.3) [9].

Comprised renal function is an important predictor of AHF outcome. A patient presenting with a blood urea nitrogen level greater than 43 mg/dL is one of the most important predictors of increased acute mortality, and creatinine is a helpful indicator of mortality, with levels >2.75 mg/dl associated with short-term adverse outcomes and decreased therapeutic responsiveness [20]. Serial determinations of electrolytes every 1–2 days (especially sodium, potassium, and magnesium) and renal function are necessary during diuresis as deterioration is a poor prognostic sign.

A major dilemma occurs when creatinine rises in the face of continued signs and symptoms of congestion because there's little evidence to guide clinicians in this setting. Most physicians continue diuresis as long as the increase in creatinine is modest, or if it is significant, the reduction or temporary discontinuation of diuretic or vasodilator therapy should be considered [22]. Liver function tests are often impaired with AHF due to hemodynamic derangements and may be useful for management and prognosis [9].

Assessment of procalcitonin levels may be considered in patients with AHF with suspected coexisting infection, particularly for the differential diagnosis of pneumonia and to guide antibiotic therapy, if considered [9].

Table 13.3 ESC guideline recommendations for diagnostic measures in AHF [9]

Diagnostic measure	COR	LOE
BNP and NT-proBNP is recommended in all patients with acute dyspnea and suspected AHF to help differentiate AHF from non-cardiac causes of acute dyspnea	I	A
A 12-lead ECG, chest X-ray, cardiac troponins, BUN, creatinine, electrolytes, glucose, CBC, LFT, and TSH are recommended	I	C
Echocardiography is recommended immediately in hemodynamically unstable AHF and within 48 hours when cardiac structure and function are either unknown or may have changed since previous studies	I	C

COR class of recommendation, *LOE* level of evidence, *BNP* B-type natriuretic peptide, *NT-proBNP* N-terminal pro B-type natriuretic peptide, *AHF* acute heart failure, *ECG* electrocardiogram, *BUN* blood urea nitrogen, *CBC* complete blood count, *LFT* liver function tests

13.13 Therapeutic Approach

Treatment Goals

- To relieve symptoms and optimize the fluid volume status
- To restore the respiratory function, gas exchange, and systemic oxygenation
- To improve hemodynamics and end-organ function
- To address any underlying cause or precipitant (myocardial ischemia, arrhythmia, infection, anemia, drugs toxicity, etc.)

The first step is the initial evaluation, airway assessment, monitoring of vital signs, and stabilization with the purpose of securing the airway, optimizing the hemodynamics and tissue oxygenation (see Fig. 13.2) [9, 22, 25].

Oxygen Therapy and/or Ventilatory Support

- Oxygen therapy is recommended in patients with AHF and SpO2 < 90% or PaO2 < 60 mmHg to correct hypoxemia with the goal of a SpO2 > 95% (> 90% in COPD patients due V/Q mismatch) [6, 9].
- Oxygen is not recommended as routine therapy in patients without hypoxemia, as it may cause vasoconstriction and reduction in cardiac output.
- Routine arterial blood gas is not needed and should be restricted to patients in whom oxygenation cannot be readily assessed by pulse oximetry. However, arterial blood gas may be useful when precise measurement of O2 and CO2 partial pressures are needed. A venous sample might acceptably indicate pH and CO2 [9].
- Noninvasive mechanical ventilation like continuous positive airway pressure or bilevel positive airway pressure is recommended by both the AHA/ACC and ESC guidelines in patients with severe pulmonary edema and respiratory distress because it improves respiratory effort and maintains adequate gas exchange [6, 9, 25]. However, recent randomized control trials failed to demonstrate a mortality benefit in comparison to standard therapy or a reduction in the rate of endotracheal intubation [2]. Important prerequisites when choosing noninvasive mechanical ventilation are hemodynamic stability, full patient cooperation, and the patient's ability to protect their own airway. The response to noninvasive mechanical ventilation should be assessed after 60 minutes.
- Mechanical ventilation is only required in the minority of AHF patients. It should be considered in severe respiratory distress, non-responders to noninvasive mechanical ventilation, those with cardiogenic shock, or at high risk of hemodynamic deterioration during intervention or inter-hospital transport. The primary indication for mechanical ventilation is respiratory failure leading to hypoxemia (SpO2 < 90% PaO2 < 6–7 kPa), hypercapnia, and/or acidosis (pH <7.3 or PaCO2 > 9–10 kPa) [2].

Circulatory Support

- Close monitoring of BP, fluid balance, and urine output are essential.
- Routine invasive hemodynamic evaluation with a pulmonary artery catheter is not indicated for the diagnosis of AHF. It may be helpful in selected cases of hemodynamically unstable patients with an unknown mechanism of deterioration. Also, routine use of an arterial line or central venous line for diagnostic purposes is not indicated [9].
- Percutaneous, short-term mechanical circulatory support may be indicated early during the initial resuscitation and stabilization phase especially when drug-resistant hypotension and pulmonary congestion are sustained. The intra-aortic balloon pump is the most widely used mechanical circulatory support therapy and can be used to bridge until the implantation of a ventricular assist device or heart transplant in the case of cardiogenic shock.

13.14 Pharmacologic Therapy

In parallel to stabilization/treatment of life-threatening conditions, improving hemodynamics and symptoms are key goals (see Fig. 13.3). This is achieved through different strategies like fluid removal, preload and afterload reduction, inotropic stimulation, and anxiety management.

While diuretics remain the mainstay of therapy, it's important to identify and address any underlying cause of the acute dyspnea, because pharmacologic treatment and interventions in the ER must be tailored to each case.

Recently novel medical therapies are being assessed for safety and effectiveness in patients hospitalized for acute heart failure once hemodynamic stability is achieved. In the most recent clinical trial PIONEER-HF, sacubitril-valsartan led to a greater reduction in the NT-proBNP concentration than enalapril therapy, suggesting that it could improve prognosis after an AHF event [26].

13.14.1 Fluid Removal

Evidence-based treatment for AHF is limited, and currently the only Class I recommendation for medical therapy is IV loop diuretics (furosemide or bumetanide) due to their higher potency and even some vasodilatory effects (see Table 13.4). IV diuretics are the first-line treatment in patients with AHF and congestion (wet) but should be avoided in patients with signs of hypoperfusion (dry). For those patients with new-onset AHF or those not receiving oral diuretics, the initial recommended dose is 20–40 mg of furosemide (or 1 mg/kg). The diuretic should be administered

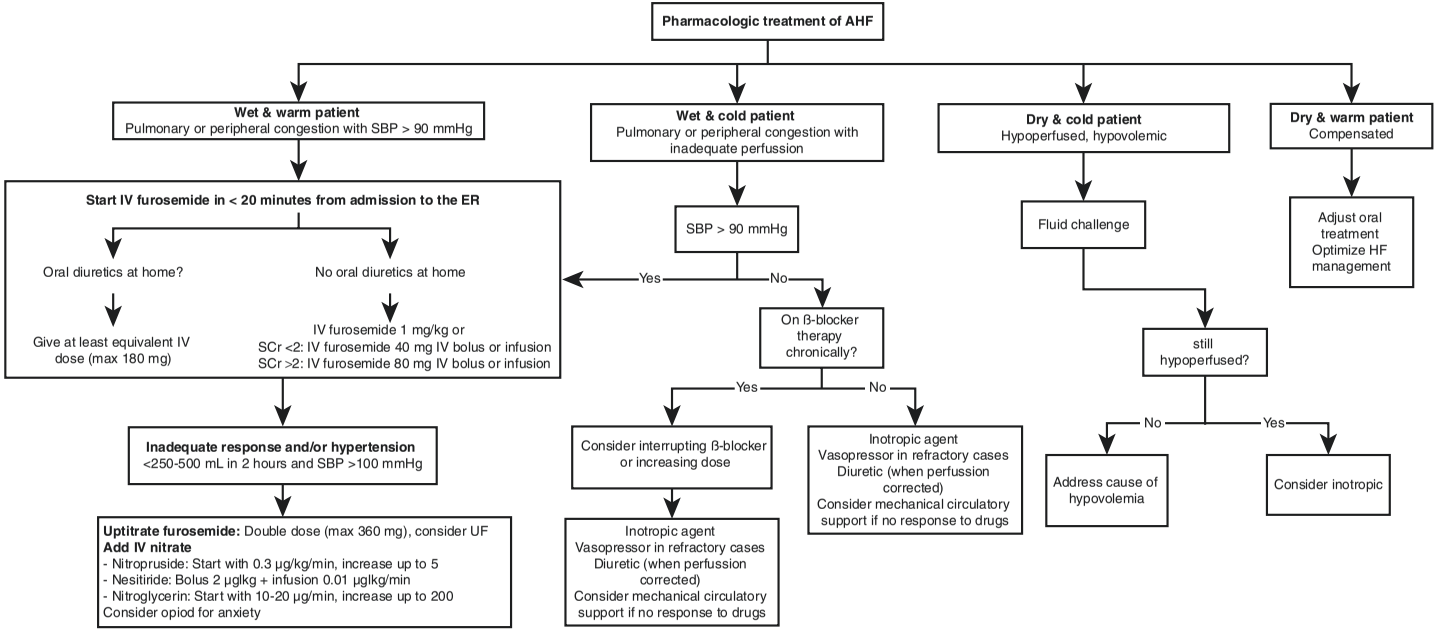

Fig. 13.3 Pharmacological treatment of acute heart failure. SBP systolic blood pressure, SCr serum creatinine, AHF acute heart failure, HF heart failure

Table 13.4 ESC guideline recommendations for medical therapy in AHF [9]

Therapy	Recommendation
First-line diuretic	Furosemide: 20–40 mg (bolus or infusion) or equivalent to chronic oral diuretic therapyBumetanide: 1–3 mg/ maximum 10 mg If the patient had chronic diuretic therapy: at least equivalent to oral therapy
Second-line diuretic	Consider adding thiazide or spironolactone (IIb/C)
Ultrafiltration	Consider in refractory cases
Vasodilators	Nitroglycerine: start with10–20 μg/min, increase up to 200 Isosorbide dinitrate: start with 1 mg/h, increase up to 10 Nitropruside: start with 0.3 μg/kg/min, increase up to 5 Nesiritide: bolus 2 μg/kg + infusion 0.01 μg/kg/min
Inotropes and/or vasopressors	Dobutamine: infusion rate 2–20 μg/kg/min (β +) Dopamine (inotropic): infusion rate 3–5 μg/kg/min (β +) Dopamine (vasopressor): >5 μg/kg/min (α and β +) Levosimendan: 12 μg/kg bolus over 10 minutes or 0.1 μg/kg/min infusion (can be increased to 0.2 or decreased to 0.05) Enoximone: 0.5–1.0 μg/kg bolus over 5–10 min or 5–20 μg/kg/min infusion Milrinone: 25–75 μg/kg bolus over 10–20 minutes or 0.375–0.75 μg/kg/min infusion Norepinephrine: 0.2–1.0 μg/kg/min infusion Epinephrine: 1 mg bolus during resuscitation every 3–5 minutes or 0.05–0.5 μg/kg/min infusion
Opiates	IIa/C recommendation to relieve dyspnea and anxiety
Thromboembolism prophylaxis	I/A recommendation with heparin or another anticoagulant

α alpha adrenergic, *β* beta-adrenergic

in the ER as soon as congestion is identified, preferably in <20 minutes. In a prospective multicenter, observational cohort study of patients presenting at the ER for AHF, early treatment (<60 minutes) with intravenous loop diuretics was associated with lower in-hospital mortality [27].

For those on chronic diuretic therapy, initial IV dose should be at least equivalent to the oral dose. The peak effect is seen at the 1rst and 2nd hour following IV administration and subsides by the 6th hour. The administration can be given either as a bolus or continuous infusion without any difference in effectiveness and immediately after patients arriving at ER [27].

- In patients with resistant edema, a loop diuretic can be titrated up, or dual treatment with a loop diuretic and thiazide (bendroflumethiazide or metolazone) or spironolactone may be used to achieve an adequate diuresis.
- Renal dose dopamine (evidence IIb/B) could potentiate the diuretic effect of loop diuretics [25].
- After acute congestion is controlled, the lowest dose should be used that is compatible with stable signs and symptoms.
- Isolated ultrafiltration is an effective alternative for the management of congestion in heart failure and has been approved by the ACC/AHA, ESC, and HFSA

clinical guidelines: (a) removes fluid in a rapid manner, (b) avoids the maladaptive renal tubular autoregulatory responses induced by diuretics, and (c) has a higher magnitude of Na + clearance. However, excessively high isolated ultrafiltration can lead to hypotension, renal hypoperfusion, and acute renal failure necessitating dialysis [2, 7, 25, 28, 29].

Endpoints for an effective diuresis include resolution of symptoms, improvement in vital signs, and improvement in end-organ function (renal and liver). The effect of fluid removal should be monitored with careful measurement of fluid intake or output, vital signs, body weight, daily serum electrolytes, BUN, and creatinine [2].

13.14.2 Preload and Afterload Reduction

IV vasodilators (nitroglycerine, isosorbide dinitrate, nitroprusside, and nesiritide) are the second most often used agent in AHF for symptomatic relief. However there is no robust data indicating any prognostic benefit (see Table 13.5). They optimize preload by decreasing venous tone and afterload by decreasing arterial tone, thus increasing the stroke volume. They are recommended for patients with pulmonary congestion which are normotensive or hypertensive (SBP > 100 mmHg) and should be avoided in hypotensive patients or patients with obstructive valvular disease or restrictive physiology [2, 6, 7, 9, 22, 25].

The ESC guidelines recommend the cautious use of opioids in selected patients for severe dyspnea and anxiety as well as to reduce the sympathetic drive. However, dose-dependent side effects and controversies regarding the potentially elevated mortality risk in these patients remain a concern [9].

In patients with CHF and ß-blocker therapy, acute cessation of the medication is associated with higher in-hospital mortality and short-term mortality. The mechanism by which mortality is increased is due to a sympathetic nervous system reactivation that can precipitate angina and arrhythmias. Evidence supports the continuation of ß-blockers at home dose unless patients require vasopressors or inotropes on admission. However contemporary guidelines haven't made any formal recommendations [30, 31]. In the ER setting, the physician in charge should decide whether to continue and increase the ß-blocker dose or to stop its administration and restart after stabilization.

13.14.3 Management of Hypotension

Inotropic agents represent a rescue therapy in patients with low cardiac output. They include sympathomimetic drugs (dobutamine, dopamine, norepinephrine, and epinephrine) phosphodiesterase inhibitors (milrinone, enoximone) and calcium sensitizers (levosimendan). However, it is noteworthy that this therapy is rarely needed

Table 13.5 Current international guidelines recommendations for the management of AHF [9, 22, 25]

	COR	LOE
European Society of Cardiology		
Oxygen therapy is recommended in patients with AHF and $SpO_2 < 90\%$	I	C
Consider NIV in patients with RR > 25 breaths/min and $SpO_2 < 90\%$ to decrease respiratory distress. It should be used carefully in hypotensive patients	IIa	B
Intubate if PaO2 < 60 mmHg, PaCO2 > 50 mmHg, pH < 7.35 and can't be managed invasively	I	C
IV loop diuretics are recommended for all patients with AHF with signs/symptoms of fluid overload to improve symptoms	I	C
First-line diuretic: furosemide 20–40 mg IV bolus or equivalent to chronic oral diuretic therapy prescribed. Either as bolus or infusion and duration is adjusted according to the patients' symptoms and status	I	B
Consider UF in refractory cases without impaired renal function	NSR	NSR
Consider vasodilators for symptomatic relief in AHF with SBP > 90 mmHg and without symptomatic hypotension	IIa	B
Consider short-term inotropes in patients with SBP < 90 mmHg and/or signs/symptoms of hypoperfusion	IIb	C
AHA/ACC guidelines		
Oxygen therapy, NIV, or intubation	NSR	NSR
HF patients with fluid overload should be treated with IV diuretics	I	B
Consider UF in refractory cases of volume overload	IIb	B
Consider UF in refractory cases of pulmonary congestion	IIb	C
Consider vasodilators plus diuretic therapy in normotensive patients	IIb	A
Consider inotropes for short-term support in selected patients	IIb	B
HFSA guidelines		
Supplemental oxygen in the presence of hypoxia is recommended	–	C
Consider NIV for severely dyspneic patients with clinical evidence of pulmonary edema	–	A
IV loop diuretics are recommended in patients with AHF		B
Consider UF in refractory cases	–	C
Consider vasodilators plus diuretic therapy for rapid improvement of congestive symptoms in AHF in the absence of symptomatic hypotension	–	B
Consider the use of inotropes in selected hypotensive patients	–	C

COR class of recommendation, *LOE* level of evidence, *BBB* bundle branch block, *NIV* noninvasive mechanical ventilation, *UF* isolated ultrafiltration

in the acute decompensated heart failure setting. Because none of these agents improve clinical outcomes and in some cases increase mortality (see Table 13.4) [2, 7, 25, 28, 29].

Patients with HFpEF presenting with hypotension should not receive inotropic therapy and may require a vasopressor in addition to diuretic therapy. Patients who develop hypotension with dynamic left ventricular outflow obstruction should not receive inotropic, since it can worsen obstruction. They should be treated with beta-blocker therapy, a vasopressor (e.g., phenylephrine or norepinephrine), and gentle

hydration if pulmonary edema is not present. Dynamic left ventricular outflow obstruction occurs in some patients with hypertrophic cardiomyopathy but is not limited to patients with that condition [32].

13.15 Additional Clinical Practice Takeaway

- Acute HF is a life-threatening medical condition requiring urgent evaluation and treatment, typically leading to urgent hospital admission.
- AHF comprises a wide spectrum of clinical conditions with different pathophysiologies and precipitating factors.
- High clinical suspicion for AHF in patients presenting with dyspnea and/or fluid congestion with or without a prior history of HF is key for prompt and effective management.
- In elderly patients presenting with the first episode of AHF, it is mandatory to exclude extensive critical coronary artery disease, myocarditis, and aortic valve disease.
- An evaluation oriented toward the assessment of systolic blood pressure, congestion, and perfusion gives the examiner a better context of the patient's underlying hemodynamic state and assists in the determination of the patient's profile.
- The diagnostic workup can orient in the classification and decision-making. However clinical correlation is fundamental for therapy initiation.
- Normal cardiac size or moderate cardiomegaly on chest X-ray in addition to symptoms and signs of acute HF could suggest HFpEF.
- Echocardiography is integral to the diagnosis of acute HF.
- BNP cutoff value of <100 pg/mL and NT-proBNP <300 pg/mL has a sensitivity, specificity, negative predictive value, and positive predictive value of 90%, 76%, 79% and 89%, respectively, to exclude HF. Unexpectedly low levels of BNP (< 100 pg/ml) can be detected, in end-stage HF, flash pulmonary edema (onset 1 hour), acute pulmonary edema secondary to papillary muscle rupture with mitral regurgitation (onset <2 hours), massive pulmonary embolism (onset 1 hour) right-sided AHF, and right ventricular myocarditis secondary to systemic lupus erythematosus.
- Routine invasive hemodynamic evaluation with a pulmonary artery catheter is not indicated for the diagnosis of AHF.
- A routine arterial blood gas is not needed and should be restricted to patients in whom oxygenation cannot be readily assessed by pulse oximetry.
- Noninvasive mechanical ventilation is recommended in AHF and respiratory distress.
- Diuretic therapy remains the mainstay therapy for AHF. However the better understanding of the underlying pathophysiology of the patient's condition can orient toward other measures like preload and afterload reduction and/or inotropic support.
- Early treatment with intravenous loop diuretics reduces in-hospital mortality.

- In a patient presenting with AHF and home therapy with ß-blockers, a continuation of these medications is associated with better in-hospital and short-term prognosis.
- Initiation of sacubitril-valsartan once hemodynamic stability is achieved leads to greater reduction in NT-proBNP than enalapril therapy alone.

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Chapter 14
Cardiac Arrest in the ER

Carlos Jerjes-Sánchez, Jathniel Panneflek and David Rodríguez

14.1 The Scope of the Problem and Definition

In the western world, 20% of all deaths due to cardiovascular failure among people between 20 and 80 years old are sudden and unexpected. Although mortality from the cardiac disease has diminished substantially, this percentage remains constant. Sudden death is most often caused by the onset of ventricular fibrillation (VF) or ventricular tachycardia, interfering with the heart's function to pump blood into the circulation and thus causing a cardiac (and circulatory) arrest [1]. Cardiac arrest is defined as loss of mechanical activity of the heart confirmed by the absence of signs of circulation [2]. The sudden cardiac arrest is defined as the sudden cessation of cardiac activity, which causes the victim to become unresponsive, showing no normal breathing patterns or signs of systemic circulation. If corrective measures are not taken rapidly, this condition will progress to sudden death. Cardiac arrest should be used to signify an event, as described above, is reversed, usually by CPR and/or defibrillation or cardioversion or cardiac pacing. Sudden cardiac death should not be used to describe events that are not fatal [3, 4].

In the emergency room (ER), cardiac arrest is presented in two forms. Either the patient arrives at the ER, already in the state of cardiac arrest, e.g., the group of patients who enter cardiac arrest in their homes or the ambulance, or the patient is admitted to the ER and subsequently enters cardiac arrest. The latter typically occurs when clinicians overlook patients with various predisposing and/or serious risk factors. These risk factors will be carefully evaluated and expounded in this section.

The survival rate of cardiac arrest is higher in ERs than any other location in hospitals. This observation is also true when compared to out-of-hospital cardiac arrest, which rarely has a favorable outcome. Neurologic outcomes were also best following cardiac arrest in the ER as well [5]. ER patients were much more likely to be during an acute myocardial infarction (MI) upon the occurrence of cardiac arrest than patients in other hospital units. Wherefore risk factors that could precipitate cardiac arrest must be considered by clinicians to promptly treat them, to

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avoid complications such as cardiac arrest. Therefore, the ER patients have a higher proportion of MI-related VF/VT as the presenting rhythm, and multiple investigations in different settings have documented that cardiac arrests due to VF/VT have a much higher survival rate than cardiac arrests with an initial rhythm of asystole or pulseless electrical activity [6]. Patients in the ER presenting cardiac arrest are also typically younger, with fewer pre-existing comorbid factors, making their diagnosis specifically challenging.

14.2 Epidemiology and Prevalence

Approximately 356,461 people are treated for out-of-hospital cardiac arrest (OHCA) annually in the United States [7]with an estimated 175,000 cases of sudden cardiac arrest (SCA) present to or occur in US ERs each year [8]. Sudden cardiac death accounts for approximately 50% of all deaths attributed to cardiovascular disease in the United States [9].

One-third of cases occur without any prior recognized heart disease; half occur without any prodromal symptoms [10]. Nonischemic dilated cardiomyopathy (NIDCM) is the second leading cause of sudden cardiac death in the United States [11].

Sudden cardiac arrest (SCA) is a complication of many forms of heart disease and on occasion presents in the absence of structural cardiac abnormalities. SCA due to ventricular arrhythmias is a daunting public health problem with 200,000–450,000 events in the United States annually [12, 13].

14.3 Etiology

In most patients who die suddenly, cardiac activity is not being monitored at the time of their collapse. As a result, the mechanism can only be inferred, based upon information obtained after the process has been initiated. The four most common etiologies leading to SCA are cardiac arrhythmias, coronary artery disease, hypertrophic cardiomyopathy, and nonischemic dilated cardiomyopathy. Table 14.1 shows a summary of the most common etiologies associated with SCA.

14.3.1 Cardiac Arrhythmias

Ventricular tachycardia (VT) or ventricular fibrillation (VF) accounts for the majority of episodes [14]. However, a bradyarrhythmia can also be responsible for some cases of SCA. The distribution is different among patients with an implantable cardioverter device (ICD); arrhythmic death accounts for 20 to 35 percent of deaths; post-shock or primary pulseless electrical activity (PEA, also called

Table 14.1 Major causes of sudden cardiac arrest

Coronary artery disease/myocardial infarction
Pulmonary embolism (in the absence of known heart disease)
Hypertrophic cardiomyopathy (presenting with)
Unexplained syncope
Familial history of sudden cardiac arrest
Atrial fibrillation
Dilated cardiomyopathy
Valvular heart disease (aortic stenosis)
Aortic dissection
Cardiac tamponade
Brugada syndrome
Long QT syndrome
Familial sudden cardiac death
Atrioventricular block

electromechanical dissociation) is a frequent cause of SCA in this setting [15]. These arrhythmias lead to asystole correlates with the duration of the arrest and may be the result of VF that has been present for several minutes or longer and then leads to the loss of all electrical activity as a result of hypoxia, acidosis, and death of myocardial tissue.

VF causes a rapid and desynchronized ventricular flutter resulting in reduced left ventricular ejection fraction [16]. VF results from multiple localized areas of micro-reentry without any organized electrical activity [17].

VF almost always occurs in the setting of underlying myocardial disease (or abnormalities in repolarization as in the long QT syndrome) that is often diffuse, resulting in heterogeneity of depolarization and the dispersion of repolarization. With regard to long QT syndrome, a prolonged QT > 500 msec can cause VF leading to compromised heart function. This change in rhythm can cause syncope, seizures, and SCA due to inadequate output [18].

The cause of long QT syndrome is congenital ion channel defects, which play a major role in causing this arrhythmia [19]. Increased risk of ACS has an association with channelopathies, mainly Ca^{2+} and K^{+} channel defects.

14.3.2 Coronary Artery Disease

One of the most common triggers for SCA is coronary artery disease (CAD) [20, 21]. In 30% of cases of CAD, VF develops as the disease progresses, which tends to lead to eventual SCA. These patients often have CAD caused by endothelial dysfunction or fibrous cap rupture [21]. The remaining 70% of patients often suffer from coronary vasospasms, which cause an obstruction leading to ST elevation [21, 22]. The onset of VF is seen during reperfusion, rendering the patient at significant risk for SCA. Patients with an ST-elevation myocardial infarction develop myocardial scarring, which can act as triger for electrical short circuits causing abnormal heart rhythms and risk for SCA [9, 22].

14.3.3 Hypertrophic Cardiomyopathy

Different types of cardiomyopathies are known to represent a common risk for the development of SCA. Patients with hypertrophic cardiomyopathy (HCM) may suffer from dyspnea due to decreased ventricular filling, angina due to restricted or reduced blood flow of the coronary arteries, palpitations due to ischemia from the reduced coronary flow, and altered electrophysiological characteristics of the heart due to the cardiomyocyte disarray [23].

In broad terms, the symptoms related to HCM are those related to heart failure, chest pain, or arrhythmias. Patients with HCM are prone to both atrial and ventricular arrhythmias. Many of these arrhythmias are asymptomatic, but some can precipitate hemodynamic collapse and SCA. SCA is a catastrophic and unpredictable complication of HCM and in some patients may be the first presentation of the disease. The assessment of arrhythmic risk and management of patients with ventricular arrhythmias (or at risk for ventricular arrhythmias) are critical components of the clinical evaluation of nearly all patients with HCM.

14.3.4 Nonischemic Dilated Cardiomyopathy

This cardiomyopathy is the second leading cause of SCA in the United States. This disease usually originates in the left ventricle and is characterized as a dilation of the left or right ventricle of the heart, leading to a decrease in systolic ventricular function [24]. This decrease in function leads to a progressive reduction in the patient's left ventricular ejection fraction, leading to inadequate tissue perfusion. Myocardial tissue hypoxia is arrhythmogenic. In the past, it was hypothesized that acidosis was to be the primary cause of cardiac arrhythmias; experimental studies [25] established that hypoxia in the absence of acidosis could also result in arrhythmias. Furthermore, a systematic review noted the correlation of ectopic rhythms with hypoxia, hypercapnia, and acidosis in myocardial tissue [26].

14.4 Pathophysiology

SCA has various etiologies, further described in the etiology subsection. However, in the ER, the main culprit for the development of SCA appears to be a marked activation of the sympathetic nervous system and the massive release of catecholamines during the stress response. Among other detrimental effects, this mainly leads to the activation of α- and β- adrenoreceptors, but the β-adrenoreceptors are proposed to have a pivotal role in the development of SCA [27]. The activation of

β-adrenoreceptor coupled Gs proteins by catecholamines leads to the formation of the cyclic AMP from ATP, activation of protein kinase A, and subsequent phosphorylation of voltage-dependent L-type calcium channels [27].

In consequence, there is an increase in the influx of Ca^{2+} into myocardial cells further triggering more release of Ca^{2+} from the sarcoplasmic reticulum via the ryanodine receptors [28]. This alteration in calcium handling is known to induce ventricular arrhythmias that are commonly associated with SCA [27]. Prolonged exposure to high levels of circulating catecholamines also results in coronary spasm causing myocardial ischemia. During this stress response, the incidence of platelet aggregation and atherosclerotic plaque rupture due to turbulence is augmented, thereby increasing the risk of CAD [29].

14.5 Risk Factors and Predictors

Most risk factors for CAD are also risk factors for SCA. These include dyslipidemia, hypertension, cigarette smoking, physical inactivity, obesity, diabetes mellitus, and a family history of a premature CAD or myocardial infarction [30]. The risk of SCA is *increased six- to tenfold* in the presence of clinically recognized heart disease and *two- to fourfold* in the presence of CAD risk factors in comparison to healthy patients [31]. A combination of cardiac arrhythmias, abnormalities of left ventricular function, and extensive coronary artery disease might increase the risk of sudden death to as high as 10% per year [31].

In the ER, a large volume of patients admitted have either a history of CAD or cardiac arrhythmias. The most common arrhythmia is atrial fibrillation. We describe the risk that patients with previous MI and atrial fibrillation have when accounting for their comorbidities, of developing SCA when admitted to the ER, in Table 14.2.

Table 14.2 Risks for a patient with previous myocardial infarction or atrial fibrillation with corresponding comorbidities

Myocardial infarction history [33]			Atrial fibrillation [34]		
	Heart rate	*p*-value		Heart rate	*p*-value
Age (> 75)	1.28 (1.08–1.52)	0.005	Age (>75)	1.44 (1.38–1.50)	< 0.001
Male sex	1.62 (1.10–2.38)	0.01	Male sex	1.38 (1.15–1.65)	0.001
Hypertension	1.70 (1.23–2.34)	0.001	Hypertension	1.55 (1.49–1.61)	< 0.001
Diabetes	1.30 (0.89–1.88)	0.2	Diabetes	1.58 (1.49–1.67)	0.960
Angina	1.59 (1.13–2.23)	0.007	History of TIA	1.24 (1.19–1.28)	< 0.001
NYHA I-II	2.77 (1.28–6.01)	0.01	NYHA I–II	1.40 (1.15–1.70)	< 0.001
NYHA III-IV	3.53 (1.09–11.45)	0.01	NYHA III–IV	1.85 (1.44–2.37	< 0.001

TIA transient ischemic attack, *NYHA* New York Heart Association

Syncope is also a predictor since observational data suggest that around 30% of patients with DCM, NYHA class III or IV symptoms, and recurrent syncope will receive an appropriate shock for ventricular arrhythmia by 1 year after implantation of an ICD, rising to around 50% by 2 years [32].

Syncope increases the risk of SCA in CAD patients even with preserved left ventricular ejection fraction (LVEF). One of the most common triggers for SCA is CAD. These findings suggest a role for this clinical marker among patients with CAD and normal LVEF, a large subgroup without any current means of SCA risk stratification [35]. In a recent trial, after adjusting for clinical factors and LVEF, syncope was associated with an increased risk of SCA (OR 2.8; 95%CI 1.68–4.85). When the analysis was restricted to subjects with LVEF ≥50%, the risk of SCA associated with syncope remained significantly elevated (adjusted OR 3.1; 95% CI 1.68–5.79) [35].

However, LVEF remains the most important predictor of SCA after MI. Reduced ejection fraction satisfies the need for an underlying "structural" heart defect that forms one of the prerequisites for a terminal cardiac event such as SCA. Other transient factors and arrhythmic mechanisms are also likely to be necessary, which is why decreased ejection fraction should be considered in addition to other factors when identifying high-risk patients [9].

14.6 Diagnosis and Risk Stratification

Moments of accelerated patient influx, and/or a high number of severely unstable patients, can convert the ER into a chaotic environment. At these moments, SCA presented in the ER can occur unexpectedly in patients who were previously triaged as "safe" or coded "green," due to presenting "mild" symptomatology.

Overlooking patients that could be prone to progressing to SCA can be avoided by promptly identifying patients with risk factors and additionally considering that all patients admitted to the ER are potentially in critical condition until proved otherwise.A study conducted to determine the prevalence of risk factors for cardiac arrest in a hospitalized population identified three significant independent positive associations with the risk of cardiac arrest [36], abnormal breath rate or shortness of breath, abnormal pulse, and reduced systolic blood pressure (Fig. 14.1).

Various arrhythmias can be the origin of "arrhythmia-induced SCA"; ECG is a readily available tool that has been proved useful in the diagnosis and stratification of ventricular tachycardia, ventricular fibrillation, and bradyarrhythmias.

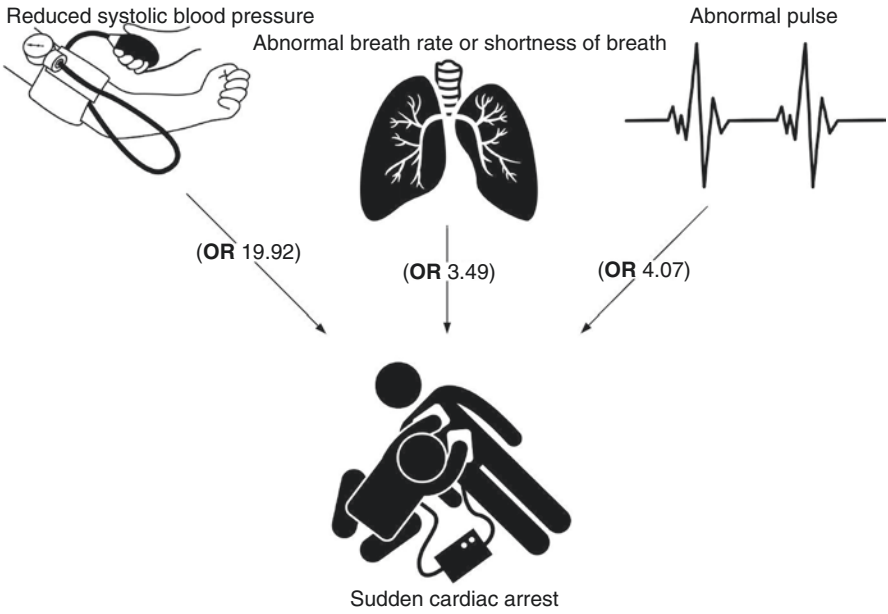

Fig. 14.1 Clinical signs that significantly increased risk of SCA. OR odds ratio

Table 14.3 ECG findings to predict cardiac arrest

Predictor (cutoff)	*OR (confidence interval)*	*p-value*
QRS duration [11](110–120 msec)	1.46 (95% CI, 1.10–1.94)	$p = 0.013$
Fragmented QRS [11]	6.73 (95% CI, 3.85–11.76)	$p = <0.001$
T wave alternans [11]	4.66 (95% CI, 2.55–8.53)	$p = <0.001$
Predictor (cutoff)	*HR (confidence interval)*	*p-value*
Atrial fibrillation [9]	0.99 (95% CI, 0.60–1.63) [9]	_____
Pathological Q wave [9]	0.67 (95% CI, 0.49–0.92) [9]	_____

However, no individual ECG finding has been found to stratify patients the risk for sudden cardiac arrest. However, one or more of ECG findings are useful components for risk stratification. Tables 14.3 and 14.4 show ECG findings and odds ratios.

Table 14.4 ECG definitions to predict cardiac arrest

QRS duration (110–120 msec)	The QRS interval ranges between 0.08 and 0.10 seconds. Durations between 0.10 and 0.12 seconds are intermediate durations, > 0.12 seconds are considered abnormal
Fragmented QRS	The presence of the R′ wave or notching of the R or S wave in the presence of narrow QRS. It indicates heterogeneous depolarization of the ventricular myocardium (due to ischemia, fibrosis, or scar, coronary microvascular dysfunction)
T wave alternans	Microvolt T wave alternans characterized as beat-to-beat fluctuation of the T wave amplitude and morphology is an electrophysiological phenomenon associated clinically with impending ventricular arrhythmias and is an important marker of arrhythmia risk
Atrial fibrillation	An abnormal and irregular heart rhythm in which electrical signals are generated chaotically throughout the heart atria, which may cause symptoms like heart palpitations, fatigue, and shortness of breath
Pathological Q wave	Q wave duration >40 msec or >25% of the QRS complex amplitude. These need to be present in at least two contiguous leads to be considered abnormal (e.g., lead II and III, not leads II and aVF)

14.7 Management

A common method used to prevent SCA is the implantation of intracardiac devices (ICDs) in patients with various risk factors. However, arrhythmic death can still occur despite recognition and termination of tachyarrhythmias by the ICD [37]. These deaths often result from electromechanical dissociation or acute cardiac mechanical dysfunction [38]. Electromechanical dissociation or bradyarrhythmias may be the mechanism of SCA in up to 40% of patients with ICDs [15]. In other cases, ICDs fail to defibrillate fatal ventricular arrhythmias. This situation may occur in the presence of an incessant VT/VF or uncontrolled refractory myocardial ischemia/infarction. Reducing delays has shown to improve survival substantially. In an outcome study of arrests, the survival rate was 74 percent for those who received their first defibrillation no later than 3 minutes after a witnessed collapse and 49% for those who received their first defibrillation after more than 3 minutes [1]. However, even the best guidelines and risk stratification tools can only be translated into improved survival if emergency services are equipped for such an approach and boast experienced clinicians who are careful to detect and monitor high-risk patients promptly. Figure 14.2 shows the steps that follow cardiac arrest detection in the ER.

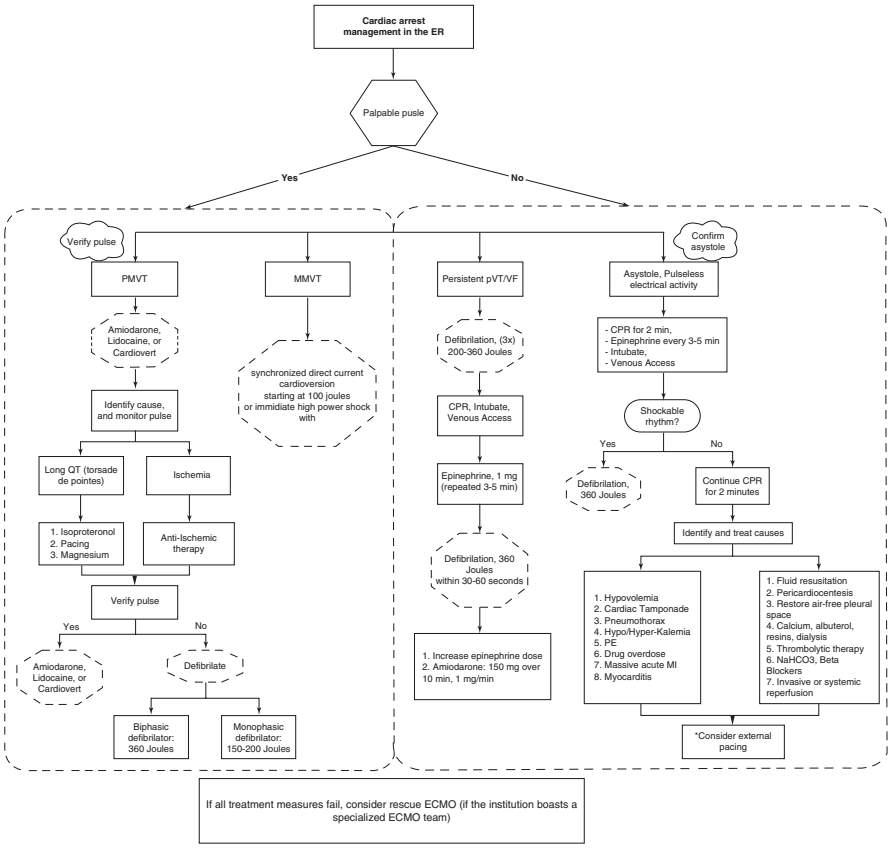

Fig. 14.2 Management of SCA. PMVT polymorphic ventricular tachycardia, MMVT monomorphic ventricular tachycardia, pVF/VT pulseless ventricular fibrillation/ventricular tachycardia

14.8 Additional Clinical Practice Takeaway Points

- Sudden cardiac death accounts for approximately 50% of all deaths attributed to cardiovascular disease in the United States.
- The four most common etiologies leading to SCA are cardiac arrhythmias, coronary artery disease, hypertrophic cardiomyopathy, and nonischemic dilated cardiomyopathy.
- Ventricular tachycardia or ventricular fibrillation accounts for the majority of episodes.
- The risk of SCA is *increased six- to tenfold* in the presence of clinically recognized heart disease.
- Eliminate delays to defibrillate patients in cardiac arrest as much as possible.
- Any given patient admitted to the ED may be prone to SCA.

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Chapter 15
Prosthetic Valve Thrombosis in the ER

Carlos Jerjes-Sánchez, David Rodríguez, Jathniel Panneflek, Francisco Nevarez, Claudia Ortiz-Ledesma, and Jose Manuel Gonzalez-Rayas

15.1 The Scope of the Problem

Prosthetic valve thrombosis (PVT) is a serious and potentially lethal complication of heart valve replacement, most often encountered with mechanical prosthetic valves (MPV) [1] than with bioprosthetic valves (BPV) [2]. The significant morbidity and mortality associated with this condition warrant rapid diagnostic evaluation [3]. PVT incidence is high in developing countries and contributes significantly to late mortality post-valve surgery [4]. Diagnosis can be a challenge due to a broad clinical presentation and a variable degree of prosthetic valve obstruction.

15.2 Prevalence

The precise incidence of early and late PVT thrombosis is difficult to ascertain. Surgical aortic valve replacement recipients had rates from 0.34% to 0.04% per year, respectively. BPV thrombosis using microsimulation models was extremely low a 0.03% per year predicted rate [2]. In retrospective analyses of mitral valve recipients with 12-month follow-up, the incidence was up to a 6%. BPV now accounts for nearly 80% of all surgical aortic valve replacements within the United States [2].

15.3 High-Clinical Suspicion

High-clinical suspicion for PVT must be considered in all patients with a history of mitral or aortic valve replacement, at least ≥1 patient- or prosthesis valve-related risk factors [2, 5], and acute or subacute clinical manifestations until proven otherwise (Fig. 15.1).

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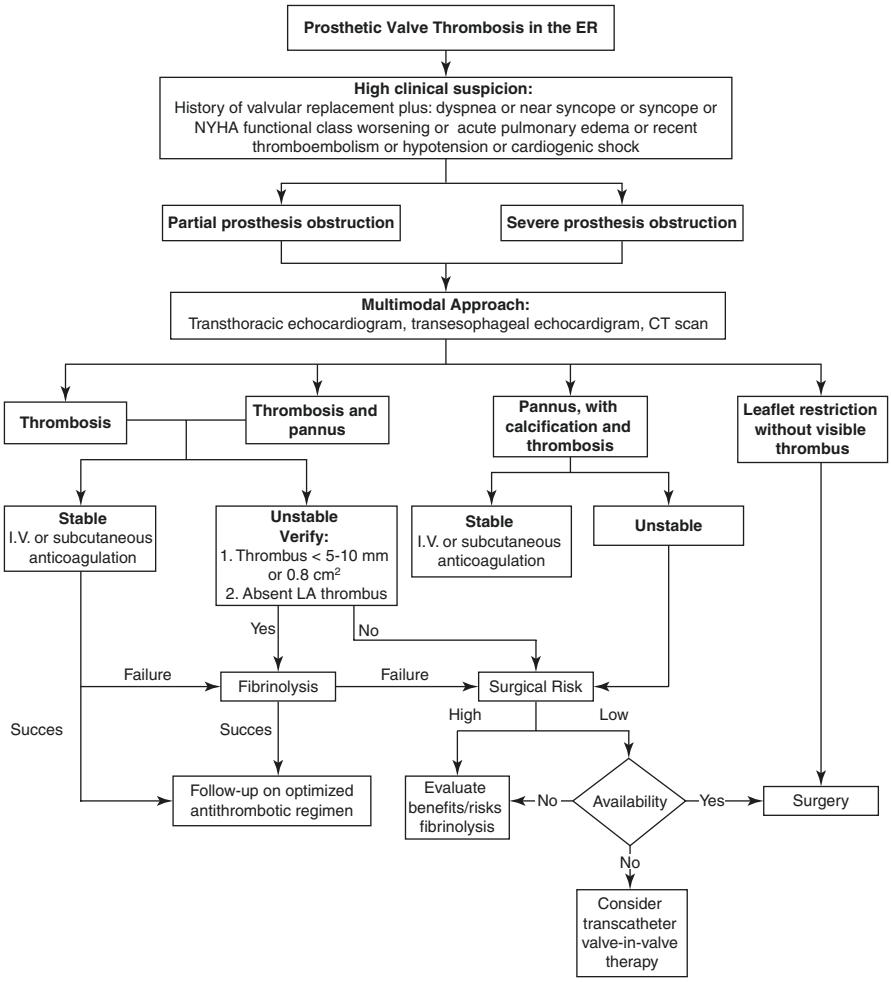

Fig. 15.1 Algorithm for the approach, diagnosis, and management of acute PVT

15.4 Thrombosis Risk Factors

MPV and BPV per se are risk factors for thrombosis [2]. The intrinsic coagulation pathway, also known as the contact activation pathway, represents the main mechanism involved. In contrast to the healthy endothelium, which actively resists thrombosis, artificial surfaces promote clotting through a complex series of interconnected processes. BPVs are less thrombogenic than their mechanical counterparts [6]. Table 15.1 describes the pathophysiological mechanisms that contribute to acute prosthetic valve thrombosis.

Table 15.1 Mechanisms and factors related to prosthetic valve acute thrombosis

Surface	Include protein adsorption (fibrinogen); adhesion of platelets, leukocytes, and red blood cells; as well as thrombin generation and complement activation
Hemostatics	Important in high-risk patients, chronic kidney diseases, diabetes mellitus, anemia, obesity, smoking, and cancer
Hemodynamic	Anything that could provoke stasis and turbulent flow, which in turn promotes hypercoagulability and platelet activity and adhesion

Table 15.2 Risk factors for prosthesis valve thrombosis

Patient-related	MPV- or BPV-related
Renal insufficiency	Incomplete prosthesis endothelialization
Obesity	Periprocedural trauma
Diabetes mellitus	Significant tissue injury
Smoking	Leaflet damage or deterioration
Anemia	Stent fracture
Cancer	Prosthesis mispositioning
Atrial fibrillation	Prosthetic hemodynamic profile
Recent systemic thromboembolism	Having a mitral valve placed over an aortic one (valve in valve therapy)
Known hypercoagulative state	First 3 months of the procedure
Heparin-induced thrombocytopenia	Larger prosthetic valve size
Low cardiac output (EF < 50%)	Pre-dilatation with balloon expandable aortic valve
The absence of OAC post-TAVR incidence 6%, compared with <2% with OAC	Higher incidence when stenting porcine BPVs than stent-less BPVs
Suboptimal OAC	Valve hemodynamic deterioration (>10 mmHg increase in transprosthetic mean gradient during follow-up)

EF ejection fraction, *OAC* oral anticoagulation, *BPV* bioprosthetic valve

Patient-related risk factors have harmful attributes such as inflammation, hypercoagulability, immunologic, as well as stasis and suboptimal treatment. MPV- or BPV-related risk factors depend on several mechanisms linked with incomplete endothelialization, valve replacement, structure, or hemodynamic valve deterioration especially in post-transcatheter valve thrombosis (absence of oral anticoagulation, valve-in-valve procedures, smaller-sized valves, and greater body mass index). Table 15.2 lists patient-related and prosthetic valve-related factors for thrombosis.

15.5 Clinical Presentation

Clinical presentation and physical findings of PVT are highly variable, often depending on the presence of partial or severe obstruction (Fig. 15.1), previous left ventricular ejection fraction, and thromboembolism location. Severe

obstruction is typically associated with clinical instability, whereas partial obstruction is often an incidental finding or can present as minor or major thromboembolism [3]. Thrombosis of a BMV has a similar clinical presentation to that of MVT.

15.6 Main Clinical Characteristics

- Dyspnea
- Loss of NYHA functional class
- Syncope
- Thromboembolism
- Cardiogenic pulmonary edema
- Hypotension
- Cardiogenic shock

15.6.1 Physical Examination

15.6.1.1 Clinical Stability

A careful clinical examination should be performed, with attention being paid to muffling or disappearance of prosthetic sounds and the appearance of a new regurgitant or obstructive murmur [3].

15.6.1.2 Clinical Instability

In patients with a high-clinical suspicion of severe prosthetic valve obstruction, clinical presentation is driven by sudden or progressive dyspnea alone or in association with several additional critical conditions. Although the physical examination should be performed, its clinical condition (respiratory failure, tachycardia, cardiac low output) makes it difficult to identify muffling or disappearance of prosthetic sounds or a new regurgitant or obstructive murmur.

15.6.2 Chest X-ray

Patients with partial obstruction usually have signs of acute pulmonary venous hypertension. In those with severe obstruction, bilateral interstitial or alveolar pulmonary edema is the rule (Fig. 15.2). Chest X-ray findings in clinical stability and instability are described in Table 15.3.

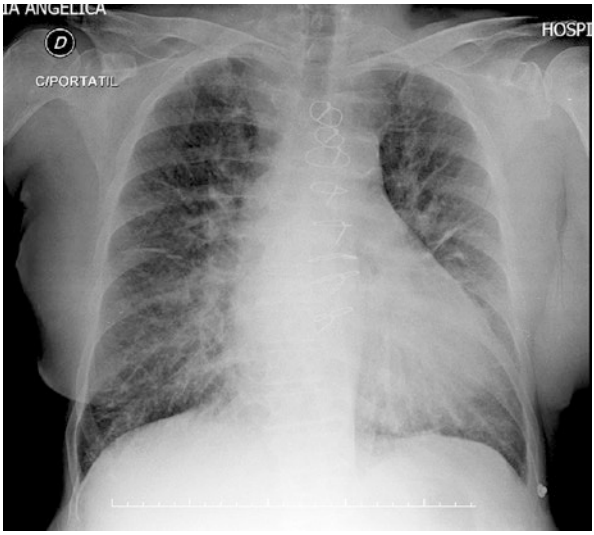

Fig. 15.2 A female patient with biological prosthetic mitral valve thrombosis. Chest X-ray is showing interstitial acute cardiogenic pulmonary edema

Table 15.3 Chest X-ray in clinical stable and unstable patients

Findings	Clinical stability	Clinical instability
Upper lobe vessels are increased in diameter greater than 3 mm in the first intercostal interspace	✓	✓
Venus hilum	✓	✓
Bronchial cuffing	✓	✓
Kerley B lines	✓	✓
Pleural effusion of lung fissures	✓	
Right or bilateral small pleural effusions	✓	
Interstitial or alveolar pulmonary edema		✓

15.6.3 Electrocardiogram

In unstable clinical patients, it is important to exclude other cardiovascular emergencies that could mimic a severe PVT such as ST-elevation myocardial infarction. In the critical state of this group of patients (respiratory failure or low cardiac output syndrome), taking an electrocardiogram (ECG) can be challenging, since artifacts secondary to patient movements can compromise interpretation. Table 15.4 describes ECG findings in patients that are clinically stable and unstable.

15.7 Multimodal Diagnosis Approach

To establish the diagnosis of prosthetic valve thrombosis secondary to a fresh thrombus, we need to exclude isolated or combined mechanisms such as fibrous

Table 15.4 Electrocardiography in clinical stable and unstable patients

Characteristics	Clinical stable	Clinical unstable
Sinus rhythm	✓	
Sinus tachycardia		✓
Left atrial dilatation	✓	
Atrial fibrillation or flutter (HR < 100 lpm)	✓	
Atrial fibrillation or flutter (HR > 100 lpm)		✓
Old myocardial infarction	✓	
Myocardial ischemia	✓	✓
Right ventricular strain	✓	✓
Left or right ventricular hypertrophy	✓	✓

HR heart rate

pannus formation (45% to 75%), calcification, leaflet restriction, and vegetation [3]. A multimodal approach (Fig. 15.1) is mandatory to identify the responsible mechanism and establish an appropriate treatment.

15.7.1 Transthoracic and Transesophageal Echocardiogram

Providing direct visualization of the prosthesis and measurement of transvalvular gradients is an essential part of the diagnostic assessment. A standard complete examination should be performed, with attention directed at transvalvular flow, gradient, and inspection of the prosthetic valve [3]. Pulmonary artery pressures and cardiac output should also be measured. The high-resolution imaging of a transesophageal echocardiogram (TEE) will provide important additional diagnostic information, which will also guide treatment (Fig. 15.3). Table 15.5 describes the echocardiographic findings in valve thrombosis.

15.7.2 Thrombus Versus Pannus

Thrombi must be differentiated from a fibrous pannus, which is usually annular in location. Pannus formation is more frequently encountered on aortic than on mitral prostheses. When observed on mitral prosthetic valves, they most often occur on the atrial side of the prosthesis. Typically presenting as a very dense immobile echo, pannus is typically encountered in patients with a normal anticoagulation profile and with subacute or chronic symptoms [3]. Table 15.6 presents clinical and echocardiographic characteristics and their presentation and/or relationship with pannus and thrombus.

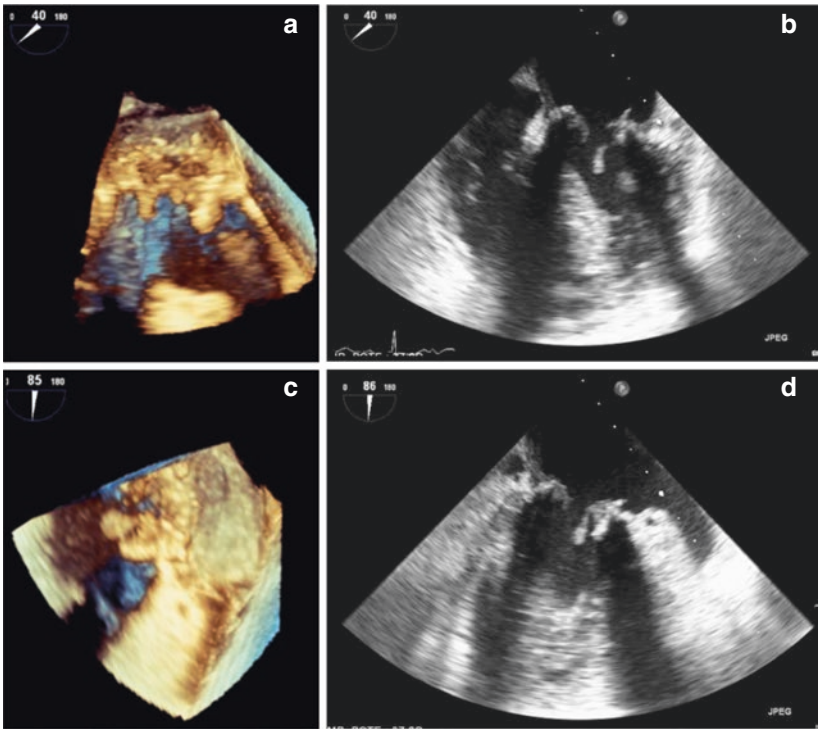

Fig. 15.3 Transesophageal echocardiogram: 3D (**a** and **c**) and 2D (**b** and **d**) images; white arrow showing thrombus in the biological prosthetic mitral valve

Table 15.5 Transthoracic and transesophageal echocardiographic findings

Direct signs	Abnormal movement of the prosthesis, an immobile hemi-disc, incomplete or delayed opening, reduced valve mobility, presence of mobile and globular thrombus with a soft echo density (like the myocardium) which may be attached to the occluded valve, the sewing ring or both, abnormal transprosthetic flow, central prosthetic regurgitation, increased cup thickness (>2 mm)
Mitral prostheses	Mean gradient >8 mmHg and effective area <1.3 cm^2
Aortic prostheses	Mean gradient >45 mmHg and effective area <0.25 cm^2

Table 15.6 Clinical and echocardiography characteristics between pannus and thrombus

Variables	Pannus	Thrombus
Dyspnea	Subacute or chronic	Acute
Suboptimal OAC (INR < 2.0)	Poor relationship	Strong relationship
Echo density (video-intensity ratio)	More >0.7 (100% specific)	Less (<0.4)
Aortic prostheses	More frequent	Less frequent
Mitral prostheses	Atrial side	---

OAC oral anticoagulation

15.7.3 Limitations of Transthoracic and Transesophageal Echocardiography

Transthoracic Echocardiogram

- Acoustic shadowing caused by the prosthesis may limit visualization of thrombus, vegetations, and pannus.
- The test is limited for morphological characterization of the etiology of PVT.
- Diagnosis is influenced by other factors: pericardial effusion, emphysema, COPD, obesity, or prior sternotomy.
- Transthoracic echocardiogram (TTE) has a 13% detection power of PVT [5].

Transesophageal Echocardiogram

- Aortic prostheses are more difficult to evaluate than mitral prostheses.
- The ventricular side of a mitral prosthesis is more difficult to evaluate than the atrial side [3].

TEE, especially three-dimensional [4], has a much greater sensitivity than TTE for the diagnosis of BMV and is also helpful in differentiating a pannus from a thrombus and in determining thrombus size accurately.

It is an important issue to differentiate small thrombi from strands or sutures. Strands are believed to be fibrin filaments, appearing as fine (1 mm), filamentous, mobile echoes of variable length (around 10 mm), most often observed on the atrial side of mitral prostheses.

15.7.4 Cardiac Computed Tomography

This imagining technique recently emerged as a complementary approach, offering excellent spatial resolution and the ability to identify a range of aortic and mitral valve replacement complications including structural valve dysfunction, thrombus development, pannus formation, and prosthetic valve infective endocarditis [7].

With cardiac computed tomography (CCT), it is important to differentiate recent (fresh) from chronic (organized) thrombosis as recent thrombi are usually suitable for thrombolytic treatment which is the case when the attenuation is <90 HU. The clot contraction owing to an increase in hemoglobin and iron concentration occurs after capillary formation and the proliferation of fibroblasts. As a consequence of this process, the attenuation of chronic thrombus is generally higher, ranging between 90 and 145 HU [8]. Tables 15.7 and 15.8 describe the CCT findings and the characteristics between pannus and thrombosis, respectively.

Table 15.7 Cardiac computed tomography findings

CT features	Reduced leaflet motion on 4D-CT
	Hypo-attenuated leaflet thickness
	Thrombus has lower measured CT attenuation values than pannus, with a suggested threshold of 145 HU to distinguish either

CT computed tomography, *HU* Hounsfield units

Table 15.8 Cardiac computed tomography characteristics between pannus and thrombosis

Variables	Pannus	Thrombosis
Timing of presentation	12 months after surgery	At any time
Attenuation value	>145 HU	<145 HU
Impact on disc motion	Yes/no	Yes
Location	Below the prosthesis	Above or below the prosthesis
CT scan appearance	Circular mass extending from the ring, contrast enhancement, calcification	Irregular lobulated mass

HU Hounsfield units

Table 15.9 Differential diagnosis

Cardiovascular	Pulmonary
Acute coronary syndrome	Chronic obstructive pulmonary disease exacerbation
Heart failure with or without preserved ejection fraction	Non-cardiogenic pulmonary edema
Pulmonary embolism	Pneumonia
New onset atrial fibrillation	Asthma
Cardiac tamponade	Fibrosis
Emergency hypertension	
Endocarditis	
Acute aortic syndromes	

15.8 Differential Diagnosis

In all patients with a history of valve replacement, acute symptoms, and clinical instability, PVT must be the first diagnosis. However, other more frequent clinical conditions should be considered and excluded. Table 15.9 shows cardiovascular and pulmonary differential diagnosis.

15.9 Laboratory Evaluation

The laboratory evaluation of a patient with high-clinical suspicion should focus on the analysis of leukocytes, hemoglobin, and renal function to exclude endocarditis. A determination of a suboptimal INR would support the diagnosis of PVT. However an INR in therapeutic ranges does not exclude it.

15.10 Treatment

In patients with clinical stability and proved PVT, unfractionated heparin, enoxaparin, or fondaparinux followed by oral anticoagulation with vitamin K antagonist could improve the outcome in most of them (Fig. 15.1). Unfractionated heparin should be used in patients in whom their clinical conditions may require thrombolysis or surgery. In patients with severe obstruction and clinical instability, physicians in charge must identify in which patients the use of high doses in short-term infusion is mandatory resulting in faster resolution of obstruction and valve aperture. This therapeutic approach could be crucial in critically ill patients where the early resolution of obstruction could be lifesaving [4]. Table 15.10 shows antithrombotic therapy recommendations in clinical stability and instability patients. Surgery depends on availability and surgery team experience. Table 15.11 summarizes the major recommendations from the European and American guidelines.

Table 15.10 Antithrombotic treatment

Clinical stability	Unfractionated heparin adjusted to weight, bolus 60 IU/Kg (maximum 4000 IU) followed by intravenous infusion 12 IU/kg/hour (maximum 1000 IU/hour)
	Enoxaparin 1 mg/kg BID or 1.5 mg OD
	Fondaparinux, <50 kg, 5 mg SC OD; 50–100 kg, 7.5 mg SC OD; >100 kg, 10 mg SC OD
	Vitamin K antagonists with INR 2–3
Clinical instability	Alteplase: Low dose, 25 mg over 6 hours by peripheral vein [4]
	Ultraslow low dose, 25 mg over 25 hours by peripheral vein [9] A bolus of 10 mg in 90 minutes infusion with unfractionated heparin [10]

Table 15.11 Current international guidelines recommendations [10]

European guidelines	COR	LOE
Mechanical valve thrombosis		
Urgent or emergent valve replacement is recommended for obstructive thrombosis in critically ill patients without severe comorbidity	I	C
Consider fibrinolysis (with 10 mg bolus of recombinant tissue plasminogen activator +90 mg of HNF in 90 minutes or infusion of 1,500,000 U streptokinase without HNF in 60 minutes), when surgery is not available or is high risk	IIa	C
Surgery should be considered in the presence of large nonobstructive thrombi (>10 mm) in prostheses without embolic complications	IIa	C
Bioprosthetic valve thrombosis		
Anticoagulation with a VKA or UFH is recommended for bioprosthetic valve thrombosis before considering reoperation	I	C
AHA/ACC guidelines [9]		
Urgent evaluation with multimodality imaging is indicated in patients with suspected mechanical prosthetic valve thrombosis to assess valvular function, leaflet motion, and the presence and extent of thrombus	I	B-NR
Urgent initial treatment with either slow-infusion low-dose fibrinolytic therapy or emergency surgery is recommended for patients with a thrombosed left-sided mechanical prosthetic heart valve presenting with symptoms of valve obstruction	I	B-NR

COR class of recommendation, *LOE* level of evidence

15.11 Additional Clinical Practice Takeaway

- Seek and rule out prosthetic valve thrombosis in every patient with previous valve replacement history and patients who report no longer hearing heart valve click.
- Central venous access must be guided by echocardiography, to avoid multiple punctures increasing potential bleeding complications.
- Unfractionated heparin is preferred over LMWH in patients with a high probability for surgical interventions and in unstable patients to avoid increase of risk if a patient requires thrombolysis after that.
- Avoid use of fluid overload in hypotensive patients, since it could precipitate or worsen ventricular dysfunction.
- Streptokinase could induce severe hypotension.
- All prosthetic valve types can develop thrombus obstruction, independently if patients are or not under effective oral anticoagulation.

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Chapter 16
Pacemaker Emergencies in the ER

Carlos Jerjes-Sánchez and Jose Manuel Gonzalez-Rayas

16.1 The Scope of the Problem

Pacemakers have won a preponderant role in today's cardiology and nowadays are used to treat a huge variety of conditions. For instance, 425 new pacemakers are implanted per 100,000 people every year in America [1]. In addition, in 2009, 737,840 pacemakers were implanted, and 264,824 were replaced worldwide. Specifically, most of them (225,567) were implanted in the United States, whereas demographically speaking, Germany had the greatest quantity of newly implanted pacemakers per million population (927). Additionally, the most common indications for pacemaker implantation are high-degree atrioventricular block and sick sinus syndrome. The most common pacing mode is VVI/VVIR, especially in developing countries [2, 3]. Furthermore, the majority of leads are transvenous and bipolar and have an active fixation [2]. All of this obligates every emergency room (ER) physician to know how to appropriately and efficiently treat a pacemaker emergency.

16.2 Prevalence

Overall issues associated with pacemakers have a prevalence ranging from <1% to 6% [4] or 3% to 7.5% [5]. Complications can be classified according to the time elapsed after the implantation in immediate (related to the procedure), intermediate, late, and in mechanical or electrical (Table 16.1).

Moreover, rates of up to 19.5% of right ventricular (RV) pacing-induced cardiomyopathy (≥10% decrease in LVEF with LVEF <50%) were related with frequent RV pacing in patients with preserved ejection fraction. Other risk factors for pacing-induced cardiomyopathy are male sex, wide native QRS duration, and frequent RV pacing (>20%) [4, 13].

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Table 16.1 Pacemaker-associated complications [4, 6–12]

Type	Time	Complications	Frequency
Mechanical	Immediate	Pneumothorax	0.9–1.2%
		Hemothorax	<1%
		Arterial puncture (could cause unnoticed placement of the lead in the arterial system)	2.7%
		An important pocket hematoma that requires intervention	3.5%
		Cardiac perforation (pericarditis and cardiac tamponade)	<1%
	Intermediate	Twiddler's syndrome	0.07% in 10 years
		Hypertrophic scar and keloid formation	NR
		Infection	0.13–19.9%
		Venous thrombosis and stenosis	1–3%
		Right-sided lead dislodgement	1.8%
		Left ventricular lead dislodgement	5.7%
		Mechanical lead complication	<1%
		Pocket pain or arm swelling	Infrequently reported
		Tricuspid valve and subvalvular apparatus injury	NR
	Late	Lead fracture	2.6–3.6%
		Infections (pocket, lead, and valve)	0.13–19.9%
Electrical	Intermediate	Runaway pacemaker event	2–4% with 30–40% mortality
		Failure to capture	NR
		Failure to pace	NR
		Failure to sense	NR
		Pacemaker-induced tachycardia	NR
	Late	Battery depletion	NR
		Left ventricular desynchrony	NR
		Failure to pace	NR
		Failure to sense	NR
		Pacemaker-induced tachycardia	NR
Mechanical and electrical	Intermediate	Significant TV insufficiency	10–39%

NR not reported

16.3 Pacemaker Functionality Aspects

Cardiac pacing has advanced a great deal since Elmqvist's and Senning's first totally implantable pacemaker in 1958 [14]. Basically, a pacemaker consists of a pulse generator and a lead or various leads implanted in the heart's chambers.

Table 16.2 Pacemaker code reaffirmed by the HRS in 2018

First letter Chamber paced	Second letter Chamber sensed	Third letter Response to a sensed event	Fourth letter Rate Modulation	Fifth letter Multisite pacing
A (atrium)	A (atrium)	I (inhibited)	R (yes)	A (atrium)
V (ventricle)	V (ventricle)	T (triggered)	O (no)	V (ventricle)
D (dual)	D (dual)	D (dual)		D (dual)
	O (none)	O (none)		O (none)

Dual: atrium + ventricle

Nowadays pacemakers are more complex, and a five-letter code, proposed by the North American Society of Pacing and Electrophysiology and the British Pacing and Electrophysiology Group and reaffirmed by the Heart Rhythm Society in 2018, is used to describe their function (Table 16.2) [15, 16].

The first letter makes allusion to the chamber paced (V for ventricle, A for atrium, and D for dual/both), the second letter refers to the chamber sensed (V for ventricle, A for atrium, D for dual/both, and O for none), the third letter indicates how the device responds to sensed stimuli (I for inhibit, T for trigger, D for dual/both, or O for nothing), the fourth letter indicates if rate response is on (R), and the fifth letter identifies if multisite pacing is used (none O, in atrium A, in ventricle V, or in both atrium and ventricle D) [4]. The most common use of the fifth letter is for biventricular pacing used for heart failure treatment [3].

Some common pacing modes are AAI/AAIR, VVI/VVIR, VDD, DDD, DDDR, and VOO/DOO [4, 17], which are hereby presented:

- AAI/AAIR: in this mode, pacing occurs in the atrium and is inhibited by a detected P wave (atrial event). It is used when the sinus node is dysfunctional, but the AV node conduction is conserved. The main advantage of this mode (when used with a single-chamber pacemaker) is that it avoids ventricular pacing and crossing the tricuspid valve. Rate response (AAIR) is added for patients with chronotropic incompetence.
- VVI/VVIR: this mode was devised to pace the ventricle in the absence of an intrinsic ventricular event or to inhibit in the presence of one (inhibition by the QRS complex). Moreover, this mode is employed in cases of chronic atrial fibrillation, infrequent pauses, or bradycardias [4]. This is explained by the fact that VVI/VVIR is unable to sense stimuli from the atrium. Rate response (VVIR) is used in patients with chronotropic incompetence. This pacing mode can be delivered by a single-chamber pacemaker with a lead in the ventricle.
- VDD: pacing can be delivered by a single lead that senses the atrium and the ventricle but only paces the ventricle. If an atrial event is detected, after a certain time interval, the ventricle is paced. On the other hand, if the intrinsic atrial impulse travels through the AV node normally or if there is an ectopic spontaneous ventricular complex resulting in a sensed ventricular event, the pacemaker is inhibited.

- DDD/DDDR: when the sinus node is functional, but the AV conduction is abnormal, a dual-chamber pacemaker may be the option. This pacing mode is able of pacing the atrium in case the frequency drops below a set value and is also capable of pacing the ventricle if the AV conduction is dysfunctional. Additionally, by sensing the atrium, the pacemaker turns the sinus node into a biosensor for increasing the heart rate when needed [17]. Moreover, rate response (DDDR) is used as an additional indicator of physical activity for increasing the heart rate.
- VOO/DOO: although only used temporarily, this mode is of great utility in certain situations. Specifically, asynchronous stimulation is employed when there is a risk of oversensing, which means that certain electromagnetic interfering signals (MRI or electrocautery, etc.) can be taken as intrinsic cardiac events. For instance, if one of these signals is detected in the atrium, the impulse could be carried to the ventricles, which may exceed the upper limit. Also, it is possible that the interfering signal is sensed in the ventricle as a native ventricular event and hence pacing would stop, leading to bradycardia or asystole in a pacemaker-dependent patient.

16.4 Most Common Indications to Implant a Pacemaker

The most common indications to implant a pacemaker, ICD, and CRT are summarized in the following table (Table 16.3).

16.5 Main Pacemaker Malfunctions/Abnormalities

Pacemaker malfunctions/abnormalities can be divided into mechanical or electrical complications:

- Mechanical complications
  - Lead damage

Table 16.3 Common indications to implant a pacemaker

Pacemaker	Third or advanced second-degree AV block
	Sinus node dysfunction
	Chronotropic incompetence
	Carotid sinus hypersensitivity
ICD	Primary or secondary prevention of sudden death because of malignant ventricular arrhythmias
CRT	To maintain AV and interventricular synchrony by biventricular stimulation for heart failure

ICD implantable cardioverter defibrillator, *CRT* cardiac resynchronization therapy

  - Infections
  - Thrombosis
  - Lead perforation
- Electrical complications
  - Failure to capture
  - Failure to pace
  - Failure to sense
  - Pacemaker-induced tachycardia
  - Runaway pacemaker syndrome
  - Battery depletion
  - Left ventricular dyssynchrony
  - Pacemaker syndrome
- Mechanical and electrical complications
  - Tricuspid regurgitation

16.6 Mechanical Complications

16.6.1 Lead Damage

Leads may experience fracture or twisting. In a few severe cases such as Twiddler's syndrome, Reel syndrome, or Ratchet mechanism, lead dislodgement may occur due to manipulation of the generator, causing it to twist inside its pocket [8, 18]. Additionally, lead's resistance is a variable factor dependent on body position or edema (to name a few), but a resistance change of >30% might imply a lead defect/damage [4]. Moreover, it is crucial to understand that the term "impedance" (measured in ohms Ω) refers to all the forces that oppose to the current flux in an electric circuit or pacemaker [19]. The normal impedance value of a lead typically ranges from 250 to 1200 Ω, with an output of 5 V [19]. In the one hand, an impedance value lower than 250 Ω suggests that the lead's insulation may be damaged (fewer forces opposing to the current flux). On the other hand, a high impedance along with a high myocardial depolarization threshold suggests a broken lead (stronger forces opposing the current flux) [19].

16.6.2 Infections

Infections are severe complications of cardiac implantable electronic devices (CIED). For instance, device-related endocarditis has an incidence of 10–23%, while infection of a pacemaker following implantation goes from 0.13% to 19.9%. Additionally, the incidence of ICD infection ranges from 0.7% to 1.2% [9].

Cardiac device infective endocarditis has a high mortality rate of 24.5–29% (with up to a year follow-up periods) and an 80–100% explantation rate [20]. Moreover, 68–93% of infections are caused by *Staphylococci* and Gram-positive bacteria, whereas less than 18% of infections are due to Gram-negative bacteria. The fact that 15% of implantable cardiac device bacteria are culture negative must be considered [20].

Most of the infections related to pacemakers occur in the implantation pocket [9]. Device infection may present a few weeks later (a most common scenario) or up to 1 year after the procedure [4]. As a result of infected leads, vegetations can appear through all the lead path, which includes the tricuspid valve, the endocardium of the right atrium, and less frequently the right ventricle [9]. Echocardiography is effective in visualizing and measuring vegetations along with evaluating the hemodynamic state of the heart. Transesophageal echocardiography must be performed in pacemaker bearers with suspected infective endocarditis [21].

Clinical presentation of systemic infections and endocarditis of the leads or valves commonly are fever, chills, positive blood cultures, and intracardiac vegetation. Pocket infection signs are swelling, redness, erosion, purulent discharge, chronic pocket pain, and alterations in the scar. Pocket fluid collection (visible with ultrasonography) and soft swelling may also present [22]. In this case, recommendations are to take a blood culture, to perform sensitivity testing (if possible), and to initiate broad-spectrum antibiotics with focus on cutaneous flora (most commonly *Staphylococcus aureus* or *Staphylococcus epidermidis*) such as vancomycin [1, 22, 23]. Needle aspiration or incision of the pocket should be avoided, and the patient must be referred to a center experienced in treating infected devices to program removal and/or antibiotic therapy [4].

In case empirical treatment needs to be initiated, a list of possible antibiotics is provided according to the "Guidelines for the diagnosis, prevention, and management of implantable cardiac electronic device infection" published on behalf of the British Society for Antimicrobial Chemotherapy (BSAC) as host organization [20]: (iv, intravenous; q, every)

- Generator pocket infection without further complications
  - Vancomycin (1 g BID iv) *or*
  - Daptomycin (4 mg/kg OD iv) *or*
  - Teicoplanin (6 mg/kg to a maximum of 1 g given at 0, 12, and 24 h and then OD)
- Lead-associated infective endocarditis or lead infection or complicated generator pocket infection with pending blood cultures, like in the scenario of severe sepsis
  - Vancomycin (1 g bid iv) AND meropenem (1 g tid iv) *or*
  - Daptomycin (8–10 mg/kg od iv) AND meropenem (1 g tid iv)
- Lead-associated infective endocarditis or lead infection or complicated generator pocket infection with negative blood cultures

– Vancomycin (1 g bid iv) AND gentamicin (1 mg/kg bid iv) *or*
– Daptomycin (8–10 mg/kg od iv) AND gentamicin (1 mg/kg od iv)

It is important to consider that doses need to be adjusted to the renal state of the patient. Moreover, daptomycin may be used to replace vancomycin in glycopeptide-intolerant patients or if nephrotoxicity is an issue. When selecting gentamicin, pre-dose levels must be <1 mg/L and post-dose levels 3–5 mg/L. Additionally, gentamicin may be replaced by meropenem.

16.6.3 Thrombosis

Venous thrombosis and stenosis are severe complications of pacemakers with an incidence of 1–3% [4]. Right atrial thrombosis is an uncommon pathology that can present asymptomatically or with signs of right-sided heart failure, obstruction, or pulmonary embolism [9]. Moreover, in 2 out of 53 autopsies performed in pacemaker bearers, a large right atrial thrombus was found. Both patients were older women and presented the thrombotic event approximately 1 month after device implantation and had signs of congestive heart failure and superior vena cava syndrome [9, 24, 25].

Echocardiography is an insightful tool for determining if the thrombus is recent or longstanding. According to Almomani et al., long-standing thrombi may contain calcium and most of the times are stationary. On the other hand, recent thrombi have a lower echo density and are highly mobile [9]. General signs for thrombosis are a pain, swelling, vein distention, and shortness of breath. As for standard venous thromboembolism, anticoagulants are the core of the treatment [1]. Finally, deciding whether to remove or change a lead or not is the responsibility of the implantation team, and it is not an emergency [1].

16.6.4 Lead Perforation

Perforation by a lead of a cardiac implantable device is an uncommon complication with an incidence of less than 1%. Moreover, perforation rates for pacemakers go from 0.1% to 0.8% and for implantable cardioverter defibrillators from 0.6% to 5.2%. This type of complication can be further divided into acute perforation, commonly resulting from the procedure, and subacute or delayed perforation, which takes place past the 1 month of implantation [9]. According to Hirschl et al., atrial perforation is more common than ventricular perforation, and ventricular perforation is more frequently caused by an implantable cardioverter defibrillator than by a pacemaker [26].

Apart from cardiac perforation, pleural perforation is also an acute complication of pacemaker implantation. Figure 16.1 depicts an anteroposterior chest X-ray of a pneumothorax case with subcutaneous emphysema after pacemaker implantation.

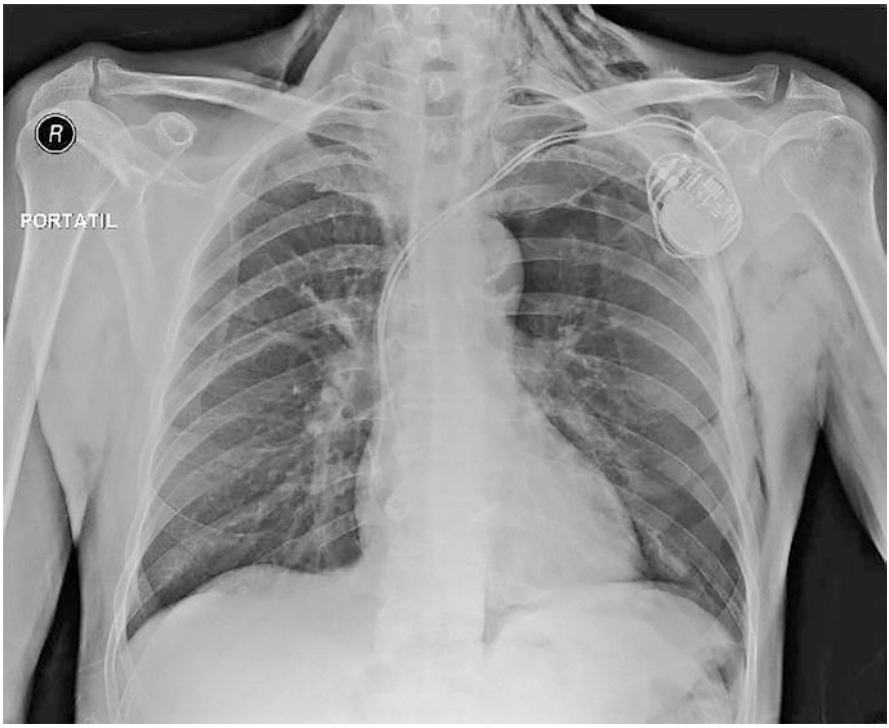

Fig. 16.1 Anteroposterior chest X-ray of a patient with pneumothorax and subcutaneous emphysema after pacemaker implantation

Almomani et al. conducted a review of 35 cases of delayed lead perforation reported in the literature in which his group concluded that the risk for cardiac tamponade and death is low [9]. Furthermore, Refaat et al. found that the symptoms accompanying a delayed perforation are variable, but some examples are syncope, chest pain, stimulation of extracardiac muscles such as the diaphragm, shortness of breath (possibly related to pneumothorax, hemothorax, hemopneumothorax, pneumomediastinum, and/or tamponade), chest discomfort (due to delayed pericarditis or mammary hematoma near the device pocket), hiccups caused by the stimulation of the phrenic nerve, swelling of the device pocket, and repetitive shocks due to a malfunctioning device. Moreover, patients may present unspecific symptoms such as dizziness or fatigue or be completely asymptomatic [27].

If the lead perforation is suspected, the following diagnostic sequence can be followed: device interrogation, chest radiography, echocardiography, and fluoroscopy [28]. Chest CT aids when other methods do not provide a clear diagnosis [9]. As such, myocardial perforation can sometimes be seen with a chest X-ray, and in much of the cases, it will show the lead's displacement to a different position from the one it was originally implanted (Fig. 16.2). Hence, when possible, it is important to compare the chest X-ray taken in the ER with a control one ideally taken within 24 h after the pacemaker implantation [29].

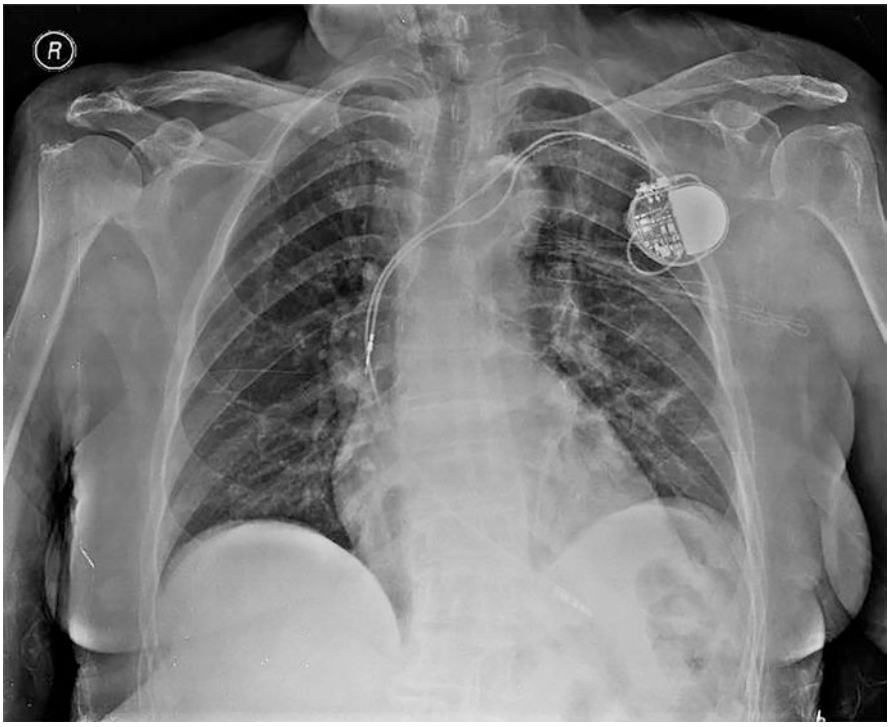

Fig. 16.2 Anteroposterior chest X-ray of a patient with dislodged and inactivated atrial lead

Two-dimensional transthoracic echocardiography is also of help to diagnose lead perforation or dislodgement, along with some accompanying pathologies such as pericardial effusion and tamponade. Since transthoracic echocardiography beam may not pass through the wire's path at first, it is important to keep in mind that multiple tomographic images should be taken to achieve a complete diagnosis [9]. Real-time 3D transthoracic echocardiography complements the 2D modality and is better and quicker to visualize the intracardiac part of the device's lead [9]. Thus, if available, real-time 3D transthoracic echocardiography should be used when lead perforation is suspected.

16.7 Electrical Complications

16.7.1 Failure to Capture

In this complication, the pacing spike is delivered, but the cardiac muscle does not depolarize. On the ECG this can be identified as pacing spikes with no atrial or ventricular complexes following [1]. Figure 16.3 depicts an example of a failure to capture on the

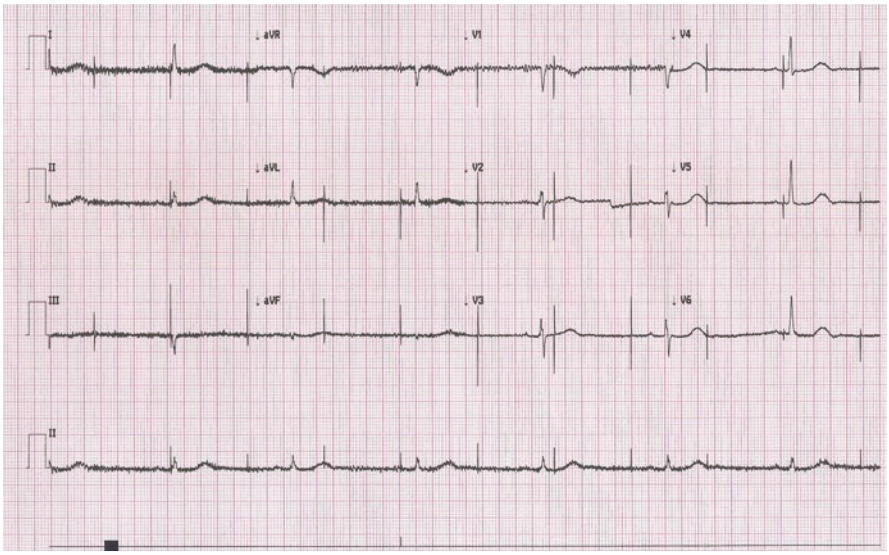

Fig. 16.3 ECG of a patient with a dislodged atrial lead (same case of Fig. 16.2) that depicts a failure to capture and to pace. On DII, pacing spikes 2, 4, 5, 7, and 9 fail to elicit a ventricular contraction. Additionally, pacing spikes 3, 6, and 8 are incorrectly delivered due to a failure to sense. ECG parameters: heart rate = 40 bpm, QRS complex = 94 ms, QT/QTc = 510/449 ms, average RR = 1485 ms, QTcB = 425 ms, QTcF = 454 ms, speed = 25 mm/s, voltage = 10 mm/mV, filter = 0.05–300 Hz W

ECG. Some common causes for this complication are lead dislodgement or malposition, inflammation of the electrode-myocardium interphase, and electrolyte imbalances. Imaging techniques, ranging from a chest X-ray or echocardiography to chest CT, are useful to determine the position of the lead. Symptoms of the disease by which a pacemaker was initially indicated can appear. Standard ACLS management is suggested, and a transcutaneous pacemaker should be considered on pacemaker-dependent patients [1].

16.7.2 Failure to Pace

Here, the pacemaker is sensing correctly but not delivering pacing spikes when needed. On the ECG, there will be no pacing spikes, and thus, the native rhythm of the patient will be observed. The most common causes are lead fracture, battery depletion, failure of the generator, and oversensing [1]. Oversensing refers to the event when the pacemaker is affected by electrical interference (muscular potentials or electrical noise) and incorrectly senses it as coming from the heart. This inhibits the delivery of stimuli.

Another important cause of oversensing is called pacemaker crosstalk. This phenomenon happens with dual-chamber devices when the lead in one chamber

delivers a pacing spike which is sensed by the lead on the second chamber as an intrinsic depolarization, therefore inhibiting the delivery of pacing spikes in the second chamber [30]. For example, the ventricular lead could sense an atrial depolarization spike as being ventricular in nature and inhibit ventricular pacing.

Causes of generator damage potentially leading to failure to pace are an internal malfunction, blunt trauma, MRI, radiation therapy, and use of electrocautery. Symptoms of pacing failure are frequently the same as those of the native pathology, such as bradycardia or high-degree atrioventricular block. Treatment consists of ACLS bradycardia management and interrogation and reprogramming of the pacemaker [1]. In the case of oversensing, switching the device into an asynchronous pacing mode (a constant frequency of 80–100 bpm) by placing a magnet over the pulse generator may help to avoid oversensing of the device (and therefore to avoid pacemaker inhibition). Extreme caution is advised in pacemaker-dependent patients [1].

16.7.3 Failure to Sense

In this malfunction, the pacemaker is not detecting the intrinsic chamber activity, and thus, regardless of the intrinsic beats, the device sends electrical impulses. Some frequent causes are lead dislodgement, lead fracture, scar tissue between the lead and myocardium interface, battery depletion, or low-amplitude cardiac signal [1]. The ECG will show inappropriately delivered pacing spikes (Fig. 16.3). Signs and symptoms of failure to sense will be those of congestive heart failure. Pacemaker under sensing must be considered when there is no obvious explanation for an exacerbation of congestive heart failure [1]. Interrogation of the device to obtain key functionality parameters is suggested alongside with pacemaker reprogramming.

16.7.4 Pacemaker-Induced Tachycardia

This complication occurs most commonly in old dual-chamber devices and is caused by atypical conduction through the heart [1]. Specifically, a retrograde P wave may initiate a reentry circuit by falling just after the preprogrammed refractory period. This will make the device deliver rapid ventricular stimuli as a result of the continuously sensed atrial impulses [1]. First-line intervention for pacemaker-induced tachycardia/runaway pacemaker syndrome is to apply a magnet since it could break the anomalous rhythm. When the above method fails in an unstable patient, possible management options are reprogramming the device or external pacing [1].

16.7.5 Runaway Pacemaker Syndrome

The present malfunction is intrinsic to the device and represents an infrequent but serious pacemaker complication with an estimated incidence of 2–4% with 30–40% mortality [7]. This malfunction also occurs with implantable defibrillators. Additionally, runaway pacemaker events have been reported to present in a wide time range, from 2 days to 9 years after implantation [7]. Nonetheless, runaway pacemaker events can occur throughout the entire lifetime of the device. They can also present intermittently and remain undetected [7].

Although some authors [1] treat runaway pacemaker syndrome and pacemaker-induced tachycardia as synonyms, they have certain specific differences and distinct treatment methods. Runaway pacemaker syndrome can present in two forms: pacemaker-induced ventricular tachycardia and extreme bradycardia as a result of ventricular capture failure (due to "rapid, low-amplitude sub-threshold pulses") [7]. In both forms mortality rates are high. Runaway pacemaker syndrome must be considered when pacing frequency exceeds the established upper limit, thus excluding pacemaker-mediated tachycardia [31].

The precise cause of runaway pacemaker is unknown, but it is associated with:

- Primary circuit failure
- Generator hermetic seal defects
- Circuit damage due to an electric scalpel or radio-frequency ablation
- Generator sterilization with heat
- Electromagnetic interference during radiotherapy [32]
- Low battery voltage [33]

It is important to mention that this syndrome is refractory to defibrillation therapy and antiarrhythmic agents since the problem is limited to the device. Poor results have been achieved by reprogramming the device or by overstimulation with a temporal electrode. Moreover, since magnet placement just disables the sensing feature of the device, this approach may be inefficient. Last treatment option is to disconnect the leads from the generator [7, 23].

16.7.6 Battery Depletion

Battery life is a variable parameter but a very important one for pacemaker-dependent patients. Hence, it is valuable to know some common clinical manifestations of a dying battery:

- Pacing mode change into an asynchronous one (VOO or AOO)
- Change on the width of the pacing spike
- Battery voltage or impedance change [19]

Two important terms to have in mind are ERI and BOL, which mean elective replacement indicator and beginning of life, respectively, and inform on the power left on the device's battery.

16.7.7 Left Ventricular Dyssynchrony

Right ventricular apical pacing is a risk factor for left ventricular dyssynchrony, which can lead to systolic and diastolic dysfunction, and ventricular remodeling. All of this is reflected clinically by worsening of heart failure. Furthermore, tissue Doppler and speckle tracking echocardiography are helpful to evaluate left ventricular dyssynchrony [9].

16.7.8 Pacemaker Syndrome

This pathology does not imply a malfunctioning pacemaker but rather a patient presenting unfavorable hemodynamics, namely, atrioventricular dissociation. This is common to see with VVI pacemakers since the synchrony between auricular and ventricular depolarization is lost. According to the Mode Selection Trial (MOST), 18.3% of the patients with sinus node dysfunction assigned to a VVIR pacing mode developed pacemaker syndrome [34]. Some of the most common symptoms presented are neurological of low cardiac output and of congestive heart failure such as general discomfort, fatigability, dyspnea, orthopnea, cough, dizziness, atypical chest discomfort, throat fullness sensation, and, less frequently, presyncope or syncope [3, 35]. Furthermore, patients may present hypotension, rales, jugular vein distention accompanied with cannon A waves, peripheral edema, and tricuspid or mitral (or both) regurgitation murmurs [3]. Lastly, when patients with a VVI pacemaker present pacemaker syndrome, a change to a dual-chamber device, such as DDD/DDDR, could be considered in some cases [3].

16.8 Mechanical and Electrical Complications

16.8.1 Tricuspid Regurgitation

Severe tricuspid regurgitation due to valve interference with an intracardiac device lead is an infrequent cause of progressive right-sided cardiac insufficiency and represented 2.8% of all the tricuspid valve surgeries [9]. Higher rates of tricuspid regurgitation were reported when more than 1 RV lead is implanted and with ICD leads because of their thickness and stiffness [12]. Tricuspid regurgitation can be functional or structural. When tricuspid regurgitation is associated with a pacemaker, the most common cause is functional (87%). On the other hand, when the regurgitation is directly induced by a pacemaker, the structural causes are divided as follows: restricted leaflet mobility (41%), adherent leaflet to the leads (37%), leaflet perforation (12%), scarring of leaflets (8%), and chordal entrapment (7%). The most commonly affected leaflet was the septal one (73%) [36].

Tricuspid valve regurgitation due to a pacemaker must be suspected in every patient with progressive right-sided cardiac insufficiency with early or late onset, without an apparent cause, and in cases that are refractory to habitual diuretic treat-

ment. Echocardiography is central to the diagnosis of tricuspid regurgitation, and both 2D and 3D modalities may be used. However, 3D echocardiography has better efficacy to evaluate the route of the lead through the tricuspid valve [9].

16.9 High-Clinical Suspicion in the ER

A pacemaker emergency must be suspected when a patient arrives at the ER with low- cardiac output symptoms (hypotension, syncope, lipothymia, dyspnea, fatigability, etc.). Additionally, lead perforation should be highly suspected in thin elderly females and in patients taking steroids or anticoagulants [27]. Moreover, device infection needs to be considered in light of *Staphylococcus aureus* bacteremia, since it is the most common infectious agent related to lead endocarditis and device pocket infection [9]. Furthermore, in a patient with an embolic event (especially pulmonary embolism) and a cardiac device, a right-sided origin of the thrombus must be suspected [21]. Pacemaker undersensing (failure to sense) must be suspected when there is no obvious explanation for congestive heart failure exacerbation [1].

16.10 Risk Factors

Although establishing clear risk factors is complicated, Refaat et al. [27] reported that patients with a lower body mass and elderly female patients were specifically vulnerable to lead perforation [9, 27]. Additionally, patients with a thin myocardial wall, possibly due to dilated myocardiopathy or a previous infarction, are also vulnerable to lead perforation. However, patients with a normal myocardium or a hypertrophic one are not considered to be at lower risk [27, 29]. Twiddler's syndrome is more common in female, elder, obese, and psychiatric patients [8]. Risk factors for pacemaker infection (pocket, endovascular leads, and valves) are diabetes, heart failure, renal failure, corticosteroid use, postoperative hematoma, lack of antibiotic prophylaxis, oral anticoagulation, previous cardiac device infection, generator change, and use of temporary pacemaker [4]. Finally, passive fixation leads and coronary sinus pacing leads (LV) have a higher risk of dislodgement [4].

16.11 Clinical Presentation

A typical patient with a malfunctioning pacemaker presents with bradycardia and/or hemodynamic instability due to abnormal stimulation. Additionally, the baseline rhythm of the patient (his indication for pacing) may manifest due to the malfunctioning device. Patients may also present tachycardia due to oversensing

(pacemaker-mediated tachycardia). In either case, low cardiac output symptoms are common. On the other hand, patients with pocket infections more commonly present local signs of erythema or edema. Finally, hemodynamic instability could also be due to severe cases of lead infection or thrombosis.

16.12 Main Clinical Characteristics

- Low cardiac output symptoms
  - Hypotension, dizziness, syncope, dyspnea, lipothymia, and fatigability
- Return to baseline rhythm before pacemaker implantation (bradycardia or advanced degree AV block)
- High pacing frequencies
- Shock or hemodynamic instability
- Suggestive signs of pocket infection such as erythema, edema, or tenderness to palpation

16.12.1 Physical Examination

Physical examination and device interrogation are the cornerstone to identify a pacemaker complication. When myocardial perforation is suspected, mammary hematoma, pericardial/pleural effusion, and chest wall bruising are key signs that may support the diagnosis [27]. Moreover, setting the device to a maximal stimulation output and hence the stimulation of the right or left hemidiaphragm or the chest wall indicate most of the times that a lead has perforated the atrial or ventricular wall. Additionally, interrogation of the device may show change in impedance, change in pacing parameters, loss of capture, elevated capture threshold, undersensing, and a noisy electrogram [27]. Nevertheless, normal parameters do not exclude lead perforation, and in case some of the above signs are found, image confirmation must be undertaken.

16.12.2 Clinical Stability

Some patients with a pacemaker complication may be asymptomatic, as in the case of lead perforations or right atrial thrombus discovered incidentally by chest CT or echocardiography, respectively [9, 26].

16.12.3 Clinical Instability

Since pacemakers are essentially antibradycardia devices, bradycardia or asystole in pacemaker-dependent patients may occur. Although some of the patients with right atrial thrombosis are asymptomatic, they can also present with symptoms of right-sided heart failure, obstruction, or embolization of the pulmonary artery [9]. Patients may present with septic shock in less than 10% of the cardiac device infection cases [20].

16.12.4 Chest X-ray

Chest X-ray is helpful in identifying twisted, fractured, or dislodged pacemaker cables (Fig. 16.3). It is also valuable to diagnose myocardial perforation by a pacemaker lead, since the migrated lead may be appreciated outside the heart. Furthermore, lead perforation must be suspected when the separation between the electrode tip and the epicardial fat is less than 3 mm [9]. In addition to posteroanterior chest radiography, a lateral projection is also of help to assess for the correct position of the device's leads [29].

16.12.5 Electrocardiogram

The electrocardiogram is an important part of the clinical assessment of a pacemaker. A functional pacemaker produces a spike or artifact on the surface ECG. Commonly, these spikes will anticipate atrial or ventricular depolarization [1]. These spikes are often difficult to appreciate, but setting the ECG filter to 150 or 300 Hz should make them more visible.

Most of the atrial leads are placed in the right atrial appendage, and thus P waves are normally positive on the inferior wall, DI, and AVL. An apical pacing lead will be seen as a left bundle block (QS or rS morphology in V1–V2 and wide QRS) since the depolarization stimulus travels from the RV to the LV. Moreover, the QRS complex will be discordant from the T wave [1]. On the other hand, a right bundle branch block suggests that the lead is in the left ventricle, which can result in thromboembolism or in ventricular arrhythmias. If this is discovered during the implantation procedure, leads must be repositioned. If this is detected after the implant, anticoagulation must be initiated, and a repositioning procedure must be planned [4].

Monophasic pacemakers (older devices) produce a clearly noticeable artifact on the ECG, while biphasic pacemakers (modern devices) produce a mostly indiscernible spike [1]. In the case of biphasic pacemakers, sometimes it is useful to increase the amplitude of the ECG to make the pacing spike noticeable [1]. Biphasic pacemakers (which can also act as monophasic) reduce the risk of over detecting muscular potentials, far-field detection, and stimulating the skeletal muscle [19]. In case

of lead perforation suspicion, right bundle branch morphology might be seen in V1, while the right ventricle is paced [27].

As it was previously stated, pacing leads are normally placed on the apex of the RV. Other implantation sites higher up in the septum are also possible, but the left bundle branch block morphology will persist. However, inferior ECG leads can have a variable axis [37]. The following table summarizes the most common electrocardiographic features found according to the lead implantation site as reported in [38] (Table 16.4).

Finally, a recently published algorithm called TBC helps to quickly assess for complications in the electrocardiograms of patients with pacemakers [39]. This method is easy to remember since each of its letters represents a sign of alarm:

- Tachycardia with spikes (T): spikes (pacing artifacts) stimulating at a frequency of 120 bpm or more (2.5 big squares [500 ms] or less after the previous QRS complex)
- Bradycardia without spikes (B): no QRS complex during a 1500 ms time period (7.5 big squares) after the previous QRS, which translates in a frequency of 40 bpm
- Chaos (C): spikes with no relation to the QRS complex (pacing artifacts within the QRS-T complex or not followed by a QRS and at different distances from the following QRS complex)

If the T criterion is found (most commonly produced by pacemaker-mediated tachycardia), elective referral to a specialist is recommended. On the other hand,

Table 16.4 Identification of lead position according to the electrocardiogram pattern

Lead position	Electrocardiographic features
RV apex (E.g. Fig. 16.4)	The impulse travels from right to left and from the apex to the base Left bundle branch block morphology VI: predominantly negative QRS of more than 120 ms Inferior leads (DII, DIII, aVF): negative QRS
A higher portion of the septum (E.g. Fig. 16.5)	The impulse travels from the right ventricle outflow tract to the inferior wall Inferior leads (DII, DIII, aVF): positive QRS Narrower QRS than with apical stimulation (leads on the higher portion of the septum are closer to the cardiac conduction system)
The lower portion of the septum (E.g. Fig. 16.6)	The impulse has two components: one travels from the inferior part of the septum to the right ventricle outflow tract and the other travels to the apex Inferior leads (DII, DIII, aVF): rS morphology R wave is proportional to the height at which the lead is implanted on the septum
Unnoticed placement of the lead in the LV	Right bundle branch block morphology
Biventricular stimulation (E.g. Fig. 16.7)	QRS has a combined morphology of the depolarization stimuli of both ventricles

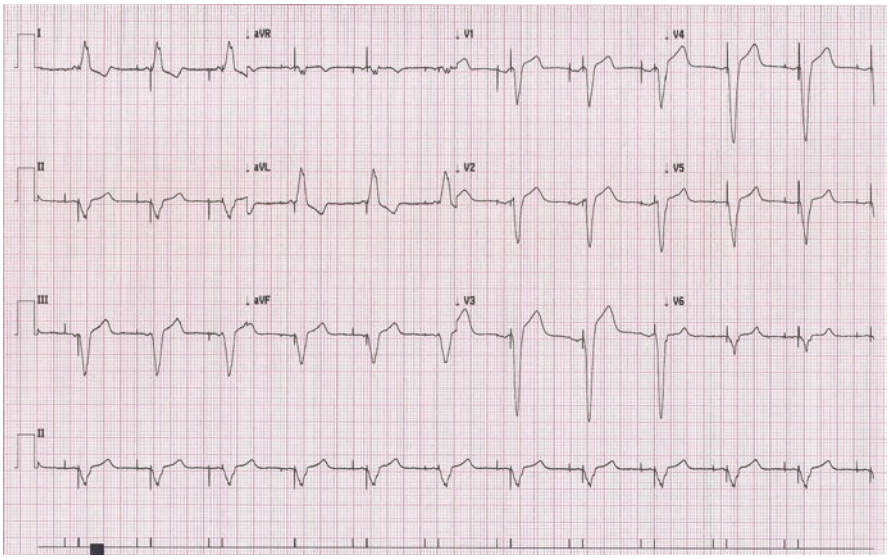

Fig. 16.4 RV apex

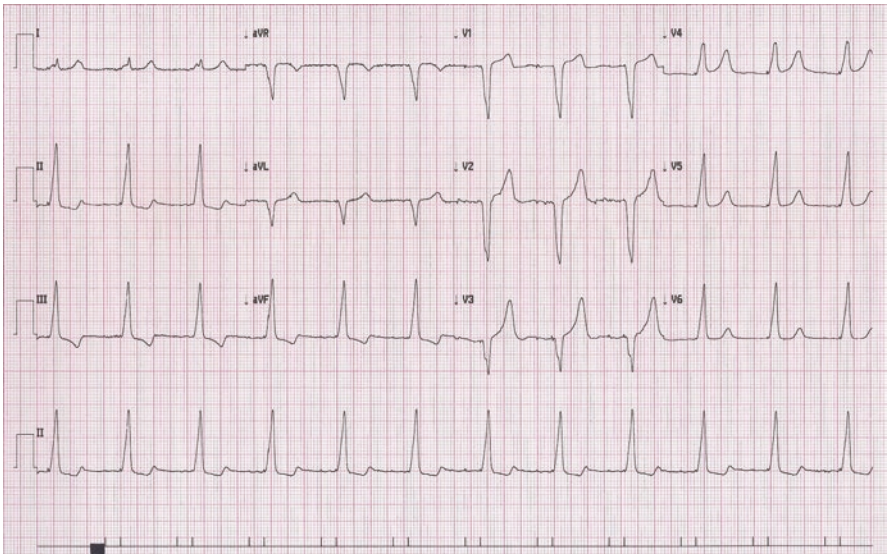

Fig. 16.5 Higher portion of the septum

both B and C require urgent pacemaker evaluation by a specialist and are indicative of severe malfunctions.

The sensitivity and specificity of this quick test are high, with 86.3% and 94.2%, respectively. Moreover, it has a positive predictive value of 88% and a negative predictive value of 93.3%, which means that if none of the above criteria are meet,

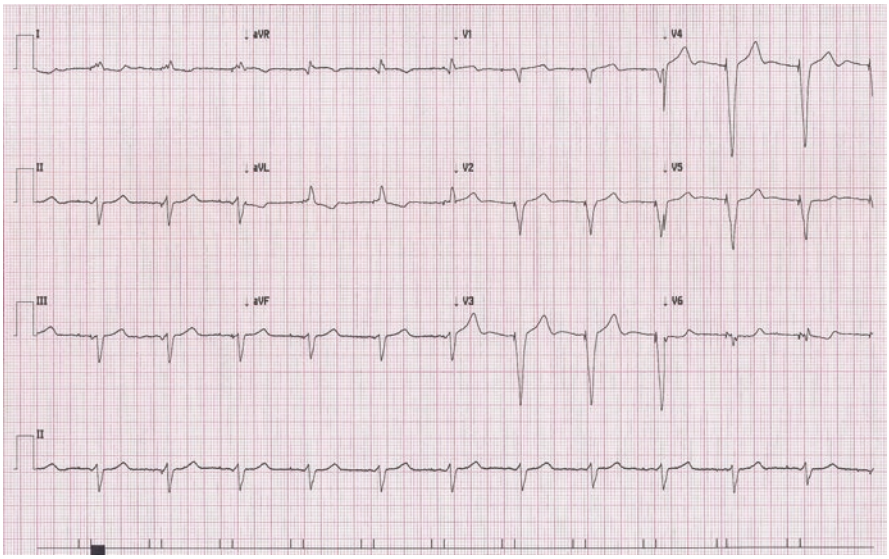

Fig. 16.6 Lower portion of the septum

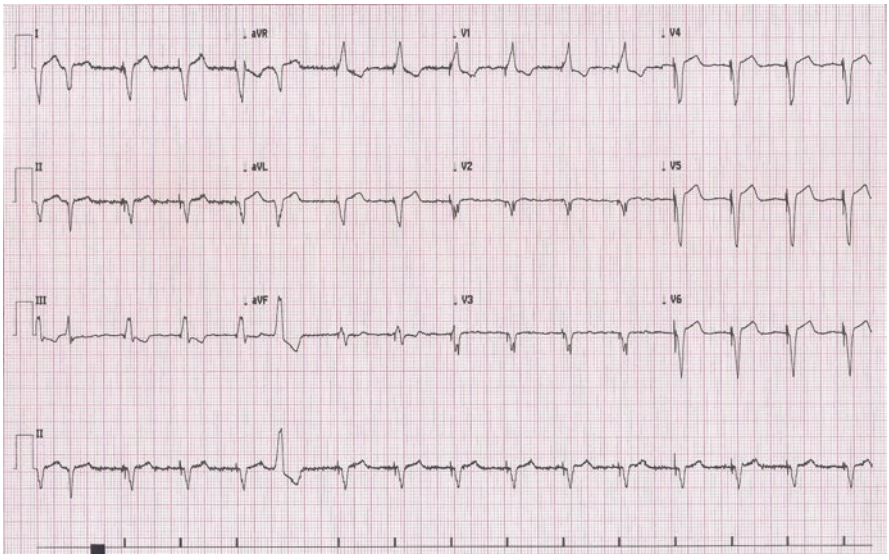

Fig. 16.7 Biventricular stimulation

the chances of finding an abnormal device are very low. Additionally, the algorithm improved the diagnostic and referral ability of non-cardiologist (including ER physicians) when dealing with patients with pacemakers. Unfortunately, atrial lead dysfunction, VOO programming, and advanced pacemaker functions are part of the limitations of this method [39].

16.12.6 *Transthoracic, Transesophageal, and 3D Echocardiography*

Echocardiography is a convenient diagnostic tool for detecting and, thus, properly treating pacemaker-related complications. Transthoracic echocardiography is useful to locate the path of pacemaker leads within the heart cavities (Figs. 16.8 and 16.9) and identify lead dislodgement, cavity perforation by lead, hemopericardium, or images suggesting a thrombus, but the diagnosis must be confirmed by other means such as transesophageal echocardiography, which is more sensible. Moreover, transesophageal echocardiography can be used to inspect for vegetations or masses with a sensibility of 92–96%, compared to a 22–30% of the transthoracic echocardiography [9]. Specifically, transesophageal echocardiography may be used when a thrombus on a pacemaker lead is suspected [40]. Real-time three-dimensional echocardiography, along with 2-dimensional echocardiography, is also helpful in the diagnosis of pacemaker complications, especially lead issues [9]. It is important to keep in mind that due to right ventricular pacing, patients may normally present paradoxical septal motion as a cause of the anticipated electrical activation of the right ventricle [9].

Transthoracic echocardiography may be limited as a result of a poor acoustic window and because of the presence of lead reverberation artifacts. Additionally,

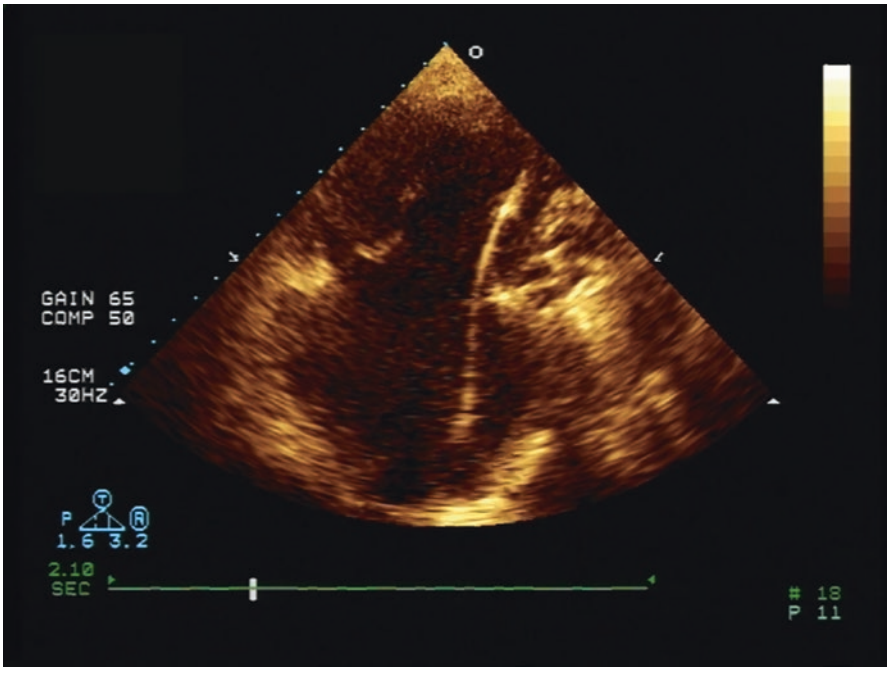

Fig. 16.8 Transthoracic echocardiography depicting a modified projection for RV which shows the complete lead path within right cavities in a patient with inactive rheumatic cardiopathy, mitral prosthetic mechanical valve, and total hip replacement

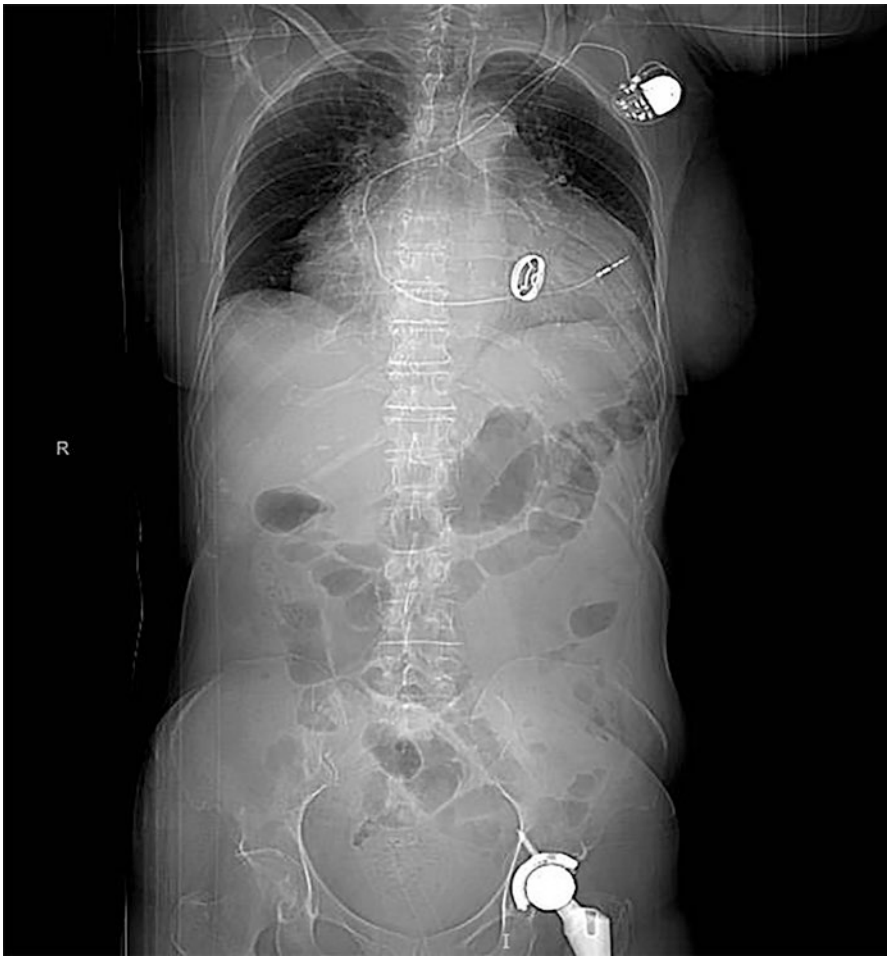

Fig. 16.9 CT scan of the patient described in Fig. 16.8 mitral prosthetic mechanical valve, total hip replacement, and a VVI pacemaker can be appreciated

sometimes it is difficult to distinguish between the lead tip, abnormal masses, or the tricuspid valve with a transthoracic echocardiogram due to poor echogenicity, limited window, or artifacts. On the contrary, transesophageal echocardiography is better to view the entire lead passage through the heart cavities. Furthermore, real-time transthoracic 3D echocardiography offers multiple views from a single acquisition and is helpful in the assessment of masses adhered to the leads [9].

Echocardiography is the preferred imaging technique to inspect masses on cardiac device leads since MRI is contraindicated in some types of pacemakers and CT is generally affected by metal artifacts. Vegetation usually looks as an oscillating intracardiac mass located on the pacemaker leads, valve leaflets, or endocardium [9]. Nevertheless, distinguishing between thrombus or vegetation as the origin of

the mass is complicated. Hence, echocardiography must always be complemented with clinical and laboratory evidence [9]. Finally, echocardiography is an operator-dependent study, and thus, having an echocardiography expert perform the studies in pacemaker patients could be an important factor to achieve a correct diagnosis.

16.12.7 Chest Cardiac Tomography (CT)

Chest CT is an important diagnostic tool for pacemaker complications. It is of special utility when lead perforation is suspected, and other diagnostic modalities were inconclusive. For instance, 15 of 100 completely asymptomatic patients with a cardiac device were incidentally diagnosed with subacute lead perforation when they underwent a CT whose primary clinical indication was other than lead perforation [26]. Leads create a star artifact when imaged with a CT, a common artifact caused by metal implants (Fig. 16.10). Commonly, the lead tip may be defined as the center of the star artifact [26].

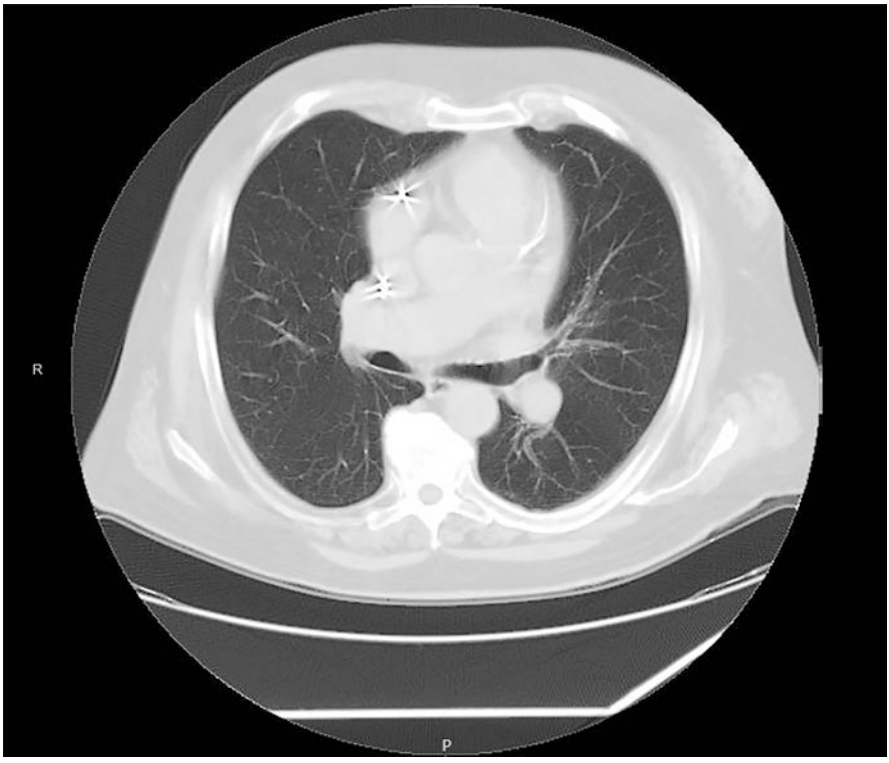

Fig. 16.10 CT scan is showing the star artifact caused by pacemaker leads

ECG synchronized chest CT can be used in the diastole phase to assess for myocardial lead perforation [29]. CT 3D reconstruction could also be performed and offers good visualization of the lead. Finally, chest CT is safe to use with cardiac device bearers with no serious or permanent complications reported [28].

16.13 Laboratory Evaluation

Laboratory test is of special utility since a failure to capture or undersensing may be due to electrolyte imbalances [30]. Moreover, blood and lead tip cultures may help to identify a pacemaker infection. Especially, *Staphylococcus aureus* bacteremia could be related to lead endocarditis or device pocket infection [9].

16.14 Multimodal Diagnosis Approach

Some pacemaker complications may be asymptomatic, but others generally present as palpitations, anxiety, lightheadedness, or as full cardiac arrest (Fig. 16.11). If a pacemaker abnormality is suspected, the patient must be connected to a cardiac monitor. Next, a 12-lead ECG (to evaluate cardiac rhythm and to look for electrical malfunctions) and a chest X-ray should be taken (to assess for mechanical problems such as a lead fracture or dislodgement). General laboratory tests are also suggested since the myocardial depolarization threshold could increase (leading to failure to capture) with electrolyte imbalances or ischemia [1].

16.15 Differential Diagnosis

Pacemaker complications are subject to be confused with a wide range of pathologies. For instance, paradoxical septal motion, which is a normal echocardiographic finding in some patients with right ventricular pacing, can also be observed in patients with RV volume/pressure overload or that have undergone cardiac surgery [9]. Additionally, observing noninfected strands adhered to the cardiac device leads is frequent. Those strands typically measure between 1 and 2 mm in width and 3 and 5 mm in length and are commonly localized in the right atrium [9]. Nevertheless, 6% of patients with an infection presented abnormal long filaments of more than 3 mm in width which were infected [9, 41]. Hence, clinical correlation is central to adequate differentiation between fibrin deposits, vegetations, or thrombi. Thus, it is vital to apply a multimodal diagnosis approach in which data from the image studies, the electrocardiogram, and the echocardiogram are fully integrated with the clinical history.

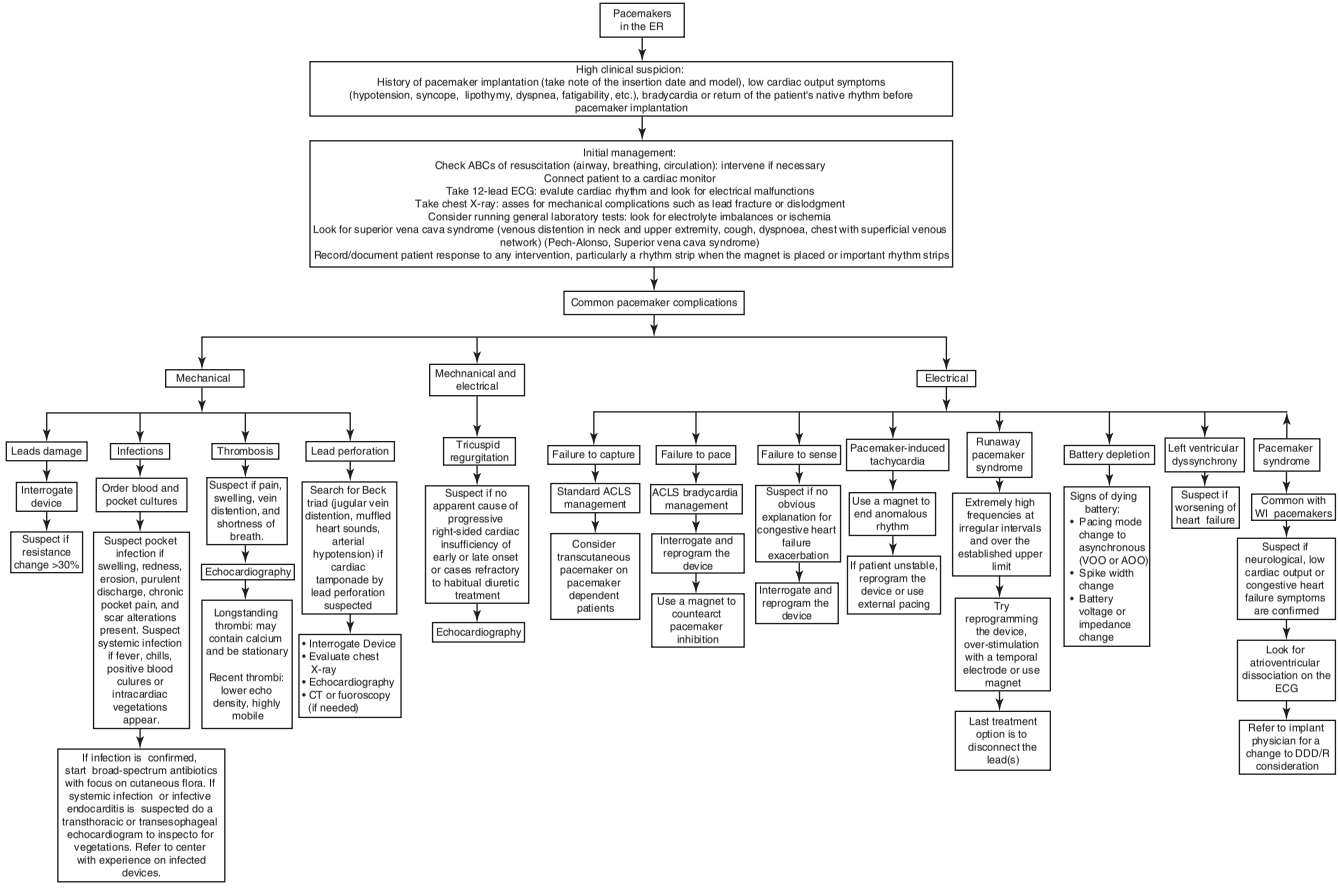

Fig. 16.11 Algorithm for pacemakers in the ER

16.16 Treatment

In case of a failure to capture, ACLS management is suggested in addition to a transcutaneous pacemaker, or a temporal venous pacemaker if available, in case of a pacemaker-dependent patient [1]. Moreover, in case of a failure to pace, ACLS bradycardia management is recommended. Then, the device must be interrogated and reprogrammed [1].

Transesophageal echocardiography is of great help when establishing treatment for device-related infections. Indeed, if the patient presents myocardial abscess or lead vegetation bigger than 5 cm, surgery may be preferred over percutaneous extraction [9]. Apart from device removal, antibiotic therapy must be started [9].

When lead perforation is confirmed, there is a vast set of possible treatments according to the characteristics of the perforation and the device. If the electrode tip is inside the mediastinum and no bleeding events are registered, then a second cable may be implanted without the retraction of the perforating lead [27]. Nevertheless, maintaining an inoperative lead must be weighed against the risk for further migration of the perforating lead. In the presence of a cardiac tamponade possibly caused by lead perforation, drainage of the pericardial effusion and conservative management are recommended [27]. Extraction must be performed in a patient with uncontrolled bleeding or evolving hematoma and lead migration outside of the pericardium with the risk of vascular, pulmonary, or adjacent structures injury [27]. When micro-perforation is suspected, indications for repositioning a lead are refractory pericarditis pain, persistent effusion, or pacemaker malfunction (pacing or sensing abnormalities) [4].

The method of choice to extract a perforating lead depends on the fixation system. If the lead has an active fixation system, transvenous extraction can be performed with a low complication risk according to some electrophysiologists [27]. The above procedure must be executed under TEE vigilance, general anesthesia, and if possible with excimer laser sheath [27]. Moreover, the procedure can be done both in the electrophysiology laboratory or in the operating room, but the cardiac surgery service must be present in case of an emergency [27]. On the other hand, if the electrode has a passive fixation system, two-stage cardiac surgery is preferred since this type of electrodes is thicker and has a higher chance of injuring tissue if retracted. Finally, the risk of bleeding or injuring nearby tissues during extraction is diminished by cutting the lead tip first [27].

16.17 Response to Magnet

The following table applies to most of the devices. For a specific list, please consult the references listed (Table 16.5).

In most of the devices, when the magnet is removed, the device will return to normal programmed function. However, reprogramming might be needed by some ICD models after being exposed to a magnet [1]. It is important to remember, that

Table 16.5 Expected CIED response to magnet application according to manufacturer [42–46]

Manufacturer	Device type	Response to magnet
Boston Scientific	Pacemaker and CRT-P	Asynchronous pacing at 100, 90, or 85 bpm (depending on the model)
		Asynchronous pacing at 85 bpm means that the device is near to the replacement date, contact the patient's device following physician
	ICD and CRT-D	Tachy therapy inhibited during magnet application
		Beeping tones produced one per second or R wave synchronous (depending on the model)
		No change to pacing therapy
	S-ICD	Tachy therapy inhibited during magnet application
		Beeping tone when the magnet is detected, then R wave synchronous beeping for 60 seconds, then beeping stops
Medtronic	IPG and CRT-P	Asynchronous pacing (DOO, VOO, or AOO) induced at 85 or 65 bpm (pacing rate may vary for some models or older devices)
		If device conditions are normal, the pacing rate will be 85 bpm If a recommended replacement time (RRT) or an electrical reset has occurred, the pacing rate will be 65 bpm
	ICD and CRT-D	Magnet application will not induce asynchronous pacing
		Magnet application can be used to check device status alerts
	ICD	If a programmed device condition (low battery voltage, lead impedance out of range, etc.) has occurred since the last time the device was interrogated, a tone will be emitted
		If the magnet is placed over the ICD for another time, the tone will be repeated
		Tachyarrhythmia detection and therapy operations are suspended while the magnet is placed
		Bradycardia pacing operations are not affected by the magnet
St. Jude Medical	Pacemaker	The device will pace asynchronously for the duration of the magnet placement (Magnet Mode parameter must be enabled)
		Devices at BOL pace at 100–98.6 bpm and at ERI at 85–86.3 (depending on the model)
		Dual-chamber mode devices (DDD, DDDR, DDI, DDIR) pace with an AV delay of 120 ms
		The device will go to a high output mode for the duration of the magnet placement if AutoCapture is enabled
		When the magnet is removed, AutoCapture will initiate a threshold search
	ICD	Tachyarrhythmia detection disabled during magnet placement
		Bradycardia pacing function is not affected

Table 16.5 (continued)

Manufacturer	Device type	Response to magnet
Biotronik	Pacemaker	Biotronik pacemakers have three different pacing modes induced by a magnet: asynchronous, synchronous, and auto (depends on manufacturer programming)
		Asynchronous mode at BOL paces at 90 bpm
		Asynchronous mode at ERI/EOL paces at 80 bpm
	ICD	Detection suspended
		No effect of a magnet on pacing
Sorin (ELA Medical)	Pacemaker	BOL asynchronous pacing at 96 bpm
		ERI asynchronous pacing at 80 bpm
	ICD	Detection and therapy suspended
		Magnet effect on pacing: pacing at 96 (BOL) or 80 (ERI) bpm

CIED cardiac implantable electronic device, *S-ICD* subcutaneous implantable cardioverter defibrillator, *ICD* implantable cardioverter defibrillator, *CRT-D* cardiac resynchronization therapy-defibrillators, *CRT-P* cardiac resynchronization therapy-pacemakers, *IPG* implantable pulse generator, *BOL* beginning of life, *ERI* elective replacement interval, *EOL* end of life

no matter the manufacturer, pacing behavior at or below EOL is unpredictable. Finally, physicians will be in warning when applying a magnet, and to ponder its usage against reprogramming the device instead, since asystole complication have been reported with it use. Consider the limited availability of technicians with the skills to reprogram the device and the time this process could take reprogramming the device (time is taken to reprogram and availability of technicians with such skills), since asystole cases have been reported [47, 48].

16.18 Electrosurgery

Electrosurgery alludes to the usage of electric scalpels during a surgical procedure. Its main risk with pacemakers is the production of electromagnetic interference potentially leading to pacing inhibition, rapid delivery of stimuli, tissue damage, or sudden change in pacing parameter (power-on reset). There are two modalities of electrosurgery monopolar and bipolar. In monopolar electrosurgery, the active electrode is included in the cautery pen, but a dispersive electrode needs to be placed on the patient. In the case of bipolar electrosurgery, both electrodes are built into the cautery pen, making the electric current to be localized. For this reason, in patients with pacemakers, bipolar electrosurgery should be used when possible. If the monopolar modality is selected, the current pathway between the active and return electrodes should avoid the generator (at least 6 inches away from the device) [49]. Additionally, cautery burst duration should be limited to 5 seconds with 5 seconds or more gap between bursts [4].

When the surgical site is below the umbilicus, and the dispersive path is placed on the lower limbs, there is no need to reprogram the device, except when several inhibition events are observed [4, 49]. In case the operation site is over the umbilicus, and

especially for pacemaker-dependent patients, the device must be interrogated before the procedure; pacing mode should be changed to asynchronous (DOO, AOO, VOO), either by reprogramming or by using a magnet; and at the end of the procedure, the device must be reprogrammed to its original parameters [4]. Finally, always have magnet ready to use during the procedure, especially if no device reprogramming is decided [49].

16.19 Magnetic Resonance Imaging (MRI): Yes or No?

MRI is a powerful diagnostic tool in clinical practice. It is estimated that half of the patients with a cardiac implantable electronic device will need an MRI scan once in their life [50]. MRI conditional systems include both a generator and leads that were specifically tested in combination. Thus, an MRI conditional generator with non-MRI conditional leads is not considered to be an MRI conditional system. Abandoned or fractured leads, epicardial leads, or components from multiple vendors make an MRI nonconditional system [50]. Especially, patients with epicardial leads should not be scanned with MRI.

The most frequent effect of MRI on pacemakers is an increase in the pacing capture threshold. Battery level could also result affected, and power-on reset events may occur [50, 51]. Apart from MRI, radiotherapy can also interfere with pacemakers, while high-dose radiation may create electrical currents in the semiconductor circuit of the device (Table 16.6) [28].

Table 16.6 Possible detrimental effects of MRI on cardiac implantable electronic devices according to HRS guidelines [50]

Effect	Comment
Force and torque induced by the magnetic field	Extremely unlikely since the generator is in a subcutaneous position and because leads contain a not significant amount of ferromagnetic material
Electrical current induced by gradient magnetic field	Might cause unintended myocardial capture or arrhythmias (atrial or ventricular)
Heating and tissue damage by radio-frequency fields	MRI nonconditional devices might heat and damage the adjunct tissue. Sensing or capture thresholds might change
Effects on reed switch activity	Reed switch activity on nonconditional devices might be affected with subsequent asynchronous pacing or inhibition of tachycardia therapies
Electrical reset	Electromagnetic interference cold cause power-on reset (backup mode) leading to inhibition of pacing, activation of tachyarrhythmia therapy, change to unipolar pacing, pacing below the threshold, battery status changes, and unreliable function
Inappropriate function and therapies	Could cause oversensing with the following consequences: asystole in pacemaker-dependent patients, inappropriate shocks in implantable cardioverter defibrillators, or programming changes

Note: Reed switch makes possible to program a device with the help of a magnet

It is important to know that MRI conditional generators have an MRI programming pathway that must be turned on before the scan and off after the scan. Scanning should be performed with the prerequisites specified for the device (**I A** HRS recommendation).

MRI conditional devices have an exempt period in which the conditionality does not apply (commonly 3 months after implantation). Despite the later, it is reasonable to perform an MRI scan during this period with a profound risk-benefit analysis (**IIa C-EO** HRS recommendation).

In the case of MRI nonconditional devices, risk-benefit must be thoroughly pondered. MRI scans are reasonable for patients with cardiac implantable electronic devices if the following criteria are meet, no fractured, epicardial, or abandoned leads, and MRI is superior to other testing modalities (**IIa B-NR** HRS recommendation). In such cases, pacemakers should be programmed to an asynchronous pacing mode, and tachyarrhythmia detection should be disabled on implantable cardioverter defibrillators (**I B-NR** HRS recommendation).

16.20 A Brief Comment on the Physical Bases of Pacemakers and MRI Compatibility

MRI has its theoretical basis on nuclear magnetic resonance (NMR) spectroscopy. This essentially consists of analyzing the radio-frequency energy absorbed and emitted by certain atomic nuclei placed in an artificial magnetic field. Hydrogen is the most commonly used atom for clinical purposes. Moreover, MRI is especially useful when imaging regions with a high quantity of water and fat since hydrogen atoms are densely present in those tissue components [50].

It is important to have in mind that MRI scan procedures require the use of the following fields: static magnetic, gradient magnetic, and radio frequency. All these fields might interfere negatively with susceptible electronic devices, including cardiac electronic implantable devices. For instance, the static magnetic field strength used by MRI scanners ranges from 0.2 to 9 Tesla, which could lead to mechanical injuries by moving objects if the appropriate security standards are not followed [50].

Apart from Tesla, gauss is an alternative unit for measuring the strength of magnetic fields [52]. To convert these units, the following formula is used:

$$1\,\text{Tesla} = 10{,}000\ \text{gauss} \tag{16.1}$$

The clinical importance of this formula resides in the fact that the "safe" magnetic field strength area is 5 gauss [50].

A final comment is to be made on the meaning of SAR, a concept commonly used when talking about the energy absorbed by a tissue due to exposure to

a radio-frequency field on MRI. Specifically, SAR is used to limit the energy delivered to a tissue to avoid thermic damage. The following formula is used to calculate SAR:

$$\mathrm{SAR} = \frac{\sigma |E|^2}{2\rho} \tag{16.2}$$

where E represents the peak electric field strength, σ the local tissue conductivity, and ρ the local tissue mass density [53]. Thus, the clinical significance of the formula is that SAR depends on both scanner parameters (electric field) and tissue factors (conductivity and mass density). As such, the effect of MRI scanning on patients with pacemakers is determined by the device, patient's tissue condition, and the pulse sequence used for the study.

16.21 Guideline Recommendations

A selection of guideline recommendations in relation to pacemaker emergencies is given in Table 16.7.

Table 16.7 Current international guideline recommendations

HRS CIED lead management and extraction [54]	COR	LOE
Drawing at least two sets of blood cultures before starting antibiotic therapy is recommended for all patients with suspected CIED infection to improve the precision and minimize the duration of antibiotic therapy	I	C-LD
Evaluation by physicians with specific expertise in CIED infection and lead extraction is recommended for patients with documented CIED infection	I	C-EO
TEE can be useful for patients with CIED pocket infection with and without positive blood cultures to evaluate the absence or size, character, and potential embolic risk of identified vegetations	IIa	B-NR
HRS MRI and radiation exposure in patients with CIEDs [50]	COR	LOE
MR conditional devices should be considered MR conditional only when the product labeling is adhered to, which includes programming the appropriate "MR mode" and scanning with the prerequisites specified for the device	I	A
It is reasonable for patients with an MR nonconditional CIED system to undergo MR imaging if there are no fractured, epicardial, or abandoned leads; the MRI is the best test for the condition, and there are an institutional protocol and a designated responsible MR physician and CIED physician	IIa	B-NR
It is recommended that for the patient with an MR nonconditional CIED who is pacing-dependent to program their device to an asynchronous pacing mode with deactivation of advanced or adaptive features during the MRI examination, and the pacing rate should be selected to avoid competitive pacing	I	B-NR

Table 16.7 (continued)

HRS CIED lead management and extraction [54]	COR	LOE
All tachyarrhythmia detections for patients with an ICD should be disabled prior to MRI	I	B-NR
For a patient with an MR nonconditional CIED who is not pacing-dependent, it is reasonable to program their device to either a nonspacing mode (OVO/ODO) or to an inhibited mode (DDI/VVI), with deactivation of advanced or adaptive features during the MRI examination	IIa	B-NR
It is reasonable to program patients with an MR nonconditional CRT device who are not pacing-dependent to an asynchronous pacing mode (VOO/DOO) with deactivation of advanced or adaptive features during the MRI examination and with a pacing rate that avoids competitive pacing	IIa	C-EO
It is recommended that patients with a CIED undergo clinical diagnostic CT without any additional device interrogation, programming, or monitoring	I	B-NR
ESC Guidelines on cardiac pacing and cardiac resynchronization therapy: magnetic resonance in patients with implanted cardiac devices [55]	COR	LOE
Conventional cardiac devices: in patients with conventional cardiac devices, MR at 1.5 T can be performed with a low risk of complications if appropriate precautions are taken	IIb	B
MR-conditional PM systems: in patients with MR-conditional PM systems, MR at 1.5 T can be done safely following manufacturer instructions	IIa	B
BSAC implantable cardiac electronic device infection [20]	COR	LOE
A chest X-ray should be carried out in all patients with suspected ICED infection	–	C
CT scanning or CT pulmonary angiography should be considered when ICED infection is suspected, and echocardiography is non-diagnostic	–	C
Echocardiography should be carried out as soon as possible (within 24 h) after a diagnosis of ICED infection is considered	–	C
Blood cultures should be taken prior to starting antimicrobial therapy	–	B
Apply meticulous aseptic technique when taking blood cultures to reduce the risk of contamination with skin commensals	–	B
Antimicrobial treatment strategies should be discussed by the multidisciplinary team and should be determined by plans to remove or attempt to salvage an infected ICED, the presence of ICED-IE, and any extracardiac foci of infection	–	C
When there is clinical evidence of generator pocket infection, empirical antimicrobial therapy should be commenced	–	C
Local antimicrobial instillation into an infected generator pocket is not recommended	–	C
The need for empirical antimicrobial treatment for ICED-LI or ICED-IE (prior to the availability of microbiological data) is a clinical decision based on the severity of the infection	–	C

COR class of recommendation, *LOE* level of evidence, *HRS* Heart Rhythm Society, *CIED* cardiac implantable electronic device, *TEE* transesophageal echocardiography, *MRI* magnetic resonance imaging, *MR* magnetic resonance, *ICD* implantable cardioverter defibrillator, *CRT* cardiac resynchronization therapy, *CT* computed tomography, *ESC* European Society of Cardiology, *T* Tesla, *PM* pacemaker, *BSAC* British Society for Antimicrobial Chemotherapy, *ICED* implantable cardiac electronic device, *ICED-IE* ICED lead-associated infective endocarditis, *ICED-LI* ICED lead infection

16.22 Additional Clinical Practice Takeaways

- It is important to remember that pacemakers are essentially antibradycardia devices. Hence, patients with a malfunctioning pacemaker may present to the ER with bradycardia or low cardiac output symptoms.
- Not all pacemaker complications imply an abnormally functioning device. For instance, pacemaker syndrome is caused by the adverse hemodynamics created by atrioventricular dissociation.
- The decision to remove or to implant a new lead without removing the previous one must be accompanied by the clinical data, a multimodality image approach (chest X-ray, echocardiography, fluoroscopy, and tomography), and device interrogation.
- If the decision has been taken to extract an electrode in the case of a subacute (late) lead perforation, the cardiac surgery service must be called even if the lead is going to be transvenous extracted or repositioned.
- In case electrosurgery is needed, try to direct the electrical current pathway at least 6 inches away from the device, and always have a pacemaker magnet ready to use during the procedure.

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Chapter 17
Cardiology Bedside Interventions in the ER

Carlos Jerjes-Sánchez and Raul del Toro-Mijares

17.1 The Scope of the Problem

Emergency rooms (ER) across the world see patients with cardiac conditions that carry high mortality if not acted upon quickly and appropriately: cardiac tamponade, acute pump failure, atrial fibrillation (AF), ventricular tachycardia (VT), and other severe forms of rhythm disorders such as complete atrioventricular (AV) block. Unfortunately, besides conventional resuscitation measures, many ER are not equipped and/or qualified to perform emergency bedside interventions that have the potential to save lives and/or create a bridge for salvage surgery. The clinical presentation and physical findings of cardiac emergencies are highly variable. Patients may be already known for their history of ischemic heart disease or rhythm disorders, or they may have participated in a recent car crash or a street fight, suffering thoracic trauma. Electrocardiogram (ECG) and imaging studies are crucial and aid in establishing the diagnosis, and some are implemented to perform the procedure (echocardiogram-guided pericardiocentesis). Additionally, in-house patients are also at risk of presenting one of the cardiac emergencies. For example, patients in the immediate postoperatory period after open-heart surgery or percutaneous coronary intervention (PCI) are at risk for severe arrhythmias and hemodynamic collapse, and it is recommended that hospital staff must also be trained and prepared to perform these lifesaving procedures. This chapter explains the indications, contraindications, complications, and technical and hemodynamic aspects of several bedside interventions in an ER setting. Some of them are performed in the ER, while others may also be needed on the floor or in the operating room. This chapter does not delve into procedures done in a nonurgent manner or in a non-ER setting, such as the implantation of a permanent pacemaker or a scheduled pericardial drainage. The following procedures will be covered in this chapter are intra-aortic balloon pump (IABP), emergency pericardiocentesis, temporary pacemaker, and electric cardioversion.

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17.2 Intra-aortic Balloon Pump

The IABP counterpulsation device is the most commonly used circulatory assist device in patients with a failing heart [1]. It consists of a catheter-inserted balloon in the proximal descending aorta that inflates in diastole and deflates just before systole starts. This precise mechanism of inflation-deflation produces direct hemodynamic benefits to the heart: it significantly improves coronary artery blood flow during diastole, and it reduces left ventricle preload and afterload during systole. Thus, myocardial work and oxygen consumption are reduced. This contributes to an improvement of 0.5–1 L/minute of cardiac output [1]. However, IABPs are not permanent devices. They serve as a temporary relief until the underlying mechanic or obstructive/ischemic problem is solved.

17.2.1 Indications and Contraindications

Indications for IABP have evolved through the years. In the past, IABP was used in patients with myocardial infarction complicated with or without cardiogenic shock and in patients undergoing high-risk percutaneous coronary intervention [2]. However, randomized studies analyzing the use of IABP in these specific situations were lacking. Hence, three important clinical trials were put underway:

- *CRISP AMI:* compared PCI with IABP vs. PCI alone in patients with ST-elevation myocardial infarction (STEMI) (the main endpoint was infarct size measured with MRI 3–5 days post-PCI) [3]
- *IABP-SHOCK II:* compared PCI/coronary artery bypass graft (CABG) with IABP vs. PCI/CABG only in patients with STEMI (the main endpoint was all-cause 30-day mortality) [4]
- *TACTICS:* compared fibrinolysis with IABP vs. fibrinolysis alone in patients with acute myocardial infarction complicated by hypotension, cardiogenic shock, or heart failure (the main endpoint was all-cause 6-month mortality) [5]

Surprisingly, these trials failed to demonstrate benefits in the main endpoints. Although the results of these trials discourage its routine use, the hemodynamic benefits of using IABP have already been described, and patients who are placed on IABP have the potential to improve clinically. Since the publication of the clinical trials mentioned above, the American Heart Associates/American College of Cardiologists (AHA/ACC) and the European Society of Cardiology (ESC) guidelines for the management of STEMI have been modified. The most current versions state the following:

- *2013 ACCF/AHA:* the use of IABP counterpulsation can be useful for patients with cardiogenic shock after STEMI who do not quickly stabilize with pharmacological therapy (Class IIa recommendation, level of evidence B) [6]

2017 ESC: the use of IABP should be considered for hemodynamic support in patients with STEMI and cardiogenic shock due to mechanical complications such as the acute rupture of papillary muscle or interventricular septum (Class IIa recommendation, level of evidence C) [7]

17.2.2 Technical Aspects of the Procedure and Device

IABPs are composed of two main parts: an 8.0–9.5 double-lumen French catheter with a polyethylene 25–50 cc balloon attached to its distal end and a console with a pump to drive the balloon [8]. When inflated, the balloon shouldn't cover more than 80–90% of the patient's descending aorta. Balloon size is selected based on patient height (Table 17.1) [8].
IABP is a catheter-inserted device. Vascular access is usually obtained through the femoral artery using the standard percutaneous Seldinger technique with a 0.030-inch guidewire. Once vascular access is obtained, the catheter is advanced and placed 1–2 cm distal to the origin of the left subclavian artery [9]. The procedure is usually guided with fluoroscopy [8]. Helium is the gas employed to inflate and deflate because its low density allows for rapid transfer from the console to the balloon [8]. A sheathless approach is considered in patients with peripheral vascular disease because this technique is associated with decreased lower limb ischemia when compared with the sheathed approach. Access via the subclavian artery, the brachial artery, and even through open-heart surgery has also been described but is not practiced routinely [9].

17.2.3 Complications

The only true contraindications of IABP are severe aortic insufficiency because it worsens regurgitation and acute aortic dissection because the catheter may inadvertently be introduced in the false lumen and extend the dissection or rupture the aorta. Aortic aneurysm, iliofemoral vascular disease, and aortic surgery are all relative contraindications [9]. The prevalence of complications can be as high as 2.7%. The most common complications are accessed zone severe bleeding, vascular injury, and limb injury [9].

Table 17.1 Intra-aortic ballon pump, balloon size based on patient height [8]

Patient height (cm)	Balloon volume size (cc)
< 152	25
152–163	34
164–183	40
>183	50

17.3 Pericardiocentesis

17.3.1 Physiology and Pathophysiology

Adequate ventricular filling is what drives adequate systolic volume. If the heart doesn't fill with enough blood, the systolic volume will be reduced, even if the heart can contract properly. The true filling pressure is cardiac transmural pressure (intracardiac pressure – intrapericardial pressure) [10]. Cardiac tamponade increases intrapericardial pressure, offsetting cardiac transmural pressure and thus compromising systolic stroke volume and cardiac output. When this happens to a certain degree, hypotension ensues.

17.3.2 Indications and Contraindications

Cardiac tamponade is a serious, life-threatening condition. It is defined as the accumulation of fluid, pus, blood, or air in the pericardial sac, such that intrapericardial pressure increases and cardiac output and cardiac filling decrease [10]. It is characterized by systolic hypotension and/or signs and symptoms of low cardiac output, jugular vein distention, and distant/muffled heart sounds (the fluid or material in the pericardial space acts as a barrier for sound transmission), called Beck's triad. Although many conditions and diseases can cause pericardial effusion, cardiac tamponade is essentially the only indication for an emergency pericardiocentesis. All other effusions can be readily scheduled for a draining procedure. Ideally, echocardiography should confirm the effusion and guide the procedure; however, under certain circumstances, an ECG-guided or even a "blind" pericardiocentesis can be done [11]. Another alternative is fluoroscopy-guided pericardiocentesis, but this is rarely used in the emergency setting. Echocardiography is preferred because it can easily be done at the bedside.

In the event of a true emergency, there are no absolute contraindications for pericardiocentesis. Albeit, tamponade due to aortic dissection, myocardial free wall rupture, or trauma are relative contraindications because these conditions will immediately need to be surgically corrected [9]. Pericardiocentesis can serve as a bridge in patients with hypotensive cardiogenic shock in these situations, but it will not solve the underlying problem, and the surgical team should be immediately called. Bleeding disorders or intake of anticoagulants or blood thinners are relative contraindications and should not stand in the way of performing an emergency pericardiocentesis [9]. Finally, as discussed above, not all pericardial effusions are an indication for emergency pericardiocentesis. However, physicians in charge should consider early pericardiocentesis in those cases with pericardial effusion, clinical stability, and atrial or ventricular diastolic collapse. These echocardiographic findings establish cardiac tamponade. Follow the diagram in Fig. 17.1 to discard pericardial effusions that do not necessarily need a pericardiocentesis.

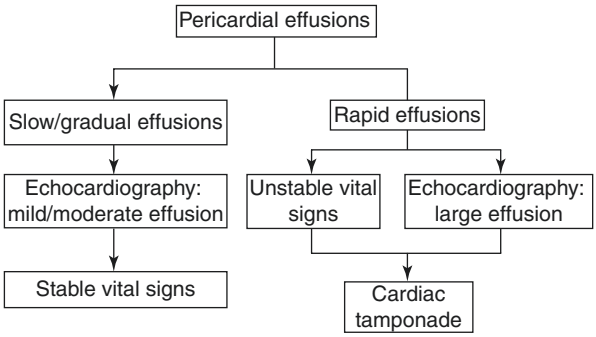

Fig. 17.1 Only pericardial effusions that cause cardiac tamponade are an indication for emergency pericardiocentesis

17.3.3 Technical Aspects of the Procedure

Kits for pericardiocentesis should be readily available in ER and intensive care units (ICU), but they can also be assembled individually. The following materials should be collected to perform a pericardiocentesis:

- 16–18G spinal needle 8–12 cm long
- Scalpel
- Sponges and antiseptic solution
- Syringe
- Three-way stopcock
- Tubing
- Echocardiogram

There are three ways of accessing the pericardial space. The traditional way is via the xiphoid process. However, in this book, we will review the transthoracic approach because it is associated with fewer complications [11].

1. Clean the precordium with antiseptic solution and drape the patient; wash hands, and use cap, mask, and surgical gown and gloves if available and timely feasible.
2. Confirm the puncture site with echocardiography: locate the area with the biggest effusion.
   (a) Usually in the 4th–6th intercostal spaces, 1/3 to 2/3 of the distance between the sternal line and the anterior axillary line
3. Puncture on the *superior costal margin* to avoid injuring the neurovascular sheath [9].
4. Continue using ultrasound if readily available to adjust needle as necessary and enter the pericardial space.
5. Locate the biggest effusion and aspirate with the syringe.
6. Continue aspirating until vital signs stabilize.
7. Remove the needle and place a bandage on the puncture site.

A xiphoid approach will be preferred if cardiopulmonary resuscitation is necessary throughout the procedure.

17.3.4 Complications

When done properly, pericardiocentesis is a simple and safe procedure. However, like any invasive procedure, it is not exempt from potential complications. Cardiac chamber puncture requiring surgery is the most common – and the most feared – major complication, occurring in 0.44% of cases [9]. The right ventricle is the most common site of puncture, although left ventricle punctures tend to be more serious because of a higher risk of bleeding. Other complications include coronary vessel laceration, hemothorax, pneumothorax, pneumopericardium, and pericardial infection. The most serious complications are related to technique and maintaining the surgical area as aseptic as possible. Careful attention must be placed to avoid injuring the internal mammary arteries, which course 3–5 cm from the parasternal border [12].

17.4 Temporary Pacemaker

17.4.1 Indications and Contraindications

Temporary pacemakers are potentially lifesaving in the setting of a severe bradyarrhythmia or tachyarrhythmia. The indications for the placement of a temporary pacemaker are essentially the same ones for the placement of a permanent pacemaker but when the latter is not available, not feasible, or when the benefits of placing a permanent pacemaker do not outweigh the risks. Like the indications for electric cardioversion, the decision to place a temporary pacemaker on a patient with AV block should be based on signs and symptoms of hypoperfusion and/or hypotension and failure to correct the arrhythmia with a pharmacological approach.

Probably the most important indication for a temporary pacemaker is bradyarrhythmia secondary to AV block. First-degree block, however, is an exception. Only second- and third-degree block is an indication for temporary pacemaker if they are symptomatic and unresponsive to initial pharmacological therapy [9]. Patients with myocardial infarction and those undergoing PCI are a subpopulation of patients particularly susceptible to these conditions.

Sinus bradycardia and sinoatrial block are indications for temporary pacemaker if two conditions are met: the patient is symptomatic and pharmacological therapies have been tried and failed (atropine and other adrenergic drugs) [9].

Reversible conditions that cause rhythm problems, such as drug toxicity, are another indication for temporary implantation of a temporary pacemaker [9]. When the reversible condition is fixed, the pacemaker is removed. A temporary pacemaker is also indicated during revisions of permanent pacemakers for infection and/or malfunction [13].

Contraindications are not absolute but proceed with caution if the patient is heavily anticoagulated or on antiplatelet medications, if the patient has a prosthetic tricuspid valve, or if the bradycardia is well tolerated.

17.4.2 Technical Aspects of the Procedure

There are four ways of temporally pacemaking the heart (we will only review the transvenous method in this chapter):

- Transvenous (most common and most comfortable for the patient)
- Transcutaneous
- Epicardial (usually after cardiac surgery)
- Transesophageal

Temporal pacemakers have two parts: a catheter with an electrode attached to its distal end and an external generator. The number of catheters connected to the external generator – and therefore to the heart – depending if single-chamber or dual-chamber pacing is required. Single-chamber pacers are usually ventricle pacers, and they are preferred because they are associated with fewer complications and only need one venous access. Single-chamber atrial pacemakers are used in the case of sinus node dysfunction and intact AV node function. Dual-chamber pacemakers require two venous accesses. One electrode is placed in the atrium, and the second electrode is placed in the ventricle. Dual-chamber pacemakers are used in myocardial infarction, especially in the setting of hemodynamic instability [9].

Transvenous pacemakers are catheter-inserted. Venous access is obtained through the left subclavian vein or the right internal jugular vein. If the need for a permanent pacemaker is anticipated, preserve the subclavian vein, and use another access point. The procedure can be done bedside or in the catheterization lab. Sterile technique should be implemented as with any other invasive procedure. If using a non-floating catheter, use fluoroscopy as a guide because these catheters are rigid and therefore carry a higher risk for perforation. Typically, in the emergency setting, a semi-floating catheter is used [9].

17.4.3 Complications

Complications from temporal pacemakers are common, occurring in over 20% of the patients [9]. They are related to either the venous access, the electrode catheters, or the electrical performance of the pacemaker (Table 17.2). Patients with temporal pacemakers are often bedridden or have limited mobility. Thus, prolonged use of temporal pacemakers is discouraged because it is associated with infection and thromboembolic events.

17.5 Electric Cardioversion

Cardioversion is a synchronized direct current discharge delivered to the heart with the objective of reverting it back to sinus rhythm during dysrhythmia. It

Table 17.2 Complications of intravenous temporary pacemakers [9]

Venous access	Pneumothorax Hemothorax Air embolism
Electrode catheters	Perforation Dislodgement Diaphragmatic stimulation Malposition Catheter-induced arrhythmias
Electrical performance	Loss of capture Oversensing Undersensing

must be differentiated from defibrillation, the unsynchronized electrical shock of the heart delivered at a random point during the cardiac cycle [14]. There are two types of cardioversion: pharmacological and electrical. While defibrillation is also an interesting topic, it is not the matter at hand and is discussed elsewhere in this book. In this subsection, we will review emergency electrical cardioversion.

17.5.1 Indications and Contraindications

Heart rhythm problems are a worldwide epidemic and an important cause of cardiac mortality. Moreover, they have highly variable presentations. AF, for example, may be completely asymptomatic, or it may present in the emergency room with hemodynamic collapse due to inappropriate ventricular diastolic filling. Thus, electrical cardioversion is potentially lifesaving in the appropriate emergency setting. There are three main indications for this procedure:

- AF (probably the most common indication) and atrial flutter
- Supraventricular tachycardia (SVT) with nonsuccess adenosine use
- Ventricular tachycardia

However, these arrhythmias are not always an indication for cardioversion. Only when they are clinically compromising the hemodynamic status of the patient or when pharmacology therapy has either failed to revert to sinus rhythm or is contraindicated will they benefit from electrical cardioversion [15–19]. For example, to make the last point clear, there are patients with AF that never undergo electrical cardioversion and are only managed with rhythm control and anticoagulation. Atrial or ventricular arrhythmias associated with pregnancy, ejection fraction <40%, critical coronary disease, mechanical cardiac prosthesis, and clinical stability should be considered for electrical cardioversion. Ventricular fibrillation is an indication for defibrillation.

17.5.2 Technical Aspects of the Procedure

Performing electrical cardioversion is technically speaking a simple procedure. However, there are various factors to consider: electrode location, energy to be discharged, waveform, pad size, handheld vs. patch, and thoracic impedance. Most importantly, the type and duration of arrhythmia in each individual patient must be reviewed and analyzed. For this reason, we will review each arrhythmia separately.

Cardioversion is indicated in AF if hemodynamic instability is present or if pharmacological cardioversion is attempted and fails. A biphasic, R wave synchronized shock of at least 150–200 joules with anteroposterior electrodeposition is recommended in these patients [9]. The use of biphasic waveform in patients with AF and flutter is further supported by other clinical trials [20, 21]. This is because of higher efficacy, lower energy requirements, and less number of shocks required. Figure 17.2 shows an algorithm for cardioverting patients in AF and hemodynamic instability.

Once again, hemodynamic status and the response to adenosine and vagal maneuvers preclude the necessity for electrical cardioversion in patients with SVT. The AHA/ACC guidelines for the management of patients with SVT describe two settings where cardioversion is indicated: SVT with hemodynamic instability not responsive to adenosine and/or vagal maneuvers and SVT without hemodynamic instability resistant to pharmacological strategies (verapamil, diltiazem, adenosine)

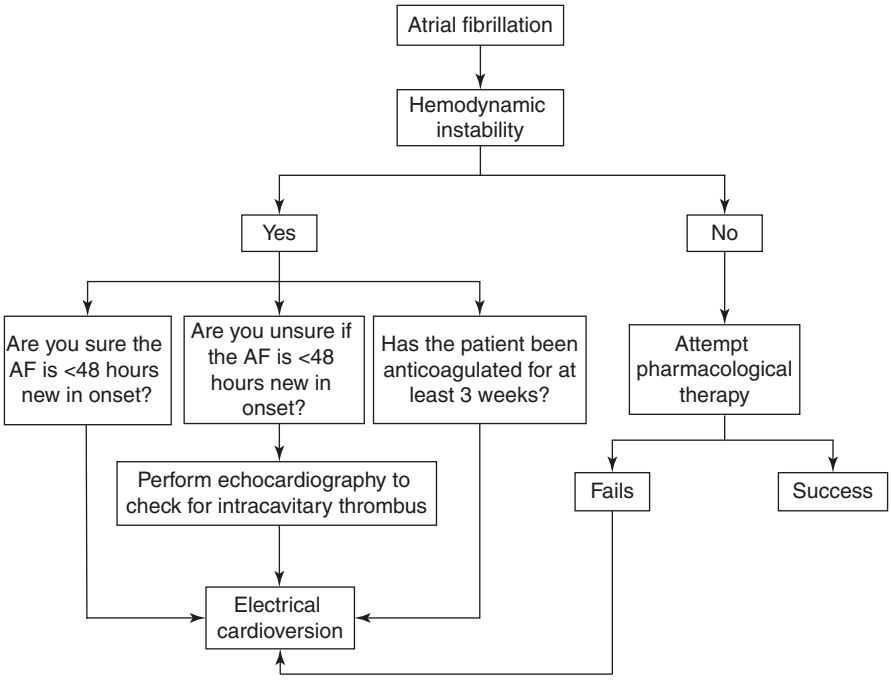

Fig. 17.2 Follow this flow diagram to establish whether a patient with atrial fibrillation is an ideal candidate for electrical cardioversion

[18]. The 2010 advanced cardiac life support adult guidelines places cardioversion as the first option in patients with SVT and hemodynamic instability but suggests the primary use of adenosine if the tachycardia is regular and has a narrow QRS complex [22]. Figure 17.3 shows an algorithm on how to approach a patient with SVT.

Prior to attempting to cardiovert a patient who is in VT, it is important to analyze the characteristics of the ECG. Before deciding to cardiovert these patients, make sure you can easily distinguish each QRS complex from each other because not all patients with VT are ideal candidates for cardioversion. Patients with undistinguishable QRS complexes are at risk of developing VF if given a shock during the T wave. Therefore, only monophasic VT with distinguishable QRS complexes is an indication for electrical cardioversion when the patient is symptomatic (hypotension, loss of consciousness, heart failure). Synchronized cardioversion of 100 joules or more should be performed in these patients immediately [9]. Polymorphic VT is not an indication for electrical cardioversion because of difficulty synchronizing the shock with the QRS complex and the risk of triggering a VF if you discharge on the T wave, as explained above. Instead, it is managed as VF [9]. Figure 17.4 shows which patients should receive electric cardioversion. Of note, cardioversion is safe for VT in pregnant patients [16].

Fig. 17.3 Patients with supraventricular tachycardias are only managed with electrical cardioversion when all other therapies have failed

Fig. 17.4 Only patients with monomorphic ventricular tachycardia should receive direct current electrical cardioversion

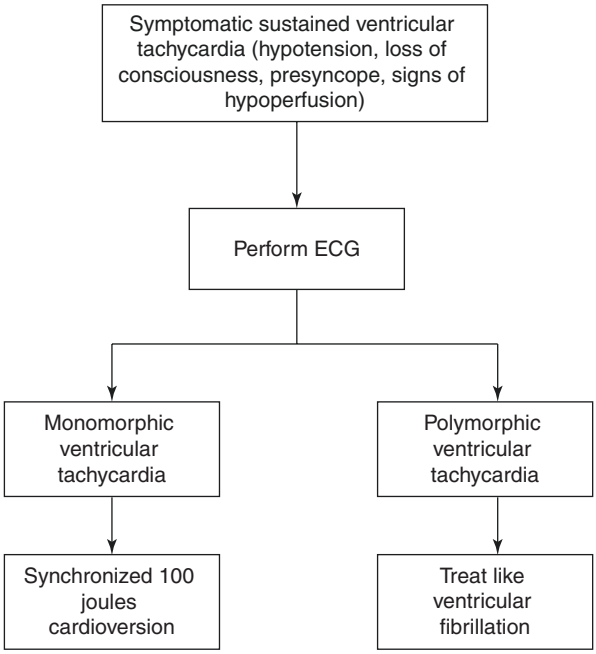

Table 17.3 Summary of main international guidelines

Intra-aortic balloon pump	
ESC	Should be considered for hemodynamic support in patients with STEMI and cardiogenic shock due to mechanical complications such as the acute rupture of papillary muscle or interventricular septum COR IIa LOE C
AHA/ACC	Can be useful for patients with cardiogenic shock after STEMI who do not quickly stabilize with pharmacological therapy COR IIa LOE B
Emergency pericardiocentesis	
ESC	Pericardiocentesis or cardiac surgery is indicated for cardiac tamponade or for symptomatic moderate to large pericardial effusions not responsive to medical therapy and for suspicion of unknown bacterial or neoplastic etiology COR I LOE C
AHA/ACC	Echocardiographic-guided pericardiocentesis has been demonstrated to be a safe and effective procedure that can be performed at the bedside[a]
Temporary pacemaker	
ESC	In the scenario of a patient with STEMI complicated by sinus bradycardia with hemodynamic intolerance or high-degree AV block without stable escape rhythm, temporary pacing is indicated in cases of failure to respond to positive chronotropic medication (epinephrine, vasopressin, and/or atropine) COR I LOE C
AHA/ACC	In patients with STEMI, temporary pacing is indicated for symptomatic bradyarrhythmias unresponsive to medical treatment COR I LOE C
Electrical cardioversion	
ESC	VT: direct current cardioversion is recommended for patients presenting with sustained VT and hemodynamic instability COR I LOE C AF: electrical cardioversion of is recommended in patients with acute hemodynamic instability to restore cardiac output
AHA/ACC	VT: patients presenting with ventricular arrhythmia with hemodynamic instability should undergo direct current cardioversion COR I LOE A AF: in hemodynamically unstable patients, electrical cardioversion is indicated COR I LOE B

ESC European Society of Cardiology, *AHA/ACC* American Heart Association/American College of Cardiology, *STEMI* ST elevation myocardial infarction, *COR* class of recommendation, *LOE* level of evidence, *VT* ventricular tachycardia, *AF* atrial fibrillation

[a]The AHA/ACC has not published guidelines on pericardial diseases but published a review on the literature

17.6 Additional Clinical Practice Takeaways

- IABP is a catheter-inserted device useful in patients with STEMI and mechanical complications (papillary muscle or ventricular septum rupture).
- Cardiac tamponade is the only true indication for emergency pericardiocentesis; it should be guided by echocardiography when possible.
- Consider early pericardiocentesis in those cases with pericardial effusion, clinical stability, and atrial or ventricular diastolic collapse by echocardiography.
- Temporary pacemakers are indicated for bradyarrhythmias with hemodynamic instability.
- Electrical cardioversion is indicated in patients with monomorphic VT and AF that is hemodynamic unstable.

- Consider electrical cardioversion in patients with atrial or ventricular arrhythmias and clinical stability associated with pregnancy, ejection fraction <40%, critical coronary disease, mechanical cardiac prosthesis.
- Table 17.3 summarizes the most relevant recommendations from the ESC and AHA/ACC guidelines for each of the procedures covered in this chapter

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