Review Article

Clinical Assessment in Acute Heart Failure

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Heart failure (HF) is defined as "a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with, or eject blood." HF has an estimated overall prevalence of 2.6%. It is becoming more common in adults older than 65 years, because of increased survival after acute myocardial infarction (AMI) and improved treatment of coronary artery disease (CAD), valvular heart disease and hypertension.[1]

Acute HF (AHF) is an increasingly common cause of hospitalizations and mortality worldwide. In the majority of patients, AHF can be attributed to worsening chronic HF, and approximately 40-50% of this group have a preserved ejection fraction. The remaining cases present with *de novo* AHF, often secondary to acute coronary syndromes.[2]

Symptoms are predominantly the result of systemic and pulmonary congestion due to elevated left ventricular (LV) filling pressures. Signs and symptoms usually improve markedly during hospitalization; however, mortality during that period remains high, ranging from 5-15%. Of those patients who survive to discharge, a further 10-15% will die within 3 months. Most patients have one or more serious comorbid conditions that contribute to a poor outcome.[3]

Initial assessment and phenotype classification

In patients with AHF, there is often a clear precipitant or trigger. It is very important to establish the precipitating causes, which may have therapeutic and prognostic implications. Approximately 60% of patients with AHF have documented CAD. Myocardial ischemia in the setting of acute coronary syndromes is a precipitant or cause, particularly in patients presenting with *de novo* AHF.[4] AHF is also often precipitated by medication and dietary non-compliance, as well as by many other conditions, which are summarized in Table 1. Once the diagnosis of AHF is confirmed, initial therapy includes removal of precipitants; if this can be carried out successfully, the patient's subsequent course may be stable.

Approximately 80% of AHF admissions initially present to the emergency department. Patients usually arrive with the classic symptoms (e.g. dyspnea, fatigue) or signs (e.g. peripheral edema) of HF. It is critical to establish the diagnosis of AHF early, as delays in diagnosis and treatment may lead to worse outcomes.[5]

The immediate assessment of patients presenting with AHF should include a thorough history and physical examination that should be complemented by ECG, chest X-ray and the necessary initial laboratory investigations (Table 2). Echocardiography is most useful in patients with suspected HF, when it is available.[6] Establishing the HF diagnosis, according to ESC guidelines, requires the conditions shown in Table 3.[2]

Table 1. Common precipitants of hospitalization for acute heart failure.

Acute coronary syndrome	Cardiac tamponade
Uncontrolled hypertension	Acute pulmonary embolism
Tachyarrhythmia / bradyarrhythmia	Aortic dissection
Concurrent infections	Anemia
Exacerbation of COPD or asthma	Alcohol abuse
Renal dysfunction	Peripartum
Thyroid dysfunction	Perioperative problems
Dietary and medication non-compliance	Drugs (NSAID, corticosteroid, negative inotropic agents, illicit drugs)

COPD – chronic obstructive pulmonary disease; NSAID – nonsteroidal anti-inflammatory drugs.

Table 2. Immediate Emergency Department assessment of heart failure.

History
Clinical examination
ECG
Chest X-ray
Initial laboratory studies:
Blood biochemistry
Cardiac biomarkers
Natriuretic peptides
Markers of renal impairment
Oxygen saturation
Echocardiogram (portable echo)

Table 3. Diagnostic requisites for heart failure (ESC HF Guidelines 2012).

HF with reduced EF	Symptoms typical of HF
	Signs typical of HF
	Reduced EF
HF with preserved EF	Symptoms typical of HF
	Signs typical of HF
	Normal or only mildly reduced LVEF and LV not dilated
	Relevant structural heart disease (LV hypertrophy, LA enlargement) and/or diastolic dysfunction

EF – ejection fraction; HF – heart failure; LA – left atrium; LV – left ventricle.

Once the diagnosis of AHF has been made, patients may be broadly categorized into phenotypes of hypertensive AHF, acute coronary syndrome (ACS), right HF, high-output HF, pulmonary edema, and cardiogenic shock (Figure 1).[7] The Killip classification is valid in acute *de novo* HF after AMI, and is used in coronary care and intensive care units. It is designed to provide a clinical estimate of the severity of myocardial derangement in the treatment of AMI (Table 4).[8]

Clinical evaluation of severity and congestion

HF is characterized by dyspnea, fatigue and signs of volume overload, which may include peripheral edema and pulmonary rales. These symptoms and signs are predominantly the result of systemic and pulmonary congestion due to elevated LV filling pressures. Patients with AHF may present insidiously or acutely, with a spectrum of clinical severity ranging from increasing dyspnea to acute pulmonary edema or cardiogenic shock.[2] Severity at presentation does not always correlate well with long-term prognosis. Patients presenting with pulmonary edema due to severe hypertension and normal LV systolic function may have an excellent prognosis. In contrast, patients presenting with only moderate dyspnea and severe LV dysfunction, may have high mortality. Overall, however, patients demonstrating clinical or hemodynamic congestion have been shown to have significantly worse rates of mortality and HF rehospitalization.[9] Clinical congestion in HF is defined as a high left ventricular

Table 4. Killip classification.

Stage I	No heart failure. No clinical signs of cardiac decompensation
Stage II	Heart failure. Diagnostic criteria include rales, S3 gallop and pulmonary venous hypertension. Pulmonary congestion with wet rales in the lower half of the lung fields
Stage III	Severe heart failure. Frank pulmonary edema with rales throughout the lung fields.
Stage IV	Cardiogenic shock. Signs include hypotension (systolic blood pressure ≤90 mmHg) and evidence of peripheral vasoconstriction, such as oliguria, cyanosis and diaphoresis.

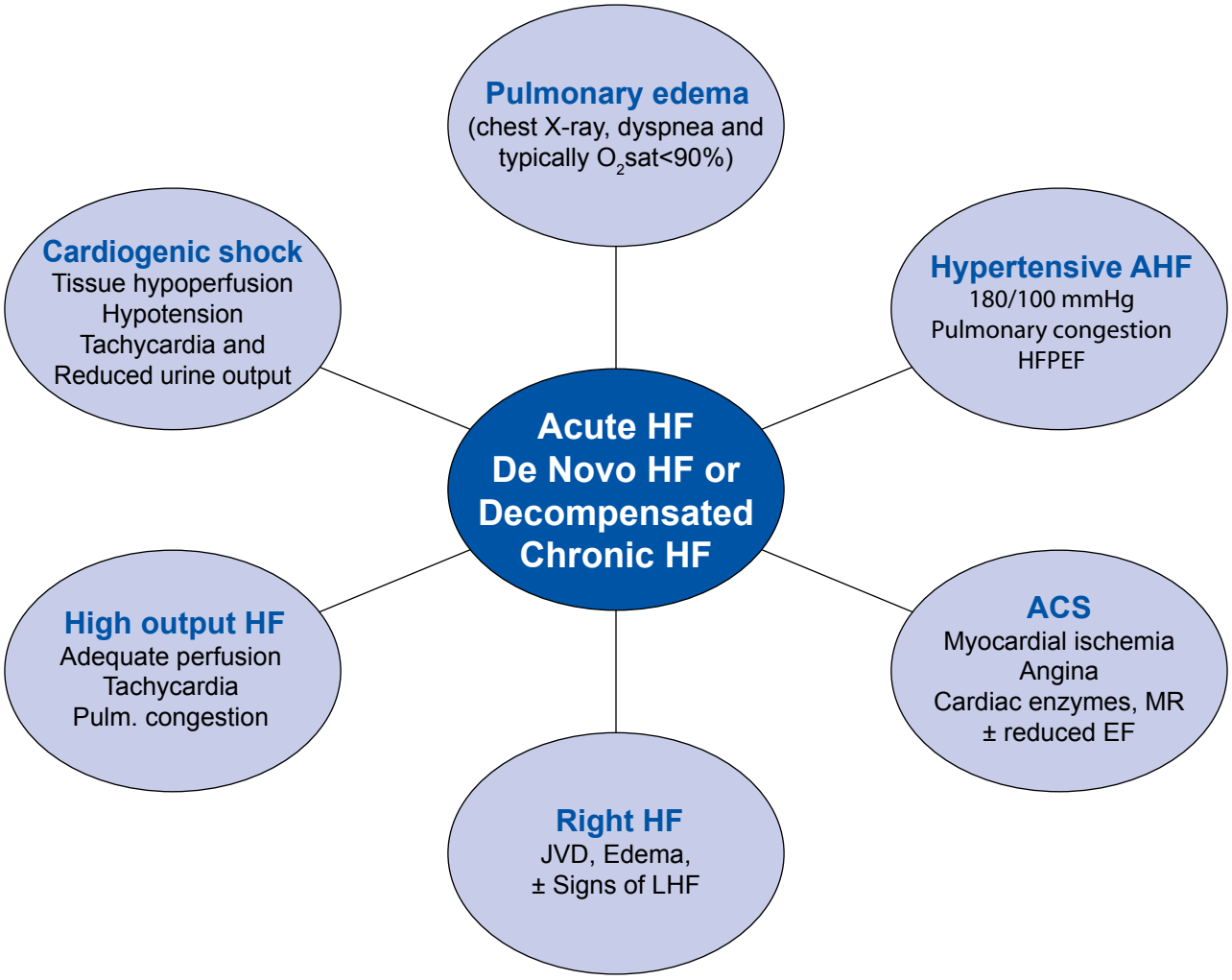

Figure 1. Clinical phenotypes at presentation of acute heart failure (AHF). JVD – jugular vein distension; MR – mitral regurgitation; LHF – left heart failure.

diastolic pressure (LVDP) associated with signs and symptoms of HF, such as rales, dyspnea, orthopnea, paroxysmal nocturnal dyspnea and edema. Elevation of LVDP in HF patients, without overt clinical congestion, has been termed "hemodynamic congestion". Often, hemodynamic congestion precedes clinical congestion by days or even weeks. In chronic HF, even severe hemodynamic congestion rarely causes rales and/or radiographic pulmonary edema.[10] This may be related to several adaptive pathophysiological changes, such as an increase in alveolar capillary membrane thickness, increased lymphatic drainage, and/or pulmonary hypertension.

The gold standard for evaluating hemodynamic congestion in HF patients is cardiac catheterization; however, its invasive nature limits its routine use in clinical practice. Numerous tools are available for the assessment of congestion, including physical examination, body weight, serum sodium, natriuretic peptides, chest X-ray and others.

Relying on a limited set of physical examination findings alone is associated with low sensitivity and poor predictive value in identifying hemodynamic congestion. In a study of patients with chronic HF, physical signs of congestion (rales, edema, and jugular venous distension [JVD]), were absent in 42% of patients with a measured pulmonary capillary wedge pressure (PCWP) ≥22 mmHg, and the combination of these signs showed only a 58% sensitivity in detecting elevated PCWP.[9] In another study of chronic HF patients, the presence of JVD, when measured carefully, had the best combination of sensitivity (81%), specificity (80%), and predictive accuracy (81%) for detection of an elevation in PCWP (≥18 mmHg).[11] Ultrasonography of the lungs using an echocardiographic probe is another potentially useful way to as-

sess pulmonary congestion. Thoracic impedance measurement, using external or implanted devices, has been investigated in recent years in assessing congestion.[12] Measuring the lead impedance of a conventional pacemaker (PM) during pacing in VVI unipolar mode may provide additional information about the severity of pulmonary congestion or advanced warning of HF decompensation. Findings from a recent study of ours suggest that a reduction in PM impedance of >60 Ω from the reference value should prompt attempts at decongestion, though further study is required to determine whether such preemptive therapy could reduce hospital admissions.[13]

Establishing the diagnosis of heart failure

History

The clinical evaluation of a patient presenting with AHF starts in the Emergency Department with the patient's carefully elicited history. Symptoms of HF include those due to excess fluid accumulation (dyspnea, orthopnea, edema, discomfort or pain from hepatic congestion, abdominal distention from ascites) and those due to a reduction in cardiac output (fatigue, weakness that is most pronounced with exertion). The history alone is insufficient to make the diagnosis of HF, yet a detailed history remains the single best discriminator to determine the acuity, etiology and rate of progression of HF.

HF is unusual in an individual with no relevant medical history (e.g. a potential cause of cardiac damage), whereas, conversely, certain features, particularly previous AMI, greatly increase the likelihood of HF in a patient with appropriate symptoms and signs. Other clinical features, such as older age, history of hypertension and use of a loop diuretic, are associated with an increased likelihood of HF. These points highlight the need to obtain evidence of a structural or functional cardiac abnormality to corroborate the diagnosis of HF.[14]

Symptoms

Although symptoms bring patients to medical attention, many of the symptoms of HF are non-specific and do not, therefore, help discriminate between HF and other problems. Symptoms that are more specific (i.e. orthopnea and paroxysmal nocturnal dyspnea), are less common and are, therefore, insensitive (Table 5).[15] Symptoms are similar for systolic and diastolic ventricular dysfunction. Dyspnea on exertion and fatigue are early, but very non-specific symptoms of HF, as is peripheral edema.

Acute and subacute presentations (days to weeks) are characterized primarily by shortness of breath at rest and/or with exertion. Also common are orthopnea, paroxysmal nocturnal dyspnea and, with right HF, right upper quadrant discomfort due to acute hepatic congestion. Patients with tachyarrhythmias may complain of palpitations with or without lightheadedness. Chronic presentations (progressive over

Table 5. Symptoms and signs of heart failure (ESC guidelines, 2012).

Symptoms	Signs
Typical:	More specific:
Breathlessness	Elevated jugular venous pressure
Orthopnea	Hepatojugular reflux
Paroxysmal nocturnal dyspnea	Third heart sound (gallop rhythm)
Reduced exercise tolerance	Laterally displaced apical impulse
Fatigue, tiredness, increased time to recover post exercise	Cardiac murmur
Ankle swelling	
Less typical:	Less specific:
Nocturnal cough	Peripheral edema (ankle, sacral, scrotal)
Wheezing	Pulmonary crepitations
Weight gain (>2 kg/week)	Reduced air entry and dullness to percussion at lung bases (pleural effusion)
Weight loss (in advanced heart failure)	
Bloated feeling	Tachycardia
Loss of appetite	Irregular pulse
Confusion (especially in elderly)	Tachypnea (>16 breaths/minute)
Depression	Hepatomegaly
Palpitations	Ascites
Syncope	Tissue wasting (cachexia)

months) differ in that fatigue, anorexia, abdominal distension and peripheral edema may be more pronounced than dyspnea. Over time, pulmonary venous capacitance accommodates to the chronic state of volume overload, leading to less or no fluid accumulation in the alveoli, despite the increase in total lung water. These patients usually present with excessive fatigue and low-output symptoms.

Dyspnea is a clinical symptom of HF usually first manifested on exertion and is the most common symptom for patients presenting with AHF. Nonetheless, HF accounts for only 30% of the causes of dyspnea in the primary care setting. Consequently, dyspnea, though more specific than fatigue, is non-specific and may be due to many other disorders, such as pulmonary disease, obesity, and anemia, that are common in the elderly population and may coexist with HF, as do other comorbidities such as chronic renal failure and diabetes mellitus. Patients with chronic pulmonary disease are at particular risk of developing arterial hypoxemia that may further aggravate HF. Chronic obstructive pulmonary disease and HF may be difficult to distinguish in some patients. Causes of fatigue also include deconditioning, sleep apnea, and depression. It is notable that there is a poor correlation between dyspnea and LV function at rest. The absence of dyspnea on exertion only slightly decreases the probability of systolic HF.[16]

Orthopnea is defined as dyspnea that occurs in the recumbent position and is usually relieved by sitting upright or by the addition of more pillows. On adoption of the recumbent position, the failing heart is unable to cope with the mobilization of fluid from dependent venous reservoirs in the abdomen and the lower extremities, which increases venous return to the thoracic compartment by 250-500 mL of fluid. As a result, left-sided filling pressures, pulmonary venous and capillary pressures rise further, with the risk of developing interstitial pulmonary edema. Orthopnea has been shown to correlate with high PCWP with a sensitivity approaching 90%.[17]

Paroxysmal nocturnal dyspnea, occurring while recumbent at night, causes the patient to wake up with severe breathlessness, which is relieved by sitting upright. It is also a result of pooling of blood in the lungs and is usually manifested as cough or wheezing. The increased pressure in the bronchial arteries, along with interstitial pulmonary edema, leads to increased airway resistance. This situation is what is described as cardiac asthma, which should be differentiated from primary asthma and other pulmonary causes of wheezing. Paroxysmal nocturnal dyspnea is an important symptom that often precedes pulmonary edema by several days and requires urgent treatment.[18]

Abdominal pain in the right upper quadrant may occur as a result of congestion of the liver and stretching of its capsule. Nausea and abdominal discomfort may also occur when there is marked congestion of the liver and gastrointestinal tract.

Patients with chronic HF often develop secondary pulmonary hypertension, which can contribute to dyspnea, as pulmonary pressures rise with exertion. These patients may also complain of substernal chest pressure, typical of **angina**. In this setting, elevated RV end-diastolic pressure leads to secondary RV subendocardial ischemia.

Clinical examination

Clinical examination, including observation of the patient, palpation and auscultation of the heart, is essential in the clinical assessment of a patient with suspected HF. The clinical examination should focus on several key features, including vital signs, the examination of heart and lungs, neck veins, abdomen and extremities.

The presence of pulmonary rales, JVD, hepatojugular reflux and pitting peripheral edema, are indicative of volume overload and enhance the probability of an HF diagnosis. The absence of any of these findings is of little help in ruling out HF. The more specific signs, such as elevated jugular venous pressure (JVP) and displacement of the apical impulse, are harder to detect and therefore less reproducible, with poor interobserver agreement. Symptoms and signs may be particularly difficult to identify and interpret in obese individuals, in the elderly, and in patients with chronic lung disease.[19] Table 6 shows the diagnostic value of clinical markers of congestion.

Vital signs

Blood pressure may be normal, low or high in patients with AHF. High blood pressure at presentation is more often the result of a high sympathetic tone (reactive hypertension), rather than chronic hypertension. There is an inverse association between blood pressure at presentation and in-hospital and post-discharge mortality, as hypertensive patients are more likely to have preserved systolic function. Hypotension is a more ominous sign, and may reflect a low

Table 6. Diagnostic value of clinical signs of congestion. Modified from Knudsen et al.[43]

Variable	Sensitivity (%)	Specificity (%)
Medical history:		
Chronic heart failure	62	87
Myocardial infarction	43	87
Hypertension	72	48
Clinical findings:		
Orthopnea	66	57
Jugular venous distention	38	90
S3 gallop rhythm	13	93
Rales	59	77
Lower extremity edema	64	74
Brain natriuretic peptide (pg/mL):		
≥100	90	75
≥200	80	87
≥300	71	90
≥400	64	92
Chest radiographic findings:		
Cardiomegaly	79	80
Cephalization	41	96
Interstitial edema	27	98
Alveolar edema	6	99
Pleural effusion	25	92
No hyperinflation	3	92
No pneumonia	4	92
Abnormal electrocardiogram	58	78

cardiac output due to severe myocardial dysfunction, acute valvular heart disease, cardiac tamponade and other causes. In patients with severe HF, a proportional pulse pressure, (systolic blood pressure – diastolic blood pressure) / systolic blood pressure, <25% predicts a cardiac index of <2.2 L/min/m^2 with high sensitivity and specificity.[20] Blood pressure should always be determined in both arms and in the legs, where there is any suspicion of coarctation or aortic dissection. A difference in systolic blood pressure between the arms of more than 10 mmHg is abnormal.[21] The potential causes of blood pressure discrepancy between arms and legs are shown in Table 7. *Pulsus paradoxus* (paradoxical pulse) is an exaggeration (>10 mmHg) of the normal inspiratory decline in arterial pressure and, amongst other pathologies, may be a sign of severe congestive HF (Table 8).[22]

Sinus tachycardia is a non-specific sign that is caused by increased sympathetic activity and is usually present in AHF, except in the presence of conduction disturbances or if the patient is taking negatively chronotropic agents, such as digoxin, beta-blockers or amiodarone. Some patients may have atrial fibrillation (usually rapid) or ventricular arrhythmias. Perfusion may be assessed by capillary refill time and physician's perception of skin temperature (i.e. warm, suggestive of adequate perfusion, or cold, suggestive of poor perfusion). Peripheral vasoconstriction with coldness, cyanosis and pallor of extremities is also caused by increased sympathetic activity.

Table 7. Causes of blood pressure discrepancy between arms and legs.

Dissecting aortic aneurysm
Peripheral arterial stenosis/occlusion
Coarctation of the aorta
Supravalvular aortic stenosis
Thoracic outlet syndrome

Table 8. Causes of *pulsus paradoxus*.

Severe congestive heart failure
Severe pulmonary emphysema
Severe asthma
Pulmonary embolism
Pericardial tamponade
Constrictive pericarditis

Pulmonary examination

Pulmonary examination often reveals rales, consistent with interstitial pulmonary edema, or wheezing. Rales should be examined after the patient has been asked to cough. In acute pulmonary edema, crackles may be accompanied by expectoration of frothy, blood-stained sputum. Pulmonary rales result from transudation of fluid from the intravascular space to the alveoli. Auscultation of rales may indicate fluid overload, but is a non-specific and insensitive marker of the absence of congestion. If rales persist at the time of discharge, it should be noted whether they are due to other conditions, such as pneumonia, interstitial fibrosis, chronic bronchitis, asthma, and emphysema, or whether persistent congestion due to HF remains. Pleural effusions can also be detected in patients with HF. They are usually bilateral and associated with dyspnea and generalized congestion.

Estimation of JVP

Measurement of JVP is not infrequently limited by patient body habitus, such as obesity or respiratory pathology. Nonetheless, when performed properly and by experienced physicians, JVP estimation is a fairly accurate and simple measurement of congestion, and is thus a potential target to monitor thera-

py.[23] Elevated JVP may identify an elevated right atrial pressure and, by inference in the absence of tricuspid or pulmonary valve disease, an elevated PCWP and left atrial pressure in patients with HF. The presence of JVD, when measured carefully, predicts elevated left-sided filling pressures with 80% sensitivity and specificity.[24,25]

Normal JVP decreases with inspiration and increases with expiration. Veins that fill at inspiration (Kussmaul sign) are a clue to constrictive pericarditis, pulmonary embolism, or right ventricular (RV) infarction. With the patient sitting at 45°, JVP can be estimated by measuring the vertical distance from the top of the internal jugular venous pulsation to the sternal angle of Louis and adding the distance from the sternal angle to the level of the mid-right atrium which has most widely been cited as 5 cm (Figure 2). The normal JVP is between 6 and 8 cm of water. A JVP of <6 cm-H_2O is suggestive of hypovolemia and a JVP >9 cm-H_2O is indicative of elevated right atrial pressures. It is preferable to examine the internal rather than the external jugular vein, since the internal jugular vein is in direct line with the superior *vena cava* and right atrium, whereas the external jugular vein is not.

The **hepatojugular reflux** may also be used to assess elevated JVP and is both sensitive and reliable. Ten seconds of firm mid-abdominal pressure applied by hand with a sustained rise in JVP of at least 3 mmHg (4 cm of blood) is considered a positive result. This sign is due to an increase in the right atrial pressure during the test, due to the inability of the failing ventricles to accommodate the increased venous return, and is found in patients with hemodynamic evidence of LV failure with secondary pulmonary hypertension. Patients with a positive response have lower LV ejection fractions and stroke volumes, higher LV filling pressures, higher mean pulmonary arterial and right atrial pressures. In patients with chronic congestive HF, a positive hepatojugular reflux sign (with or without increased JVP), a third heart sound (S3), and radiographic pulmonary vascular redistribution are independent predictors of increased PCWP.[17] In the absence of isolated RV failure, seen in some patients with RV infarction, a positive test suggests a PCWP of ≥15 mmHg.[26]

Cardiac palpation

Examining the apical impulse by the posterior approach with the patient in the sitting position is the best method for appreciating subtle abnormalities

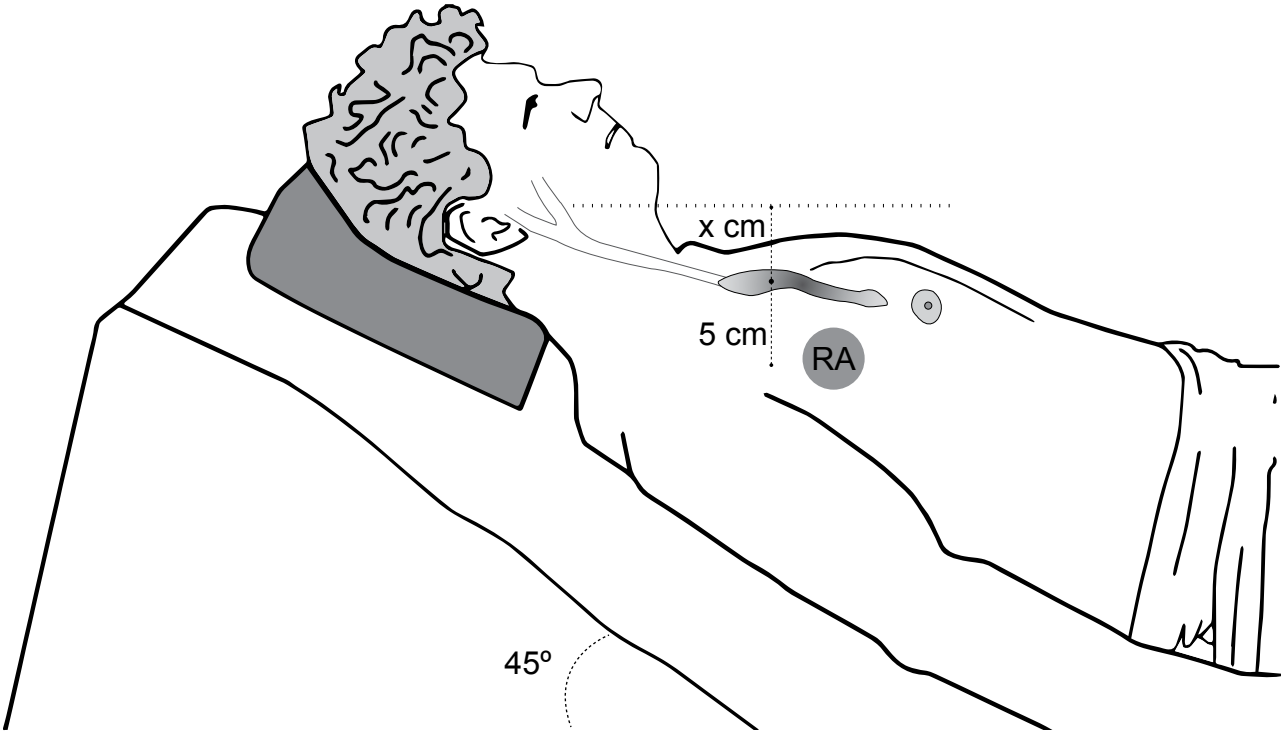

Figure 2. Clinical estimation of jugular venous pressure (JVP). The vertical distance from the right atrium (RA) to the sternal angle of Louis is estimated as 5 cm. The additional vertical distance from the angle to the height of observed venous distention (x cm) is added to obtain the JVP estimate.

of precordial motion. The normal apical impulse occurs during early systole, with an outward motion imparted to the chest wall. An outward precordial apical motion occurring in late systole is abnormal. In LV enlargement the apical impulse is laterally displaced, beyond the mid-clavicular line, is wide or diffuse (>3 cm in diameter), and can be palpated in two adjacent intercostal spaces. In LV hypertrophy without dilatation the apical impulse is localized, non-displaced, late and sustained. In the presence of an LV aneurysm, or pseudoaneurysm, the apical impulse is displaced and delayed with rocking motion. If the apical impulse is maximal in the epigastrium one should consider emphysema and an enlarged RV. If the apical impulse is not palpable and the patient is hemodynamically unstable, consider cardiac tamponade as the first diagnosis. Significant overlap of sites of maximal pulsation occurs in LV and RV overload states. Generally, pulsations of increased blood flow are dynamic and quick, whereas pulsations due to pressure overload cause a sustained impulse. Abnormal pulsations at the right upper sternal border (aortic area) should suggest an aortic aneurysm.[27] In patients with pulmonary hypertension, signs can include increased intensity of P2, a murmur of pulmonary insufficiency, a parasternal lift, and a palpable pulmonic tap (felt in the left second intercostal space).

Cardiac auscultation

Cardiac auscultation may reveal either a third and/or a fourth heart sound suggestive of cavitary dilatation or decreased compliance of the LV, respectively. A new or changed murmur usually represents valvular abnormalities, which may reflect altered ventricular geometry.[17]

A **third heart sound (S3)** is more common in severe HF, being associated with poor prognosis. The timing of S3 (ventricular filling gallop) relates to the peak of rapid ventricular filling with rapid flow deceleration and indicates an increased LV end-diastolic pressure. An RV S3 may be augmented with inspiration. Despite being relatively uncommon findings, a third heart sound and displaced cardiac apex are good predictors of LV dysfunction and effectively rule in the diagnosis of systolic HF.[28] An S3 in a patient with mitral regurgitation (MR) implies severe regurgitation or a failing LV or both. An S3 is less common in conditions that cause thick, poorly compliant ventricles—for example, LV hypertrophy that occurs with pressure overload states such as aortic stenosis or hypertension—until late in the disease. An S3 may occur in hypertrophic obstructive cardiomyopathy with normal systolic function. An S3 gallop is associated with left atrial pressures exceeding 20 mmHg, increased LV end-diastolic pressures (>15 mmHg), and elevated serum brain natriuretic peptide (BNP) concentrations. However, there is appreciable interobserver variability in the ability to detect an S3, such that an S3 has a low sensitivity (e.g. 9%) but high specificity (e.g. 99%) for the clinical diagnosis of HF.[28] The pericardial knock of constrictive pericarditis is similar to an S3 and is associated with a sudden arrest of ventricular expansion in early diastole. It is of higher frequency than S3, occurs slightly earlier in diastole, may vary with respiration, and is more widely transmitted.[29]

A **fourth heart sound (S4)** is thought to originate within the ventricular cavity and results from a forceful atrial contraction into a ventricle that has limited distensibility, due, for example, to hypertrophy or fibrosis. It is not heard in healthy young persons or in atrial fibrillation. Common pathologic states in which an S4 is often present include aortic stenosis, arterial hypertension, hypertrophic obstructive cardiomyopathy, pulmonary stenosis and ischemic heart disease. In patients with aortic stenosis who are younger than 40 years, the presence of an S4 usually indicates significant obstruction. A loud S4 can be heard in acute MR (e.g. with ruptured *chordae tendineae*) or regurgitation of recent onset where the left atrium has not yet significantly dilated. With chronic MR, the left atrium dilates, becomes more distensible and generates a less forceful contraction. Under these circumstances, an S4 is usually absent. An S4 can also originate from the right ventricle. A right-sided S4 is increased in intensity with inspiration, is often associated with large jugular venous a waves, and is best heard along the left sternal border rather than at the apex, which is the usual site of an S4 from the LV. The presence of a right-sided S4, in association with pulmonary stenosis, indicates severe pulmonary valve obstruction.

A systolic murmur in the posterior thorax may be heard in coarctation, aortic dissection, anterior mitral leaflet syndrome (with posteriorly directed jet of MR), and peripheral pulmonary artery stenosis. A systolic murmur due to mitral or tricuspid regurgitation may be heard even in the absence of primary valve disease and is termed a functional regurgitant murmur; it is due to dilatation of the mitral or tricuspid annulus when the left or right ventricle is en-

larged. Chronic MR in HF patients causes volume overload, resulting in further LV remodeling and worsening MR. Moderate to severe MR is noted in 40-50% of patients with AHF and LV systolic dysfunction, and is associated with worse outcomes.[30]

The murmur of mild aortic regurgitation (AR) may be difficult to appreciate and hence clinically "silent". This murmur is best heard with the patient in the sitting position, leaning forward, in held expiration. Consider AR when there is a wide arterial pulse pressure, especially in young or middle-aged patients. The murmur of AR is typically early diastolic (immediately after S2) and decrescendo in timing. Severe AR, especially if acute, may be associated with markedly increased LV end-diastolic pressures. These pressures will decrease the gradient between the aorta and the LV in diastole, and the murmur will taper rapidly. In mild AR, the LV end-diastolic pressure remains normal, the gradient persists throughout most of diastole, and the murmur may persist longer into diastole. With severe, chronic AR, there is often a wide pulse pressure, a systolic ejection murmur that usually peaks early (related to increased aortic flow). The murmur of AR is often best heard along the left sternal border. The clinical triad of hypertension, chest pain, and right sternal border transmission of the AR murmur should suggest proximal aortic dissection.[17]

Additional physical examination

Abdominal examination may reveal hepatomegaly as a result of passive congestion, hepatojugular reflux or ascites. The liver can pulsate during systole in the presence of tricuspid regurgitation. The epigastric site may be the location of the maximal cardiac impulse in patients with emphysema or an enlarged right ventricle.

Extremity examination may reveal peripheral edema, particularly in the dependent portions of the body. Perfusion may be assessed by capillary refill time and physician's perception of skin temperature.[24] Peripheral edema is a key manifestation of HF, but is not specific and usually absent in patients treated with diuretics. It is related to extracellular volume expansion, is accompanied by weight gain and is progressive. It is usually bilateral and symmetrical, painless, pitting, and occurs first in the lower extremities in ambulatory patients (feet and ankles). In bedridden patients, edema may be found over the sacrum and scrotum. Edema to mid-calf may reflect an increase of >2 liters in extracellular fluid volume. In severe untreated cases the edema may become generalized with hepatic congestion, ascites and pleural effusions (anasarca). Generalized edema is often accompanied by resistance to oral diuretic treatment and necessitates special manipulation.[31]

In HF patients, peripheral edema is usually associated with a high right atrial pressure that is most commonly due to left-sided HF. An elevated JVP improves the specificity of edema as a sign of congestion. After treatment, patients should have no more than trace edema unless they have preexisting edema of non-cardiac etiology. HF should be distinguished from other causes of edema, including venous thrombosis or insufficiency, hypoalbuminemia, renal sodium retention, drug side effect (e.g. calcium channel blocker), and cirrhosis. Figure 3 shows some examples with clinical signs of congestion.

Cerebral signs, such as confusion, disorientation, sleep or mood disturbances, may be observed in advanced HF, particularly in the presence of hyponatremia. These symptoms may be the first manifestation of HF in elderly patients.

Initial laboratory assessment

Several laboratory investigations are recommended in the ESC guidelines as part of the routine diagnostic evaluation of patients with suspected HF. Laboratory testing can help identify alternative diagnoses and potentially reversible causes of HF and should thus include a range of tests, as indicated in Table 9.[32] Additional laboratory tests should be performed based on physician discretion to evaluate further causes or identify comorbid conditions that require enhanced control.

A **complete blood count** may suggest concurrent or alternate conditions. Anemia or infection can exacerbate preexisting HF. Anemia, hyponatremia, hyper-/hypokalemia and renal dysfunction are relatively common and are important for both immediate management considerations and prognosis. Anemia is an independent predictor of in-hospital mortality in symptomatic patients with severe HF and an elevated post-discharge mortality risk.[33]

Serum electrolytes, blood urea nitrogen and creatinine may indicate associated conditions. Hyponatremia generally indicates severe HF, though it may occasionally result from excessive diuresis. Hyponatremia occurs in approximately 25% of patients with AHF and commonly remains uncorrected during hos-

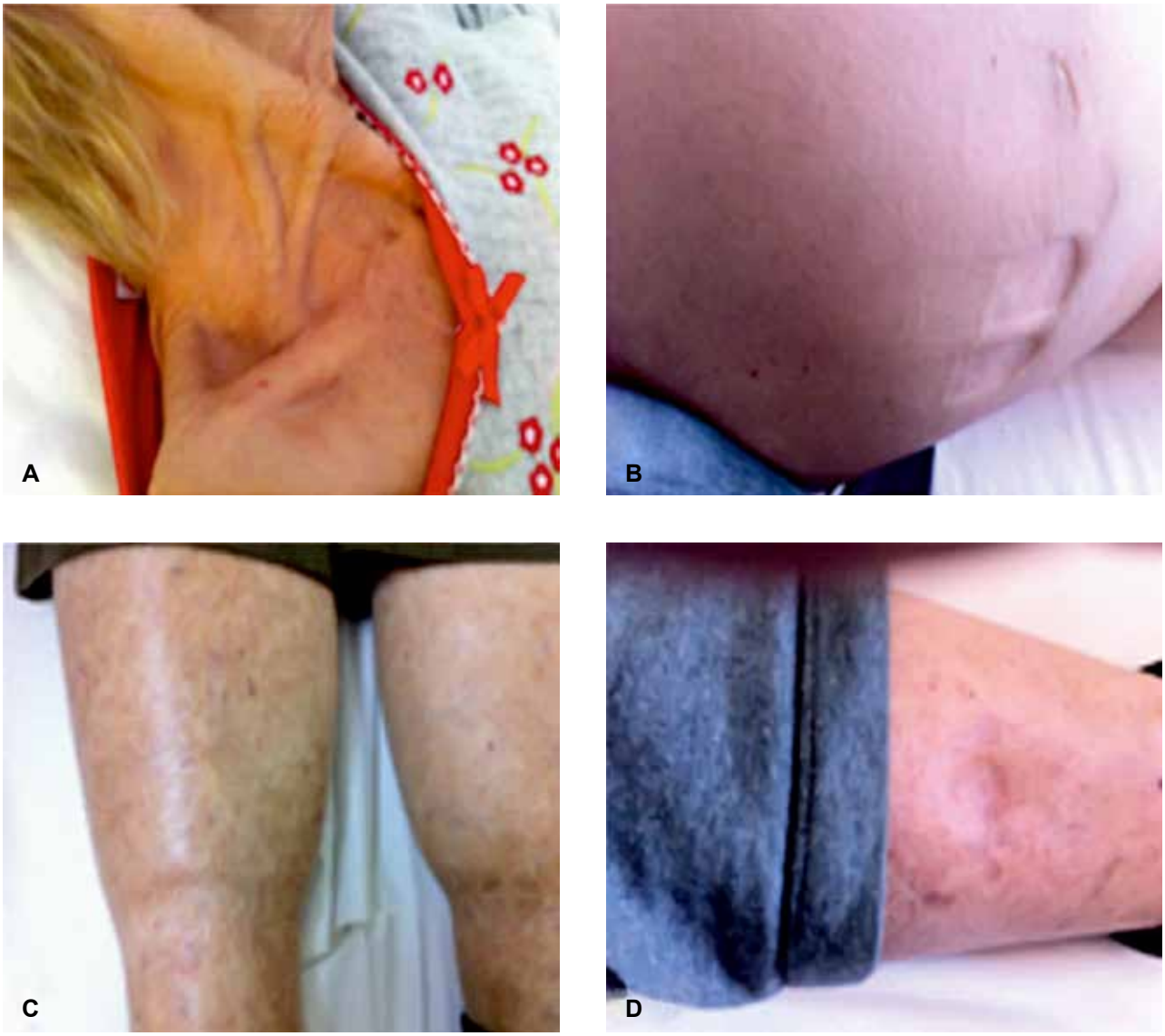

Figure 3. Clinical signs of congestion. a) Jugular venous distension, b) ascites with pitting abdominal wall edema, c) peripheral edema to thighs, d) pitting edema of the shin.

pitalization. Admission serum sodium is an independent predictor of an increased length of hospital stay for cardiovascular causes and increased in-hospital and post-discharge mortality.[32] Renal impairment may be caused by and/or contribute to HF exacerbation. Renal dysfunction consistently predicts poor outcomes in HF in both chronic and acute settings. Increases in urea in HF may reflect congestion and fluid retention, as well as cardiac and renal dysfunction, whereas elevation in creatinine is more specific for changes in GFR. Recently, urea was found to be a better predictor of outcome than creatinine or estimated GFR in AHF. Elevations in urea disproportionate to the rise in creatinine (20:1 for urea vs. creatinine in mg/dL or serum urea >10% of the value of serum creatinine in mmol/L) may also reflect dehydration. A **fasting blood glucose** test or glycated hemoglobin (HbA1c) is necessary to detect underlying diabetes mellitus. **Liver function tests** may be affected by hepatic congestion. Elevated total bilirubin and gamma-glutamyl transferase levels in particular carry a significant independent predictive value.[34]

Cardiac biomarkers associated with myocardial injury, such as troponin I or T, are important prognostic markers in AHF patients and should be obtained in patients in whom ACS is a concern, or in whom additional risk stratification is warranted. Current practice guidelines recommend the selective use

Table 9. Laboratory evaluation for heart failure.

Complete blood count
Serum electrolytes
Liver function tests
Renal function tests
Serum glucose
Thyroid-stimulating hormone
Urinalysis
Troponin
Natriuretic peptides
Arterial blood gases

Table 10. Causes of elevated natriuretic peptide levels.

Cardiac	Non-cardiac
Heart failure:	Acute pulmonary embolism
Systolic dysfunction	Pulmonary hypertension
Diastolic dysfunction	Anemia
Coronary artery disease	*Cor pulmonale*
Hypertension with left ventricular hypertrophy	Renal insufficiency
Valvular heart disease	Septic shock
Atrial fibrillation	Hyperthyroidism

of biomarkers as well as noninvasive and invasive techniques for the initial assessment of HF.[35]

Natriuretic peptides – BNP and N-terminal pro-BNP (NT-proBNP) – are neurohormones specifically secreted from the cardiac chambers, particularly the ventricles, in response to volume and pressure overload. The plasma concentrations of natriuretic peptides (NP) are increased in patients with LV dysfunction. Measurement of NP is a class I, level of evidence A, recommendation in the ACC/AHA guidelines, and a IIa/C indication in the ESC guidelines, when the diagnosis of AHF is in question, to help distinguish it from other causes of dyspnea.[36] Multiple systematic reviews have concluded that NP levels can effectively rule out a diagnosis of HF, because of their high negative predictive value.[37] Limited evidence also supports monitoring the reduction of NP levels in the acute and outpatient settings. A 30-50% reduction in BNP level at hospital discharge showed improved survival and reduced re-hospitalization rates, whereas persistently elevated values, despite optimal treatment, portend a poor prognosis. Most dyspneic patients with HF have BNP values above 400 pg/mL, while values below 100 pg/mL have a very high negative predictive value for HF as a cause of dyspnea. In the range between 100-400 pg/mL, plasma BNP concentrations are neither very sensitive nor specific for detecting or excluding HF. Nonetheless, there is no recognized definitive cutoff value that ensures the diagnosis of HF, and the positive predictive value of elevated plasma BNP or NT-proBNP in the diagnosis of HF is limited. Atrial fibrillation (AF) is associated with higher levels of BNP in the absence of HF. Other diagnoses, such as pulmonary embolism, right HF and pulmonary hypertension, should also be considered in patients with elevated plasma BNP/NT-proBNP concentrations. NP levels increase with age and are higher in women, blacks, patients with renal failure, and some acute non-cardiac illnesses such as sepsis (Table 10). Furthermore, the utility of NP levels may be limited by the fact that their production and release may lag behind acute changes in hemodynamic measurements. Despite this limitation, NP levels add greater diagnostic value to the history and physical examination than other initial laboratory tests (ECG, chest X-ray and blood tests). Consequently, elevated NP levels should be interpreted in the context of other clinical information, as they may lend weight to the diagnosis of HF or trigger consideration of HF, but should not be used in isolation to diagnose HF.[38]

Electrocardiogram (ECG)

The ECG is one of the most useful investigations in a patient with suspected HF and is recommended as a first line diagnostic test in the guidelines.[2] An ECG should be performed in all patients presenting with suspected AHF in the emergency department, as it provides diagnostic and prognostic information and helps in guiding treatment. Most patients with HF due to systolic dysfunction have significant abnormalities on the ECG. A normal ECG in patients presenting acutely makes systolic dysfunction unlikely, with a 98% negative predictive value. In patients with a non-acute presentation, a normal ECG has a somewhat lower negative predictive value (likelihood about 10-14%).[39]

The ECG is particularly important for identifying evidence of acute or prior myocardial infarction or acute ischemia. The ECG may also show evidence of LV hypertrophy, giving a possible clue to the etiology of HF. Ischemia may cause symptoms of dyspnea similar to HF and may also cause or exacerbate HF. The ECG is useful for identifying other causes of dyspnea in patients with suspected HF. Heart rate and rhythm abnormalities can significantly affect myocardial oxygen demands, cardiac output and coronary perfusion.

Both excessive tachycardia and bradycardia reduce cardiac output and can precipitate or intensify HF.[40] Rhythm disturbances, such as heart block, atrial fibrillation, atrial flutter, ventricular ectopy and ventricular tachycardia, should be assessed.

Atrial fibrillation is found in approximately 20-30% of patients with AHF. A rapid ventricular response may precipitate AHF, and may be particularly harmful in patients with diastolic dysfunction, who rely on atrial contraction to augment stroke volume. In addition, the rapid heart rate reduces the time for diastolic filling, further impairing diastolic function. Sustained ventricular or atrial arrhythmias in patients hospitalized for AHF are associated with increased sudden cardiac death (SCD) and non-arrhythmic death. Non-sustained ventricular tachycardia is an independent marker of the risk of SCD in HF patients and impacts ICD implantation decision. Precipitants of arrhythmias, such as electrolyte disturbances, proarrhythmic drugs and digoxin toxicity, should be assessed and corrected when present.

Intraventricular conduction disorders are common in patients with AHF. These findings are important for decisions about treatment. A prolonged QRS duration over 120 ms is usually associated with ventricular mechanical dyssynchrony, which leads to worsening ventricular function. It is present in approximately 40% of patients with reduced systolic function who are hospitalized for worsening HF and is associated with worse outcomes.[2] Cardiac resynchronization therapy has been shown to improve cardiac output without increasing myocardial energy expenditure in patients with left bundle branch block and HF, and can improve functional status, reduce hospitalizations, and improve mortality. In patients with pacemakers or ICDs, the device should be interrogated to determine the underlying rhythm, to see whether the device is functioning properly and if the programming is optimal.[41]

Although the ECG may be less predictive of HF than the BNP/NT-pro-BNP level, it may show findings that favor the presence of a specific cause of HF. The most common abnormalities on the ECG in HF are shown in Table 11.

Chest radiography in HF

The chest X-ray is recommended as a first line diagnostic test in HF, particularly in the evaluation of patients who present with dyspnea, to differentiate HF from primary pulmonary disease.[4] Radiographic imaging of the chest enables assessment for pulmonary congestion, cardiomegaly, pericardial and pleural effusions, and the presence of pulmonary disease, pneumothorax or infection. Chest X-ray findings suggestive of HF include cardiomegaly (cardiothoracic ratio >50%), cephalization of the pulmonary vessels, Kerley B-lines, and pleural effusions (Table 12).[42]

The absence of cardiomegaly does not exclude HF, as this is a usual finding in acute HF and in patients with HF with preserved EF. Moreover, the absence of chest X-ray findings of HF (e.g. cardiomegaly, vascular redistribution, and interstitial or alveolar

Table 11. Most common ECG abnormalities in HF.

Abnormality	Causes
Sinus tachycardia	Decompensated HF, anemia, fever, hyperthyroidism
Sinus bradycardia	Beta-blockade, digoxin, ivabradine, verapamil, diltiazem
	Antiarrhythmics
	Hypothyroidism
	Sick sinus syndrome
Atrial tachycardia/ flutter/fibrillation	Hyperthyroidism, infections, mitral valve disease
	Decompensated HF, infarction
Ventricular arrhythmias	Ischemia, infarction, cardiomyopathy, myocarditis, hypokalemia, hypomagnesaemia, digitalis overdose
Myocardial ischemia/ infarction	Coronary artery disease
Q waves	Infarction, hypertrophic cardiomyopathy, LBBB, pre-excitation
LV hypertrophy	Hypertension, aortic valve disease, hypertrophic cardiomyopathy
AV block	Infarction, drug toxicity, myocarditis, sarcoidosis, genetic cardiomyopathy, Lyme disease
Low QRS voltage	Obesity, emphysema, pericardial effusion, amyloidosis
QRS duration ≥120 ms and LBBB morphology	Electrical and mechanical dyssynchrony

HF – heart failure; LV – left ventricular; AV – atrioventricular; LBBB – left bundle branch block.

Table 12. Chest X-ray in heart failure. Adapted from Mueller-Lenke et al 2006.[44]

	Sensitivity (%)	Specificity (%)
Cardiomegaly	64	70
Cephalization	20	93
Vascular prominent hilum	17	72
Hilar haziness	22	94
Peribronchial cuffing	17	96
Kerley B lines	23	96
Haziness of pulmonary vessels	18	98
Peripheral extension of pulmonary vessels	10	96
Interstitial edema	29	93
Alveolar edema	12	99
Right sided pleural effusion	11	91
Left sided pleural effusion	11	93
Bilateral pleural effusion	20	95

edema), does not exclude a high PCWP. Radiographic signs of pulmonary congestion are absent in 50% of patients with PCWP of 16-29 mmHg and in 40% of patients with PCWP ≥30 mmHg.[43]

A systematic review of the utility of the chest X-ray to diagnose LV dysfunction concluded that redistribution and cardiomegaly were the best predictors of increased preload and reduced EF, respectively (Table 12).[43] Neither finding, however, was sufficient to make a definitive diagnosis of HF. In a multicenter study, alveolar edema, interstitial edema, and cephalization all had a specificity of >90% for HF, but only cardiomegaly had a sensitivity >50%.[44] The chest X-ray may be very helpful for establishing not only the diagnosis but also the cause of heart failure (Figure 4).

Echocardiography

The declining skill of physicians in clinical examination, the low sensitivity and specificity of most signs, and the large interobserver variability in their detection highlight the need for objective assessment of cardiac function. In patients with symptoms and signs of HF, bedside echocardiography is helpful for determining whether ventricular function and hemodynamics are consistent with HF and for identifying its cause. Echocardiography, including two-dimensional, pulsed and continuous wave Doppler, color Doppler and tissue Doppler imaging, is the primary imaging tool for the structural and functional assessment of AHF patient. The transthoracic Doppler echocardiogram is recognized by the ESC guidelines as the most important investigation for the patient with suspected HF. Echocardiographic applications in AHF are shown in Table 13.[45]

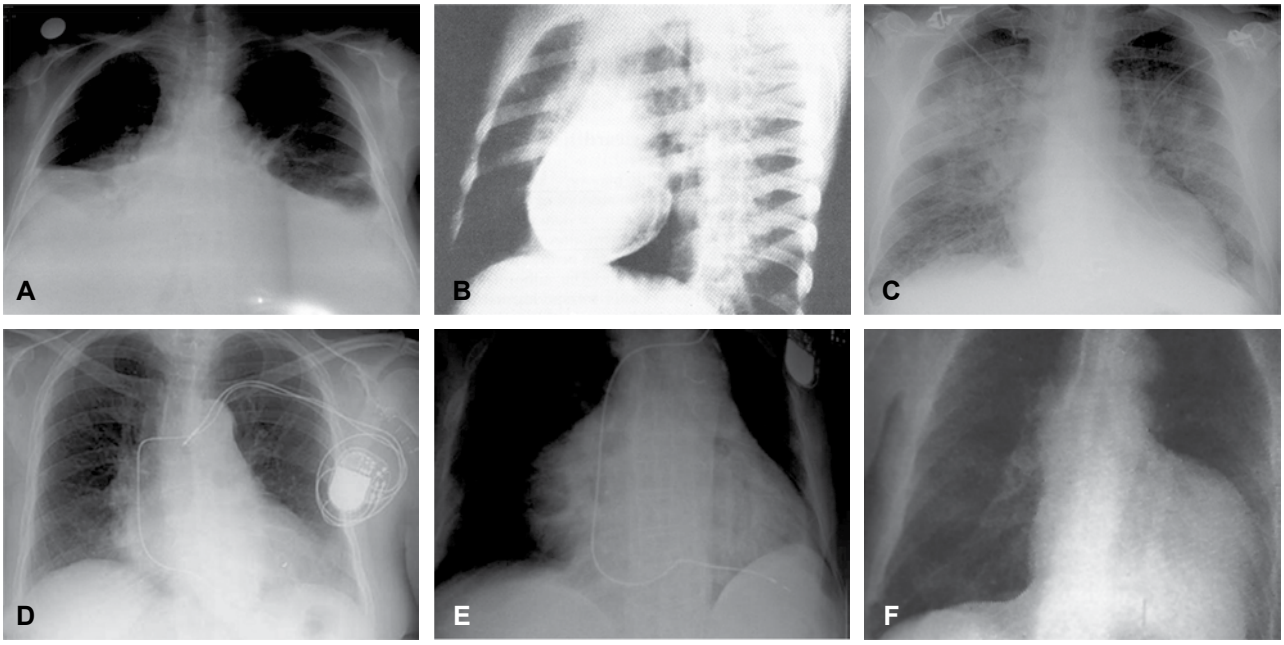

Figure 4. Chest X-ray in heart failure. a) pleural effusion, b) constrictive pericarditis with calcific pericardium, c) pulmonary edema, d) heart failure with pacemaker lead problem, e) cardiomegaly due to right atrial and right ventricular dilatation with small pericardial effusion, f) cardiomegaly with double apex due to left ventricular pseudoaneurysm.

Table 13. Applications of echocardiography in acute heart failure.

Assist in diagnosis of acute heart failure:
Chamber volumes, pressures and function
Wall thickness
Valve function
Pericardium
Determine heart failure etiology:
Coronary artery disease
Hypertension
Non-ischemic etiology
• Dilated
• Restrictive
• Hypertrophic
Categorizing heart failure:
Right and/or left ventricular dysfunction
Reduced or preserved ejection fraction
Estimate the severity of congestion
Assessment of hemodynamics
Transesophageal echocardiography
Guide heart failure treatment
Assessment of prognosis

Measurement of atrial and ventricular sizes may be helpful in identifying the cause and chronicity of disease. For example, patients with idiopathic dilated cardiomyopathy typically have both left and right atrial and ventricular enlargement (four-chamber dilatation) with decreased left systolic ventricular function. Estimation of right atrial pressure can be performed by measuring the diameter and collapsibility of the inferior *vena cava*. Dilatation of the LV on echocardiography (LV end-diastolic dimension >7.5 cm) is associated with a poor prognosis in AHF patients. The severity of valvular dysfunction can also be estimated. Pericardial disease includes thickening, suggestive of constrictive pericarditis or effusion, that may or may not be associated with tamponade.

Echocardiography is the most widely accepted and commonly used noninvasive tool for identifying systolic or diastolic dysfunction and should be performed after the initial evaluation to confirm the presence of HF. Regional wall-motion abnormalities in a coronary distribution are suggestive of coronary heart disease, but segmental abnormalities also occur commonly in patients with dilated cardiomyopathy. The most important consideration when categorizing HF is whether LVEF is preserved or reduced. LVEF may be obtained by visual estimation, which is limited by subjectivity and level of expertise, or by a quantified, objective method for measurement of LV systolic function, such as the biplane method. A reduced LVEF in systolic HF is a powerful predictor of mortality. Nonetheless, as many as 40-50% of patients with HF have diastolic HF with preserved LV function. Patients with diastolic HF are more likely to be women, older, and to have hypertension, atrial fibrillation, and LV hypertrophy, but no history of CAD. The diagnosis of diastolic dysfunction can also be made via methodologies that demonstrate abnormal LV relaxation or diastolic stiffness (Table 14).

Echocardiography combined with Doppler imaging may also be utilized to assess hemodynamics non-

Table 14. Common echocardiographic measures of left ventricular diastolic dysfunction in patients with heart failure (ESC Guidelines 2012).

Measurement	Abnormality	Clinical implications
e´	Decreased (<8 cm/s septal, <10 cm/s lateral, or <9 cm/s average)	Delayed LV relaxation
E/e´ ratio[a]	High (>15)	High LV filling pressure
	Low (<8)	Normal LV filling pressure
	Intermediate (8-15)	Grey zone (additional parameters necessary)
Mitral inflow E/A ratio[b]	"Restrictive" (>2)	High LV filling pressure
		Volume overload
	"Impaired relaxation" (<1)	Delayed LV relaxation
		Normal LV filling pressure
	Normal (1-2)	Inconclusive (may be "pseudonormal")
Mitral inflow during Valsalva manoeuvre	Change of the "pseudonormal" to the "impaired relaxation" pattern (with a decrease in E/A ratio ≥0.5)	High LV filling pressure (unmasked through Valsalva)
(A pulm-A mitral) duration	>30 ms	High LV filling pressure

invasively. In addition, tissue Doppler imaging variables, including the ratio of early transmitral velocity to tissue Doppler early mitral annular velocity (E/e'), have been shown to correlate with LV filling pressures. An E/e' ratio >15 suggests a PCWP >15 mm Hg, when e' is the mean of medial and lateral mitral annulus early diastolic velocities.[45]

Pulmonary hypertension is prevalent in AHF patients who have either reduced or preserved EF. Doppler echocardiography may be used to assess the presence of pulmonary hypertension via the estimation of pulmonary artery systolic pressure through tricuspid regurgitant or pulmonary artery acceleration velocities. The cardiac output can be estimated by pulsed-wave Doppler from the left ventricular outflow tract. In expert hands, the echocardiographic probe may also be used to assess pulmonary congestion by ultrasonography of the lungs.[46]

Transesophageal echocardiography is recommended in patients who have inadequate transthoracic echo windows, in patients with complex valvular conditions, in suspected endocarditis, in congenital heart disease, or to exclude a thrombus in the left atrial appendage in patients with atrial fibrillation. Overall, echocardiography plays a crucial role in the setting of the final diagnosis of HF (Figure 5).

Conclusion

HF is a common clinical syndrome that results from the impaired ability of the ventricle to fill with or eject blood. AHF results from multiple causes, including CAD, hypertension and valvular heart disease. The cardinal symptoms of HF include dyspnea and fatigue, which can occur at rest in severe cases and with exertion in milder cases. For the dyspneic patient in the acute care setting, a history and physical examination should be performed and a chest radiograph, electrocardiogram and echocardiogram should be obtained. A natriuretic peptide level may also help to clarify the diagnosis.

A thorough clinical examination, combined with the patient's medical history, will often deliver the diagnosis, severity, a sense of prognosis, and comorbidities. It also serves as a base for devising a rational, safe and effective treatment plan and determining whether the patient would benefit from hospitalization. Obtaining a detailed history and physical exami-

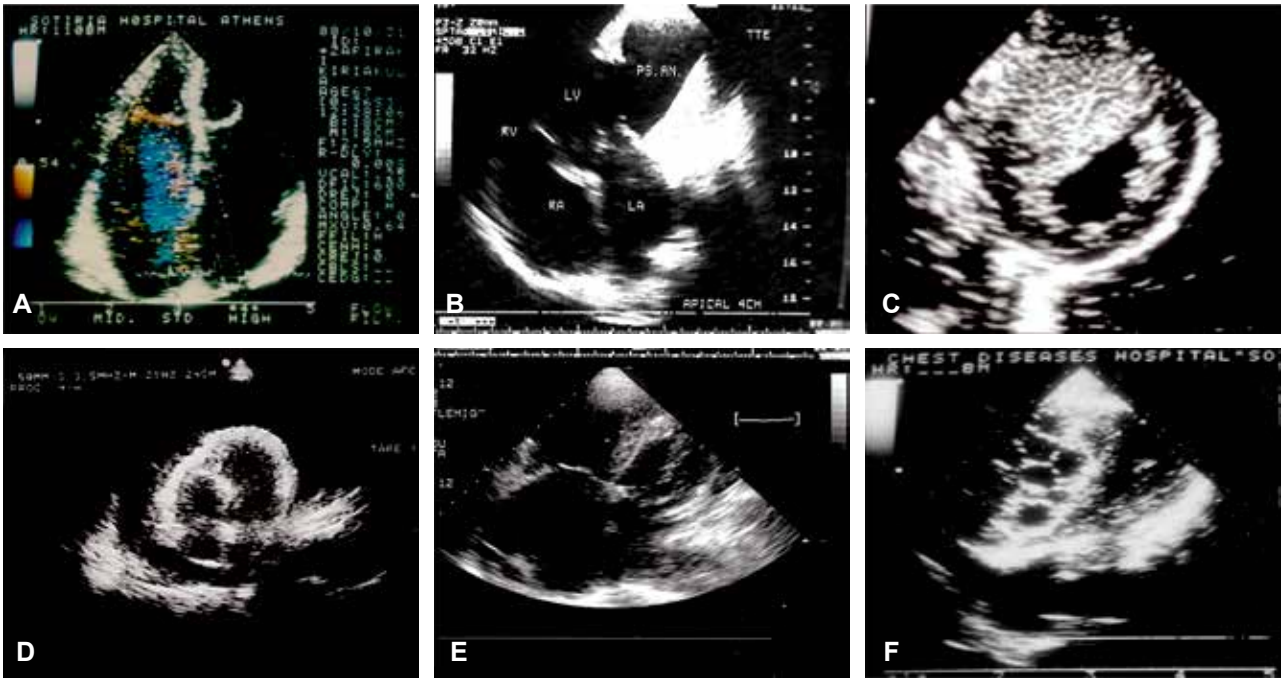

Figure 5. Echocardiography plays a crucial role in setting the final HF diagnosis. a) Restrictive cardiomyopathy (increased cardiothoracic ratio on chest x-ray and biatrial dilatation on echocardiogram), b) left ventricular pseudoaneurysm following previous myocardial infarction, c) hypertrophic cardiomyopathy, d) pericardial effusion with cardiac tamponade, e) right atrial and right ventricular dilatation with pulmonary hypertension, f) right ventricular hydatid cyst in a patient with right heart failure.

nation is also the best means of keeping testing under control and avoiding unnecessary studies; it provides the context within which to assess and validate the interpretation of study results, arrange their positioning in the overall management plan, and resolve the conflicting results of various studies.

The principal limitation of clinical examination in HF is the requirement for the examiner to perform it effectively. Much of the joy of medicine resides in the perpetual learning and professional growth that occurs with clinical experience at the bedside over time and in the sense of accomplishment in obtaining at the bedside the majority of the information needed to confidently determine a patient's diagnosis. Furthermore, observing, palpating, probing and auscultating during the physical examination are perhaps the most powerful ways of convincing patients and their families that you care deeply about your patient.

Medical education and residency training have undergone many changes in the last few decades, partly because of the advent of modern technologies. Training is increasingly focused on the use of technologies such as echocardiography in the diagnosis of cardiac conditions. With the increased focus on technology, less emphasis has been placed on the physical examination. Discussion of the clinical examination occupies about 60% of the chapter on HF in an old textbook of cardiology (1970), but only about 6.6% in a modern cardiology book and the ESC Heart Failure Guidelines of 2012. This does not indicate that physical examination is at risk of extinction. With the innumerable newer diagnostic modalities available, we now have the tools to correlate, refine and perfect the physical examination to a level beyond that at any other time in its history. We must try hard to improve this already excellent diagnostic tool and perhaps regain what is being lost with the retirement and passing of our outstanding bedside clinicians. The HF specialists may well be the last bastion of the protection and survival of the clinical examination and are in the best position to keep this investigative tool alive and vibrant. Medical education and residency training must better incorporate the use of clinical skills and evidence-based clinical tools in the evaluation, diagnosis, and management of HF.

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