Heart Failure

KEY POINTS

1. **Systolic heart failure** (HF) is caused by impaired ventricular ejection of blood. **Diastolic HF** results from impaired relaxation and filling of the left ventricle during diastole.
2. Symptomatic HF has a 1-year mortality of almost 50%.
3. The most common cause of HF is left ventricular systolic dysfunction, which typically results from **coronary artery disease**.
4. Symptoms of HF include *dyspnea, orthopnea, paroxysmal nocturnal dyspnea, fatigue, exercise intolerance, peripheral edema, and weight gain*.
5. Signs of HF include jugular venous distension, extra heart sounds (S_3 in left-sided HF and S_4 in patients with increased resistance to ventricular filling), pulmonary crackles, wheezing, pleural effusion, and pitting edema.
6. Initial testing should include *electrolytes* with *blood urea nitrogen* and *creatinine*, *complete blood count*, PA and lateral *chest x-ray*, *electrocardiogram*, and *echocardiography*. Cardiac catheterization is usually performed when no obvious cause for the HF is found or when myocardial ischemia is suspected.
7. Chest x-ray findings of HF may be obscured or distorted if there is underlying lung disease, and findings may be absent in patients with chronic HF.
8. HF is an unlikely cause of dyspnea in the emergency room when an untreated patient has normal levels of B-type natriuretic peptide.
9. Angiotensin-converting enzyme (**ACE**) inhibitors improve mortality, symptoms, left ventricular ejection fraction, and exercise tolerance and reduce hospitalizations. ACE inhibitors should be initiated early during the treatment of HF before excessive diuresis has occurred.
10. Patients who develop a cough or angioedema with ACE inhibitor therapy should be switched to an angiotensin receptor blocker (ARB).
11. Patients who develop significant renal insufficiency or hyperkalemia with ACE inhibitor or ARB therapy should be switched to combination hydralazine and isosorbide dinitrate.
12. Some **beta-blockers** such as carvedilol and bisoprolol improve morbidity and mortality in patients with HF, but should be initiated only after the patient's condition has stabilized and the volume status has been normalized.

13. **Digoxin** reduces hospitalization rates and improves symptoms and quality of life but does not lower mortality in patients with HF.
14. Mineralocorticoid receptor antagonists have shown promise in HF when used with ACE inhibitors but their concomitant use may be limited by hyperkalemia.
15. Clinical trials testing medications for diastolic HF are limited. ACE inhibitors and ARBs may improve exercise capacity and reduce the risk of hospitalization. Diuretics are appropriate for volume management but should be used with caution because these patients are sensitive to excessive preload reduction.
16. Upon discharge, patients should be educated about dietary salt and fluid restriction and should weigh themselves daily on the same scale. Early identification and treatment of HF can reduce the likelihood of hospitalization.

DEFINITIONS

Heart failure (HF): Clinical syndrome characterized by signs and symptoms of volume overload and reduced organ perfusion.
Systolic heart failure: HF caused by impaired ventricular ejection of blood.
Diastolic heart failure: HF resulting from impaired relaxation and filling of the left ventricle during diastole. Diastolic HF can occur in patients with normal systolic function or can coexist with systolic HF. Since the normal lower limit of the ejection fraction is arbitrary, distinguishing between diastolic HF and systolic HF is sometimes difficult. At many medical facilities, an ejection fraction below 50% is considered abnormal.

EPIDEMIOLOGY

HF affects nearly 5 million Americans and accounts for at least 20% of hospital admissions among people over 65 years of age.
Symptomatic HF has a 1-year mortality of almost 50%, conferring a worse prognosis than most cancers. As many as one-half of the patients with HF have normal or only minimally reduced systolic function, and are diagnosed with diastolic HF.

PATHOPHYSIOLOGY

Systolic Heart Failure

When the myocardium is weakened, the body attempts to maintain perfusion to vital organs by improving cardiac output and using systemic vasoconstriction to redistribute blood flow.

Reduced renal perfusion leads to activation of the renin–angiotensin–aldosterone system, which causes extracellular volume expansion that raises end-diastolic volume and improves stroke volume via the Frank-Starling mechanism (this law states that increases in end-diastolic volume lead to increases in contractility and stroke volume).

Catecholamines improve cardiac output by increasing heart rate and contractility. These compensatory neurohormonal mechanisms are initially beneficial but become deleterious over time.

The systemic vasoconstriction increases the workload of the heart, which can lead to further myocardial deterioration. The raised diastolic pressures are transmitted to the pulmonary and systemic veins, and can cause pulmonary congestion and peripheral edema. Catecholamine activation may worsen coronary ischemia or induce cardiac arrhythmias. Activation of the renin–angiotensin system causes sodium and water retention and may promote further cardiovascular injury, including left ventricular hypertrophy and remodeling.

Diastolic Heart Failure

Diastolic HF occurs when there is reduced myocardial relaxation (e.g., from ischemia, myocyte hypertrophy, aging), increased passive stiffness of the ventricle (e.g., from infiltrative diseases such as hemochromatosis and amyloidosis), or limited ventricle mobility (e.g., from pericardial tamponade or extrinsic compression by tumor).

In patients with left ventricular hypertrophy, ischemia may contribute to diastolic HF even when there are no significant coronary stenoses, because the elevated diastolic pressures may impair blood flow through capillaries and small resistance vessels.

Causes and Precipitants

The most common cause of HF is left ventricular systolic dysfunction, which typically results from coronary artery disease (Box 2-1). These patients may have a history of myocardial infarction or may have viable but underperfused myocardium. In patients with a history of HF, a

frequent precipitant is dietary or fluid indiscretion or medication non-compliance. Tachyarrhythmias (most commonly atrial fibrillation) may reduce cardiac output by limiting the duration of ventricular filling, increasing myocardial oxygen demands, and eliminating ‘‘atrial kick.’’ Atrial kick refers to atrial contraction, which promotes ventricular filling during diastole.
Loss of atrial kick may precipitate HF in patients with stiffened ventricles from diastolic dysfunction. Myocardial infarction or ischemia can cause ventricular stiffening (diastolic dysfunction), reduced muscle mass for pumping blood, valvular leakage from papillary muscle dysfunction, and increased oxygen demand from pain and tachycardia, all of which may precipitate or contribute to HF.
Systemic infections or hyperthyroidism increase the metabolic rate, which increases the workload on the heart. Newly prescribed medications may cause salt retention, myocardial depression, or arrhythmias.

SYMPTOMS

1. **Dyspnea**, orthopnea (dyspnea upon lying supine), and paroxysmal nocturnal dyspnea are common symptoms of pulmonary congestion. Patients with paroxysmal nocturnal dyspnea describe wakening from sleep with shortness of breath. The presence and severity of orthopnea can be assessed by asking (a) ‘‘*With how many pillows do you sleep*?’’ and (b) ‘‘*With how many pillows did you sleep weeks/months ago*?’’ If there is an increase in the number of pillows, ask what symptoms prompted the change. When orthopnea is severe, patients may be unable to sleep in bed and may choose to sleep in a recliner or chair.

2. **Fatigue**, exercise intolerance, and mental obtundation are symptoms of poor cardiac output.

3. Peripheral **edema** suggests right-sided HF.

4. **Weight gain** results from fluid retention.

SIGNS

The goal of the focused physical exam is to determine volume status and to search for potential precipitants of the HF.

1. Jugular Venous Distension

Jugular venous pressure (JVP), which reflects right atrial pressure (central venous pressure), is estimated by examining the internal jugular veins. We do not recommend using the external jugular vein pulsations to estimate central venous pressure, because valves in these veins may lead to inaccurate readings.
To assess JVP, turn the patient's head slightly away from the side being examined and elevate the head of the bed to at least 30 degrees until the jugular venous pulsations are visible in the lower part of the neck.
Several features help differentiate internal jugular pulsations from carotid pulsations. The internal jugular vein is not visible (lies deep to the sternocleidomastoid muscles), is rarely palpable, and the level of its pulsations drops with inspiration or as the patient becomes more upright.
The jugular vein pulsations usually have two elevations and two troughs. The first elevation (a wave) corresponds to the slight rise in atrial pressure resulting from atrial contraction.
The first descent (x descent) reflects a fall in atrial pressure that starts with atrial relaxation. The second elevation (v wave) corresponds to ventricular systole when blood is entering the right atrium from the vena cavae while the tricuspid valve is closed. Finally, the second descent (y descent) reflects falling right atrial pressure as the tricuspid valve opens and blood drains from the atrium into the ventricle.

Once the highest point of internal jugular pulsation has been identified, the vertical distance between this point and the sternal angle represents the JVP. Regardless of the patient's position, the sternal angle remains approximately 5 cm above the right atrium. Venous pressure greater than 3 to 4 cm above the sternal notch is considered elevated, suggesting right-sided HF, constrictive pericarditis, tricuspid stenosis, or superior vena cava syndrome.

2. Heart

The heart examination should include assessment of the cardiac impulse (lateral displacement suggests cardiomegaly), heart rate (decompensated HF causes tachycardia), rhythm, murmurs (such as aortic stenosis or mitral regurgitation), and extra heart sounds (S_3 or S_4).
An S_3 is a soft, low-frequency sound caused by vibrations of the ventricular walls, valves, and supporting structures as blood decelerates in the left ventricle

during rapid ventricular filling. Although an S_3 is normal in some healthy children and young athletes, the presence of an S_3 in older adults suggests an abnormality, such as left HF or mitral regurgitation.
The fourth heart sound (S_4) is caused by vibrations in the ventricular walls and supporting structures as blood from atrial contraction decelerates in the ventricle. An S_4 occurs when there is increased resistance to ventricular filling (diastolic dysfunction). A loud, widely split S_2 supports the diagnosis of pulmonary hypertension.
Muffled heart sounds and a globular heart on chest x-ray suggest a pericardial effusion and should prompt assessment for pulsus paradoxus (more than 10 mmHg fall in systolic blood pressure with inspiration).

Box 2-1. Common Precipitants of Heart Failure
Anemia
Dietary indiscretion
Hypertension
Hyperthyroidism
Infection, endocarditis
Medications (see Table 2-1)
Myocardial infarction
Myocarditis
Noncompliance with medications or fluid
restriction
Pregnancy
Pulmonary embolism
Tachyarrhythmias or bradyarrhythmias
Adapted from Givertz MM, Colucci WS, Braunwald E. Clinical aspects of heart failure: pulmonary edema, high-output failure. In: Zipes DP, Libby P, Bonow RO, Braunwald E, editors.
Braunwald's Heart Disease: A Textbook of Cardiovascular Med icine, 7th ed. Philadelphia. WB Saunders; 2005.

3. Lungs

a. **Crackles**

The crackles (‘‘Velcro’’ sound) of HF are described as ‘‘wet’’ as compared to the ‘‘dry’’ crackles of pulmonary fibrosis, and are caused by air moving through fluid-filled airways. In mild HF, crackles will be limited to the lung bases.

Atelectasis also causes bibasilar crackles, but the crackles of atelectasis clear after several repeated inspirations. Crackles will be detected higher in the chest with worsening severity of HF. Crackles may be absent in patients with chronic HF even in the setting of elevated pulmonary capillary wedge pressure. Also, crackles may be difficult to hear in patients with emphysema or other coexisting pulmonary diseases.

b. **Pleural Effusion**

Pleural effusions in patients with HF usually do not require thoracentesis, and typically resolve with diuresis. Although effusions are classically transudative, diuretic therapy can cause the effusion to become exudative. In this setting, the traditional Light’s criteria used to differentiate transudative from exudative pleural effusions may be misleading and it may be more appropriate to use the pleural fluid/serum albumin gradient. A gradient >1.2 g/dL suggests that the effusion is likely due to HF.

c. **Wheezing**

Some patients with pulmonary edema develop wheezing. Potential mechanisms include reflex bronchoconstriction from elevation of pulmonary or bronchial vascular pressure, and decreased airway size from intraluminal edema and bronchial mucosal swelling.

4. Pitting Edema

Right-sided HF reduces venous return to the heart and causes pitting edema of the lower extremities. Because gravity plays an important role in the formation of edema, patients who are predominantly bed-bound may have very little lower extremity edema even when there is profound fluid overload. In these cases, the pitting edema may be detected at the sacrum or along the lower back. Peripheral edema may be absent in patients with chronic HF.

5. Cheyne-Stokes Respiration

Cheyne-Stokes respiration is a breathing disorder of sleep seen in almost one-half of HF patients with ejection fractions below 40%. Cheyne-Stokes breathing is characterized by a crescendo–decrescendo alteration in tidal volume separated by periods of apnea or hypopnea. The mechanisms for Cheyne-Stokes respiration are not fully understood, but may include increased central nervous system sensitivity to changes in arterial partial pressures of oxygen and carbon dioxide. Therapeutic options include medical optimization

of HF, nocturnal oxygen therapy, and nasal continuous positive airway pressure.

6. Other Findings

Other findings of right-sided HF include hepatosplenomegaly, ascites, and imaging evidence of bowel wall edema (which may affect medication absorption). Other findings of left-sided HF and poor cardiac output include mental obtundation, cool skin, and cachexia.

LABORATORY DATA

Initial laboratory testing should include:

1. Electrolytes, blood urea nitrogen, creatinine, and complete blood count (with differential if infection is suspected)

2. PA and lateral chest x-ray

Classic chest x-ray findings of HF include:
a) Cardiomegaly—defined on chest x-ray as a ‘‘cardiothoracic ratio’’ (horizontal width of the heart divided by the widest internal diameter of the thorax) above 0.5
b) Large hila with indistinct vessel margins
c) Cephalization of flow—present when upper lobe vessels in an upright patient are larger than the lower lobe vessels at approximately the same distance from the hilum (normally, the upper lobe vessels are smaller than the lower lobe vessels because gravity directs most blood flow to the lung bases). Cephalization of flow implies elevated left heart pressures.
d) Pleural effusions
e) Kerley B lines—imply interstitial edema and occur when fluid thickens the interlobular septa, causing short lines to appear perpendicular to the pleural surface
f) Alveolar edema
g) Peribronchial cuffing—develops when fluid extravasates from peri-bronchial vessels and outlines the bronchi. The bronchi appear as dark circles surrounded by a water-dense ring.

h) Fluid in the interlobar fissures

Many of these findings may be obscured or distorted if there is underlying lung disease. Findings may be absent in patients with chronic HF who have longstanding elevations in pulmonary capillary wedge pressure

3. Electrocardiography

Electrocardiography (ECG) may demonstrate abnormal cardiac rhythm, ischemia, prior evidence of myocardial infarction, or left ventricular hypertrophy.

4. B-type Natriuretic Peptide

B-type natriuretic peptide (BNP) is primarily produced in the ventricles in response to ventricular strain or stretch. This hormone has shown initial promise in rapidly differentiating HF from lung disease in patients presenting to the emergency department with acute dyspnea.
BNP levels <50 pg/mL may have a negative predictive value for HF as high as 96% (i.e., the probability of not having HF given a BNP <50 pg/ml is 96%). Therefore, HF is an unlikely cause of dyspnea in an untreated patient with normal BNP levels, and echocardiography may be unnecessary in this setting.

5. Echocardiography

Findings on history, physical examination, the ECG, and chest x-ray occur with similar frequencies in both systolic and diastolic HF. Therefore, these symptoms and signs cannot be used to reliably differentiate systolic HF from diastolic HF. For this reason, two-dimensional, M-mode echocardiography should be obtained in all patients presenting with HF unless this test has been performed recently and there has been no interval change in the patient's medical history. Echocardiography provides useful information about the left ventricular ejection fraction, valvular dysfunction, regional wall motion abnormalities, ventricular hypertrophy, pericardial disease, and pulmonary hypertension. Echocardiography may also diagnose a dilated (4-chamber enlargement) or restrictive (''starry sky'') cardiomyopathy or diastolic dysfunction. Echocardiographic evidence for diastolic HF includes normal systolic function and reversal of the ''E to A'' ratio. The E wave refers to the peak velocity of blood flow across the mitral valve during early diastolic filling. The A wave corresponds to peak velocity of blood flow across the mitral valve during atrial contraction. Normally, the E-wave velocity is greater than the A-wave velocity, and the E to A ratio is approximately 1.5. In early diastolic dysfunction, the stiff heart relaxes slowly. In this setting, atrial contraction contributes relatively more to ventricular filling and there is reversal of the E to A ratio (<1.0). In patients with severe diastolic dysfunction, the very high end-diastolic left ventricular pressures

significantly limit the contribution of atrial contraction to left ventricular filling and the E to A ratio rises again, often to greater than 2.0.

CARDIAC CATHETERIZATION

Cardiac catheterization is usually performed when there is no obvious cause for the HF or when myocardial ischemia is suspected (for example, when patients describe angina or if there is objective evidence of myocardial infarction). Cardiac catheterization can also demonstrate impaired ventricular relaxation and filling by providing a direct measurement of ventricular diastolic pressure.

TREATMENT

Medications

(Table 2-3)

Table 2-3. Medications for Treating Heart Failure

Medication Class	Comments
Diuretics	Use early in the course of treatment. Use intravenous route initially.
Angiotensin-converting enzyme (ACE) inhibitors	Monitor for hyperkalemia. Use with caution if there is coexisting renal insufficiency. May cause cough. Preferred over angiotensin receptor blockers (ARBs).
Angiotensin receptor blockers	Monitor for hyperkalemia. Use with caution if there is coexisting renal insufficiency. Do not cause cough.
Beta-blockers	Start with low dose and titrate slowly. Do not initiate in the setting of acute heart failure.Reduce the beta-blocker dose during a heart failure exacerbation.
Digoxin	Improves symptoms and reduces hospitalizations but does not reduce mortality.
Aldosterone antagonists	Monitor for hyperkalemia. Eplerenone has fewer side effects than spironolactone (gynecomastia).
Hydralazine and nitrates	Reduce mortality but effect is not as large as for ACE inhibitors. Use only if patient is intolerant of ACE inhibitors and ARBs.

Medical Therapy for Diastolic Heart Failure

Clinical trials testing medications for the treatment of diastolic HF are limited. ACE inhibitors and ARBs may improve exercise capacity and reduce hospitalizations for diastolic HF. Diuretics are appropriate for volume management, but these medications should be used with caution because patients with diastolic dysfunction are sensitive to excessive preload reduction. In patients with diastolic dysfunction and atrial fibrillation or other tachyarrhythmias, beta-blockers or non-dihydropyridine calcium channel blockers can be used to slow the heart rate and lengthen diastole so that the ventricle has a longer filling time.

Hospital Discharge Instructions

Prior to hospital discharge, patients should be educated about dietary salt and fluid restriction and should be instructed to weigh themselves daily on the same scale. The home furosemide dose should be doubled if the weight increases by 2 lb over the course of 1 day. The patient should call his/her physician if the weight increases by 5 lb or if clinical signs develop, such as a change in the number of pillows needed to sleep, reduced exercise tolerance, or peripheral edema.

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