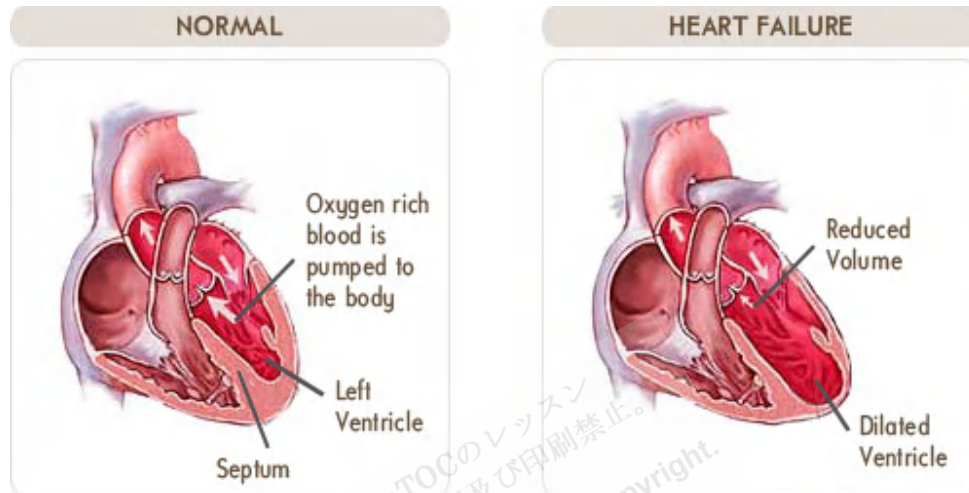


Heart Failure

Heart Failure (HF)(Congestive Heart Failure)



<http://www.terumoheart.com/images/uploads/heart-failure.jpg>

*Heart failure (HF) is a syndrome of **ventricular dysfunction**. **Left ventricular failure** causes shortness of breath and fatigue, and **right ventricular failure** causes peripheral and abdominal fluid accumulation; the ventricles can be involved together or separately. Diagnosis is initially clinical, supported by chest x-ray, **echocardiography**, and levels of **plasma natriuretic peptides**. Treatment includes diuretics, ACE inhibitors, angiotensin II receptor blockers, β -blockers, aldosterone antagonists, digitalis, specialized implantable pacemakers, and correction of the underlying disorder.*

HF affects about 5 million people in the US; > 500,000 new cases occur each year.

Physiology

Cardiac contractility (force and velocity of contraction), **ventricular performance**, and **myocardial O₂** requirements are determined by preload, afterload, substrate availability (eg, **O₂**, **fatty acids**, **glucose**), heart rate and rhythm, and amount of viable **myocardium**. **Cardiac output** (CO) is the product of stroke volume and heart rate; it is also affected by **venous return**, **peripheral vascular tone**, and **neurohumoral** factors.

Preload is the loading condition of the heart at the end of its relaxation phase (**diastole**) just before contraction (**systole**). Preload represents the degree of end-diastolic fiber stretch and end-diastolic volume, which is influenced by ventricular diastolic pressure and the composition of the myocardial wall. Typically, left ventricular (LV) end-diastolic pressure, especially if higher than normal, is a reasonable measure of preload. **LV**

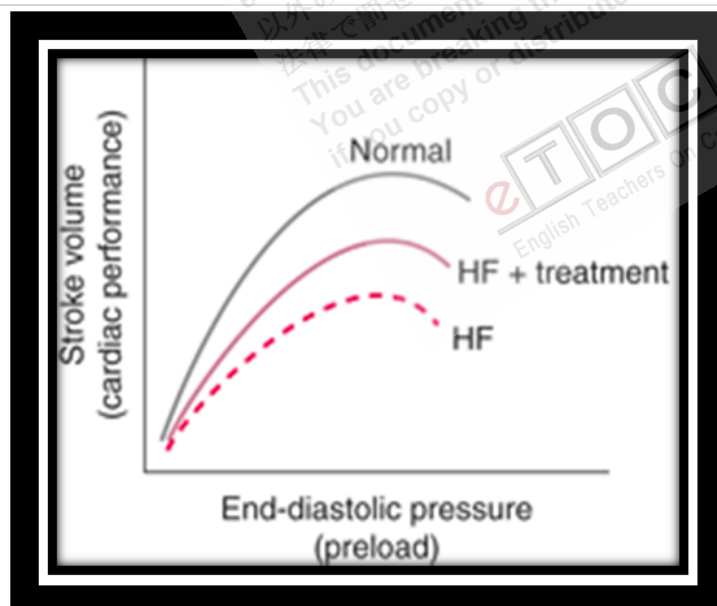
dilation, **hypertrophy**, and changes in **myocardial distensibility** (compliance) modify preload.

Afterload is the force resisting **myocardial fiber contraction** at the start of **systole**; it is determined by chamber pressure, volume, and wall thickness at the time the **aortic valve** opens. Clinically, systemic systolic BP at or shortly after the aortic valve opens represents peak **systolic wall stress** and approximates afterload.

The **Frank-Starling principle** describes the relationship between **preload** and **cardiac performance**. It states that, normally, **systolic contractile performance** (represented by stroke volume or CO) is proportional to preload within the normal physiologic range. Contractility is difficult to measure without cardiac **catheterization** but is reasonably reflected by the ejection fraction (EF), which is the percentage of end-diastolic volume ejected with each contraction (LV stroke volume/end-diastolic volume); contractility can generally be adequately assessed noninvasively with echocardiography.

Fig. 1

Frank-Starling principle.



Normally (top curve), as preload increases, cardiac performance also increases. However at a certain point, performance plateaus, then declines. In heart failure (HF) due to systolic dysfunction (bottom curve), the overall curve shifts downward, reflecting

reduced cardiac performance at a given preload, and as preload increases, cardiac performance increases less. With treatment (middle curve), performance is improved, although not normalized.

Cardiac reserve is the ability of the heart to increase its performance above resting levels in response to emotional or physical stress; body O₂ consumption may increase from 250 to ≥1500 mL/min during maximal exertion. Mechanisms include increasing heart rate, **systolic** and **diastolic volume**, **stroke volume**, and **tissue extraction** of O₂ (the difference between O₂ content in arterial blood and mixed venous or **pulmonary artery blood**). In well-trained young adults during maximal exercise, heart rate may increase from 55 to 70 beats/min at rest to 180 beats/min, and CO may increase from 6 to ≥ 25 L/min. At rest, arterial blood contains about 18 mL O₂/dL of blood, and mixed venous or pulmonary artery blood contains about 14 mL/dL. O₂ extraction is thus about 4 mL/dL, but when demand is increased, it may increase to 12 to 14 mL/dL. This mechanism also helps compensate for reduced tissue blood flow in HF.

Pathophysiology

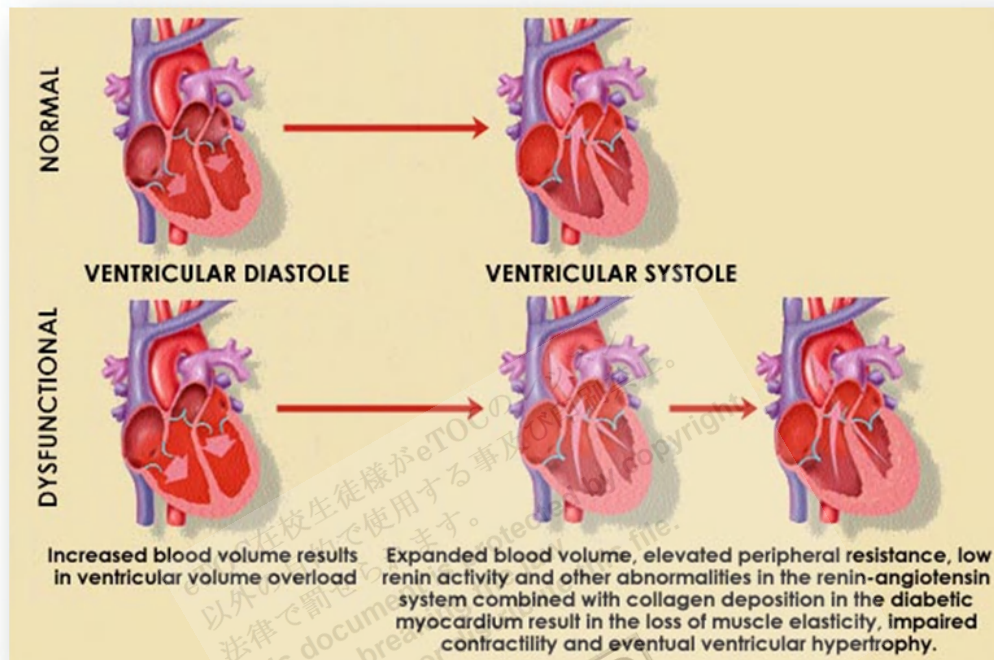
In HF, the heart may not provide tissues with adequate blood for metabolic needs, and cardiac-related elevation of **pulmonary** or **systemic venous pressures** may result in organ congestion. This condition can result from abnormalities of systolic or diastolic function or, commonly, both. Although a primary abnormality may be a change in **myocyte function**, there are also changes in collagen turnover of the **extracellular matrix**. Cardiac structural defects (eg, **congenital defects, valvular disorders**), rhythm abnormalities (including persistently high heart rate), and high metabolic demands (eg, from **thyrotoxicosis**) also can cause HF.

Systolic dysfunction: In **systolic dysfunction**, the **ventricle** contracts poorly and empties inadequately, leading initially to increased diastolic volume and pressure and decreased EF. Many defects in energy utilization, energy supply, **electrophysiologic** functions, and contractile element interaction occur, with abnormalities in intracellular Ca modulation and cAMP production.

Predominant systolic dysfunction is common in HF due to **MI**, **myocarditis**, and **dilated cardiomyopathy**. Systolic dysfunction may affect primarily the LV or the right ventricle (RV); LV failure often leads to RV failure.

Diastolic dysfunction: In **diastolic dysfunction** (also called HF with preserved systolic function or HF with preserved/normal EF), **ventricular filling** is impaired, resulting in reduced **ventricular end-diastolic volume**, increased **end-diastolic**

pressure, or both. Contractility and hence EF remain normal; EF may even increase as the poorly filled LV empties more completely to maintain CO. Markedly reduced LV filling can cause low CO and systemic symptoms. Elevated left **atrial pressures** can cause **pulmonary hypertension** and **pulmonary congestion**.



<http://sleepapneadisorder.info/wp-content/uploads/2010/07/Left-Ventricular-Diastolic-Dysfunction.jpg>

Diastolic dysfunction usually results from impaired **ventricular relaxation** (an active process), increased ventricular stiffness, **valvular disease**, or constrictive **pericarditis**. Acute **myocardial ischemia** is also a cause of diastolic dysfunction. Resistance to filling increases with age, probably reflecting myocyte loss and increased interstitial collagen deposition; thus, **diastolic dysfunction** is particularly common among the elderly. Diastolic dysfunction predominates in **hypertrophic cardiomyopathy**, disorders with ventricular hypertrophy (eg, **hypertension**, **significant aortic stenosis**), and **amyloid infiltration** of the **myocardium**. LV filling and function may also be impaired if marked increases in RV pressure shift the **interventricular septum** to the left.

Diastolic dysfunction is increasingly being recognized as a cause of HF. Estimates vary, but about 50% of patients with HF have diastolic dysfunction and a normal EF; the prevalence increases with age.

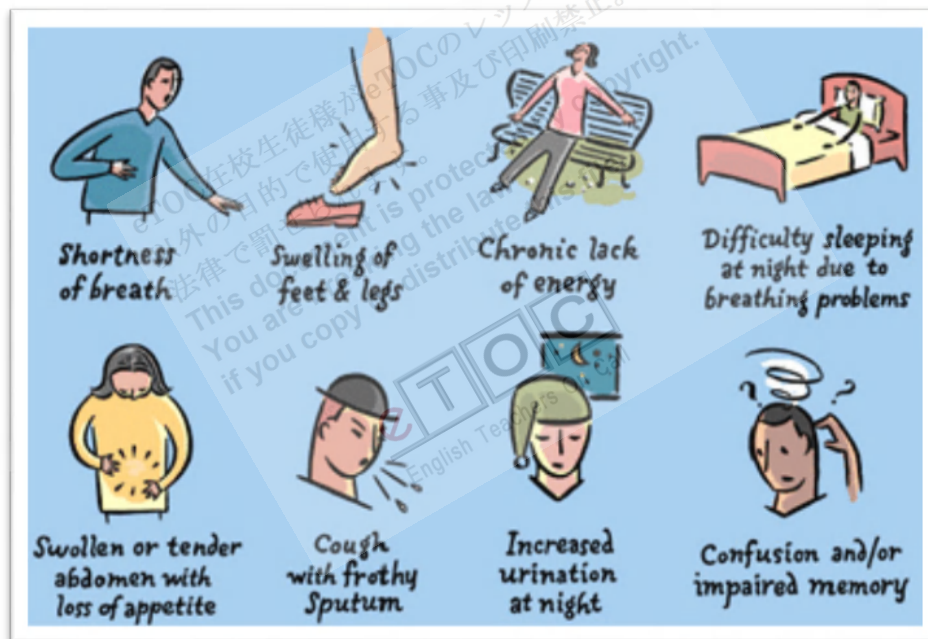
LV failure: In failure due to LV dysfunction, CO decreases and **pulmonary venous pressure** increases. When **pulmonary capillary pressure** exceeds the **oncotic pressure** of plasma proteins (about 24 mm Hg), fluid extravasates from the **capillaries** into the interstitial space and **alveoli**, reducing **pulmonary compliance** and increasing the work of breathing. **Lymphatic drainage** increases but cannot compensate for the increase in pulmonary fluid. Marked fluid accumulation in alveoli (pulmonary edema) significantly alters ventilation-perfusion (V/Q) relationships: **Deoxygenated pulmonary arterial blood** passes through poorly ventilated alveoli, decreasing systemic arterial oxygenation (PaO_2) and causing dyspnea. However, dyspnea may occur before V/Q abnormalities, probably because of elevated pulmonary venous pressure and increased work of breathing; the precise mechanism is unclear. In severe or chronic LV failure, pleural effusions characteristically develop in the right **hemithorax** and later bilaterally, further aggravating dyspnea. Minute ventilation increases; thus, PaCO_2 decreases and blood pH increases (**respiratory alkalosis**). Marked interstitial edema of the small airways may interfere with ventilation, elevating PaCO_2 —a sign of impending respiratory failure.

RV failure: In failure due to **RV dysfunction**, **systemic venous pressure** increases, causing fluid extravasation and consequent edema, primarily in dependent tissues (feet and ankles of ambulatory patients) and abdominal viscera. The liver is affected most, but the stomach and intestine also become congested; fluid accumulation in the peritoneal cavity (ascites) can occur. RV failure commonly causes moderate hepatic dysfunction, with usually modest increases in conjugated and unconjugated **bilirubin**, PT, and **hepatic enzymes** (eg, alkaline phosphatase, AST, ALT). The impaired liver breaks down less aldosterone, further contributing to fluid accumulation. Chronic venous congestion in the **viscera** can cause **anorexia**, **malabsorption** of nutrients and drugs, **protein-losing enteropathy** (characterized by diarrhea and marked **hypoalbuminemia**), chronic GI blood loss, and rarely **ischemic bowel infarction**.

Cardiac response: If ventricular function is impaired, a higher preload is required to maintain CO. As a result, the ventricles are remodeled over time: The LV becomes less **ovoid** and more **spherical**, **dilates**, and **hypertrophies**; the RV dilates and may hypertrophy. Initially compensatory, these changes eventually increase diastolic stiffness and wall tension (ie, diastolic dysfunction develops), compromising cardiac performance, especially during physical stress. Increased wall stress raises O_2 demand and accelerates **apoptosis** (programmed cell death) of **myocardial cells**. Dilatation of the **ventricles** can also cause **mitral** or **tricuspid valve regurgitation** with further increases in **end-diastolic volumes**.

Hemodynamic responses: With reduced CO, tissue O₂ delivery is maintained by increasing O₂ extraction and sometimes shifting the **oxyhemoglobin** dissociation curve to the right to favor O₂ release.

Reduced CO with lower systemic BP activates **arterial baroreflexes**, increasing sympathetic tone and decreasing **parasympathetic tone**. As a result, heart rate and **myocardial contractility** increase, **arterioles** in selected **vascular beds** constrict, **venoconstriction** occurs, and Na and water are retained. These changes compensate for reduced **ventricular performance** and help maintain **hemodynamic homeostasis** in the early stages of HF. However, these compensatory changes increase cardiac work, preload, and afterload; reduce **coronary** and **renal perfusion**; cause fluid accumulation resulting in congestion; increase K excretion; and may cause **myocyte necrosis** and **arrhythmias**.



<http://1.bp.blogspot.com/-Rq6t3eTS4KU/UDz9X1so2DI/AAAAAAAAA88/DWgi-KpQ68/s1600/Heart-failure-Symptoms.gif>

Renal responses: As cardiac function deteriorates, renal blood flow and GFR decrease, and blood flow within the kidneys is redistributed. The filtration fraction and filtered Na decrease, but **tubular resorption** increases, leading to Na and water retention. Blood flow is further redistributed away from the kidneys during exercise, but renal blood flow improves during rest, possibly contributing to **nocturia**.

Decreased perfusion of the kidneys (and possibly decreased **arterial systolic** stretch secondary to declining ventricular function) activates the **renin-angiotensin-**

aldosterone system, increasing Na and water retention and renal and **peripheral vascular tone**. These effects are amplified by the intense **sympathetic activation accompanying HF**.

The **renin-angiotensin-aldosterone-vasopressin** (antidiuretic hormone [ADH]) system causes a cascade of potentially deleterious long-term effects. **Angiotensin II** worsens HF by causing **vasoconstriction**, including efferent renal vasoconstriction, and by increasing aldosterone production, which not only enhances Na reabsorption in the **distal nephron** but also causes **myocardial** and **vascular collagen deposition** and fibrosis. Angiotensin II increases **norepinephrine** release, stimulates release of ADH, and triggers apoptosis. Angiotensin II may be involved in vascular and myocardial hypertrophy, thus contributing to the remodeling of the heart and peripheral **vasculature**, potentially worsening HF. **Aldosterone** can be synthesized in the heart and vasculature independently of angiotensin II (perhaps mediated by **corticotropin**, **nitric oxide**, **free radicals**, and other stimuli) and may have deleterious effects in these organs.

HF that causes **progressive renal dysfunction** (including that renal dysfunction caused by drugs used to treat HF) contributes to worsening HF and has been termed the **cardiorenal syndrome**.

Neurohumoral responses: In conditions of stress, **neurohumoral** responses help increase heart function and maintain BP and **organ perfusion**, but chronic activation of these responses is detrimental to the normal balance between **myocardial-stimulating** and **vasoconstricting hormones** and between **myocardial-relaxing** and **vasodilating** hormones.

The heart contains many **neurohumoral receptors** (α_1 , β_1 , β_2 , β_3 , **angiotensin II type 1 [AT₁] and type 2 [AT₂]**, **muscarinic**, **endothelin**, **serotonin**, **adenosine**, **cytokine**); the role of these receptors is not yet fully defined. In patients with HF, β_1 receptors (which constitute 70% of cardiac β receptors) are **downregulated**, probably in response to intense sympathetic activation. The result of **downregulation** is impaired **myocyte contractility** and increased heart rate.

Plasma **norepinephrine** levels are increased, largely reflecting **sympathetic nerve stimulation** because plasma **epinephrine** levels are not increased. Detrimental effects include **vasoconstriction** with increased preload and afterload, direct **myocardial damage** including **apoptosis**, reduced **renal blood flow**, and activation of other **neurohumoral systems**, including the **renin-angiotensin-aldosterone-ADH** system.

ADH is released in response to a fall in BP via various **neurohormonal stimuli**. Increased ADH decreases **renal excretion** of free water, possibly contributing to **hyponatremia** in HF. ADH levels in HF with normal BP vary.

Atrial natriuretic peptide is released in response to increased atrial volume and pressure; brain (B-type) **natriuretic peptide** (BNP) is released from the **ventricle** in response to **ventricular stretching**. These peptides enhance renal excretion of Na, but in patients with HF, the effect is blunted by decreased renal perfusion pressure, receptor downregulation, and perhaps enhanced **enzymatic degradation**.

Because **endothelial dysfunction** occurs in HF, fewer **endogenous vasodilators** (eg, nitric oxide, prostaglandins) are produced, and more **endogenous vasoconstrictors** (eg, endothelin) are produced, thus increasing afterload.

The failing heart and other organs produce **tumor necrosis factor** (TNF)- α . This **cytokine** increases catabolism and is possibly responsible for **cardiac cachexia** (loss of lean tissue $\geq 10\%$), which may accompany severely symptomatic HF, and for other detrimental changes. The failing heart also undergoes metabolic changes with increased free fatty acid utilization and decreased glucose utilization; these changes may become therapeutic targets.



<http://photos2.demandstudios.com/DM->

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Changes with aging: Age-related changes in the heart and cardiovascular system lower the threshold for expression of HF. **Interstitial collagen** within the **myocardium** increases, the myocardium stiffens, and **myocardial relaxation** is prolonged. These changes lead to a significant reduction in diastolic LV function, even in healthy elderly people. Modest decline in **systolic function** also occurs with aging. An age-related decrease in myocardial and vascular responsiveness to **β -adrenergic stimulation** further impairs the ability of the cardiovascular system to respond to increased work demands.

As a result of these changes, peak exercise capacity decreases significantly (about 8%/decade after age 30), and CO at peak exercise decreases more modestly. This decline can be slowed by regular physical exercise. Thus, elderly patients are more prone than are younger ones to develop HF symptoms in response to the stress of systemic disorders or relatively modest cardiovascular insults. Stressors include infections (particularly pneumonia), **hyperthyroidism**, **anemia**, **hypertension**, **myocardial ischemia**, **hypoxia**, **hyperthermia**, **renal failure**, **perioperative IV fluid loads**, nonadherence to drug regimens or to low-salt diets, and use of certain drugs (including NSAIDs, β -blockers, and certain Ca channel blockers).

Etiology

Both cardiac and systemic factors can impair cardiac performance and cause or aggravate HF.

Table 1

Causes of Heart Failure	
Type	Examples
Cardiac	
Myocardial damage	MI Myocarditis Cardiomyopathy Some chemotherapy drugs
Valvular	Aortic stenosis

disorders	Mitral regurgitation
Arrhythmias	Bradyarrhythmias Tachyarrhythmias
Conduction defects	AV node block Left bundle branch block
Reduced substrate availability (eg, of free fatty acids or glucose)	Ischemia
Infiltrative or matrix disorders	Amyloidosis Chronic fibrosis Hemochromatosis
Systemic	
Disorders that increase demand for CO	Hyperthyroidism Paget's disease
Disorders that increase resistance to output (afterload)	Aortic stenosis Hypertension
AV = atrioventricular; CO = cardiac output.	

Classification

The traditional distinction of left and right ventricular failure is somewhat misleading because the heart is an integrated pump, and changes in one chamber ultimately affect

the whole heart. However, these terms indicate the major site of **pathology** leading to HF and can be useful for initial evaluation and treatment. Other common descriptive terms include acute or **chronic**; **congestive**; **high output** or **low output**; **systolic** or **diastolic**; **dilated** or **nondilated**; and **ischemic**, **hypertensive**, or **idiopathic dilated cardiomyopathy**.

LV failure characteristically develops in **ischemic heart disease**, **hypertension**, **mitral** or aortic **valvular regurgitation**, **aortic stenosis**, most forms of **cardiomyopathy**, and congenital heart disorders (eg, ventricular septal defect or patent **ductus arteriosus** with large shunts).

RV failure is most commonly caused by previous **LV failure** (which increases **pulmonary venous pressure** and leads to **pulmonary arterial hypertension**, thus overloading the RV) or by a severe lung disorder (when it is called **cor pulmonale**). Other causes are multiple **pulmonary emboli**, **RV infarction**, **primary pulmonary hypertension**, **tricuspid regurgitation** or **stenosis**, **mitral stenosis**, **pulmonary artery** or **valve stenosis**, **pulmonary venous occlusive disease**, or **congenital disorders** such as **Ebstein's anomaly** or **Eisenmenger's syndrome**. Some conditions mimic RV failure, except cardiac function may be normal; they include volume overload and increased **systemic venous pressure** in **polycythemia** or **overtransfusion**, **acute renal failure** with retention of Na and water, obstruction of either **vena cava**, and **hypoproteinemia** from any cause resulting in low **plasma oncotic pressure** and **peripheral edema**.

Biventricular failure results from disorders that affect the whole **myocardium** (eg, viral myocarditis, amyloidosis, Chagas disease) or long-standing LV failure causing RV failure.

High-output HF results from a persistently high CO, which may eventually result in an inability of a normal heart to maintain adequate output. Conditions that may increase CO include severe **anemia**, **beriberi**, **thyrotoxicosis**, **advanced Paget's disease**, **arteriovenous fistula**, and **persistent tachycardia**. CO is high in various forms of **cirrhosis**, but much of the observed fluid retention is due to **hepatic mechanisms**.

Cardiomyopathy is a general term reflecting disease of the **myocardium**. Most commonly, the term refers to a primary disorder of the **ventricular myocardium** that is not caused by **congenital anatomic defects**; **valvular**, **systemic**, or **pulmonary vascular disorders**; **isolated pericardial**, **nodal**, or **conduction system disorders**; or **epicardial coronary artery disease** (CAD). The term is sometimes used to reflect

etiology (eg, **ischemic** vs **hypertensive cardiomyopathy**). Cardiomyopathy does not always lead to **symptomatic HF**. It is often idiopathic and is classified as **dilated congestive**, **hypertrophic**, **infiltrative-restrictive**, or **apical-ballooning cardiomyopathy**.

Symptoms and Signs

Manifestations differ depending on the extent to which the LV and RV are initially affected. Clinical severity varies significantly and is usually classified according to the New York Heart Association system; the examples of ordinary activity may be modified for elderly, debilitated patients. Severe LV failure may cause **pulmonary edema** or **cardiogenic shock**.

Table 2

New York Heart Association (NYHA) Classification of Heart Failure			
NYHA Class	Definition	Limitation	Example
I	Ordinary physical activity does not cause undue fatigue, dyspnea, or palpitations.	None	Can complete any activity requiring ≤ 7 MET: <ul style="list-style-type: none"> • Carry 11 kg up 8 steps • Carry objects weighing 36 kg • Shovel snow • Spade soil • Ski • Play squash, handball, or basketball • Jog or walk 8 km/h
II	Ordinary physical activity causes fatigue, dyspnea, palpitations, or angina.	Slight	Can complete any activity requiring ≤ 5 MET: <ul style="list-style-type: none"> • Sexual intercourse without stopping • Garden

- Roller skate
- Walk 7 km/h on level ground
- Climb one flight stairs at a normal pace without symptoms

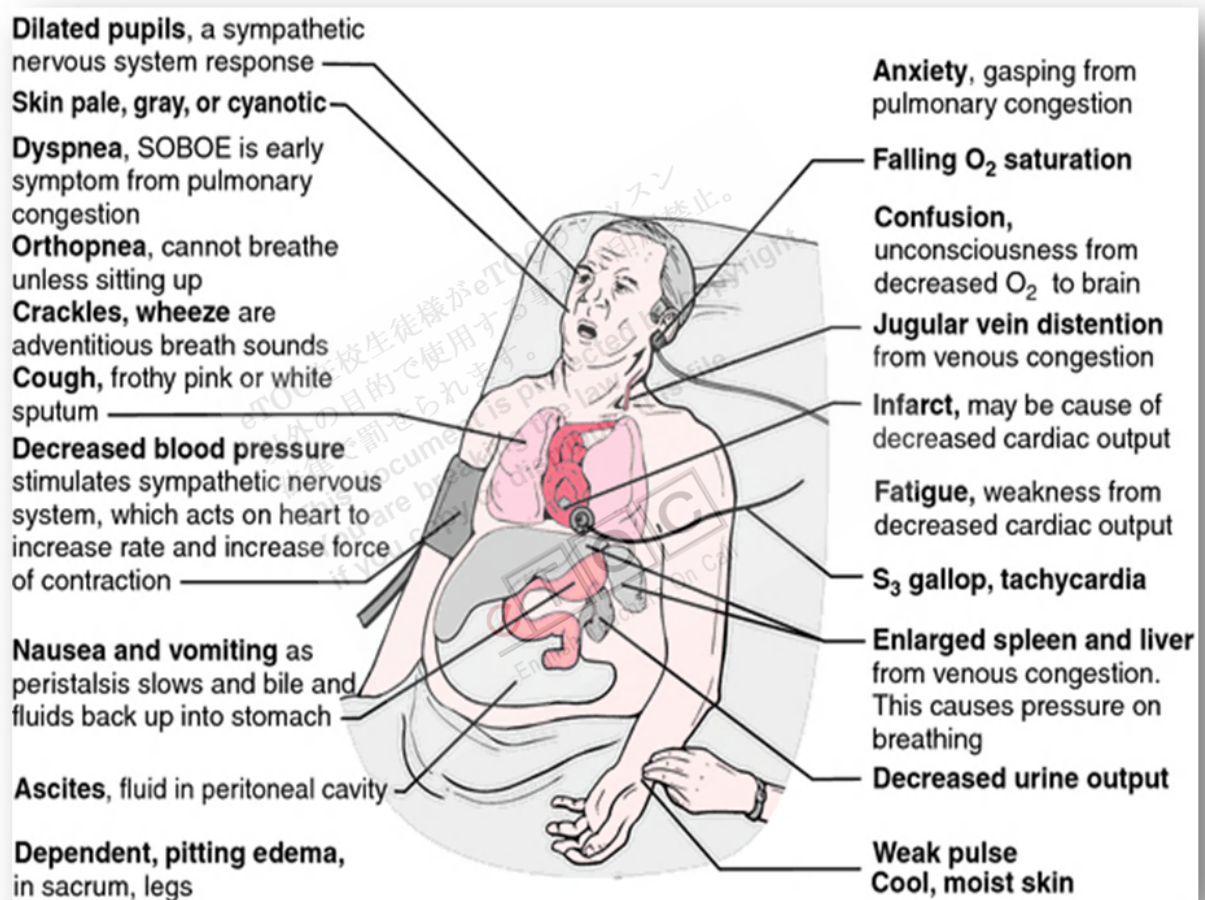
III	Comfortable at rest; less than ordinary physical activity causes fatigue, dyspnea, palpitations, or angina.	Moderate	Can complete any activity requiring ≤ 2 MET: <ul style="list-style-type: none"> • Shower or dress without stopping • Strip and make a bed • Clean windows • Play golf • Walk 4 km/h
IV	Symptoms occur at rest; any physical activity increases discomfort.	Severe	Cannot do or cannot complete any activity requiring ≥ 2 MET; cannot do any of the above activities

MET = metabolic equivalent task.

History: In LV failure, the most common symptoms are **dyspnea**, reflecting **pulmonary congestion**, and fatigue, reflecting low CO. Dyspnea usually occurs during exertion and is relieved by rest. As HF worsens, dyspnea can occur during rest and at night, sometimes causing **nocturnal cough**. Dyspnea occurring immediately or soon after lying flat and relieved promptly by sitting up (**orthopnea**) is common as HF advances. In **paroxysmal nocturnal dyspnea** (PND), dyspnea awakens patients several hours after they lie down and is relieved only after they sit up for 15 to 20 min. In severe HF, periodic cycling of breathing (**Cheyne-Stokes respiration**—a brief period of increased breathing [**hyperpnea**] followed by a brief period of no breathing [**apnea**])—can occur during the day or night; the sudden **hyperpneic phase** may awaken the patient from sleep. This breathing differs from PND in that the hyperpneic phase is short, lasting only a few seconds and resolving in < 1 min. PND is associated with pulmonary congestion, and **Cheyne-Stokes** respiration with low CO. **Sleep-related breathing**

disorders, such as **sleep apnea**, are common in HF and may aggravate HF. Severely reduced **cerebral blood flow** and **hypoxemia** can cause **chronic irritability** and impair mental performance.

In RV failure, the most common symptoms are ankle swelling and fatigue. Sometimes patients feel a sensation of fullness in the abdomen or neck. **Hepatic congestion** can cause **right upper quadrant abdominal discomfort**, and stomach and intestinal congestion can cause anorexia and abdominal bloating.



<http://img2.tfd.com/mk/H/X2604-H-14.png>

Less specific HF symptoms include **cool peripheries**, **postural light-headedness**, **nocturia**, and decreased **daytime micturition**. Skeletal muscle wasting can occur in severe **biventricular failure** and may reflect some disuse but also increased **catabolism** associated with increased **cytokine production**. Significant weight loss (**cardiac cachexia**) is an ominous sign associated with high mortality.

In the elderly, presenting complaints may be atypical, such as **confusion**, **delirium**, **falls**, **sudden functional decline**, **nocturnal urinary incontinence**, or **sleep disturbance**. Coexisting cognitive impairment and depression may also influence assessment and therapeutic interventions and may be worsened by the HF.

Examination: General examination may detect signs of systemic disorders that cause or aggravate HF (eg, **anemia**, **hyperthyroidism**, **alcoholism**, **hemochromatosis**).

In **LV failure**, **tachycardia** and **tachypnea** may occur. Patients with severe LV failure may appear visibly **dyspneic** or **cyanotic**, **hypotensive**, and **confused** or **agitated** because of **hypoxia** and **poor cerebral perfusion**. Some of these less specific symptoms (eg, confusion) are more common in the elderly.

Central cyanosis (affecting all of the body, including warm areas such as the tongue and **mucous membranes**) reflects severe **hypoxemia**. Peripheral **cyanosis** of the lips, fingers, and toes reflects low blood flow with increased O₂ extraction. If vigorous massage improves nail bed color, **cyanosis** may be peripheral; increasing local blood flow does not improve color if cyanosis is central.

Cardiac findings in **LV systolic dysfunction** include a diffuse, sustained, and laterally **displaced apical impulse**; audible and occasionally palpable 3rd (S₃) and 4th (S₄) heart sounds, and an **accentuated pulmonic component** (P₂) of the 2nd heart sound (S₂). A **pansystolic murmur** of **mitral regurgitation** at the apex may occur. Pulmonary findings include inspiratory **basilar crackles** that do not clear with coughing and, if **pleural effusion** is present, dullness to percussion and diminished breath sounds at lung bases.

Signs of RV failure include nontender peripheral pitting edema (digital pressure leaves visible and palpable imprints, sometimes quite deep) in the feet and ankles; an enlarged and sometimes pulsatile liver palpable below the right costal margin; abdominal swelling and ascites; and visible elevation of the jugular venous pressure, sometimes with large *a* or **vwaves** that are visible even when the patient is seated or standing. In severe cases, peripheral edema can extend to the thighs or even the sacrum, scrotum, lower abdominal wall, and occasionally even higher. Severe edema in multiple areas is termed **anasarca**. **Edema** may be asymmetric if patients lie predominantly on one side.

With **hepatic congestion**, the liver may be palpably enlarged or tender, and **hepatojugular** or **abdominal-jugular reflux** may be detected. Precordial palpation may detect the left parasternal lift of RV enlargement, and auscultation may detect the

murmur of **tricuspid regurgitation** or the RV S₃ along the left sternal border; both findings are augmented upon inspiration.

Diagnosis

- Sometimes only clinical evaluation
- Chest x-ray
- **Echocardiography**
- Sometimes **BNP** or **N-terminal-pro-BNP** (NT-pro-BNP) levels
- ECG and other tests for etiology as needed

Clinical findings (eg, **exertional dyspnea** or **fatigue**, **orthopnea**, **edema**, **tachycardia**, **pulmonary crackles**, **S₃**, **jugular venous distention**) suggest HF but are not apparent early. Similar symptoms may result from COPD or recurrent pneumonia or may be erroneously attributed to obesity or old age. Suspicion for HF should be high in patients with a history of MI, hypertension, or **valvular disorders** or **murmurs** and should be moderate in any elderly or diabetic patient.

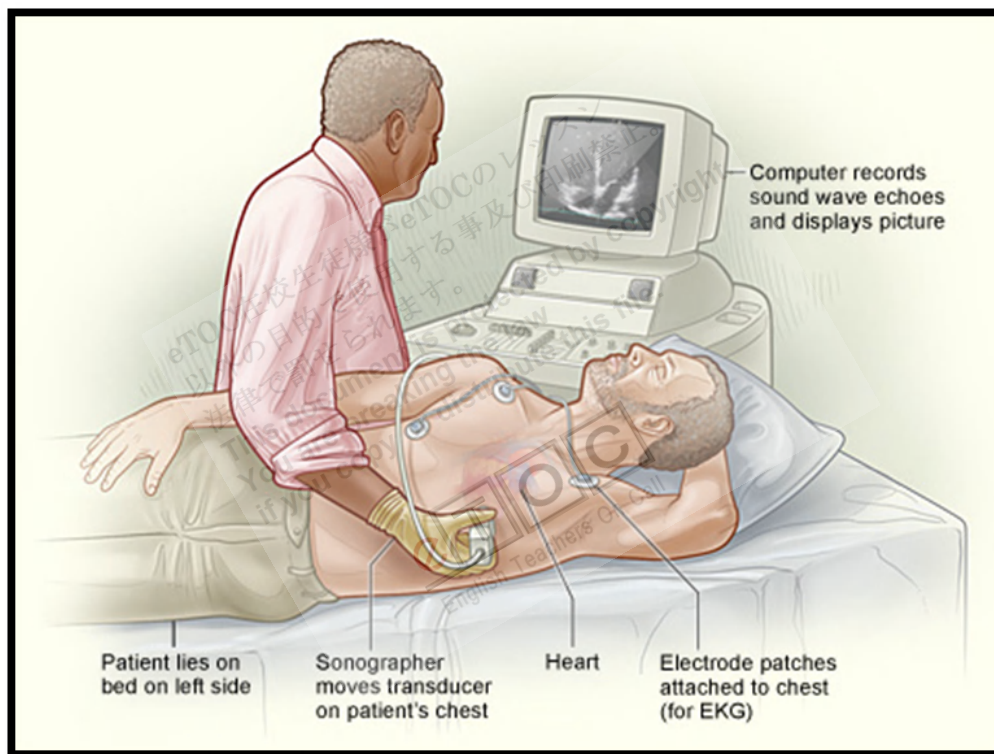
Chest x-ray, ECG, and an objective test of cardiac function, typically echocardiography, should be done. Blood tests, except for BNP levels, are not used for diagnosis but are useful for identifying cause and systemic effects.

Chest x-ray: Chest x-ray findings suggesting HF include an enlarged **cardiac silhouette**, **pleural effusion**, fluid in the **major fissure**, and horizontal lines in the periphery of lower **posterior lung fields** (Kerley B lines). These findings reflect chronic elevation of left atrial pressure and **chronic thickening** of the **intraalveolar septa** due to **edema**. **Upper lobe pulmonary venous congestion** and **interstitial** or **alveolar edema** may also be present. Careful examination of the cardiac silhouette on a lateral projection can identify specific ventricular and **atrial chamber enlargement**. The x-ray may also suggest alternative diagnoses (eg, **COPD**, **pneumonia**, **interstitial pulmonary fibrosis**, **lung cancer**).

ECG: ECG findings are not diagnostic, but an abnormal ECG, especially showing previous **MI**, **LV hypertrophy**, **left bundle branch block**, or **tachyarrhythmia** (eg, **rapid atrial fibrillation**), increases suspicion for HF and may help identify the cause. An entirely normal ECG is uncommon in chronic HF.

Imaging: Echocardiography can help evaluate chamber dimensions, valve function, **EF**, **wall motion abnormalities**, **LV hypertrophy**, and **pericardial effusion**. **Intracardiac thrombi**, **tumors**, and **calcifications** within the **heart valves**, **mitral annulus**, and

aortic wall abnormalities can be detected. Localized or segmental **wall motion abnormalities** strongly suggest underlying CAD but can also be present with **patchy myocarditis**. **Doppler** or **color Doppler echocardiography** accurately detects **valvular disorders** and **shunts**. Doppler studies of **mitral** and **pulmonary venous inflow** often help identify and quantify LV **diastolic dysfunction**; tissue Doppler imaging is more accurate. Measuring LVEF can distinguish between predominant diastolic dysfunction (EF > 0.50) and systolic dysfunction (EF < 0.40). It is important to re-emphasize that HF can occur with a normal LVEF. **Three-dimensional echocardiography** may become important but currently is available only in specialized centers.



http://www.nhlbi.nih.gov/health/health-topics/images/echo_setup.jpg

Radionuclide imaging also can help assess **systolic** and **diastolic function**, previous **MI**, and **inducible ischemia** or **myocardial hibernation**. Cardiac MRI provides accurate images of cardiac structures and is becoming more widely available. In many centers, multimode imaging (eg, **stress MIBI** [**thallium** and **sestamibi stress tests**] plus CT **angiography**) is becoming common, although there is growing concern about the **radiation dose** with **CT angiography**.

Blood tests: **Serum BNP** levels are high in HF; this finding may help when clinical findings are unclear or other diagnoses (eg, COPD) need to be excluded. It may be particularly useful for patients with a history of both **pulmonary** and **cardiac disorders**. **NT-pro-BNP**, an inactive moiety created when pro **BNP** is cleaved, can be used similarly.

Recommended blood tests include **CBC, creatinine, BUN, electrolytes** (including Mg and Ca), **glucose, albumin**, and **liver function tests**. **Thyroid function tests** are recommended for patients with atrial fibrillation and for selected, especially elderly, patients.

Other tests: **Coronary angiography** is indicated when CAD is suspected or the etiology of HF is uncertain. **Cardiac catheterization** with **intracardiac pressure** measurements may be helpful in the diagnosis of **restrictive cardiomyopathies** and **constrictive pericarditis**.

Endocardial biopsy is sometimes done when an **infiltrative cardiomyopathy** is strongly suspected but cannot be confirmed with noninvasive imaging (eg, cardiac MRI).

Prognosis

Generally, patients with HF have a poor **prognosis** unless the cause is correctable. Mortality rate at 1 yr from first hospitalization for HF is about 30%. In chronic HF, mortality depends on severity of symptoms and **ventricular dysfunction** and can range from 10 to 40%/yr. Specific factors that suggest a poor prognosis include **hypotension, low EF, presence of CAD, troponin release, elevation of BUN, reduced GFR, hyponatremia**, and **poor functional capacity** (eg, as tested by a 6-min walk test).

HF usually involves gradual deterioration, interrupted by bouts of severe **decompensation**, and ultimately death, although the time course is being lengthened with modern therapies. However, death can also be sudden and unexpected, without prior worsening of symptoms.

End-of-life care: All patients and family members should be taught about disease progression. For some patients, improving quality of life is as important as increasing quantity of life. Thus, it is important to determine patients' wishes about **resuscitation** (eg, endotracheal intubation, CPR) if their condition deteriorates, especially when HF is already severe. All patients should be reassured that symptoms will be relieved, and they should be encouraged to seek medical attention early if their symptoms change significantly. Involvement of pharmacists, nurses, social workers, and clergy, who may

be part of an **interdisciplinary team** or **disease management program** already in place, is particularly important in **end-of-life care**.

Treatment

- Diet and lifestyle changes
- Treatment of cause
- Drugs (numerous classes)
- Sometimes device therapy (eg, implantable cardioverter-defibrillator, biventricular pacing)
- Multidisciplinary care



<http://3.bp.blogspot.com/PX0prAHl0hg/TMAe0U1L8XI/AAAAAAAAAns/oaELNOi7m4k/s1600/lifestyle+change.jpg>

Immediate inpatient treatment is required for patients with acute or worsening HF due to certain disorders (eg, **acute MI**, **atrial fibrillation** with a very **rapid ventricular rate**, **severe hypertension**, **acute valvular regurgitation**), as well as for patients with **pulmonary edema**, **severe symptoms**, **new-onset HF**, or **HF** unresponsive to outpatient treatment. Patients with mild exacerbations of previously diagnosed HF can be treated at home.

The primary goal is to diagnose and to correct or treat the disorder that led to HF.

Short-term goals include relieving symptoms and improving **hemodynamics**; avoiding **hypokalemia**, **renal dysfunction**, and **symptomatic hypotension**; and correcting **neurohumoral activation**.

Long-term goals include correcting **hypertension**, preventing **MI** and **atherosclerosis**, improving **cardiac function**, reducing **hospitalizations**, and improving survival and quality of life. Treatment involves dietary and lifestyle changes, drugs, devices, and sometimes **percutaneous coronary interventions** or surgery.

Treatment is tailored to the patient, considering causes, symptoms, and response to drugs, including adverse effects. Treatment of **systolic** and **diastolic dysfunction** has become more similar, although there are more evidence-based therapies for **systolic HF**.

General management: General measures, especially patient and caregiver education and diet and lifestyle modifications, are important for all HF patients.

- Education
- Na restriction
- Appropriate weight and fitness levels
- Correction of underlying conditions

Patient and caregiver education are critical to long-term success. The patient and family should be involved in treatment choices. They should be taught the importance of drug adherence, warning signs of decompensation, and how to link cause with effect (eg, increased salt in the diet with weight gain or symptoms).

Many centers (eg, specialized outpatient clinics) have integrated health care practitioners from different disciplines (eg, HF nurses, pharmacists, social workers, rehabilitation specialists) into multidisciplinary teams or outpatient HF management programs. These approaches can improve outcomes and reduce hospitalizations and are most effective in the sickest patients.



<http://schoolofbeinghealthy.com/wp-content/uploads/2009/07/Want-to-enjoy-good-health-change-your-lifestyle.jpg>

Dietary Na restriction helps limit **fluid retention**. All patients should eliminate salt in cooking and at the table and avoid salted foods; the most severely ill should limit Na to < 2 g/day by consuming only low-Na foods. Monitoring daily morning weight helps detect Na and water accumulation early. If weight increases > 2 kg over a few days, patients may be able to adjust their **diuretic dose** themselves, but if weight gain continues or symptoms occur, patients should seek medical attention. Intensive case management, particularly by monitoring drug adherence and frequency of unscheduled visits to the physician or emergency department and hospitalizations, can identify when intervention is needed. Specialized HF nurses are valuable in education, follow-up, and dosage adjustment according to predefined protocols.

Patients with **atherosclerosis** or **diabetes** should strictly follow a diet appropriate for their disorder. **Obesity** may cause and always aggravates the symptoms of HF; patients should attain a body mass index (BMI) of 21 to 25.

Regular light activity (eg, walking), tailored to symptoms, is generally encouraged. Activity prevents skeletal muscle deconditioning, which worsens functional status; whether this measure improves survival is under study. Rest is appropriate during acute **exacerbations**. The role of formal exercise rehabilitation programs is being studied; initial results appear favorable.

If **hypertension, severe anemia, hemochromatosis, uncontrolled diabetes, thyrotoxicosis, beriberi, alcoholism, Chagas' disease, or toxoplasmosis** is successfully treated, patients may dramatically improve. Significant **myocardial ischemia** should be treated aggressively; treatment may include **revascularization** by **percutaneous coronary intervention** or **bypass surgery**. Management of extensive **ventricular infiltration** (eg, in amyloidosis) remains unsatisfactory.

Arrhythmias: It is important to identify and treat the cause of an **arrhythmia**.

- Electrolytes are normalized.
- Atrial and ventricular rate are controlled.
- Sometimes antiarrhythmic drugs are given.

Sinus tachycardia, a common compensatory change in HF, usually subsides when HF treatment is effective. If it does not, associated causes (eg, **hyperthyroidism, pulmonary emboli, fever, anemia**) should be sought. If it persists despite correction of causes, a β -blocker, given in gradually increasing doses, should be considered.

Atrial fibrillation with an uncontrolled ventricular rate must be treated; the target resting **ventricular rate** is typically < 80 beats/min. β -Blockers are the treatment of choice, although rate-limiting Ca channel blockers may be used cautiously if **systolic function** is preserved. Adding **digoxin** or **low-dose amiodarone** may help some patients. Routine conversion to and maintenance of sinus rhythm has not been shown to be superior to rate control alone in a recent large clinical trial. If rapid **atrial fibrillation** does not respond to drugs, permanent pacemaker insertion with complete or partial ablation of the **atrioventricular node** may be considered in selected patients.

Isolated ventricular premature beats, which are common in HF, do not require specific treatment. However, optimization of HF treatments and correction of **electrolyte abnormalities** (especially K and Mg) reduce the risk of ventricular arrhythmias. Sustained ventricular tachycardia that persists despite correction of cause (eg, low K or Mg, ischemia) and optimal medical treatment of HF may require an antiarrhythmic drug. **Amiodarone** and β -blockers are the drugs of choice because other **antiarrhythmics** have adverse **proarrhythmic** effects when **LV systolic dysfunction** is present. Because amiodarone increases **digoxin levels**, the digoxin dose should be decreased by half. Because long-term use of amiodarone can cause adverse effects, a low-dose (200 to 300 mg po once/day) is used when possible; blood tests for liver function and thyroid-stimulating hormone are done every 6 mo, and if chest x-ray is abnormal or dyspnea worsens significantly, chest x-ray and pulmonary function tests are done yearly to check for **pulmonary fibrosis**. For sustained **ventricular arrhythmias**, **amiodarone** may be required; to reduce risk of sudden death, a loading dose of 400 to 800 mg po bid is given for 1 to 3 wk until rhythm control is adequate, then dose is decreased over 1 mo to a maintenance dose of 400 mg po once/day.

Device therapy: Use of an **implantable cardioverter-defibrillator** (ICD) or **biventricular pacing** is appropriate for some patients.

An ICD is recommended for patients with an otherwise good life expectancy if they have **symptomatic sustained ventricular tachycardia** (especially if it causes syncope), **ventricular fibrillation**, or an LVEF persistently < 0.30 while receiving good medical therapy.

Biventricular pacing (cardiac resynchronization therapy [CRT]) may relieve symptoms and reduce HF hospitalizations for patients who have HF, LVEF < 0.35, and a widened QRS complex (> 0.12 sec). Better ways of detecting **ventricular dyssynchrony** may help identify patients most likely to respond to CRT. CRT devices are effective but expensive, and patients must be appropriately selected.

Ultrafiltration (venovenous filtration) can be useful in selected hospitalized patients with severe volume overload if they have not responded well to **diuretic therapy** and have rising **serum creatinine (cardiorenal syndrome)**. Long-term benefits are still unclear.

An **intra-aortic counterpulsation balloon pump** is helpful in selected patients who have a good chance of recovery (eg, acute HF following MI). LV assist devices are implantable pumps that augment LV output. They were initially used only as a short-term intervention to maintain patients with severe HF awaiting transplant but are sometimes now used for extended periods (1 to 2 yr) in patients who are not transplant candidates. However, although survival can be prolonged, few patients are able to recover sufficiently to tolerate device removal.

Surgery: Surgery may be appropriate when certain underlying disorders are present. Usually, surgery in HF patients should be done in a specialized center. Surgical closure of **congenital** or acquired **intracardiac shunts** can be curative. **Coronary artery bypass grafting** to reduce **ischemia** may help some patients with ischemic cardiomyopathy and is currently being studied in a large clinical trial of HF patients with **ischemic systolic dysfunction**. If HF is primarily due to a **valvular disorder**, valve repair or replacement is considered. Patients with primary **mitral regurgitation** are more likely to benefit than patients with mitral regurgitation secondary to LV dilation, in whom **myocardial function** is likely to continue to be poor postoperatively. Surgery is preferably done before **myocardial dilation** and damage become irreversible.



**“I already diagnosed myself on the Internet.
I’m only here for a second opinion.”**

<http://www.heart-valve-surgery.com/Images/second-opinion-cartoon.jpg>

Heart transplantation is the treatment of choice for patients < 60 who have severe, refractory HF and no other life-threatening conditions and who are highly adherent to management recommendations. Some older patients with otherwise excellent health may be considered. Survival is 82% at 1 yr and 75% at 3 yr; however, mortality rate while waiting for a donor is 12 to 15%. Human organ donation remains low. LV assist devices can be a bridge to transplantation or recovery in carefully selected patients.

Experimental therapies: **Artificial hearts** are not yet a viable alternative. **Stem cell transplantation** is in early-stage trials. Surgical options studied include implantation of restraining devices to reduce progressive dilation and a **modified aneurysmectomy** called surgical ventricular restoration, but neither showed clinical benefit.

Dynamic cardiomyoplasty, endocardial laser therapy, and excision of segments of **dilated myocardium** are no longer recommended.

Persistent HF: After treatment, symptoms often persist. Reasons include persistence of the underlying disorder (eg, **hypertension, ischemia, valvular regurgitation**) despite treatment; suboptimal treatment of HF; drug nonadherence; excess intake of dietary Na or alcohol; and presence of an undiagnosed **thyroid disorder, anemia,** or **supervening arrhythmia** (eg, **atrial fibrillation with rapid ventricular response, intermittent ventricular tachycardia**). Also, drugs used to treat other disorders may interfere with HF treatment. **NSAIDs, thiazolidinediones** (eg, pioglitazone) for diabetes, and short-acting **dihydropyridine** or **nondihydropyridine Ca** channel blockers can worsen HF and should be avoided unless no alternative exists; patients who must take such drugs should be followed closely.

Drugs

- Symptom relief: Diuretics, nitrates, or digoxin
- Long-term management and improved survival: ACE inhibitors, β -blockers, aldosterone receptor blockers, or angiotensin II receptor blockers (ARBs)

All these drug classes have been studied in systolic dysfunction, but fewer have been adequately studied in diastolic dysfunction. However, ACE inhibitors, ARBs, and β -blockers are generally used to treat diastolic HF. In patients with severe diastolic dysfunction, diuretics and nitrates should be used in lower doses because these patients do not tolerate reduced BP or plasma volume well. In patients with **hypertrophic cardiomyopathy, digoxin** is not effective and may be harmful. All patients should be given clear and explicit information about their drugs, including the importance of timely prescription renewal and adherence to therapy, how to recognize adverse effects, and when to contact their physician. Research is seeking plasma

biomarkers that may predict which patients might respond best to which drug or drug combination.

Diuretics: Diuretics are given to all patients with symptomatic systolic dysfunction and current or previous volume overload; dose is adjusted to the lowest dose that stabilizes weight and relieves symptoms. Loop diuretics are preferred. **Furosemide** is used most often, starting at 20 to 40 mg po once/day, increased to 120 mg once/day (or 60 mg bid) if needed based on response and renal function. **Bumetanide** is an alternative. In refractory cases, **furosemid** 40 to 160 mg IV, **ethacrynic** acid 50 to 100 mg IV, **bumetanide** 0.5 to 2 mg po or 0.5 to 1.0 mg IV, **ormetolazone** 2.5 to 10 mg po may have an additive effect. IV infusion of furosemide (5 to 10 mg/h) may be helpful in selected patients with severe edema. Loop diuretics (particularly when used with **metolazone**) may cause **hypovolemia** with **hypotension**, **hyponatremia**, **hypomagnesemia**, and **severe hypokalemia**. The dose of diuretic required acutely can usually be gradually reduced when HF improves, and the diuretic may be stopped if other drugs improve heart function and clear HF symptoms. Using larger than required doses of diuretics lowers CO, impairs renal function, causes **hypokalemia**, and increases mortality. **Serum electrolytes** are monitored, initially daily (when diuretics are given IV) and subsequently as needed, particularly after a dose increase.

A K-sparing diuretic, either **spironolactone** or **eplerenone** (which are **aldosterone receptor blockers**), can be added to offset the K-losing effects of higher-dose loop diuretics. **Hyperkalemia** may result, especially when ACE inhibitors or ARBs are also taken, so electrolytes must still be monitored, especially during a dehydrating illness that could cause renal dysfunction. These drugs may have particular benefit in chronic RV failure, in which hepatic congestion results in elevated aldosterone levels as its metabolism is reduced.

Thiazide diuretics are not normally used as a single agent unless hypertension is present but may be added to furosemide for added **diuresis**.

Reliable patients are taught to take additional diuretic doses as needed when weight or peripheral edema increases. They should seek medical attention promptly if weight gain persists.

Experimental ADH blockers increase water excretion and serum Na levels and may cause less **hypokalemia** and renal dysfunction. Their clinical role remains to be defined.

ACE inhibitors: All patients with **systolic dysfunction** are given oral ACE inhibitors unless contraindicated (eg, by plasma creatinine > 2.8 mg/dL [$> 250 \mu\text{mol/L}$], bilateral renal artery stenosis, renal artery stenosis in a solitary kidney, or previous **angioedema** due to ACE inhibitors).

ACE inhibitors reduce production of angiotensin II and breakdown of **bradykinin**, mediators that affect the **sympathetic nervous system**, **endothelial function**, **vascular tone**, and **myocardial performance**. **Hemodynamic effects** include arterial and **venous vasodilation**, sustained decreases in LV filling pressure during rest and exercise, decreased systemic vascular resistance, and favorable effects on ventricular remodeling. ACE inhibitors prolong survival and reduce HF hospitalizations. For patients with atherosclerosis and a vascular disorder, these drugs reduce MI and stroke risk. For patients with diabetes, they delay onset of **nephropathy**. Thus, ACE inhibitors may be used in patients with diastolic dysfunction and any of these disorders.

The starting dose typically should be low (usually one fourth to one half of the target dose depending on BP and renal function); the dose is gradually adjusted upward over 8 wk as tolerated, then continued indefinitely. Usual target doses of representative drugs **include enalapril** 10 to 20 mg bid, **lisinopril** 20 to 30 mg once/day, **ramipril** 5 mg bid, **and captopril** 50 mg tid.



<http://www.glasbergen.com/wp-content/gallery/heart/heart36.gif>

If the **hypotensive effect** (more marked in patients with **hyponatremia** or **volume depletion**) is troublesome, it can often be minimized by separating administration of other BP-lowering drugs or reducing the dose of concomitant diuretics. ACE inhibitors often cause mild to moderate reversible serum creatinine elevation due to **vasodilation** of the **efferent glomerular arteriole**. An initial 20 to 30% increase in creatinine is no reason to stop the drug but does require slower increases in dose, reduction in **diuretic dose**, or avoidance of NSAIDs. Because aldosterone's effect is reduced, K retention may result, especially in patients receiving K supplements. Cough occurs in 5 to 15% of patients, probably because **bradykinin** accumulates, but other causes of cough should also be considered. Occasionally, rash or **dysgeusia** occurs. **Angioedema** is rare but can be life threatening and is a contraindication to this class of drugs. Alternatively, ARBs can be used, although rarely cross-reactivity is reported. Both are contraindicated in pregnancy.

Serum electrolytes and renal function should be measured before an ACE inhibitor is started, at 1 mo, and after each significant increase in dose or change in clinical condition. If dehydration or poor renal function due to acute illness develops, the ACE inhibitor dose may need to be reduced or the drug may be temporarily withheld.

ARBs: These drugs are not demonstrably superior to ACE inhibitors but are less likely to cause cough and **angioedema**; they may be used when these adverse effects prohibit ACE inhibitor use. ACE inhibitors and ARBs are equally effective post MI; however, their equivalence is less clear in chronic HF, and the best dose is still under study. Usual oral target doses are **valsartan** 160 mg bid, **candesartan** 32 mg once/day, and **losartan** 50 to 100 mg once/day. Introduction, upward **titration**, and monitoring of ARBs and ACE inhibitors are similar. Like ACE inhibitors, ARBs can cause reversible renal dysfunction, and the dose may need to be reduced or withheld temporarily during an acute dehydrating illness.

Adding an ARB to a regimen of an ACE inhibitor, β -blocker, and diuretic should be considered for HF patients with persistent symptoms and repeated hospitalizations. Such combination therapy requires increased monitoring of BP, **serum electrolytes**, and renal function.

Aldosterone receptor blockers: Because **aldosterone** can be produced independently of the **renin-angiotensin system**, its adverse effects are not inhibited completely even by maximal use of ACE inhibitors and ARBs. Thus, the **aldosterone receptor** blockers **spironolactone**, 25 to 50 mg po once/day, and **eplerenone**, 10 mg po once/day (does not cause **gynecomastia** in males), can reduce mortality, including

from sudden death, in patients with LVEF < 30% and **severe chronic HF or acute HF complicating acute MI**. K supplements should be stopped. Serum K and creatinine should be checked every 1 to 2 wk for the first 4 to 6 wk and after dose changes; dose is lowered if K is between 5.5 and 6.0 mEq/L and stopped if K is > 6.0 mEq/L, if creatinine increases above 2.5 mg/dL (220 μ mol/L), or if ECG changes of **hyperkalemia** are present. These drugs are usually not used in patients receiving both an ACE inhibitor and an ARB because of the high risk of hyperkalemia and renal dysfunction.

β -Blockers: β -Blockers, unless otherwise contraindicated (by **asthma, 2nd- or 3rd-degree atrioventricular block**, or previous intolerance), are an important addition to ACE inhibitors for chronic systolic dysfunction in most patients, including the elderly, and for **diastolic dysfunction** in **hypertension** and **hypertrophic cardiomyopathy**. They are best started when the patient has no evidence of pulmonary congestion. Some of these drugs improve LVEF, survival, and other major cardiovascular outcomes in patients with chronic systolic dysfunction, including those with severe symptoms. β -Blockers are particularly useful for diastolic dysfunction because they reduce heart rate, prolonging **diastolic filling time**, and possibly improve **ventricular relaxation**.

The starting dose should be low (one fourth of the target daily dose), then the dose is gradually increased over 8 wk as tolerated. The acute negative inotropic effects of **β -blockade** may cause cardiac depression and fluid retention. In such cases, a temporary increase in **diuretic dose** and slower upward titration of the β -blocker dose is warranted. Tolerance may improve over time, and efforts should be made to reach target doses. Usual oral target doses are **carvedilol** 25 mg bid (50 mg bid for patients \geq 85 kg), **bisoprolol** 10 mg once/day, **and metoprolol** 50 to 75 mg bid (**tartrate**) or 200 mg once/day (**succinate extended-release**). **Carvedilol**, a **3rd-generation nonselective β -blocker**, is also a vasodilator with **α -blocking** and **antioxidant effects**; it is the preferred and most widely studied β -blocker but is more expensive in many countries. Some β -blockers (eg, **bucindolol**, **xamoterol**) do not appear beneficial and may be harmful.

During a severe, **acute decompensation**, β -blockers should not be started until patients are stabilized and have little evidence of fluid retention. For patients already taking a β -blocker, the dose may be temporarily reduced or, in severe decompensation, temporarily withheld but restarted and titrated again when patients are stable. For milder decompensations, the β -blocker dose should be continued with a temporary increase in diuretic dose.

After initial treatment, heart rate and **myocardial O₂ consumption** decrease, and stroke volume and filling pressure are unchanged. With the slower heart rate, diastolic function improves. Ventricular filling returns to a more normal pattern (increasing in early diastole), which appears less restrictive. Improved **myocardial function** is measurable in some patients after 6 to 12 mo but may take longer; EF and CO increase, and LV filling pressure decreases. Exercise capacity improves.

Vasodilators: **Hydralazine** plus **isosorbide dinitrate** may help patients truly intolerant of **ACE inhibitors** or **ARBs** (usually because of significant renal dysfunction), although long-term benefit of this combination is limited. In African-American patients, this combination may also provide some additional benefits when added to standard therapy. As **vasodilators**, these drugs improve hemodynamics, reduce **valvular regurgitation**, and increase exercise capacity without causing significant renal impairment. Hydralazine is started at 25 mg po qid and increased every 3 to 5 days to a target total dose of 300 mg/day, although many patients cannot tolerate > 200 mg/day because of hypotension. **Isosorbide dinitrate** is started at 20 mg po tid (with a 12-h nitrate-free interval) and increased to a target of 40 to 50 mg tid. Whether lower doses (frequently used in clinical practice) provide long-term benefit is unknown. In general, vasodilators have been replaced by ACE inhibitors, which are easier to use, are usually better tolerated, and have greater proven benefit.

Nitrates alone can relieve HF symptoms; patients can be taught to use **sublingual nitroglycerin** spray as needed for **acute dyspnea** and a **transdermal patch** for **nocturnal dyspnea**. Nitrates are safe, effective, and well tolerated and are particularly helpful in patients with HF and angina. Adverse effects include hypotension and headache.

Other vasodilators such as Ca channel blockers are not used to treat systolic dysfunction. **Short-acting dihydropyridines** (eg, nifedipine) and **nondihydropyridines** (eg, diltiazem, verapamil) may be deleterious. However, **amlodipine** and **felodipine** are well tolerated and may be useful for patients with HF and associated angina or hypertension. Both drugs may cause peripheral edema; rarely, amlodipine causes pulmonary edema. **Felodipine** should not be taken with grapefruit juice, which significantly increases plasma levels and adverse effects by inhibiting cytochrome P-450 metabolism. In patients with diastolic dysfunction, Ca channel blockers may be used as needed to treat hypertension or ischemia or to control ventricular rate in atrial fibrillation. **Verapamil** may be used in **hypertrophic cardiomyopathy**.

Digitalis preparations: These drugs inhibit the Na-K pump (Na^+ , K^+ -ATPase). As a result, they cause weak positive **inotropism**, reduce sympathetic activity, block the **atrioventricular node** (slowing the ventricular rate in atrial fibrillation or prolonging the PR interval in **sinus rhythm**), reduce **vasoconstriction**, and improve renal blood flow. **Digoxin** is the most commonly prescribed digitalis preparation. It is excreted by the kidneys; elimination half-life is 36 to 40 h in patients with normal renal function.



“An aspirin a day will help prevent a heart attack if you have it for lunch instead of a cheeseburger.”

<http://newbodyandmind.com/blog/wp-content/uploads/2012/01/cholesterol-cartoon.png>

Digoxin has no proven survival benefit but, when used with diuretics and an ACE inhibitor, may help control symptoms and reduce the likelihood of hospitalization. Digoxin is most effective in patients with large LV end-diastolic volumes and an S_3 . Acute withdrawal **of digoxin** may increase the hospitalization rate and worsen symptoms. In patients with normal renal function, digoxin, 0.125 to 0.375 mg po once/day depending on age, sex, and body size, achieves full digitalization in about 1 wk (5 half-lives). More rapid digitalization can be achieved with digoxin 0.5 mg IV over 15 min followed by 0.25 mg IV at 8 and 16 h or with 0.5 mg po followed by 0.25 mg po at 8, 16, and 24 h. Prescription patterns vary widely by physician and by country, but in general, doses are lower than those used in the past, and a trough (8- to 12-h post-dose) digoxin level of 1 ng/mL is acceptable.

Toxicity is a concern, especially in patients with renal dysfunction and perhaps in women. These patients may need a lower oral dose, as may elderly patients, patients

with a low lean body mass, and patients also taking **amiodarone**; patients > 80 kg may need a higher dose. Digoxin (and all digitalis glycosides) has a narrow therapeutic window. The most important toxic effects are life-threatening **arrhythmias** (eg, ventricular fibrillation, ventricular tachycardia, complete **atrioventricular block**). **Bidirectional ventricular tachycardia**, **nonparoxysmal junctional tachycardia** in the presence of **atrial fibrillation**, and **hyperkalemia** are serious signs of digitalis toxicity. **Nausea**, **vomiting**, **anorexia**, **diarrhea**, **confusion**, **amblyopia**, and, rarely, **xerophthalmia** may occur. If **hypokalemia** or **hypomagnesemia** (often due to diuretic use) is present, lower doses and serum levels can still cause toxicity. Electrolyte levels should be monitored in patients taking diuretics and digoxin, so that abnormalities can be prevented if possible; **K-sparing diuretics** may be helpful.

When digitalis toxicity occurs, the drug should be stopped; **electrolyte abnormalities** should be corrected (IV if abnormalities are severe and toxicity is acute). Patients with severe toxicity are admitted to a monitored unit, and digoxin immune **Fab** (**ovine antidigoxin antibody fragments**) is given if **arrhythmias** are present or if significant **overingestion** is accompanied by a serum K of > 5 mEq/L. This drug is also useful for glycoside toxicity due to plant ingestion. Dose is based on the steady-state serum digoxin level or total amount ingested. **Ventricular arrhythmias** are treated with **lidocaine** or **phenytoin**. **Atrioventricular block** with a slow ventricular rate may require a temporary **transvenous pacemaker**. Isoproterenol is contraindicated because it increases risk of ventricular arrhythmia.

Other drugs: Various positive inotropic drugs have been evaluated in HF but, except **fordigoxin**, they increase mortality risk. Regular outpatient IV infusions of **inotropes** (eg, dobutamine) increase mortality and are not recommended. Drugs under study include **Ca sensitizers** (eg, levosimendan), **cytokine blockers**, **endothelin blockers**, **matrix metalloproteinase (MMP) inhibitors**, and **immune modulators**.

Reference: <http://www.merckmanuals.com>