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Defining and Treating Heart Failure

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In many aspects the term *congestive heart failure* is a misnomer that continues to be used in the vernacular and the medical literature. Congestive heart failure, which is due to the inability of the heart to maintain adequate cardiac output, should be viewed as either left sided (left ventricle, LV) or right sided (right ventricle, RV), and systolic and/or diastolic in character. Despite suggestions that differences between systolic and diastolic failure can be made clinically, few physicians (if any) can correctly distinguish between the two 100% of the time. Successful distinction between systolic and diastolic dysfunction requires the use of noninvasive tests such as echocardiography (transthoracic or transesophageal) and radionuclide ventriculograms as discussed in Chapter 31, and invasive testing such as ventriculography performed during cardiac catheterization. The importance of coronary artery disease as a cause of death is well established, but many clinicians underestimate the significance of death in patients with class IV congestive heart failure (Table 32.1) for which the average survival time (5 years) is less than that for a patient who has recently developed acquired immunodeficiency syndrome (7 years).

In this chapter we discuss many of the various forms of heart failure, define right-sided and left-sided causes as well as systolic and diastolic failure, and review available treatment options.

TABLE 32.1. New York Heart Association classification of heart failure.

Class	Symptom
I	No symptom
II	Comfortable at rest; may have exertional symptoms
III	Fairly comfortable at rest; symptomatic with activity
IV	Symmptomatic at rest; symptoms worse with exertion

What Is Heart Failure?

Heart failure is the inability of the heart to adequately supply blood flow (cardiac output) to itself and the rest of the body. The workload placed on the heart is determined by a number of factors that can be grouped into three different categories: preload, contractility, and afterload. Each factor applies to both the right side and left side of the heart, as shown in Figures 32.1 and 32.2, respectively. Decisions concerning drug treatment and the use of mechanical assist devices such as an intraaortic balloon pump (IABP) are based on these factors (Figure 32.3) and the patient's response to treatment. We now look at each of these independent variables.

Preload

Preload is the return of venous blood to the heart, which is then pumped out of the heart through the arteries of the body. On the right side of the heart, blood is returned via the superior and inferior vena cava, with smaller amounts returning from the lungs (azygos and bronchial veins) and heart (coronary sinus). Venous return to the left side of the heart arrives via the pulmonary vein. If the right side of the heart is unable to accept or receive this blood, or if it is unable to pump the blood into the lungs, volume overload (Figure 32.1) will occur. This is accompanied by distention of neck veins and leg edema. The patient will report leg swelling and possibly weight gain. Clinically there will be evidence of lower extremity and/or sacral edema, depending on whether the patient has been bedridden. Other evidence of RV volume overload includes elevated right atrial pressures (>8–10 mm Hg) and an increased lift over the left lower sternal border that can best be appreciated by the heel of the examiners hand. Sternal lifts re-

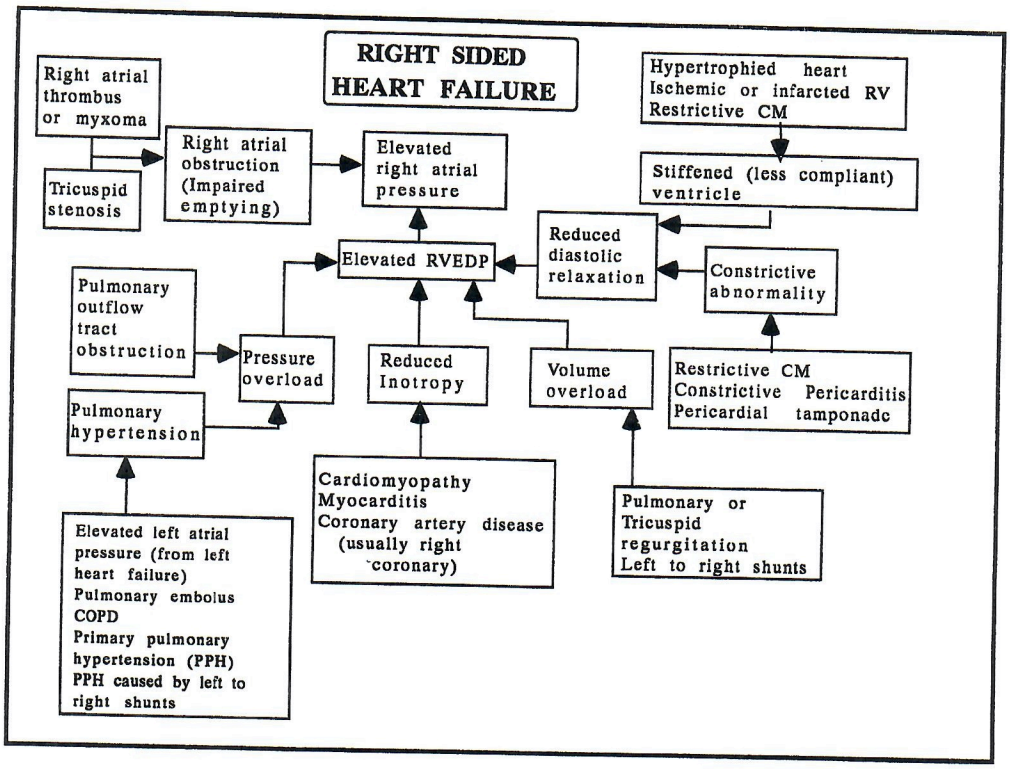

FIGURE 32.1. Right-sided heart failure. Problems that result in right-sided heart failure cause elevations in right atrial pressure either as a result of right atrial obstruction or problems with volume overload, pressure overload, inotropic or chronotropic problems, and/or diastolic dysfunction.

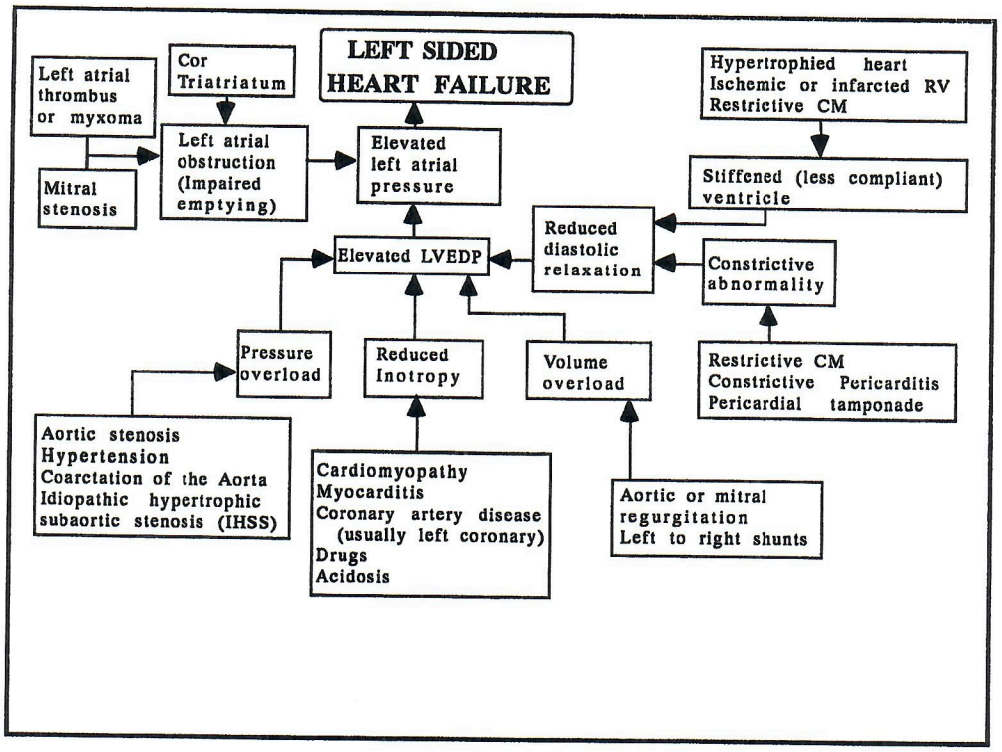

FIGURE 32.2. Left-sided heart failure. Elevations in left atrial pressure or obstruction to left atrial emptying can result in increased left atrial pressure, precipitating left-sided heart failure. Obstructions to left atrial emptying include masses, congenital abnormalities, or stenotic valves. Additional problems arise from preload, inotropic, chronotropic, and afterload disorders.

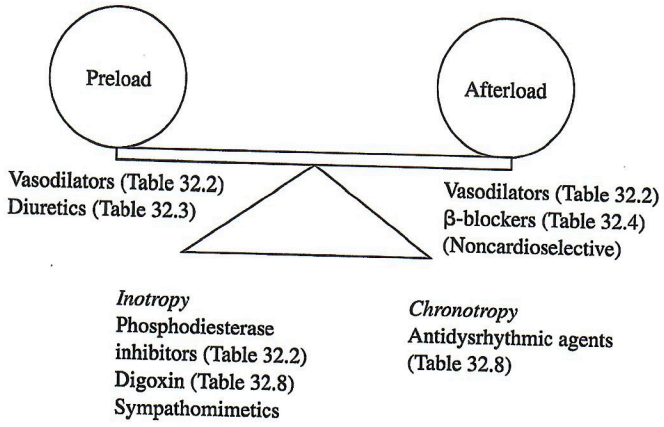

FIGURE 32.3. Determinants of myocardial workload. Workload on the heart increases with increased preload and afterload. Reduced inotropy or increased rhythm problems (chronotropy) may exacerbate myocardial dysfunction.

sulting from volume overload are brisk in character, whereas lifts resulting from pressure overload have a slow, sustained lift. Third heart sounds (S_3) are associated with volume overload (increased preload) states, although they may occasionally be heard in healthy individuals (<35–40 years of age) or during the last trimester of pregnancy. When an S_3 occurs from right ventricular overload, it is heard over the left lower sternal border where the RV is normally positioned. Enlargement of the RV can also be seen as an enlarged cardiac silhouette (5 o'clock position) on posteroanterior chest radiographs. Lateral views demonstrate a concomitant loss of retrosternal airspace.

An example of acute RV overload is seen in patients who have an acute anteroseptal myocardial infarction (anteroseptal MI) with rupture of the interventricular septum, known as a ventricular septal defect (VSD). This acute anteroseptal MI with associated VSD accounts for approximately 2% of all MI–related deaths. Unless systemic vascular resistance (SVR) is reduced, the blood pressure, which is greater in the LV than in the RV, will cause a shunting of blood from the LV to the RV into the pulmonary artery, finally returning it to the left side of the heart where the entire process can repeat itself.

This increased blood flow from the LV through the VSD into the RV and finally into the pulmonary artery will be represented by increased RV and pulmonary capillary occlusion/wedge pressures (PCOP/PCWP), and by increased vascular markings on the chest radiograph. Initial findings of pulmonary edema begin with cephalization (increased vascular markings in the apices of the lungs) and perivascular cuffing (fluid accumulation immediately around the pulmonary vessels) once the PCOP exceeds 15 to 18 mm Hg. This is the necessary pressure needed to overcome the osmotic pressure that serves to maintain serum within blood vessels of the body.

The holosystolic murmur associated with a VSD can sometimes be confused with an acute rupture of the mitral valve apparatus (acute mitral regurgitation), but can be differentiated clinically by the "thrill" felt over the RV when the examiner places the palm of his/her hand on the patient's chest, and/or by echocardiogram. An S_4 will be heard over the less compliant (stiffened) left ventricle as a result of the MI, whereas an S_3 will be heard over the fluid-overloaded RV. As fluid continues to accumulate in the lungs, perihilar prominence, perivascular cuffing, cephalization, Kerley's B-lines, and pleural effusions will be seen on the chest radiograph. Effusions are more common in the right costophrenic angle when unilateral but are frequently seen bilaterally. Such an effusion is transudative in character.

Management of an acute anteroseptal MI with VSD requires simultaneous mechanical and medical treatment. This requires the placement of an IABP to improve the LV cardiac output by decreasing aortic resistance to forward blood flow, thereby decreasing the shunting of blood from the LV to the RV. Dopamine is needed concomitantly to reduce SVR. Caution must be exercised when dosing the dopamine because treatment is aimed at reducing the SVR (blood pressure), thereby enhancing blood flow from the LV to the aorta, minimizing the shunting of blood through the VSD to the RV as described above. Low-dose dopamine (1–5 mg/kg per minute) activates the dopaminergic and β_2-receptors, producing vasodilation of the renal and mesenteric arteries, with lesser dilatation of the coronary and cerebral arteries. This effectively lowers SVR, improves the movement of blood from the LV to the aorta, and reduces the shunting of blood through the VSD. When the amount of dopamine is increased (5–10 mg/kg per minute), the β_1-receptors are activated, which increases the contractility of the heart (Figure 32.3) but does not improve the SVR. When even higher doses of dopamine are used, the α-receptors are activated, which produces vasoconstriction and increases the SVR and shunting of blood from the LV through the VSD into the RV, which in turn causes further deterioration of the patient.

A team approach including a cardiologist or angiologist, cardiovascular surgeon, and others must decide on the best time for surgical repair of the VSD. The best outcome is usually obtained if surgery can be delayed until sufficient healing has occurred for a surgical patch to be secured into place. However, deterioration of the patient may require emergent surgery at less than optimal times even though this has been associated with a greater than 50% mortality.

Medical and surgical treatment of almost everything in medicine must focus on both the cause and the associated symptoms. Many cases of fluid overload (increased preload) can be treated using medications that reduce the preload of the heart by vasodilatation or diuresis.

These medications include but are not limited to those shown in Tables 32.2 and 32.3, which list many of the available angiotensin-converting enzyme inhibitors, nitrates, phosphodiesterase inhibitors, antihypertensive agents, and diuretics currently available. Many of these medications may need to be given intravenously if there is evidence of gastrointestinal edema (frequently seen with peripheral edema), because edema of the gastrointestinal wall is associated with decreased absorption of oral medicines. Caution must be exercised when using diuretics, particularly when patients are also receiving β-adrenergic blocking agents (Table 32.4) or digitalis glycosides. If too much fluid is removed from a patient (e.g., in the treatment of peripheral edema) by diuretic agents, the patient could experience electrolyte abnormalities and/or hypovolemic shock. Digitalis toxicity can easily occur when hypokalemia, hypomagnesemia, hypercalcemia, and hypercapnia exist and is particularly a problem when patients are receiving diuretic therapy or anything else that may adversely affect electrolyte levels. In the end you cannot treat electrocardiogram results, Swan–Ganz catheter readings, blood test results, or anything else and forget about the patient without having potential adverse effects on the patient.

Other causes of elevated right atrial pressure include impaired atrial emptying, which may be caused by stenotic valves, intra-atrial masses, or chamber abnormalities, as shown in Figures 32.1 and 32.2. These are most easily detected with an echocardiogram, although computed tomography, magnetic resonance imaging, and auscultory changes may be present. Figures 32.1 and 32.2 also list various causes of pressure overload, reduced inotropy, and diastolic dysfunction, some of which we discuss later.

Myocardial Contractility

Myocardial contractility, the pumping action of the heart, is dependent on two independent factors: inotropy and chronotropy. Inotropy is the "force" of contraction and is sometimes expressed as the pressure produced by the ventricle (usually the LV) in a given amount of time (dP/dT). This is frequently equated to the ejection fraction of a ventricle (RV or LV), which can be detected by echocardiography, radionuclide ventricu-

TABLE 32.2. Vasodilators used to treat preload and afterload.

Medication	Preload*	Afterload*	Usual daily dose	Peak effect	Duration of effect
Angiotensin-converting enzyme inhibitors					
Captropril	3	4	12.5–25 mg	1–2 h	4–8 h
Enalapril	3	4	5–40 mg	4–8 h	18–30 h
Lisinopril	3	4	5–40 mg	4–6 h	18–30 h
Quinapril	3	4	5–40 mg	2–3 h	24 h
Fosinopril	3	4	20–40 mg	3 h	12 h
Moexipril	3	4	10–80 mg	1–2 h	12–14 h
Nitrates					
Sublingual nitroglycerin	4	1	0.4 mg	1–3 min	30–60 min
Oral, sustained release	4	1	2.5–9 mg	60 min	8–12 h
Paste	4	1	1–2 in	15 min	4 h
Transdermal	4	1	2.5–15 mg/24 h	30 min	24 h
Intravenous	4	1	25–500 μg/min	Minutes	Minutes
Phosphodiesterase inhibitors					
Milrinone	4	2	12.5 μg/kg loading dose; 0.2–0.7 μg/kg/min	5–15 min	6–12 h
Amrinone	4	2	5–10 μg/kg/min	5 min	6 h
Direct-acting vasodilators					
Hydralazine	0	3	10–100 mg every 6 h	1–4 h	12–24 h
Minoxidil	0	3	10–40 mg	1–3 h	24–48 h
Nitroprusside	3	3	5–150 μg/min	Minutes	1–3 min
Prostacyclin	3	3	5–15 ng/kg/min	Research	Research
Adrenergic blockers					
Phenoxybenzamine	2	2	10–20 mg every 8 h	1–2 min	24 h
Phentolamine	2	2	50 mg every 6 h	1–2 min	20 min
Prazosin	3	2	1–5 mg every 6 h	3 h	6–8 h
Terazosin	2	3	1–5 mg	2–3 h	12–24 h
Calcium channel blockers					
Nifedipine, sustained release	2	4	30–90 mg	1–3 h	8–12 h
Diltiazem, sustained release	1	1	60–120 mg	1–3 h	8–12 h
Verapamil, sustained release	0	2	40–120 mg	1–3 h	8–12 h

*Preload and afterload graded from 0 (no effect) to 4 (greatest effect).

TABLE 32.3. Diuretics used to treat preload.

Medication	Site of action	Usual daily dose	Peak effect	Duration of effect
Thiazides				
Chlorothiazide	Distal tubule	250–500 mg	4 h	6–12 h
Hydrochlorothiazide	Distal tubule	25–100 mg	4 h	>12 h
Chlorthalidone	Distal tubule	25–100 mg	6 h	24 h
Metolazone	Distal and proximal tubule	2.5–20 mg	2 h	12–24 h
Trichlormethiazide	Distal tubule	4–8 mg	6 h	24 h
Loop diuretics				
Furosemide	Ascending limb, loop of Henle	20–80 mg	1–2 h	6 h
Ethacrynic acid	Ascending limb, loop of Henle	25–100 mg	2 h	6–8 h
Bumetanide	Ascending limb, loop of Henle	0.5–2 mg	1–2 h	4–6 h
Potassium-sparing agents				
Spironolactone	Distal tubule	50–200 mg	2–3 d	2–3 d
Triamterene	Distal tubule	100–200 mg	6–8 h	12–16 h
Amiloride	Distal tubule	5–10 mg	6–10 h	24 h

TABLE 32.4. β-Adrenergic blocking agents used to treat heart rate and afterload.

Medication	Cardioselective (β_1)	Usual daily dose	Peak effect	Duration of effect
Acebutolol	Yes	200–1200 mg	3–8 h	≤24 h
Atenolol	Yes	25–200 mg	2–4 h	24–48 h
Labetalol*	No	400–800 mg	2–4 h	8–12 h
Metoprolol	Yes (up to 100 mg)	50–300 mg	2–4 h	24–48 h
Nadolol	No	20–120 mg	2–4 h	24–48 h
Pindolol	No	20–60 mg	1–2 h	<24 h
Propranolol	No	40–480 mg	2–4 h	24–48 h
Timolol	No	20–60 mg	2 h	20–24 h

*Also has alpha (vasoconstrictive) effect.

lograms, or cardiac catheterization (of the LV). Chronotropy is the rate and rhythm of the heart as influenced by the sympathetic and parasympathetic nervous system, thyroid function, atrial and/or ventricular irritability (ischemia or MI), medications, and so forth.

The overall strength (inotropy) of myocardial muscle fibers can be weakened by any of a number of factors. These include the dilated cardiomyopathies (DCMs), which are shown in Table 32.5, along with hypertrophic cardiomyopathy (HCM), restrictive cardiomyopathy (RCM), and obliterative cardiomyopathy (OCM). An example of iatrogenically induced DCM includes patients who have received more than 450 mg/m^2 of one of the two anthracycline agents: doxorubicin and daunorubicin.

TABLE 32.5. Cardiomyopathies (CM).

	Dilated CM	Hypertrophic CM	Restrictive CM	Obliterative CM*
Morphology†	Biventricular dilatation	Hypertrophy of involved regions	Thickened noncompliant heart	Space-occupying lesions
Chamber size	Increased	Normal or decreased	Normal or increased	Frequently decreased
LVEDP	Increased	Normal or increased	Increased	Usually increased
SV	Decreased	Normal or increased	Normal or decreased	Normal or decreased
EF	Decreased	Increased	Normal or decreased	Normal or decreased
CO	Decreased	Normal	Normal or decreased	Normal or decreased
Diastolic compliance	Normal or decreased	Decreased	Decreased	Decreased
Causes	Adriamycin	Aortic stenosis	Amyloidosis	
	Alcohol	Idiopathic hypertrophic subaortic stenosis	Friedreich's ataxia	Hypereosinophilic syndromes
	Amyloidosis	Mitral stenosis	Glycogen storage diseases	
	Diabetes mellitus		Infiltrative disease	
	Hypophosphatemia		Löffler's endocarditis	
	Rheumatic fever			
	Viral infection/myocarditis			

*Restrictive–obliterative cardiomyopathies (considered by many to be an extension of restrictive CM).
†LVEDP, left ventricular end-diastolic pressure; SV, stroke volume; EF, ejection fraction; CO, cardiac output.

Other causes of DCM include diabetes (diabetic patients have four to five times the prevalence of DCM compared with nondiabetic individuals) and other endocrine disorders such as Cushing's disease, thyrotoxicosis, acromegaly, myxedema, pheochromocytoma, and uremia. Various chemicals (lead, cobalt, alcohol, steroids, and chemotherapy agents) and infectious agents (viruses and *Trypanosoma cruzi*, which causes Chagas' disease), as well as hypophosphatemia can also cause DCM. DCM disorders also include postpartum cardiomyopathy and acquired immune deficiency syndrome cardiomyopathy. Although specific treatments for postpartum cardiomyopathy and acquired immune deficiency syndrome cardiomyopathy produce unimpressive results, patients should still receive symptomatic treatment.

Acute MI is an example of an injury to the heart that affects both inotropic and chronotropic function. During an MI, part of the heart muscle goes without adequate blood flow for a sufficient amount of time (1–4 hours) to result in permanent damage to the heart. Early intervention (within 1–4 hours) with thrombolytic agents may reduce the amount of damage done and improve early survival, although it is questionable whether long-term survival is increased unless lifestyle changes and control of risk factors (see Chapters 30 and 64) are successfully implemented.[1,2] Successful thrombolysis results in rapid washout of creatine kinase–myocardial band and dysrhythmias, and resolution of electrocardiographic abnormalities (Table 32.6). Changes in coronary blood flow can be documented in the cardiac catheterization laboratory (Table 32.7) or by myocardial perfusion imaging (see Chapter 31).

Coronary artery bypass graft surgery and/or the use of an IABP may be indicated, depending on the patient's presentation and clinical course. The use of other ventricular assist devices (hemopump, etc.) and intravenous medications such as glucose–insulin–potassium have not demonstrated any additional benefit despite initial hopes. In fact, the use of glucose–insulin–potassium has been associated with significant hypokalemia, dysrhythmias, and death in the clinical setting. Patients who have recently had an MI should not be prophylactically treated with lidocaine unless they demonstrate ventricular ectopy. Patients who have been given lidocaine but do not have ventricular premature beats have demonstrated increased mortality.

Additional approaches to treating DCMs include removal of offending agents; anticoagulation if a thrombus is present or is expected; and treatment of associated dysrhythmias (Table 32.8), including digitalis if either atrial fibrillation is present of if the left ventricular ejection fraction is less than 30%. In the absence of atrial fibrillation or systolic dysfunction (reduced left ventricular ejection fraction) there is no evidence to support the use of digitalis glycosides at this time, and potential problems can occur in patients with hypercapnia or those with electrolyte abnormalities, as noted above. Likewise, digitalis should not be used in patients with amyloidosis because of potential toxicity problems. Additional treatments for DCMs include preload and afterload reduction when appropriate.

In addition to inotropic problems, chronotropic issues must also be addressed. A list of many of the current antidysrhythmic agents used today is included in Table 32.8. Some patients are extremely dependent upon the "atrial kick" that occurs at the end of diastole and provides the final one-third of ventricular filling from the atria immediately preceding systole. These patients may benefit from implantation of atrial-ventricular sequential pacemakers. Other patients with dysrhythmias refractory to medical therapy may benefit from implantation of an automatic implantable cardiofibrillator device, which can both sense and defibrillate lethal dysrhythmias.

TABLE 32.6. Sequence of electrocardiographic changes occurring during transmural (Q-wave) myocardial infarction.

Hyperacute (peaked) T waves
ST-segment elevation
Q-wave development
T-wave inversion
Resolution of ST segments

TABLE 32.7. Thrombolysis in myocardial infarction flow.

0	No flow
1	Minimal flow distal to stenosis
2	Complete but sluggish flow distal to stenosis
3	Normal flow

Afterload

Afterload is the resistance against which the heart must work to eject blood from the ventricles into the arteries of the body. As shown in Figures 32.1 and 32.2, resistance can be provided by stenotic valves, obstructions, hypertension, and shunts. Afterload can best be understood by considering the law of La Place (Figure 32.4), where T is the tension (work) placed on the heart, P is the ventricular pressure, r is the radius of the ventricular cavity, and h is the height (thickness) of the ventricular wall. Hypertrophy of the ventricular wall can be either a primary problem or secondary to volume overload and so forth, as shown in Table 32.9.

In addition to increasing the workload on the heart, myocardial thickening impairs blood flow through the coronary arteries. Because coronary arteries receive most of their blood flow during diastole, any increase in wall tension of the heart will increase the resistance to blood flow, subsequently decreasing coronary blood flow and its delivery of oxygen to the heart, further limiting the amount of work the heart is able to do.

TABLE 32.8. Antiarrhythmic agents.*

Medication	Onset of action	Duration of action	Half-life ($t_{1/2}$)	Indication
Class IA agents (sodium channel blockers)				
Moricizine	2 h	10–24 h	1.5–3.5 h	Life-threatening VT, VPB
Quinidine	0.5 h	6–8 h	6–7 h	APBs, VPBs, SVT, VT
Procainamide	0.5 h	>3 h	2.5–4.5 h	APBs, VPBs, SVT, VT
Disopyramide	0.5 h	6–7 h	4–10 h	APBs, VPBs, SVT, VT
Class IB agents (shorten repolarization)				
Lidocaine (intravenous)	1–5 min	0.25 h	1–2 h	VPBs, VT
Phenytoin	0.5–1 h	24 h	22–36 h	VPBs, VT, Digitalis toxicity
Tocainide	0.5–2 h	6–12 h	11–15 h	VPBs, VT
Mexiletine	30–120 min	6–12 h	10–12 h	VPBs, VT
Class IC agents (depress repolarization)				
Flecainide†	1–6 h	12–24 h	12–27 h	Life-threatening VT
Encainide†	0.5–1.5 h	Variable	1–2 h	Life-threatening VT
Propafenone‡	3.5 h	12–24 h	2–10 h	Life-threatening VT, SVT, AF
Class II agents (β-blockers, slow atrioventricular conduction)				
Propranolol	0.5 h	3–5 h	2–3 h	SVT
Esmolol (intravenous)	<5 min	Very short	0.15 h	SVT
Acebutolol	2–3 h	24–30 h	3–4 h	VPBs
Class III agents (prolong action potential)				
Bretylium (intravenous)	1–5 min	6–8 h	5–10 h	VF, VT
Amiodarone	Days to weeks	Weeks to months	26–107 d	Refractory VT, SVT
Sotalol	2–4 h	12 h	12 h	VT
Class IV agents (slow calcium channel blockers)				
Verapamil	0.5 h	6 h	3–7 h	SVT
Other agents				
Digoxin	0.5–2 h	>24 h	30–40 h	AF
Adenosine (intravenous)	34 s	1–2 min	<10 s	SVT

*Dosage depends on clinical scenario.
†May precipitate heart failure.
‡Propafenone is also a weak calcium channel blocker.
AF, atrial fibrillation; APB, atrial premature beats; SVT, supraventricular tachycardia; VF, ventricular fibrillation; VPB, ventricular premature beats; VT, ventricular tachycardia.

TABLE 32.9. Primary and secondary causes of cardiac hypertrophy.

Primary causes	
Right sided	Left sided
Left heart failure	Aortic stenosis
Primary pulmonary disease	Coarctation of the aorta
Pulmonary stenosis	Hypertension
Secondary causes	
Volume overload	
Athletic heart	
Aortic regurgitation	
Mitral regurgitation	
Reactive hypertrophy	
Ischemic cardiomyopathy	
Myocardial infarction	

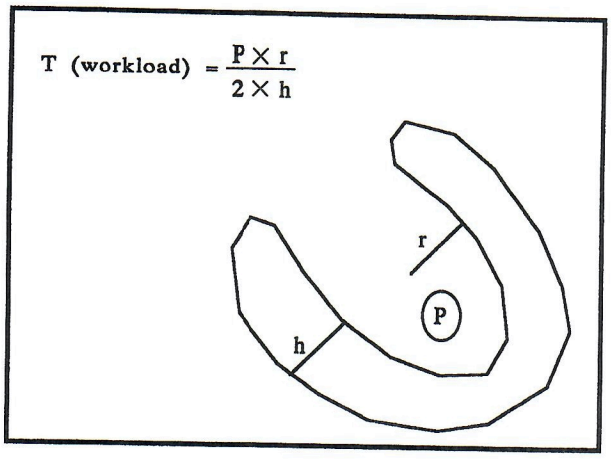

FIGURE 32.4. La Place's law. The workload (tension) on the heart is increased when LV pressure increases or the LV dilates. The heart attempts to compensate by hypertrophy of the ventricle (increased wall thickness, *h*). Both increased preload *(r)* and afterload *(P)* can increase the workload on the heart, resulting in myocardial hypertrophy. See text for full details.

HCMs include abnormalities that may or may not cause obstruction of the aortic outflow tract (Figures 32.1 and 32.2). Clinical thickening of a ventricular chamber resulting from hypertension is usually associated with an increased intensity in valve closure for either the aortic or pulmonic valve. This increased intensity is caused by differences in pressure on either side of the valve. Stenotic valves, which may cause HCM, have less mobility and are therefore associated with less intense valve closure.

Stenotic valves on the left side of the heart are relatively easy to distinguish because mitral stenosis presents as a diastolic rumble best auscultated at the apex with the bell of the stethoscope while the patient lies in the left lateral decubitus position. Mitral stenosis is frequently associated with dypsnea, angina, hemoptysis, hoarseness, and cough. On auscultation there is an opening snap when the stenotic mitral valve opens. The more severe the stenosis, the shorter the S2–opening snap interval.

In contrast to mitral stenosis, aortic stenosis is a systolic murmur heard best at the right upper sternal border and typically radiates to both carotid arteries. Aortic sclerosis sounds similar but does not tend to radiate to the carotid arteries. Distinction between the two is best made by echocardiography. Aortic stenosis is associated with syncope, angina, and dyspnea. The onset of dyspnea suggests left ventricular dysfunction and is indicative of patient mortality within 6 to 18 months unless successfully relieved. As aortic stenosis worsens, there is further delay in the opening of the aortic valve, with delayed peaking of the systolic ejection murmur occurring later and later in the murmur. This produces a delayed carotid upstroke known as *parvus et tardus* and a decrease in the intensity of aortic valve (A2) closure.

For the patient with HCM a distinction must be made between aortic stenosis and idiopathic hypertrophic subaortic stenosis, which produces outflow tract obstruction. Idiopathic hypertrophic subaortic stenosis is also known as asymmetric septal hypertrophy and hypertrophic obstructive cardiomyopathy. The distinction between aortic stenosis and idiopathic hypertrophic subaortic stenosis frequently requires the use of echocardiography, but differences in the hemodynamics of these murmurs can be detected clinically by performing maneuvers that change LV blood volume, as shown in Table 32.10. Treatment of mitral stenosis, aortic stenosis, and idiopathic hypertrophic subaortic stenosis may be accomplished medically or surgically, depending on the severity of the disease.[3,4]

In addition to the three previous determinants of cardiac workload (preload, contractility, and afterload), failure of the heart to adequately relax can also lead to right-sided and left-sided failure, as shown in Figures 32.1 and 32.2, respectively. Examples include stiffened and constrictive abnormalities such as RCM. The classic feature of RCM disorders is impedance of diastolic filling of the ventricle(s) with subsequent abnormal diastolic function. As shown in Table 32.5, there are a variety of diseases that can lead to RCM, including but not limited to amyloidosis, pseudoxanthoma elasticum, radiation damage (from treatment of lymphomas or other tumors), endomyocardial fibrosis (also known as Löffler's endocarditis), tumors (primary or secondary), glycogen storage diseases, and hemochromatosis.

An important distinction in the evaluation of RCM is to differentiate between "constrictive pericarditis," which may respond to pericardial stripping, and "restrictive cardiomyopathy." Evaluation of left and right ventricular chamber pressures will reveal the classical diastolic dip and plateau morphology known as the *square root sign.* Diastolic dysfunction is evidenced by an elevation in the diastolic pressures. Although it may be necessary to perform an endomyocardial biopsy to distinguish between these two disorders and their cause, some important clues can be provided by comparing the left and right ventricular chamber pressures. If diastolic pressures are equal for both ventricular chambers then the patient typically has a constrictive pericarditis, whereas patients with RCM will usually have greater end-diastolic pressures in the LV.

It is also important to differentiate between constrictive pericarditis and cardiac tamponade. Differentiation between the two is important because cardiac tamponade requires removal of the pericardial effusion to prevent hemodynamic collapse. This occurs when right atrial and RV filling are impaired because of the greater pressure generated by the LV, resulting in a bulging of the interventricular septum into the RV cavity, which impedes RV filling. Reduced RV filling results in less blood reaching the LV, which subsequently results in decreased cardiac output and hemodynamic collapse. Removal of the pericardial fluid can be done by either pericardiocentesis or a surgical window. True differentiation between constrictive pericarditis and cardiac tamponade may require echocardiography, but they should normally be distinguishable clinically, as shown in Table 32.11.

TABLE 32.10. Differentiation aortic stenosis (AS) from idiopathic hypertrophic subaortic stenosis (IHSS).

			Murmur intensity		
	Carotid upstroke	After ventricular premature beat	Isoprel of hand grip	Valsalva's maneuver	Amyl nitrate
AS	Parvus et tardus (slow and delayed)	Increased	Normal or decreased	Decreased	Increased
IHSS	Bisferiens (spike and dome)	Decreased	Increased	Increased	Increased

TABLE 32.11. Differentiating between cardiac tamponade and constrictive pericarditis.

Clinical findings	Cardiac tamponade	Constrictive pericarditis
Elevated jugular venous pulse	Yes	Yes
Kussmaul's sign	No	Yes
Pulsus paradoxus	Yes	No
Clear lungs	Yes	Yes
Heart sounds	Normal to decreased	Pericardial knock
Ascites	No	Yes
Edema	No	Yes
Chest x-ray—cardiomegaly	Often	No (may see pericardial calcification)
Swan-Ganz catheter	Prominent X-descent	Prominent Y-descent
Electrocardiogram (electrical alternans)	Yes	No
Echocardiogram (pericardial fluid)	Yes	No

The fourth and final group of cardiomyopathies (Table 32.5) includes the OCMs and comprises any process that produces a mass effect within any chamber of the heart. This includes tumors, asymmetric septal hypertrophy, Löffler's endocarditis at the apex of the heart, and so forth. Treatment is directed at eliminating the obstruction (obliteration) to blood flow and providing symptomatic relief.

Clinically a thickened, less compliant ventricle will have a fourth heart sound (S_4). This is caused by blood entering a stiffened ventricle that has increased ventricular end-diastolic pressure (LVEDP or RVEDP) that the incoming blood must move against. Pressure overload in the ventricles (S_4) can result in hypertrophy of the ventricle, whereas volume-overloaded ventricles (S_3) first experience dilatation, although the presence of one state can eventually lead to the other. Treatment must be focused on both the primary cause and the resulting symptoms.

There are a wide variety of medications available for the treatment of systemic hypertension (defined in millimeters of mercury or as SVR), but there has been limited success in the treatment of pulmonary hypertension (defined in millimeters of mercury or as pulmonary vascular resistance). Medications useful for the treatment of SVR include those listed in Tables 32.2, 32.3, and 32.4. The use of β-adrenergic blocking agents (Table 32.4) may also be of use in the treatment of certain atrial dysrhythmias (Table 32.8). Caution should be exercised when using these drugs when there is evidence of systolic dysfunction either clinically, echocardiographically, by nuclear imaging, or by cardiac catheterization.

Systolic Versus Diastolic Failure

Classically, ventricular function has been looked at in many ways including volume–pressure curves. Although initially somewhat difficult to understand, step-by-step analysis makes them quite easy to follow and understand. Figure 32.5 shows the volume–pressure loop for a normal LV. Blood volume inside the LV is represented on the x-axis, whereas LV pressure is displayed on the y-axis. Systole begins with mitral valve closure (MVC), preventing additional blood from entering the left ventricle. At this time the ventricle begins contraction, but blood is not ejected from the ventricle until the aortic valve opens (AVO). This period of contraction is known as isovolumetric contraction (IVC) because there is no change in blood volume within the LV. During the IVC the pressure in the ventricle rises until it exceeds the aortic pressure. Once this happens the aortic valve opens (AVO) and left ventricular ejection of blood begins. With the ejection of blood into the aorta the LV blood volume drops from 100 mL to 35–40 mL. Left ventricular ejection continues until the pressure in the aorta exceeds that in the ventricle and the aortic valve closes (AVC), ending systole.

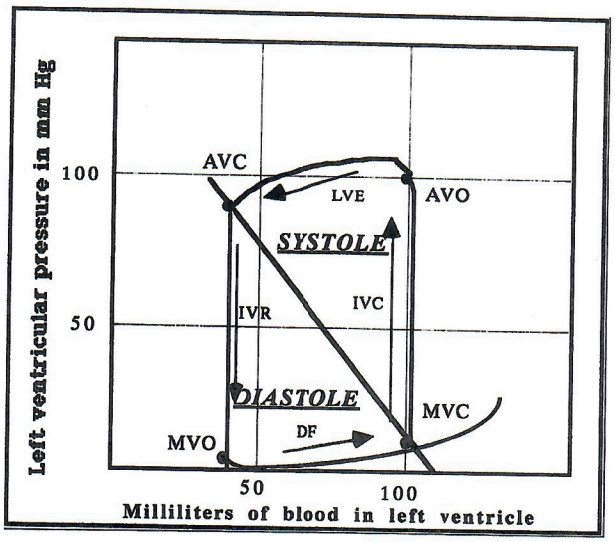

FIGURE 32.5. Volume–pressure relationships of a normal left ventricle. Systole begins with MVC and concludes with AVC, at which time diastole begins. Diastole ends with MVC, where LVEDP and left ventricular end-diastolic volume (LVEDV) are seen. See text for full details.

With the end of systole, ventricular contraction has been completed and ventricular relaxation (diastole) begins. During this time, known as isovolumetric relaxation (IVR), blood does not enter the ventricle although the pressure decreases due to relaxation of the ventricle. Diastolic filling of the LV begins when the left atrial pressure exceeds the left ventricular pressure, resulting in mitral valve opening (MVO) because of the pressure of the left atrial blood. The volume of blood in the LV increases from 35 to 40 mL to approximately 100 mL. The last part of ventricular diastolic filling occurs with atrial contraction, and diastole is completed with MVC, and systole begins again.

When systolic failure occurs, there is an increase in both left ventricular end-diastolic volume (LVEDV) and LVEDP, as represented by the example in Figure 32.6. In this example, increased LVEDV is evidenced by comparing the volume present at MVC, which is greater for the systolic failure loop (A_1MVC) than the normal volume–pressure loop (A_2MVC), 125 and 100 mL, respectively. Because

$$(1)\,\%\ \text{LVEF} = [(\text{LVESV} - \text{LVEDV})/\text{LVEDV}] \times 100$$

where LVEF is the left ventricular ejection fraction, LVESV is the left ventricular end-systolic volume, and LVEDV is the left ventricular end-diastolic volume, we can now calculate the LVEF for each of the two ventricles in question.

Normal ventricle: LVEF = (LVESV − LVEDV)/LVEDV = (100 − 35)/100 = 65%

Systolic failure ventricle: LVEF = (LVESV − LVEDV)/LVEDV = (125 − 80)/125 = 36%

As expected, the ventricle with an increased LVEDV represents a ventricle with reduced systolic function (LVEF). It is also obvious from the volume–pressure loop that to increase the LVEF we must reduce the SVR and/or increase the contractility of the ventricle.

An increase in LVEDP (A_1MVC) is also seen when pressure at end-diastole (MVC) is compared with the normal (A_2MVC) end-diastolic pressure. In this example LVEDP is 20 mm Hg for the systolic failure ventricle, as opposed to 10 mm Hg for the normally functioning ventricle. With an LVEDP of 20 mm Hg (which should represent PCOP), the patient will be dyspneic and have pulmonary edema, which requires preload reduction.

In contrast to systolic failure, diastolic dysfunction is caused by a failure of the ventricle to adequately relax. As a result, LVEDP is elevated as shown in Figure 32.7. Because the ventricle is stiffened, the pressure within the left ventricle increases rapidly during diastolic filling, resulting in early closure of the mitral valve (MVC) once pressure in the LV exceeds that in the left atria. This reduces the LVEDV without decreasing the LVEF.

Diastolic failure ventricle: LVEF = (LVESV − LVEDV)/LVEDV = (80 − 35)/35 = 56%

Although LVEF is normal, the actual stroke volume (SV = LVESV − LVEDV) is reduced, with an SV of 45 mL for the LV with diastolic failure and 65 mL for the

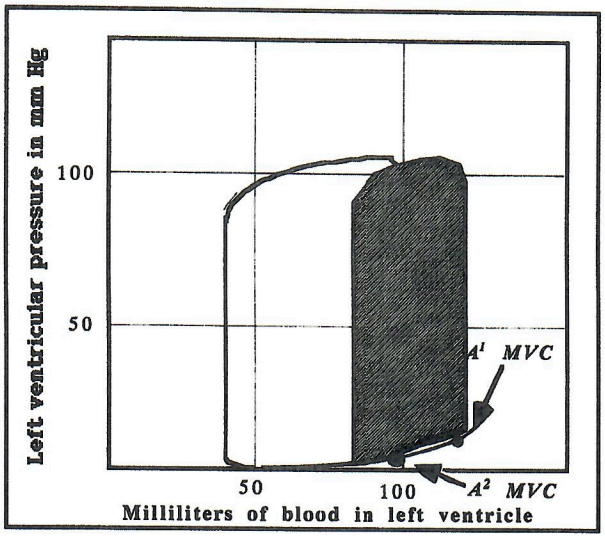

FIGURE 32.6. Systolic failure as represented by the volume–pressure loop. The normally functioning LV is represented by the open loop, and the ventricle with impaired systolic function is represented by the hashed loop. Both the LVEDV and LVEDP are elevated with systolic failure. See text for full details.

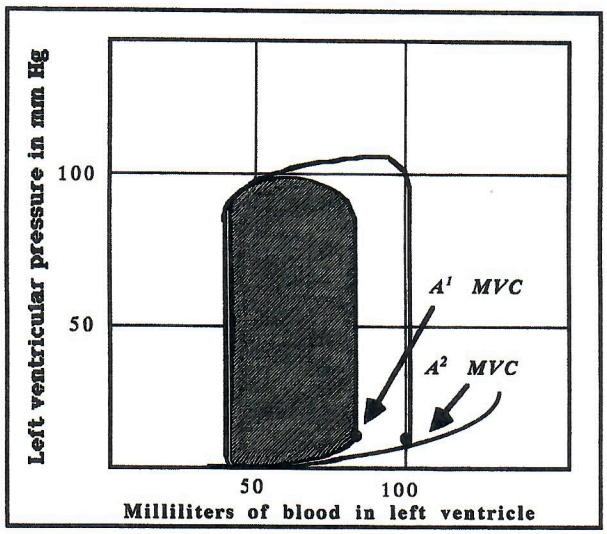

FIGURE 32.7. Diastolic failure as represented by the volume–pressure relationships. The hashed loop represents a ventricle with diastolic failure with an elevated LVEDP and reduced LVEDV as compared with the normally functioning LV, represented by the open loop.

normal ventricle. Therefore, treatment of diastolic dysfunction must focus on improving ventricular relaxation and not on increasing contractility, as many people mistakenly attempt with digitalis or inotropic agents. LVEF should be determined in each case to decide if inotropic support is needed. Similar volume–pressure loops can be drawn for RV function, although the pressures are lower for the right side of the heart.

Right-Sided Versus Left-Sided Heart Failure

By examining and understanding these volume–pressure relationships it is easy to see that treatment of systolic failure should focus on reducing both the LVEDV and LVEDP, whereas treatment of diastolic function should focus on decreasing the LVEDP without further compromising LVEDV, which could make matters worse. Successful treatment requires recognition of the underlying cause, assessment of systolic and diastolic function, and a determination as to whether the problem is right sided, left sided, or biventricular. A classic example of how important this becomes is in the treatment of an acute MI. Treatment typically includes oxygen, morphine sulfate for pain control and diuretic effect, heparin and thrombolytic agents, pressor support (dopamine, dobutamine, isoproterenol, etc.) if needed, alternative medications where available,[5,6] interventional techniques (angioplasty, stents, atherectomy, etc.), and mechanical support (IABP) and/or bypass surgery. If the left ventricle is involved, then diastolic dysfunction along with decreased inotropy and chronotropy frequently occur. In this setting, pulmonary edema (increased PCOP) may easily happen, worsening the overall scenario. Diuretics may be required but must be given cautiously so as not to deplete the intravascular volume, which could worsen the LVEDV and systolic function.

Patients who have an inferior wall MI should routinely have right precordial leads placed so they may be tested for evidence of RV infarction. This can occur in 20% to 30% of the cases of inferior wall MI. Inferior wall MIs have also been associated with the Bezold-Jarisch reflex, which consists of bradycardia, vasodilatation, and hypotension due to involvement of the parasympathetic (phrenic) nerve running along the inferior aspect of the heart/diaphragm. Patients presenting with these symptoms should not receive β-adrenergic blocking agents because of an already slowed heart rate. In patients with a RV MI, the right atrial and RV end-diastolic pressure (RVEDP) may be elevated but the PCOP will usually be low or normal. This is because the RV is a passive conduit (volume pump under low pressure) to the lungs, in contrast to the LV, which is a pressure pump. Part of the overall treatment of RV MI includes cautiously giving intravenous fluid to increase the PCOP and secure LV filling to maintain adequate LV cardiac output. The distinction between right-sided and left-sided infarction of the heart becomes extremely important, as evidenced by this example.

Cardiac Transplantation

Unfortunately heart failure, from whatever cause, may ultimately be untreatable despite changes in dietary habits, adjustment in medications, pacemakers, artificial valves, mechanical assist devices, and/or emergency surgery. As mentioned at the beginning of this chapter, patients with New York Heart Association class IV failure can have shorter lifespans than patients in the early stages of acquired immunodeficiency syndrome.

Once the available treatments have been exhausted, the one remaining hope for many patients remains cardiac transplantation.[7] The overall 1-year survival rate for transplant recipients remains at 70%. Many factors are involved in determining whether a person is an appropriate transplant candidate and whether an organ is available. Combination heart–lung transplants are frequently reserved for patients with congenital heart disease, pulmonary hypertension, or Eisenmenger's syndrome. Despite considerable work in the field of artificial hearts, latissimus dorsi muscle flap surgeries, and other valiant efforts, the vast majority of patients die while awaiting a heart transplant, with one third of these dying suddenly.

Conclusion

An adequate approach to the treatment of heart failure requires that one understand the mechanism behind the problem. To do this it is important to distinguish between right ventricular, left ventricular, and biventricular failure, as well as systolic and diastolic dysfunction. Physical examination skills, history-taking skills, and the use of appropriate diagnostic tests to elucidate the underlying pathology while looking for treatable and perhaps reversible causes are all required. Focusing on appropriate interventions for preload, contractility (inotropy and chronotropy), and afterload dysfunction can improve the overall management of the patient's condition. Careful monitoring of a patient's response to treatment is extremely important because it allows the physician to maximize patient benefit and minimize problems. It is important to remember that it is the patient you are treating and not pressure measurements obtained from a Swan–Ganz catheter or a laboratory report. Successful treatment of heart failure requires a team approach that includes a cardiologist or angiologist, a cardiovascular surgeon, and others.

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