Non pharmacological manganite of chronic heart failure.

Definition:

HF is a clinical syndrome characterized by typical symptoms (e.g. breathlessness, ankle swelling and fatigue) that may be accompanied by signs (e.g. elevated jugular venous pressure, pulmonary crackles and peripheral oedema) caused by a structural and/or functional cardiac abnormality, resulting in a reduced cardiac output and/ or elevated intracardiac pressures at rest or during stress. [85]

Signs and symptoms

Signs and symptoms of heart failure include the following:

Exertional dyspnea and/or dyspnea at rest

Orthopnea

Acute pulmonary edema

Chest pain/pressure and palpitations

Tachycardia

Fatigue and weakness

Nocturia and oliguria

Anorexia, weight loss, nausea

Exophthalmos and/or visible pulsation of eyes

Distention of neck veins

Weak, rapid, and thready pulse

Rales, wheezing

S 3 gallop and/or pulsus alternans

Increased intensity of P 2 heart sound

Hepatojugular reflux

Non pharmacological manganite of chronic heart failure.

Ascites, hepatomegaly, and/or anasarca

Central or peripheral cyanosis, pallor

Diagnosis

Heart failure criteria, classification, and staging

The Framingham criteria for the diagnosis of heart failure consists of the concurrent presence of either two major criteria or one major and two minor criteria.[1]

Major criteria comprise the following:

Paroxysmal nocturnal dyspnea

Weight loss of 4.5 kg in 5 days in response to treatment

Neck vein distention

Rales

Acute pulmonary edema

Hepatojugular reflux

S 3 gallop

Central venous pressure greater than 16 cm water

Circulation time of 25 seconds or longer

Radiographic cardiomegaly

Pulmonary edema, visceral congestion, or cardiomegaly at autopsy

Minor criteria (accepted only if they cannot be attributed to another medical condition) are as follows:

Nocturnal cough

Dyspnea on ordinary exertion

Non pharmacological manganite of chronic heart failure.

A decrease in vital capacity by one third the maximal value recorded

Pleural effusion

Tachycardia (rate of 120 bpm)

Hepatomegaly

Bilateral ankle edema

The New York Heart Association (NYHA) classification system categorizes heart failure on a scale of I to IV,[2] as follows:

Class I: No limitation of physical activity

Class II: Slight limitation of physical activity

Class III: Marked limitation of physical activity

Class IV: Symptoms occur even at rest; discomfort with any physical activity

The American College of Cardiology/American Heart Association (ACC/AHA) staging system is defined by the following four stages[3] :

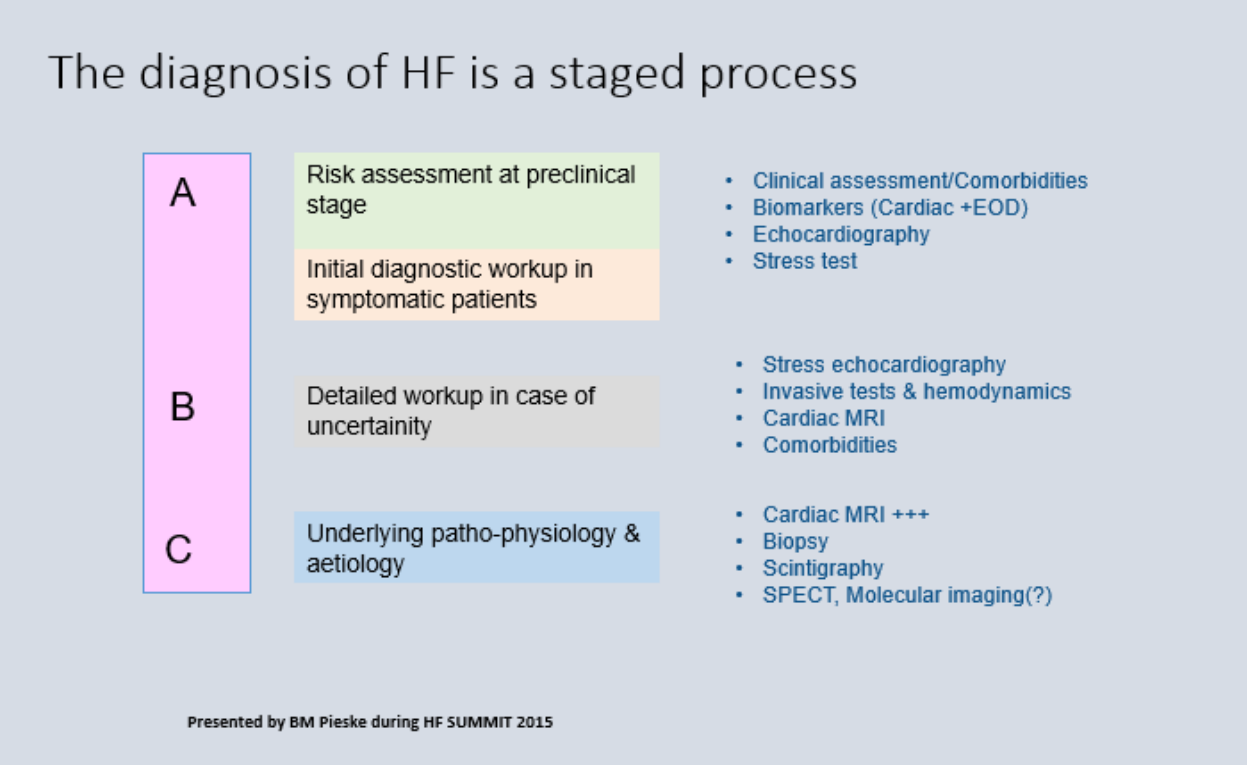
Stage A: High risk of heart failure but no structural heart disease or symptoms of heart failure

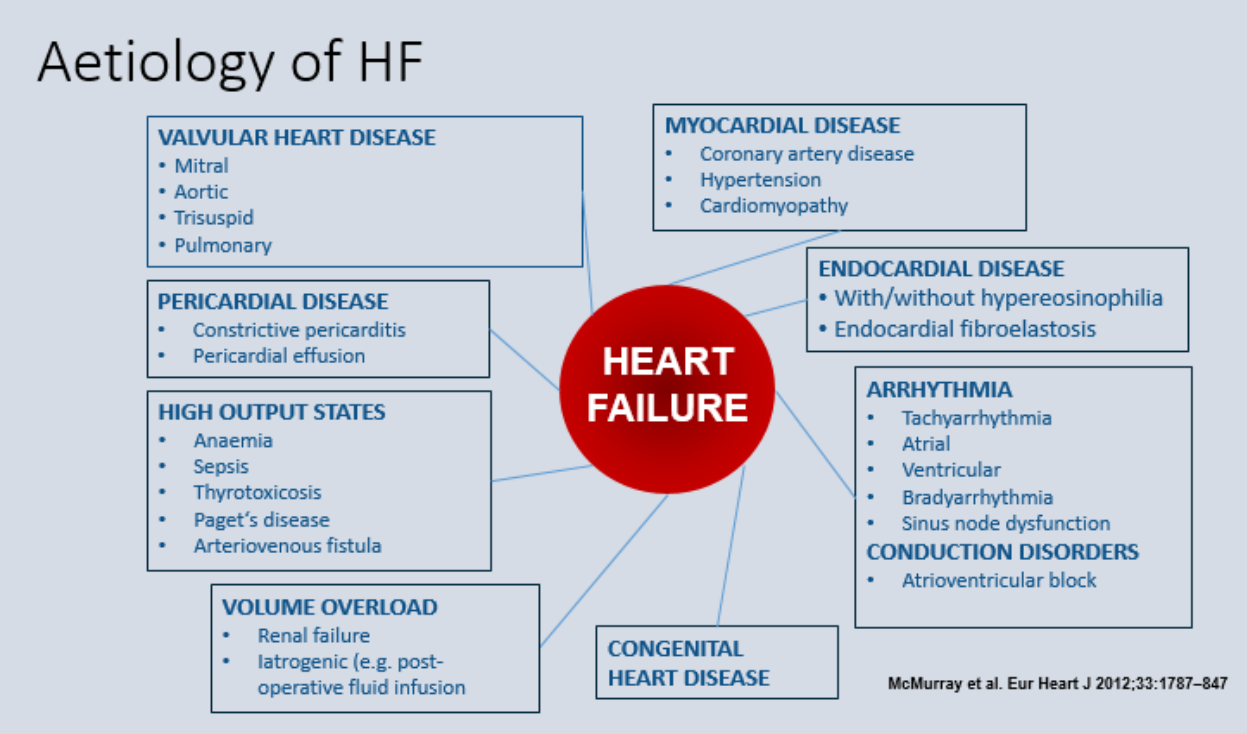
Stage B: Structural heart disease but no symptoms of heart failure

Stage C: Structural heart disease and symptoms of heart failure

Stage D: Refractory heart failure requiring specialized interventions

Non pharmacological manganite of chronic heart failure.





Non pharmacological manganite of chronic heart failure.

Testing

The following tests may be useful in the initial evaluation for suspected heart failure[3, 4, 5] :

Complete blood count (CBC)

Iron studies

Urinalysis

Electrolyte levels

Renal and liver function studies

Fasting blood glucose levels

Lipid profile

Thyroid stimulating hormone (TSH) levels

B-type natriuretic peptide levels

N-terminal pro-B-type natriuretic peptide levels

Electrocardiography

Chest radiography

Two-dimensional (2-D) echocardiography

Nuclear imaging [6]

Maximal exercise testing

Pulse oximetry or arterial blood gas

Laboratory studies for heart failure should include a complete blood count (CBC), electrolyte levels, and hepatorenal function studies. Imaging studies such as chest radiography and two-dimensional echocardiography are recommended in the initial evaluation of patients with known or suspected heart failure. B-type natriuretic peptide (BNP) and N-terminal pro-B-type

natriuretic peptide (NT-proBNP) levels can be useful in differentiating cardiac and noncardiac causes of dyspnea.

In acute heart failure, patient care consists of stabilizing the patient's clinical condition; establishing the diagnosis, etiology, and precipitating factors; and initiating therapies to provide rapid symptom relief and survival benefit. Surgical options for heart failure include revascularization procedures, electrophysiologic intervention, cardiac resynchronization therapy (CRT), implantable cardioverter-defibrillators (ICDs), valve replacement or repair, ventricular restoration, heart transplantation, and ventricular assist devices (VADs).

The goals of pharmacotherapy are to increase survival and to prevent complications. Along with oxygen, medications assisting with symptom relief include diuretics, digoxin, inotropes, and morphine. Drugs that can exacerbate heart failure should be avoided (nonsteroidal anti-inflammatory drugs [NSAIDs], calcium channel blockers [CCBs], and most antiarrhythmic drugs). (See Medication for more information.)

For further information, see the Medscape Drugs & Diseases articles Pediatric Congestive Heart Failure, Congestive Heart Failure Imaging, Heart Transplantation, Pediatric Heart Transplantation, Coronary Artery Bypass Grafting, and Implantable Cardioverter-Defibrillators.

Pathophysiology

The common pathophysiologic state that perpetuates the progression of heart failure is extremely complex, regardless of the precipitating event. Compensatory mechanisms exist on every level of organization, from the subcellular all the way through to organ-to-organ interactions. Only when this network of adaptations becomes overwhelmed does heart failure ensue.[7, 8, 9, 10, 11]

Adaptations

Most important among the adaptations are the following[12] :

- The Frank-Starling mechanism, in which an increased preload helps to sustain cardiac performance
- Alterations in myocyte regeneration and death

Non pharmacological manganite of chronic heart failure.

- Myocardial hypertrophy with or without cardiac chamber dilatation, in which the mass of contractile tissue is augmented
- Activation of neurohumoral systems

The release of norepinephrine by adrenergic cardiac nerves augments myocardial contractility and includes activation of the renin-angiotensin-aldosterone system [RAAS], the sympathetic nervous system [SNS], and other neurohumoral adjustments that act to maintain arterial pressure and perfusion of vital organs.

In acute heart failure, the finite adaptive mechanisms that may be adequate to maintain the overall contractile performance of the heart at relatively normal levels become maladaptive when trying to sustain adequate cardiac performance.[13]

The primary myocardial response to chronic increased wall stress is myocyte hypertrophy, death/apoptosis, and regeneration.[14] This process eventually leads to remodeling, usually the eccentric type. Eccentric remodeling further worsens the loading conditions on the remaining myocytes and perpetuates the deleterious cycle. The idea of lowering wall stress to slow the process of remodeling has long been exploited in treating heart failure patients.[15]

The reduction of cardiac output following myocardial injury sets into motion a cascade of hemodynamic and neurohormonal derangements that provoke activation of neuroendocrine systems, most notably the above-mentioned adrenergic systems and RAAS.[16]

The release of epinephrine and norepinephrine, along with the vasoactive substances endothelin-1 (ET-1) and vasopressin, causes vasoconstriction, which increases calcium afterload and, via an increase in cyclic adenosine monophosphate (cAMP), causes an increase in cytosolic calcium entry. The increased calcium entry into the myocytes augments myocardial contractility and impairs myocardial relaxation (lusitropy).

The calcium overload may induce arrhythmias and lead to sudden death. The increase in afterload and myocardial contractility (known as inotropy) and the impairment in myocardial lusitropy lead to an increase in myocardial energy expenditure and a further decrease in cardiac output. The increase in myocardial energy expenditure leads to myocardial cell death/apoptosis, which results in heart failure and further reduction in cardiac output,

perpetuating a cycle of further increased neurohumoral stimulation and further adverse hemodynamic and myocardial responses.

In addition, the activation of the RAAS leads to salt and water retention, resulting in increased preload and further increases in myocardial energy expenditure. Increases in renin, mediated by a decreased stretch of the glomerular afferent arteriole, reduce delivery of chloride to the macula densa and increase beta1-adrenergic activity as a response to decreased cardiac output. This results in an increase in angiotensin II (Ang II) levels and, in turn, aldosterone levels, causing stimulation of the release of aldosterone. Ang II, along with ET-1, is crucial in maintaining effective intravascular homeostasis as mediated by vasoconstriction and aldosterone-induced salt and water retention.

The concept of the heart as a self-renewing organ is a relatively recent development.[17] This paradigm for myocyte biology created an entire field of research aimed directly at augmenting myocardial regeneration. The rate of myocyte turnover has been shown to increase during times of pathologic stress.[14] In heart failure, this mechanism for replacement becomes overwhelmed by an even faster increase in the rate of myocyte loss. This imbalance of hypertrophy and death over regeneration is the final common pathway at the cellular level for the progression of remodeling and heart failure.

Angiotensin II

Research indicates that local cardiac Ang II production (which decreases lusitropy, increases inotropy, and increases afterload) leads to increased myocardial energy expenditure. Ang II has also been shown in vitro and in vivo to increase the rate of myocyte apoptosis.[18] In this fashion, Ang II has similar actions to norepinephrine in heart failure.

Ang II also mediates myocardial cellular hypertrophy and may promote progressive loss of myocardial function. The neurohumoral factors above lead to myocyte hypertrophy and interstitial fibrosis, resulting in increased myocardial volume and increased myocardial mass, as well as myocyte loss. As a result, the cardiac architecture changes which, in turn, leads to further increase in myocardial volume and mass.

Non pharmacological manganite of chronic heart failure.

Myocytes and myocardial remodeling

In the failing heart, increased myocardial volume is characterized by larger myocytes approaching the end of their life cycle.[19] As more myocytes drop out, an increased load is placed on the remaining myocardium, and this unfavorable environment is transmitted to the progenitor cells responsible for replacing lost myocytes.

Progenitor cells become progressively less effective as the underlying pathologic process worsens and myocardial failure accelerates. These features—namely, the increased myocardial volume and mass, along with a net loss of myocytes—are the hallmark of myocardial remodeling. This remodeling process leads to early adaptive mechanisms, such as augmentation of stroke volume (Frank-Starling mechanism) and decreased wall stress (Laplace law) and, later, to maladaptive mechanisms such as increased myocardial oxygen demand, myocardial ischemia, impaired contractility, and arrhythmogenesis.

As heart failure advances, there is a relative decline in the counterregulatory effects of endogenous vasodilators, including nitric oxide (NO), prostaglandins (PGs), bradykinin (BK), atrial natriuretic peptide (ANP), and B-type natriuretic peptide (BNP). This decline occurs simultaneously with the increase in vasoconstrictor substances from the RAAS and the adrenergic system, which fosters further increases in vasoconstriction and thus preload and afterload. This results in cellular proliferation, adverse myocardial remodeling, and antinatriuresis, with total body fluid excess and worsening of heart failure symptoms.

ACC/AHA stages of heart failure

The American College of Cardiology/American Heart Association (ACC/AHA) developed a classification that described the development and progression of heart failure and that "recognizes that there are established risk factors and structural prerequisites for the development of [heart failure] and that therapeutic interventions introduced even before the appearance of [left ventricular] dysfunction or symptoms can reduce the population morbidity and mortality of [heart failure]."[3] Table 3, below, summarizes the development of heart failure.

Non pharmacological manganite of chronic heart failure.

Table 1. ACC/AHA Stages of Heart Failure Development.

Level	Description	Examples	Notes
A	At high risk for heart failure but without structural heart disease or symptoms of heart failure	Patients with coronary artery disease, hypertension, or diabetes mellitus without impaired LV function, LVH, or geometric chamber distortion	• Patients with predisposing risk factors for developing heart failure • Corresponds with patients with NYHA class I heart failure
B	Structural heart disease but without signs/symptoms of heart failure	Patients who are asymptomatic but who have LVH and/or impaired LV function	
C	Structural heart disease with current or past symptoms of heart failure	Patients with known structural heart disease and shortness of breath and fatigue, reduced exercise tolerance	• The majority of patients with heart failure are in this stage • Corresponds with patients with NYHA class I-IV heart failure
D	Refractory heart failure requiring specialized interventions	Patients who have marked symptoms at rest despite maximal medical therapy	• Patients in this stage may be eligible to receive mechanical circulatory support, receive continuous inotropic infusions,

			undergo procedures to facilitate fluid removal, or undergo heart transplantation or other procedures • Corresponds with patients with NYHA class IV heart failure

LV = left ventricle; LVH = LV hypertrophy; NYHA = New York Heart Association.

Source: Yancy CW, Jessup M, Bozkurt B, et al, for the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2013 Oct 15;128(16):e240-327.[3]

Treatment:

Approach Considerations

Medical care for heart failure includes a number of nonpharmacologic, pharmacologic, and invasive strategies to limit and reverse its manifestations.[3, 4, 15] Depending on the severity of the illness, nonpharmacologic therapies include dietary sodium and fluid restriction; physical activity as appropriate; and attention to weight gain. Pharmacologic therapies include the use of diuretics, vasodilators, inotropic agents, anticoagulants, beta-blockers, and digoxin.

Invasive therapies for heart failure include electrophysiologic intervention such as cardiac resynchronization therapy (CRT), pacemakers, and implantable cardioverter-defibrillators (ICDs); revascularization procedures such as coronary artery bypass grafting (CABG) and

percutaneous coronary intervention (PCI); valve replacement or repair; and ventricular restoration.[3, 4, 13, 14, 15]

Heart transplantation has been the criterion standard for therapy when progressive end-stage heart failure occurs despite maximal medical therapy, when the prognosis is poor, and when there is no viable therapeutic alternative.[3, 4, 5] However, mechanical circulatory devices such as ventricular assist devices (VADs) and total artificial hearts (TAHs) can bridge the patient to transplantation; in addition, VADs are increasingly being used as permanent therapy.[4]

Comorbidities to consider

Coronary artery disease

Patients with heart failure should be evaluated for coronary artery disease, which can lead to heart failure (see Etiology). Not only may this condition be the underlying cause in up to two thirds of heart failure patients with low ejection fraction, but coronary artery disease may also play a role in the progression of heart failure through mechanisms such as endothelial dysfunction, ischemia, and infarction, among others.[3]

Patients with coronary artery disease with modestly reduced ejection fraction and angina have demonstrated symptomatic and survival improvement with coronary artery bypass grafting (CABG) in studies; however, the trials did not include individuals with heart failure or those with severely reduced ejection fractions.[3] In patients with angina and ventricular dysfunction, evaluation with coronary angiography should not be delayed (see Catheterization and Angiography). Noninvasive cardiac testing is not recommended in patients with significant ischemic chest pain, as revascularization is advised in these patients independent of their degree of ischemia/viability.[3]

Although there are no reports of controlled trials evaluating heart failure without angina and their outcomes with coronary revascularization, surgical revascularization is recommended in those with significant left main stenosis and in those with extensive noninfarcted but hypoperfused and hypocontractile myocardium on noninvasive testing.[3] In patients with heart failure and reduced left ventricular (LV) ejection fraction but without angina, it has not yet been determined whether routine evaluation of possible myocardial ischemia/viability and coronary artery disease should be performed.[3]

Non pharmacological manganite of chronic heart failure.

For patients with heart failure from LV dysfunction without chest pain and without a history of coronary artery disease, coronary angiography may be useful in young patients to exclude congenital coronary anomalies. However, because clinical outcomes have not been shown to improve in patients without angina, coronary angiography may not be as useful in older patients for evaluating the presence of coronary artery disease.[3] Some experts nonetheless suggest excluding coronary artery disease whenever possible, particularly in the presence of diabetes or other conditions associated with silent myocardial ischemia, because LV function may show improvement with revascularization.[3]

In general, if coronary artery disease has already been excluded as the cause of abnormalities in LV function, it is not necessary to perform repeated evaluations for ischemia (invasive or noninvasive) provided the patient's clinical status has not changed to suggest the development of ischemic disease.[3]

Valvular heart disease

Valvular heart disease may be the underlying etiology or an important aggravating factor in heart failure.[3, 4, 5]

Sleep apnea

Sleep apnea has an increased prevalence in patients with heart failure and is associated with increased mortality[4] due to further neurohormonal activation, although randomized, controlled data are lacking. Patients with heart failure and suspected sleep-disordered breathing or excessive daytime sleepiness should undergo a formal sleep assessment.[13] [15]

Sleep apnea should be treated aggressively in heart failure patients. Guidelines recommend providing oxygen supplementation and continuous positive airway pressure (CPAP).[4, 13, 15] However, the recommendations differ on the use of adaptive servo-ventilation (ASV): The 2017 focused update guideline of the 2013 American College of Cardiology/American Heart Association/Heart Failure Society of America (ACC/AHA/HFSA) guidelines indicates ASV causes harm in patients with New York Heart Association (NYHA) class II-IV heart failure with reduced ejection fraction (HFpEF) and central sleep apnea,[13] whereas the 2016 European Society of Cardiology (ESC) indicates that ASV may be considered for treating noctural hypoxemia in those with heart failure and sleep apnea.[4]

Non pharmacological manganite of chronic heart failure.

A long-term study involving 283 heart failure patients who had an implanted cardiac resynchronization device with cardioverter-defibrillator concluded that obstructive sleep apnea (OSA) and/or central sleep apnea (CSA) are independently associated with an increased risk for ventricular arrhythmias requiring cardioverter-defibrillator therapies.[106]

Anemia

Anemia is also common in chronic heart failure. Whether anemia is a reflection of the severity of the heart failure or contributes to worsening heart failure is not clear. Potential etiologies of anemia in heart failure involve poor nutrition, angiotensin-converting enzyme inhibitors (ACEIs), the renin-angiotensin-aldosterone system (RAAS), inflammatory cytokines, hemodilution, and renal dysfunction. Anemia in heart failure is associated with increased mortality.[16]

The 2010 HFSA,[5] 2013 ACC Foundation (ACCF)/AHA,[3] 2016 ACC/AHA/HFSA,[14] and 2016 ESC guidelines[4] made no recommendations regarding the administration of iron to patients with heart failure, although the ACC/AHA noted that several small studies suggested a benefit in mild anemia and heart failure,[3] and the ESC observed that intravenous (IV) ferric carboxymaltose may potentially lead to sustainable improvements in function, symptoms, and quality of life.[4] However, the ACC/AHA's 2017 focused update to the 2013 guidelines has a class IIb recommendation for IV iron replacement for patients with NYHA class II and III heart failure and iron deficiency (ferritin < 100 ng/mL or 100-300 ng/mL if transferrin saturation < 20%).[13] In addition, their class III recommendation is to avoid using erythropoietin-stimulating agents in patients with heart failure and anemia to improve morbidity and mortality owing to a lack of benefit.[13]

Cardiorenal syndrome

Cardiorenal syndrome reflects advanced cardiorenal dysregulation manifested by acute heart failure, worsening renal function, and diuretic resistance. It is equally prevalent in patients with HFpEF and those with LV systolic dysfunction. Worsening renal function is one of the three predictors of increased mortality in hospitalized patients with heart failure regardless of the LVEF.

Cardiorenal syndrome can be classified into the following five types[17] :

Non pharmacological manganite of chronic heart failure.

- CR1: Rapid worsening of cardiac function leading to acute kidney injury (HFpEF, acute heart failure, cardiogenic shock, and right ventricular [RV] failure)
- CR2: Worsening renal function due to progression of chronic heart failure
- CR3: Abrupt and primary worsening of kidney function leading to acute cardiac dysfunction (heart failure, arrhythmia, ischemia)
- CR4: Chronic kidney disease leading to progressive cardiac dysfunction, LV hypertrophy (LVH), and diastolic dysfunction
- CR5: Combination of cardiac and renal dysfunction due to acute and chronic systemic conditions

The pathophysiology of CR1 and CR2 is complex and multifactorial, involving neurohormonal activation (RAAS, sympathetic nervous system, arginine vasopressin, natriuretic peptides, adenosine receptor activation), low arterial pressure, and high central venous pressure, leading to lower transglomerular perfusion pressure and decreased availability of diuretics to the proximal nephron. This results in an increased reabsorption of sodium and water and poor diuretic response—hence, diuretic resistance despite escalating doses of oral or IV diuretics.

Treatment of cardiorenal syndrome in patients with heart failure is largely empirical, but it typically involves the use of combination diuretics, vasodilators, and inotropes as indicated.[109] Ultrafiltration is recommended for symptomatic relief by the ACC/AHA guidelines for patients with heart failure that is refractory to diuretic therapy.[3, 13] The 2017 ACC/AHA focused update noted the following five criteria may be indications for renal replacement therapy in these patients[13] :

- Oliguria unresponsive to fluid resuscitation measures
- Severe hyperkalaemia (potassium level >6.5 mmol/L)
- Severe acidemia (pH < 7.2)
- Serum urea level above 25 mmol/L (150 mg/dL)
- Serum creatinine over 300 µmol/L (>3.4 mg/dL)

A sudden increase in creatinine levels can be seen after the initiation of diuretic therapy, and it is often mistakenly considered evidence of overdiuresis or intravascular depletion (even in the presence of fluid overload). A common error in this situation is to decrease the dose of ACEIs, angiotensin-receptor blockers (ARBs), and/or diuretics, or to even withdraw

one of these agents. In fact, when diuresis or ultrafiltration is continued, patients demonstrate improved renal function, decreased total body fluid, and increased response to diuretics, as central venous pressure falls.

Low-dose dopamine has been used in combination with diuretic therapy, on the supposition that it can increase kidney perfusion. Data have been contradictory, however. In a randomized controlled study, Giamouzis et al found that the combination of low-dose furosemide and low-dose dopamine was equally as effective as high-dose furosemide for kidney function in patients with acute decompensated heart failure.[19] In addition, patients who received dopamine and furosemide were less likely to have worsened renal function or hypokalemia at 24 hours.[19]

Use of nesiritide, a synthetic natriuretic peptide, to increase diuresis in these cases has not been studied. A meta-analysis of several trials using nesiritide suggested the potential of worsening renal function, although this has not been demonstrated in prospective trials. Results of the Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure (ASCEND-HF) trial suggested that, although nesiritide is safe, it does not provide additional efficacy when added to standard therapy.[111] In another large study comprising 7141 patients with decompensated heart failure, the use of nesiritide did not have an effect on renal function, rehospitalization, and mortality, albeit there was a small but nonsignificant impact on dyspnea when used in conjunction with other therapies.[18]

The Efficacy of Vasopressin Antagonism in Heart Failure Outcome Study with Tolvaptan (EVEREST) trial showed that the addition of the vasopressin antagonist tolvaptan to diuretic therapy facilitates diuresis in acute heart failure. However, tolvaptan had no impact on mortality or hospitalizations in this setting.[20]

Adenosine receptor antagonists have been proposed for protecting renal function in acute heart failure. However, in a double-blind, placebo-controlled trial, the adenosine A1−receptor antagonist rolofylline demonstrated no benefit for patients hospitalized for acute heart failure with impaired renal function.[21]

A meta-analysis performed by Badve et al suggested that treatment with beta-blockers reduced all-cause mortality in patients with chronic kidney disease and systolic heart failure (risk ratio, 0.72).[22]

Non pharmacological manganite of chronic heart failure.

Atrial fibrillation

Many patients with heart failure also have atrial fibrillation, and the two conditions can adversely affect each other. However, in the AFFIRM (Atrial Fibrillation Follow-up Investigation of Rhythm Management) trial, there was no difference in stroke, heart failure exacerbation, or cardiovascular mortality in patients treated with rhythm control (amiodarone) and patients treated with rate control.[116] All of these patients require anticoagulation for stroke prevention, which can be achieved by using warfarin or a direct thrombin inhibitor (no need to follow protime).

A meta-analysis found that patients with LV systolic dysfunction who underwent catheter ablation for atrial fibrillation demonstrated significant improvements in LVEF, and their risk for recurrent atrial fibrillation or atrial tachycardia after catheter ablation was similar to that in patients with normal LV function after ablation.[23] However, patients with LV systolic dysfunction were more likely to require repeat procedures.

In contrast, MacDonald et al reported that in patients with advanced heart failure and severe LV systolic dysfunction, radiofrequency ablation for persistent atrial fibrillation resulted in long-term restoration of sinus rhythm in only 50% of cases.[118] Radiofrequency ablation also failed to improve such secondary outcomes as walking distance or quality of life, and the rate of related serious complications was 15%.

Nonpharmacologic Therapy

Patients with heart failure can benefit from attention to exercise, diet, and nutrition.[3, 5] Restriction of activity promotes physical deconditioning, so physical activity should be encouraged. However, limitation of activity is appropriate during acute heart failure exacerbations and in patients with suspected myocarditis. Most patients should not participate in heavy labor or exhaustive sports.

A 2012 meta-analysis showed that aerobic exercise training, particularly over the long term, can reverse left ventricular remodelling in clinically stable heart failure patients, whereas strength training had no effect on remodelling.[24]

Non pharmacological manganite of chronic heart failure.

Because nonadherence to diet and medication can have rapid and profound adverse effects on patients' clinical status, close observation and follow-up are important aspects of care.[3, 4] Patient education and close supervision, including surveillance by the patient and family, can improve adherence. These measures also facilitate early detection of weight gain or slightly worsened symptoms, which often occur several days before major clinical episodes that require emergency care or hospitalization. Patients can then alert their clinicians, who may be able to prevent such episodes through prompt intervention.

Dietary sodium restriction to 2-3 g/day is recommended. Fluid restriction to 2 L/day is recommended for patients with evidence of hyponatremia (Na < 130 mEq/dL) and for those whose fluid status is difficult to control despite sodium restriction and the use of high-dose diuretics. Caloric supplementation is recommended for patients with evidence of cardiac cachexia.

An analysis of concentrations of plasma eicosapentaenoic acid (EPA), a long-chain omega-3 fatty acid, in the Cardiovascular Health Study identified plasma phospholipid EPA concentration as being inversely related to incident congestive heart failure.[120] These results support additional studies on the potential benefits of omega-3 fatty acids for primary prevention of heart failure.

The GISSI-HF (Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico) trial, which included nearly 7000 patients with systolic heart failure (any LV ejection fraction) who received either 1 g of omega-3 polyunsaturated fatty acids (PUFAs) or placebo daily, demonstrated that the PUFA regimen had a small but significant reduction in both all-cause mortality and all-cause mortality/hospitalization for cardiovascular causes.[25]

Electrophysiologic Intervention

Devices for electrophysiologic intervention in heart failure include pacemakers, cardiac resynchronization therapy (CRT) devices, and implantable cardioverter-defibrillators (ICDs). CRT should be considered in patients with NYHA class II-IV, an LVEF of 35% or less, normal sinus rhythm and a QRS duration of 150 ms or longer, with a left bundle branch pattern.[3, 13]

Non pharmacological manganite of chronic heart failure.

In April 2014, the FDA approved 10 Medtronic biventricular pacemakers, some with defibrillators and some without, for use in patients with less severe systolic heart failure and atrioventricular (AV) block.[26, 27] Approval was based on a study of 691 patients with first-, second-, or third-degree AV block, New York Heart Association (NYHA) class I-III heart failure, and left ventricular ejection fraction (LVEF) below 50%, in which biventricular pacing over 3 years reduced all-cause mortality by 26%, reduced heart failure-related urgent care, and increased LV end-systolic volume index by more than 15%.[26, 27]

Pacemakers

Maintaining a normal chronotropic response and AV synchrony may be particularly significant for patients with heart failure.[4] Because right ventricular (RV) pacing may worsen heart failure due to an increase in ventricular dysynchrony, placement of a dual-chamber pacemaker in heart failure patients in the absence of symptomatic bradycardia or high-degree AV block is not recommended.

Implantable cardioverter-defibrillators

The role of implantable cardioverter-defibrillators (ICDs) has rapidly expanded. Sudden death is 5-10 times more common in patients with heart failure than in the general population. ICD placement results in remarkable reductions in sudden death from ischemic and nonischemic sustained ventricular tachyarrhythmias in heart failure patients. (See also the Medscape Reference articles Implantable Cardioverter-Defibrillators and Pacemakers and Implantable Cardioverter Defibrillators.)

In moderately symptomatic heart failure patients with an LVEF of 35% or less, primary prevention with an ICD provides no benefit in some cases but substantial benefit in others. A model based on routinely collected clinical variables can be used to predict the benefit of ICD treatment, according to a study by Levy et al.[28] Using data from the placebo arm of the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) with their risk prediction model, Levy et al showed that patients could be classified into five groups on the basis of predicted 4-year mortality. In the treatment arm, ICD implantation decreased the relative risk of sudden cardiac death by 88% in patients with the lowest baseline mortality risk but only by 24% in the highest-risk group.

ICD treatment decreased relative risk of total mortality by 54% in the lowest-risk group but only by 2% in the highest-risk group.[28]

It is important to note that use of the SCD-HeFT model has not been prospectively validated for risk stratification in the decision for ICD implantation. More trials are needed.

Cardiac resynchronization therapy/biventricular pacing

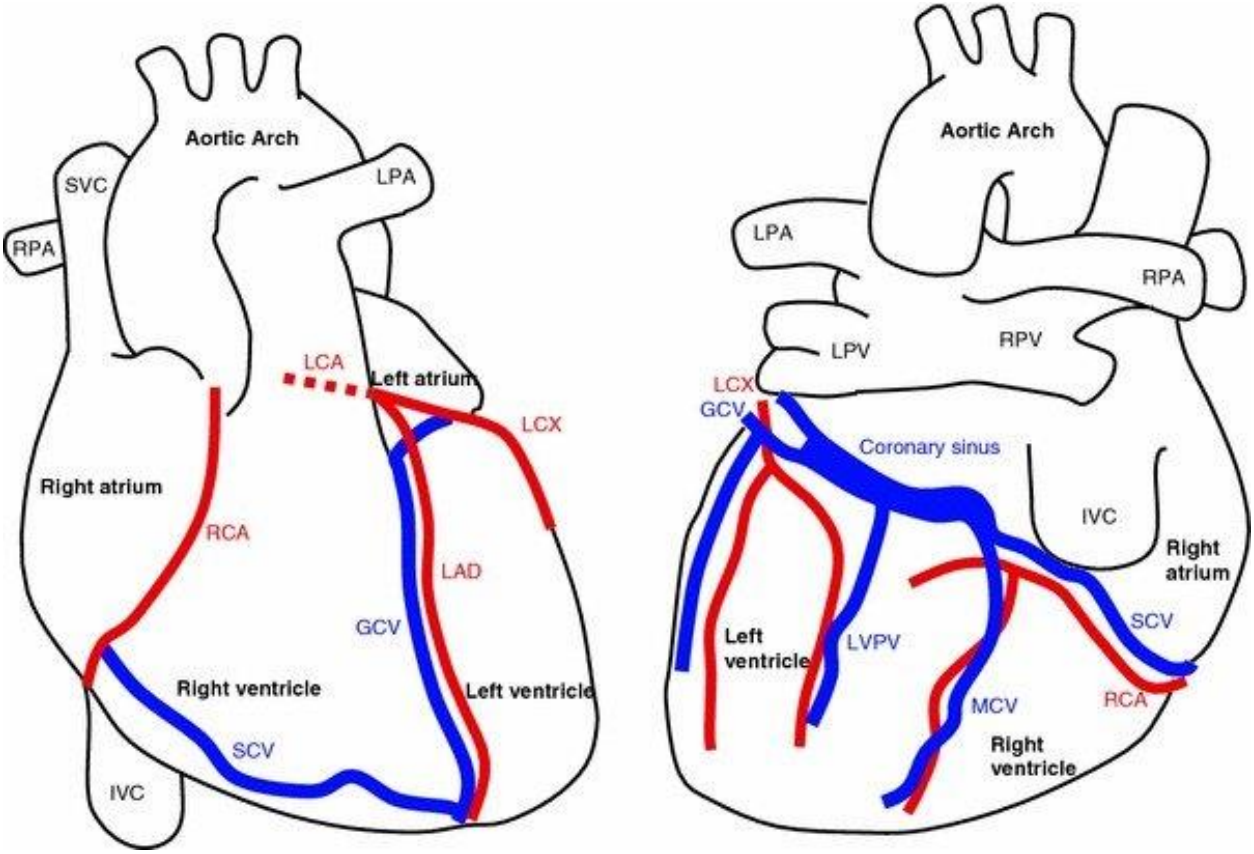
Patients with heart failure and interventricular conduction abnormalities (roughly defined as those with a QRS interval >120 ms) are potential candidates for cardiac resynchronization therapy (CRT) by means of an inserted biventricular pacemaker. CRT aims to improve cardiac performance by restoring the heart's interventricular septal electrical and mechanical synchrony.[5, 165] Thus, it reduces presystolic mitral regurgitation and optimizes diastolic function by reducing the mismatch between cardiac contractility and energy expenditure.[29]

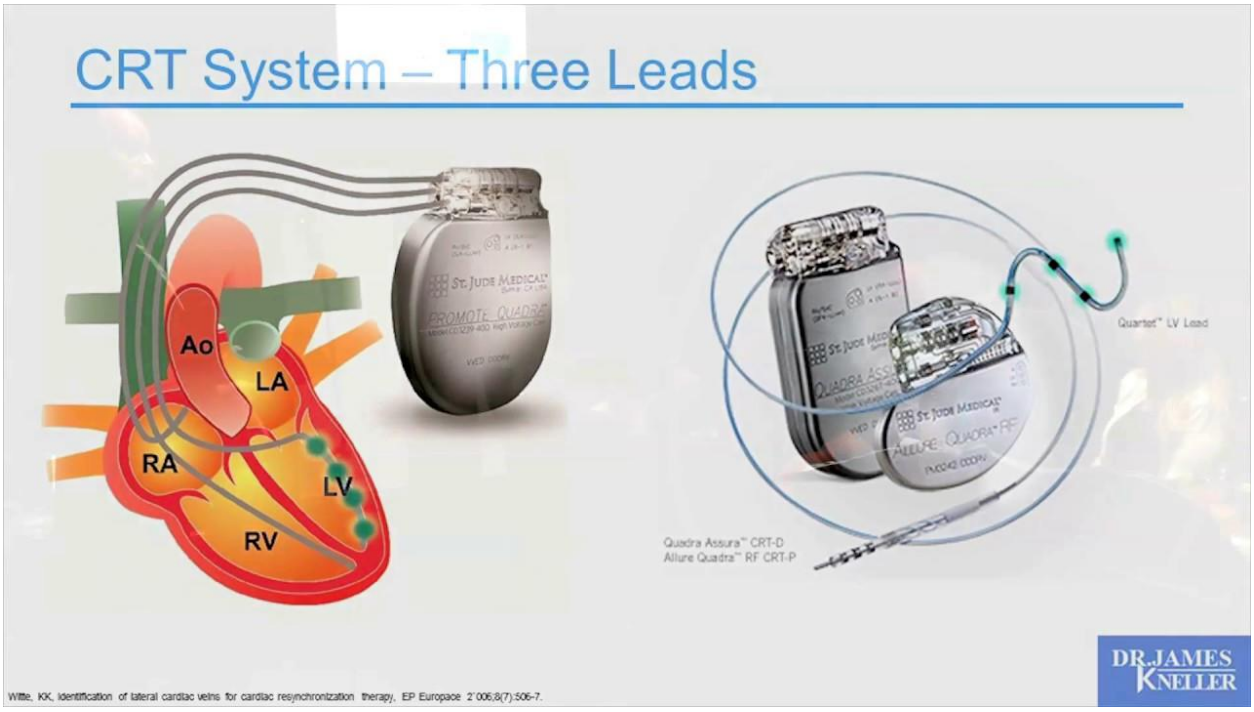
The combination of biventricular pacing with ICD implantation (CRT-ICD) may be beneficial for patients with NYHA class II heart failure, an LVEF of 30% or less, and a QRS duration longer than 150 ms. The Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy (MADIT-CRT) and Resynchronization/Defibrillation for Ambulatory Heart Failure Trial (RAFT) investigators reported significant improvement in mortality and morbidity with CRT-ICD treatment versus ICD alone in this group of patients.[30]

Patients with unfavorable coronary sinus anatomy often cannot have a CRT properly placed adjacent to the posterolateral wall of the LV. A study by Giraldi et al suggests that in such patients, a mini-thoracotomy allows for proper lead placement.[30] These patients, when compared to those who had typical transvenous placement (thus not allowing for the preferred posterolateral wall lead placement), had improved outcomes in terms of improved EF and decreased end-systolic volume.[30]

Regarding technique, three cardiac leads are placed transvenously: an atrial lead, an RV lead, and an LV lead (which is threaded through the coronary sinus and out one of its lateral wall tributaries). Surgeons have assisted difficult transvenous LV placements by epicardially inserting LV leads using a number of techniques (eg, mini-thoracotomy, thoracoscopy, robotically assisted methods).

Non pharmacological manganite of chronic heart failure.





Clinical trials of cardiac resynchronization therapy

Several prospective, randomized trials have been performed to evaluate the effectiveness of CRT. The Multicenter InSync Randomized Clinical Evaluation (MIRACLE) study group demonstrated an improvement in NYHA functional class, quality of life, and LVEF.[31]

As noted above, the MADIT-CRT demonstrated reduction in the risk of heart failure events in patients treated with CRT plus an ICD over that of individuals treated with ICD alone. This randomized trial included 1820 patients with an EF of 30% or less, a QRS duration of 130 ms or more, and NYHA class I or II symptoms.[32] During an average follow-up of 2.4 years, death from any cause or a nonfatal heart failure event occurred in 17.2% of patients in the CRT-ICD group versus 25.3% of patients in the ICD-only group. In particular, there was a 41% reduction in the risk of heart failure events in patients in the CRT group, which was evident primarily in patients with a QRS duration of 150 ms or more. CRT was associated with a significant reduction in LV volume and improvement in the EF. No significant difference occurred between the two groups in the overall risk of death.[32]

In a follow-up to MADIT-CRT, women seemed to achieve a better response result from resynchronization therapy than men, with a significant 69% reduction in death or heart failure and a 70% reduction in heart failure alone. Those benefits were associated with consistently greater echocardiographic evidence of reverse cardiac remodeling.[34]

Additional findings from MADIT-CRT concerned the relative effects of metoprolol and carvedilol in heart failure patients with devices in place.[33] The key variables were (a) rate of hospitalization for heart failure or death and (b) incidence of ventricular arrhythmia.

Treatment with carvedilol yielded a significantly lower rate of hospitalization for heart failure or death than treatment with metoprolol (23% vs 30%), a reduction that was especially pronounced in patients undergoing CRT with implantable cardioverter-defibrillator (CRT-D), including those with left bundle-branch block (LBBB).[33] The incidence of ventricular arrhythmia was 26% with metoprolol and 22% with carvedilol. There was a clear dose-dependent relation for carvedilol, which was not seen for metoprolol.

In addition to augmenting functional capacity, CRT also appears to favorably affect mortality. The Cardiac Resynchronization-Heart Failure (CARE-HF)

trial, which studied CRT placement in patients with NYHA class III or IV heart failure due to LV systolic dysfunction and cardiac dyssynchrony, showed a 36% reduction in death with biventricular pacing.[35]

In the Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) trial, biventricular pacing reduced the rate of death from any cause or hospitalization for any cause by approximately 20%. The COMPANION trial was conducted in patients with NYHA class III or IV heart failure due to ischemic or nonischemic cardiomyopathies and a QRS interval of at least 120 ms. The addition of a defibrillator to biventricular pacing incrementally increased the survival benefit, resulting in a substantial 36% reduction in the risk of death compared with optimal pharmacologic therapy.[38]

In both the CARE-HF and the COMPANION studies, mortality was largely due to sudden death.[35, 38]

Noting that high percentages of RV apical pacing could promote LV systolic dysfunction, the investigators from Biventricular versus Right Ventricular Pacing in Heart Failure Patients with Atrioventricular Block (BLOCK-HF) trial found that biventricular pacing improved outcomes in patients with AV block and NYHA class I-III heart failure over that of RV pacing.[39] A total of 691 volunteers received a pacemaker or ICD with leads in both ventricles (the LV lead was kept inactive in about half of participants). At follow-up (average, 37 months), 55.6% of the patients in the RV pacing group had died or had worsening heart failure, compared with 45.8% in the biventricular pacing group. The rate of adverse events was comparable in the two groups, and most problems occurred during the first month.[39]

Revascularization Procedures

Coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) are revascularization procedures that should be considered in selected patients with heart failure and coronary artery disease (CAD). The choice between CABG and PCI depends on the following factors:

- Patient comorbidities
- Procedural risk
- Coronary anatomy
- Likely extent of viable myocardium in the area to be revascularized

- Ischemic symptoms
- Left ventricular (LV) function
- Presence of hemodynamically significant valvular disease

In patients who are at low risk for CAD, findings from noninvasive tests such as exercise electrocardiography (ECG), stress echocardiography, and stress nuclear perfusion imaging should determine whether subsequent angiography is indicated.[3, 4, 5]

Studies of medical versus surgical therapy for CAD have historically focused on patients with normal LV function. However, a significantly increased survival rate after CABG in a subset of patients with an LV ejection fraction (EF) below 50%, in comparison with the survival rate in patients who were randomly selected to receive medical therapy, was demonstrated in the Veterans Affairs Cooperative Study of Surgery. This survival benefit was particularly evident at the 11-year follow-up point (50% CABG vs 38% medical therapy).[40] However, at 18-year follow-up, overall survival rates were 30% for the CABG group and 33% for the medical therapy group; the investigators noted that CABG appeared to be effective for reducing mortality solely in those with a poor natural history and did not reduce the myocardial infarction incidence or combined incidence infarction or death.[41] Patients with low risk and a good prognosis with medical therapy received no survival benefit with CABG at any point during the follow-up period.

Surgical revascularization prolonged survival to a greater degree than did medical therapy in most clinical and angiographic subgroups in the Coronary Artery Surgery Study (CASS) of patients with left main equivalent disease.[42] Of importance, this study demonstrated that surgical therapy markedly improved the 5-year cumulative survival rate in patients with an EF of less than 50% (80% vs 47%).[40]

These early randomized trials were limited by their inclusion of patients who had what is currently considered a good EF. That is, many patients referred for coronary revascularization live with EFs below 35%.

According to a number of studies, surgical revascularization can benefit patients who have ischemic heart failure and substantial areas of viable myocardium in the following ways:

- Reduced mortality rates
- Improved New York Heart Association (NYHA) classification

- Favorable alteration of LV geometry
- Increased LVEFs

For example, surgical revascularization confers a dramatic survival benefit in patients with a substantial amount of hibernating myocardium (ie, regions of the heart that are dysfunctional under ischemic conditions but that can regain normal function after blood flow is restored).[179, 180] For patients with at least 5 of 12 segments showing myocardial viability, revascularization has been found to result in a cardiac mortality of 3%, versus 31% for medically treated patients with viable myocardium.

Coronary artery bypass grafting

The role of CABG in patients with CAD and heart failure has been unclear. Clinical trials from the 1970s that established the benefit of CABG for patients with CAD excluded patients with an EF below 35%. In addition, major advances in medical therapy and cardiac surgery have taken place since these trials.[43]

Investigators from Yale University and the University of Virginia, among many others, published their results of CABG in patients with extremely poor LV function who were on the transplant waiting list. Elefteriades et al reported that in patients with EFs below 30% who underwent CABG, the survival rate was 80% at 4.5 years.[44] This figure approaches that of cardiac transplantation. Kron et al reported a similar 3-year survival rate (83%) in patients who underwent coronary artery bypass with an EF below 20%.[45]

STICH trial

The Surgical Treatment for Congestive Heart Failure (STICH) study found no significant difference between medical therapy alone and medical therapy plus CABG with respect to death from any cause (the primary study outcome).[43, 184, 185] STICH included 1212 patients with an EF of 35% or less and CAD amenable to CABG. Patients were randomized to either CABG with intensive medical therapy or medical therapy alone and followed up for a median of 56 months.

There was no difference between the treatment groups for all-cause mortality.[43] Owing to the lack of significant difference in the primary endpoint, the secondary endpoints should be viewed cautiously. Except for 30-day mortality, secondary study results favored CABG; compared with

study patients assigned to medical therapy alone, patients assigned to CABG had lower rates of death from cardiovascular causes and of death from any cause or hospitalization for cardiovascular causes. Surprisingly, the presence of viable, hibernating myocardium was not predictive of improved outcomes from CABG.[43]

Taken together, these findings suggest that in the absence of severe angina or left main disease, medical therapy alone remains a reasonable option for patients with an EF of 35% or less and CAD. Furthermore, current methods of assessing myocardial viability/hibernating myocardium may not accurately predict benefit from revascularization, although cardiac magnetic resonance imaging offers a promise of accuracy in identifying viable myocardium and predicting the success of revascularization in patients with low EFs.

Results from the STICH Extension Study (STICHES), which evaluated the long-term, 10-year outcomes of CABG in 1212 patients with ischemic cardiomyopathy and an ejection fraction of 35% or less, concluded that the rates of death from any cause, death from cardiovascular causes, and death from any cause or hospitalization for cardiovascular causes were significantly lower in patients who underwent CABG and received medical therapy than among those who received medical therapy alone.[46]

The adoption of techniques on and off cardiopulmonary bypass, as well as beating-heart techniques for revascularization, highlight the aim of treating high-risk patients.[186] The surgery in the STICH trial was performed with these modern surgical advantages. Preventive strategies include the increased use of bilateral mammary and arterial grafting.[47]

Valvular Surgery

Valvular heart disease may be the underlying etiology or an important aggravating factor in heart failure.[3, 4, 5]

Aortic valve replacement

Diseases of the aortic valve can frequently lead to the onset and progression of heart failure. Although the natural histories of aortic stenosis and aortic regurgitation are well known, patients are often followed up conservatively after they present with clinically significant heart failure.

Non pharmacological manganite of chronic heart failure.

Heart failure is a common indication for aortic valve replacement (AVR), but one must be cautious in patients with a low left ventricular ejection fraction (LVEF) and possible aortic stenosis. Assessment of contractile reserve with dobutamine has been demonstrated as a reliable method to determine which patients with low EF and aortic stenosis may benefit from AVR.[48]

If no contractile reserve is present (a finding that suggests some ventricular reserve), the outcome with standard AVR is poor. In this situation, transplantation might be the only option, although the use of percutaneous valves, an apical aortic conduit, or a left ventricular assist device (LVAD) may offer an intermediate solution.

Indications

Decision making regarding valve surgery should not be delayed by medical treatment. Be cautious in using vasodilators (angiotensin-converting enzyme inhibitors [ACEIs], angiotensin-receptor blockers [ARBs], and nitrates) in patients with severe aortic stenosis, as these agents may cause significant hypotension.[3, 4, 5, 13]

Surgery is recommended in selected patients with symptomatic heart failure and severe aortic stenosis or severe aortic regurgitation, as well as in asymptomatic patients with severe aortic stenosis or severe aortic regurgitation and impaired LVEF (< 50%). This intervention may be considered in patients with a severely reduced valve area and LV dysfunction.

Patient survival

Of the three classic symptoms of aortic stenosis—syncope, angina, and dyspnea—dyspnea is the most robust risk factor for death. Only 50% of patients with dyspnea in this setting are still alive within 2 years.[49] Angina is associated with a mortality risk of 50% within 5 years, whereas syncope confers a 50% mortality risk in 3 years.

In contrast, the age-corrected survival rate for patients undergoing AVR for aortic stenosis is similar to that for the normal population.[190] Once patients develop severe LV dysfunction, however, the results of AVR are somewhat guarded.[50] Because of poor LV function, these patients are unable to develop significant transvalvular gradients (ie, low-output, low-gradient aortic stenosis).

A critical aspect of the decision for or against AVR is whether the ventricular dysfunction is truly valvular or reflects other forms of cardiomyopathy, such as ischemia or restrictive processes. Valvular dysfunction improves with AVR; other forms do not.

Precise measurement of the area of the aortic valve is difficult, because the calculated area is directly proportional to cardiac output. Also, the Gorlin constant varies at lower outputs. Therefore, in this situation, valvular areas might be considered critically small when at surgery the valve is found to be only moderately diseased.

Preoperative evaluation with dobutamine testing to increase contractile reserve or with vasodilator-induced stress echocardiography by using the continuity equation rather than the Gorlin formula can be helpful in making this distinction. The results can guide the physician or surgeon in determining whether the patient is a candidate for the relatively high-risk procedure.[51] Nevertheless, because of the possibility of ventricular recovery and lengthened patient survival, most patients with heart failure and aortic stenosis are offered valve replacement.[193]

Surgical timing

Timing of surgical intervention for aortic insufficiency is more challenging in patients just described than in patients with aortic stenosis. However, as before, once symptoms occur and once evidence of LV structural changes become apparent, morbidity and mortality due to aortic insufficiency increase.[52]

As with aortic stenosis, early intervention before the onset of severe LV dysfunction is crucial to improving the survival of patients with aortic insufficiency, as was shown in a retrospective review from the Mayo Clinic.[53, 196] In this study, in which 450 patients who underwent AVR for aortic insufficiency were compared according to ranges of EF (< 35%, 35-50%, >50%), although the group with severe dysfunction had an operative mortality of 14%, the EF improved, and the group's 10-year survival rate was 41%.[53]

Mitral valve repair

Mitral valve regurgitation can either cause or result from chronic heart failure. Its presence is an independent risk factor for cardiovascular morbidity and

mortality.[54] In addition to frank rupture of the papillary muscle in association with acute myocardial infarction (MI), chronic ischemic cardiomyopathies result in migration of the papillary muscle as the ventricle dilates. This dilation causes tenting of the mitral leaflets, restricting their coaptation.

Dilated cardiomyopathies can have similar issues, as well as annular dilatation. In addition to mitral regurgitation, the alteration in LV geometry contributes to volume overload, increases LV wall tension, and leaves patients susceptible to exacerbations of heart failure.[55]

Mitral valve surgery in patients with heart failure has gained favor because it abolishes the regurgitant lesion and decreases symptoms. The pathophysiologic rationales for repair or replacement are to reverse the cycle of excessive ventricular volume, to allow for ventricular unloading, and to promote myocardial remodeling.

Among other researchers, a group from Michigan advocated mitral repair in the population with heart failure. Bolling and colleagues demonstrated that mitral valve repair increased the EF, improved NYHA classes from 3.9 to 2.0, and decreased the number of hospitalizations, although the results were reproducible by other centers.[199] Additional effects with repair in these patients were an increase in coronary blood flow reserve afforded by the reduction in LV volume.[60]

Despite the potential benefits of mitral reconstruction surgery, a retrospective review showed no reduction in long-term mortality among patients with severe mitral regurgitation and significant LV dysfunction who underwent mitral valve repair. Mitral valve annuloplasty was not predictive of clinical outcomes and did not improve mortality. Factors associated with lower mortality were ACEI use, beta blockade, normal mean arterial pressures, and normal serum sodium concentrations.[61] The results of this analysis were not overly surprising. For example, in most patients in this situation, heart failure is not due to flail leaflets but is secondary to ventricular dysfunction.

In evaluating studies of heart failure with mitral regurgitation, it is important to separate the etiology (eg, ischemic vs dilated) as well as the surgical approaches. Future trials must be designed to distinguish differences between various surgical strategies, such as annuloplasty, resuspension of

the papillary muscle, secondary chordal transection, ventricular reconstruction, passive restraints, and chordal-sparing valve replacement. A paramount goal with these procedures is for the patient to have little or no residual mitral regurgitation.[61]

Indications

Consider mitral valve surgery in patients with heart failure and severe mitral valve regurgitation whenever coronary revascularization is an option.[4] Candidates would include the following[4] :

- Patients with severe mitral regurgitation due to an organic structural abnormality or damage to the mitral valve in whom symptoms of heart failure develop
- Patients with an LVEF greater than 30%
- Patients with severe ischemic mitral regurgitation and an LVEF greater than 30% when coronary artery bypass grafting (CABG) is planned

Cardiac resynchronization therapy (CRT) should be considered in eligible patients with functional mitral regurgitation, as it may improve LV geometry and papillary muscle dyssynchrony as well as potentially reduce mitral regurgitation.[4]

Annuloplasty

Treatment of cardiomyopathy-associated mitral regurgitation most commonly involves the insertion of either a complete or a partial band attached to the annulus of the mitral valve. Thus, mitral repair deals with only one aspect of the patient's overall pathophysiologic condition. That is, annuloplasty rings may assist with tenting of the leaflet, but they do not address displacement of the papillary muscle with ventricular scarring.[62] In many patients, the underlying problem (ie, primary myopathy) continues unabated.

In general, ischemic mitral regurgitation is a ventricular problem. Many operations allow for coaptation and no mitral regurgitation when the patient leaves the operating room. However, as the LV continues to dilate, mitral regurgitation often recurs. Therefore, it is overambitious to say that annuloplasty cures this condition. As a result, many other approaches have been attempted (eg, chordal cutting, use of restraint devices, papillary relocation). However, results have been mixed.

Non pharmacological manganite of chronic heart failure.

Mitral valve replacement

If repair is deemed improbable, mitral replacement should be performed. Traditional mitral valve replacement includes complete resection of the leaflets and the chordal attachments. This destruction of the subvalvular apparatus results in ventricular dysfunction. In patients with mitral regurgitation and heart failure, preservation of the chordal attachments to the ventricle with valve replacement might provide results similar to, or even better than, those of annuloplasty.[63]

Although the benefits in terms of quality of life (decreased heart failure) might not portend increased survival in these high-risk patients, they likely keep low-EF mitral valve interventions in the armamentarium of surgeons who manage heart failure.

A relatively recent approach to functional and degenerative mitral valve regurgitation is percutaneous mitral valve repair, using devices such as the MitraClip system. The EVEREST (Endovascular Valve Edge-to-Edge Repair Study II) randomized trial reported low rates of morbidity and mortality and reduction of acute mitral regurgitation to less than 2+ in the majority of patients, with sustained freedom from death, surgery, or recurrent mitral regurgitation in a substantial proportion of patients.[64]

A systematic review and meta-analysis of data from 2615 patients over nine studies found that percutaneous edge-to-edge mitral valve repair with the MitraClip is likely to be a safe and effective option in patients with both functional and degenerative mitral regurgitation. Similarly, data from the German Transcatheter Mitral Valve Interventions (TRAMI) Registry found comparable MitraClip results for procedural safety of percutaneous mitral valve repair, efficacy, and clinical improvement after 1 year between patients with severely impaired LVEF (EF < 30%) and those with preserved LV function (EF >50%). Over two thirds (69.5%) of those with an EF below 30% improved by one or more NYHA functional class, a significantly higher proportion than the 56.8% of patients with preserved LV function whose NYHA class improved ($P< 0.05$).[65]

Ventricular Restoration

Non pharmacological manganite of chronic heart failure.

After a transmural myocardial infarction (MI) occurs, the ventricle pathologically remodels from its normal elliptical shape to a spherical shape. This change in geometry is in part responsible for the constellation of symptoms associated with heart failure and decreased survival.[66]

Several ventricular restoration techniques exist. All aim to correct the above-described pathologic alteration in geometry. Most approaches involve incising and excluding nonviable myocardium with either patch or primary reconstruction to decrease ventricular volume.

The Batista procedure (reduction left ventriculoplasty) was designed with the intent of providing ventricular restoration, but it was associated with high failure rates. Although the initial enthusiasm for ventricular resection to treat nonischemic dilated cardiomyopathies has faded, a long-established finding is that resection of dyskinetic segments associated with left ventricle (LV) aneurysms can increase patients' functional status and prolong life.[67]

The success of early lytic and percutaneous therapy for acute MI has decreased the incidence of true LV aneurysms. As such, ventricular restoration now focuses on excluding relatively subtle regions of akinetic myocardium.

Benefits from ventricular restoration using the technique described by Dor were reported in by the International Reconstructive Endoventricular Surgery Returning Torsion Original Radius Elliptical Shape to the Left Ventricle (RESTORE) group. The investigators reported that among the patients studied, ejection fractions (EFs) increased from 29.6% to 39.5%, the end-systolic volume index decreased, and New York Heart Association (NYHA) functional classes improved from 67% class III/IV patients before surgery to 85% class I/II patients after surgery.[68]

The major study of ventricular reconstruction has been the STICH trial. Investigators randomly assigned 1000 patients with an EF below 35%, coronary artery disease that was amenable to coronary artery bypass grafting (CABG), and dominant anterior LV dysfunction that was amenable to surgical ventricular reconstruction to undergo either CABG alone or CABG with surgical ventricular reconstruction (SVR) and found that SVR reduced the end-systolic volume index by 19%, as compared with a reduction of 6% with CABG alone. The median follow-up was 48 months. Cardiac symptoms and exercise tolerance improved to a similar degree in both groups.

However, no significant difference was observed in death from any cause and hospitalization for cardiac causes. On the basis of these results, SVR cannot be recommended for routine use in patients with ischemic cardiomyopathy and dominant anterior left ventricular dysfunction. [69]

Extracorporeal Membrane Oxygenation

In some cases of extreme cardiopulmonary failure (ie, American College of Cardiology/American Heart Association [ACC/AHA] stage D), the only recourse is complete support with extracorporeal membrane oxygenation (ECMO). ECMO provides both oxygenation and circulation of blood, allowing the lungs and heart time to recover. Unlike cardiopulmonary bypass, whose duration of use is measured in hours, ECMO can be used for 3-10 days.

For ECMO, one cannula is placed percutaneously via the right jugular vein or femoral vein into the right atrium, or it is placed surgically into the right atrial appendage, and another cannula is placed arterially either in the femoral artery or in the aortic arch. The drained venous blood is pumped through the ECMO device, where it is oxygenated, warmed, and anticoagulated. It is then returned to the arterial circulation.

ECMO devices can be used for short-term circulatory support in patients who are expected to recover from a major cardiac insult. Despite encouraging results with ECMO for the management of cardiogenic shock, most patients requiring circulatory assistance can be helped with ventricular support alone. [50]

Ventricular Assist Devices

Ventricular assist devices (VADs) are invaluable tools in the treatment of heart failure, particularly in those with advanced heart failure.A number of these devices are available to support the acutely or chronically decompensated heart (ie, American College of Cardiology/American Heart Association [ACC/AHA] stage D). Depending on the particular device used, the right ventricle (RV) and left ventricle (LV) can be assisted with a LV assist device (LVAD), a RVAD, or a biventricular assist device (BiVAD). An alternative term for a VAD is a ventricular assist system (VAS).[69]

In concept, LVADs, RVADs, and BiVADs are similar. Blood is removed from the failing ventricle and diverted into a pump that delivers blood to either the

aorta (in the case of an LVAD) or the pulmonary artery (in the case of an RVAD). An exception is the Impella device, which is inserted percutaneously into the LV; it draws blood from the LV and expels it into the ascending aorta.

LVADs can often be placed temporarily. In patients with acute, severe myocarditis or those who have undergone cardiotomy, this approach can serve as a bridge to recovery, unloading the dysfunctional heart and perhaps allowing reverse remodeling; in patients with end-stage heart failure, it can serve as a bridge to heart transplantation,[3, 4, 5,] allowing them to undergo rehabilitation and possibly go home before transplantation.

Long-term use (ie, destination therapy rather than bridge therapy) may be a consideration when no definitive procedure is planned.[4] Patients with severe heart failure who are not transplant candidates and who otherwise would die without treatment are candidates for lifetime use of VADs. Destination therapy with LVADs is superior to medical therapy in terms of quantity and quality of life, according to the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) trial and several later studies.[70]

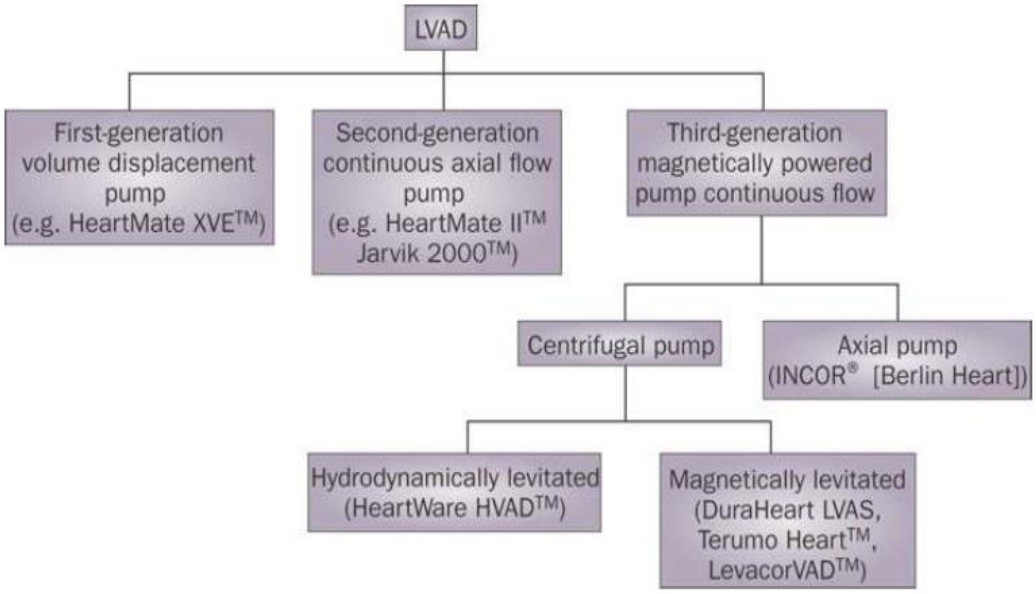
In the United States, several Food and Drug Administration (FDA)–approved options are available for bridging the patient to recovery and transplantation. These options continue to change and evolve. Some examples include the following:

- Abiomed AB5000 Ventricle
- AB Portable Driver
- Thoratec CentriMag Blood Pump
- Thoratec PVAD (Paracorporeal Ventricular Assist Device)
- Thoratec IVAD (Implantable Ventricular Assist Device)
- HeartMate XVE LVAD (also known as HeartMate I)
- HeartMate II LVAS
- TandemHeart Percutaneous LVAD
- HeartAssist 5 Pediatric VAD

The HeartMate LV and HeartWare HVAD assist systems are the only LVADs that are approved by the US Food and Drug Administration (FDA) for destination therapy. Other devices are also under study in the United States for use as destination therapy (eg, Jarvik 2000 VAS[71]).

The HeartMate XVE LVAD does not require warfarin anticoagulation, unlike another well-known first-generation pulsatile pump, the Novacor LVAD. The newer axial-flow pumps (eg, HeartMate II LVAS, Jarvik 2000, HeartAssist 5 Pediatric VAD) are relatively small and easy to insert, and they reduce morbidity; however, these devices do require anticoagulation.

Potential complications of VADs include mechanical breakdown, infection, bleeding, and thromboembolic events. Despite these potential drawbacks, however, the survival rate for patients receiving VADs is roughly 70%. This rate is impressive given the severity of illness in this cohort of patients. Furthermore, the evolving technology raises a host of clinical and physiologic questions that, when studied and answered, continue to advance the field.



Selected trials

In the REMATCH study, survival rates of medically treated and LVAD-treated patients were, respectively, 25% and 52% at 1 year and 8% and 23% at 2 years.[72] This study offered the first prospective, randomized data of very ill, non–transplant-eligible patients with heart failure receiving optimal medical therapy versus an early-generation HeartMate LVAD. In addition to survival advantage, LVAD recipients had improvements in several measures of quality of life.

Non pharmacological manganite of chronic heart failure.

Modifications in technique and perioperative care have reduced the rates of LVAD-related morbidity and mortality observed in the REMATCH trial. Although REMATCH was a single study in very high risk patients, the data serve as proof of concept for the future development of VAD technologies.

Despite the need for an external energy source, most patients can use mechanical circulatory devices in the outpatient setting. Many patients have lived productive lives for longer than 4-6 years with their original device (depending on the device).

Starling et al used INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support) data to determine that following postmarket approval by the FDA, the HeartMate II LVAS, a continuous-flow LVAD, continues to have excellent results as a bridge to heart transplantation relative to other types of LVADs in the following measures[73] :

- The 30-day operative mortality was 4% for the group receiving the HeartMate II compared with 11% for other LVADs
- Ninety-one percent of the group receiving the HeartMate II reached transplantation, cardiac recovery, or ongoing LVAD support by 6 months, compared with 80% for the group receiving other LVADs
- Renal function test measurements such as creatinine and blood urea nitrogen levels were lower in the HeartMate II group
- For all adverse events, the rates were similar or lower for the group that received the HeartMate II, with bleeding being the most frequent adverse event for both groups
- Survival for patients remaining on support at 1 year was 85% for the HeartMate II group, versus 70% for the group with other LVADs
- Relative to baseline, both groups had significant improvement of quality of life at 3 months of support, which was sustained through 12 months

In another study, Ventura et al used a large national data registry to compare posttransplant outcomes between pulsatile-flow (HeartMate XVE [HeartMate I]) and continuous-flow (HeartMate II) LVADs as bridges to transplantation and found similar 1- and 3-year survival rates but less risk of early allograft rejection and sepsis with the HeartMate II device.[74]

Patients with class IV stage D heart failure who are symptomatic despite optimal medical heart failure therapy for 45 of 60 days or who require

inotropic support for 14 days or intra-aortic balloon pump (IABP) support for 7 days and have no contraindication for anticoagulation are eligible for implantation on LVAD HM II as destination therapy if they are not eligible for or do not desire cardiac transplantation. The INTERMACS registry has established a patient profile (1-7) that determines urgency to implantation and assesses risk and survival at 90 days.

Recommendations for clinical management of continuous-flow LVAD assist providers with standardized care for this patient population.Bleeding, infection, and stroke are postimplantation complications, and death may occur due to right heart failure, sepsis, or stroke. A multidisciplinary approach to LVAD implantation is needed, as destination therapy identifies patients at high risk for complications and the need to optimize these patients medically before surgery. In a report from INTERMACS, 1-year survival for destination-therapy patients was 61% for pulsatile devices and 74% for continuous-flow devices.[75]

Heart Transplantation

Selected patients with severe heart failure, debilitating refractory angina, ventricular arrhythmia, or congenital heart disease that cannot be controlled despite pharmacologic, medical device, or alternative surgical therapy should be evaluated for heart transplantation.[5] The patient must be well informed, motivated, and emotionally stable; have a good social support network; and be capable of complying with intensive medical treatment.[4]

Since Christiaan Barnard performed the first orthotopic heart transplantation in 1967, the world has seen tremendous advancement in the field of cardiac transplantation. For patients with progressive end-stage heart failure despite maximal medical therapy who have a poor prognosis and no viable alternative form of treatment,[4] heart transplantation has become the criterion standard for therapy.[3]

Compared to patients who receive only medical therapy, transplant recipients have fewer rehospitalizations; marked functional improvements; enhanced quality of life; more gainful employment; and longer survival, with 50% surviving 10 years postoperatively. Heart transplantation is associated with a 1-year survival rate of 83%; subsequently, survival decreases in a linear manner by approximately 3.4% per year.

Non pharmacological manganite of chronic heart failure.

Careful selection of donors and recipients is critical for ensuring good outcomes. In addition, transplant teams must strive to minimize potential perioperative dangers, including ischemic times, pulmonary hypertension, mechanical support, and cardiogenic shock. [76]

Indications

Absolute indications for heart transplantation include hemodynamic compromise following heart failure, such as in the following scenarios[3] :

- Refractory cardiogenic shock
- Dependence on intravenous (IV) inotropic support for adequacy of organ perfusion
- Peak oxygen consumption per unit time (VO_2) below 10 mL/kg/min
- Severe ischemic symptoms with consistent limitations of routine activity that are not amenable to revascularization procedures (coronary artery bypass grafting [CABG], percutaneous coronary intervention [PCI])
- Recurrent symptomatic ventricular arrhythmias despite all therapeutic interventions

Relative indications for heart transplantation include the following[3] :

- Peak VO_2 between 11 and 14 mL/kg/min (or 55% of predicted) with major limitation of routine activities
- Recurrent unstable ischemia that is not amenable to other treatment
- Recurrent instability of fluid balance/renal function despite patient compliance with medical therapy

In the absence of other indications, however, the following are not sufficient indications for heart transplantation[3] :

- Low left ventricular ejection fraction (LVEF)
- History of New York Heart Association (NYHA) class III/IV heart failure symptoms
- Peak VO_2 above 15 mL/kg/min (and >55% predicted)

Contraindications

Heart transplantation is contraindicated in patients with the following conditions[4] :

Non pharmacological manganite of chronic heart failure.

- Active infection
- Severe peripheral arterial or cerebrovascular disease
- Irreversible pulmonary hypertension
- Active malignancy
- Significant renal failure (creatinine clearance < 30 mL/min)
- Systematic disease with multiorgan involvement
- Other serious comorbidity with a poor prognosis
- Body mass index (BMI) avove 35 kg/m ^{2}
- Current alcohol or drug use
- Insufficient social supports to achieve compliant care

Note that the Heart Failure Society of America (HFSA) indicates that cardiomyoplasty and partial left ventriculectomy (Batista operation) is not recommended to treat heart failure, nor should it be used as an alternative to heart transplantation.[5]

Coronary graft atherosclerosis

The Achilles heel of the long-term success of heart transplantation is the development of coronary graft atherosclerosis, the cardiac version of chronic rejection. Coronary graft atherosclerosis is uniquely different from typical coronary artery disease in that it is diffuse and is usually not amenable to revascularization.

Shortage of donor hearts

In the United States, fewer than 2500 heart transplantation procedures are performed annually; between January 1988 and September 2017, an average of 2350 people received heart transplants per year. Each year, an estimated 10-20% of patients die while awaiting a heart transplant. Of the 5 million people with heart failure, approximately 30,000 to 100,000 have such advanced disease that they would benefit from transplantation or mechanical circulatory support.This disparity between the number of patients needing transplants and the availability of heart donors has refocused efforts to find other ways to support severely failing hearts. .[77]

Non pharmacological manganite of chronic heart failure.

Total Artificial Heart

The creation of a suitable total artificial heart (TAH) for orthotopic implantation has been the subject of intense investigation for decades.[235] In 1969, Dr Denton Cooley implanted the Liotta TAH (which is no longer made) into a high-risk patient after failing to wean the patient off cardiopulmonary bypass after left ventricular (LV) aneurysm repair. The patient was sustained until a donor heart became available after 3 days, but the patient subsequently died of pneumonia and multiple organ failure. Compared with LV assist devices (LVADs), the TAH has several potential advantages, including the ability to assist patients with severe biventricular failure; a lack of device pocket and thus a lessened risk of infection; and the opportunity to treat patients with systemic diseases (eg, amyloidosis, malignancy) who are not otherwise candidates for transplantation.[79]

Two TAHs have received the most attention:

- SynCardia (formerly CardioWest) TAH
- AbioCor TAH

The SynCardia TAH is a structural cousin of the original Jarvik-7 TAH that was implanted into patient Barney Clark with great publicity in 1982. In 2004, investigators reported data that allowed this device to receive FDA approval for use as a bridge to transplantation.

The AbioCor TAH involves a novel method of transcutaneous transmission of energy, freeing the patient from external drivelines. The patient exchanges the external battery packs, which can last as long as 4 hours. This TAH is unique in that it is the first TAH to use coils to transmit power across the skin; therefore, no transcutaneous conduits are needed. This feature allows for the advantages of a closed system, which potentially reduces sources of infection, a known complication of earlier devices.

The first clinical implantation of the AbioCor TAH was performed in July 2001. Before the end of 2004, 14 patients had received this device as part of a trial in patients whose expected survival was less than 30 days. Although all subsequently died, 4 patients were ambulatory after surgery, and 2 were discharged from the hospital to a transitional-care setting. One of the discharged patients was discharged on postoperative day 209. A limitation of the AbioCor TAH is its large size, which permits its implantation in only

50% of men and 20% of women. In 2006, the FDA approved the Abiocor TAH as a permanent TAH for humanitarian uses.

The SynCardia and AbioCor TAHs require recipient cardiectomy before implantation. The devices are similar in that they are sewn to atrial cuffs and to the great vessels after the native heart is explanted.

A European study involving the CARMAT TAH is evaluating survival on this device of patients with advance heart failure at 180 days postimplant or survival to cardiac transplantion if occurring before 180 days postimplant.[80]

Despite several decades of effort, the clinical application of artificial-heart technology remains immature. However, with the approval of the SynCardia and AbioCor devices as well as with new efforts to create small pumps, TAHs will ultimately be routine components of heart failure surgery for very sick patients with heart failure and biventricular failure.

Non pharmacological manganite of chronic heart failure.

Guidelines:

Nonpharmacologic Therapy

By definition, stage A patients are at high risk for heart failure but do not have structural heart disease or symptoms of heart failure. For these individuals, guidelines from the American College of Cardiology Foundation/American Heart Association (ACCF/AHA), Heart Failure Society of America (HFSA), European Society of Cardiology recommend nonpharmacologic management focused on prevention through reduction of risk factors. Measures include the following[3, 4, 5] :

- Treat hypertension and lipid disorders
- Encourage smoking cessation
- Discourage heavy alcohol intake and illicit drug use
- Control and/or prevent diabetes mellitus
- Encourage physical activity
- Encourage weight reduction if obese or overweight

For patients with chronic heart failure, the ACCF/AHA, HFSA, and ESC recommend regular aerobic exercise to improve functional capacity and symptoms.[3, 4, 5] However, ACCF/AHA cautions that limitation of activity is appropriate during acute heart failure exacerbations and in patients with suspected myocarditis. Most patients should not participate in heavy labor or exhaustive sports.[3]

The ACCF/AHA and ESC recommend specific patient education to facilitate self-care and close observation and follow-up are important aspects of care. Close supervision, including surveillance by the patient and family, home-based visits, telephone support, or remote monitoring should be provided to improve adherence.[3, 5]

Dietary sodium should be restricted to 2-3 g/day according the ACCF/AHA and HFSA,[3, 5] although the ACCF/AHA notes that evidence to support this recommendation is inconclusive.[3]

Fluid restriction to 2 L/day is recommended for patients with evidence of hyponatremia (Na < 130 mEq/dL) and for those whose fluid status is

difficult to control despite sodium restriction and the use of high-dose diuretics.[3, 4, 5]

The ACCF/AHA, HFSA, and ESC guidelines recommend caloric supplementation for patients with evidence of cardiac cachexia.[3, 4, 5] The HFSA recommends against the use of anabolic steroids for these patients.[5]

The HFSA recommends against naturoceutical use for relief of symptomatic heart failure or for the secondary prevention of cardiovascular events.[5] Avoid natural or synthetic products containing ephedra (ma huang), ephedrine, or its metabolites, as well as products that have significant drug interactions with digoxin, vasodilators, beta blockers, antiarrhythmic drugs, and anticoagulants.[5]

Electrophysiologic Intervention

The 2010 Heart Failure Society of America (HFSA) guidelines indicate that device therapy is an integral part of the treatment of heart failure and that considerations such as the nature and severity of the condition and any patient comorbidities are essential in optimizing the use of this therapy.[5] The Committee for Practice Guidelines (CPG) of the European Society of Cardiology (ESC) as well as the American College of Cardiology, American Heart Association, and Heart Rhythm Society (ACC/AHA/HRS) emphasized the importance of medical devices in heart failure in their respective 2010 and 2012 focused updates on these interventions.[15]

Pacemakers

Because right ventricular (RV) pacing may worsen heart failure due to an increase in ventricular dysynchrony, the 2010 HFSA Practice Guidelines recommend against placement of a dual-chamber pacemaker in heart failure patients in the absence of symptomatic bradycardia or high-degree atrioventricular (AV) block.[5]

The ACC/AHA heart failure guidelines recommend consideration of cardiac resynchronization therapy (CRT) for patients with heart failure who have indications for permanent pacing (eg, first implant, upgrading of a conventional pacemaker) and New York Heart Association (NYHA) class III-IV symptoms or those who have an left ventricular ejection fraction

(LVEF) below 35% despite being on optimal heart failure therapy and who may have a dependence on RV pacing.[3, 81] These recommendations also include patients with NYHA class II symptoms and the presence of left bundle-branch block (LBBB) with a QRS duration that is at least 150 ms. The ESC guidelines have similar recommendations.[4]

Implantable cardioverter-defibrillators

ACC Foundation (ACCF)/AHA guidelines recommend placing an implantable cardioverter-defibrillator (ICD) in virtually all patients with an LVEF below 35%. The ACCF/AHA and ESC recommend ICD placement for the following categories of heart failure patients[3, 4, 77] :

- Patients with LV dysfunction (LVEF ≤35%) from a previous myocardial infarction (MI) who are at least 40 days post-Ml
- Patients with nonischemic cardiomyopathy; with an LVEF of 35% or less; in NYHA class II or III; receiving optimal medical therapy; and expected to survive longer than 1 year with good functional status
- Patients with ischemic cardiomyopathy who are at least 40 days post-MI; have an LVEF of 30% or less; are in NYHA functional class I; are on chronic optimal medical therapy; and are expected to survive longer than 1 year with good functional status
- Patients who have had ventricular fibrillation (VF)
- Patients with documented hemodynamically unstable ventricular tachycardia (VT) and/or VT with syncope; with an LVEF below 40%; on optimal medical therapy; and expected to survive longer than 1 year with good functional status

Cardiac resynchronization therapy/biventricular pacing

The ACCF/AHA guidelines recommend cardiac resynchronization therapy (CRT) for patients in sinus rhythm or atrial fibrillation with a QRS duration of 120 ms or longer (the greatest benefit is in patients with a QRS >150 ms) and an LVEF of 35% or less with persistent, moderate-to-severe heart failure (NYHA class III and functional NYHA class IV) despite optimal medical therapy.[3] A 2012 update of ACC/AHA/HRS guidelines on CRT expanded class I indications to patients with NYHA class II symptoms and LBBB duration of 150 ms or longer.[81] Additional CRT recommendations include[3, 81] :

Non pharmacological manganite of chronic heart failure.

- Patients with a reduced LVEF and a QRS of 150 ms or longer who have NYHA I or II symptoms
- Patients with a reduced LVEF who require chronic pacing and in whom frequent ventricular pacing is expected
- CRT is not recommended for patients with NYHA class I or II symptoms and non-LBBB pattern with a QRS duration shorter than 150 ms
- CRT is not indicated in patients who are not expected to survive for more than 1 year due to their comorbidities or frailty

The ESC guidelines gives class I recommendations for the use of CRT in the following groups[4] :

- Symptomatic patients in sinus rhythm with a QRS duration of 150 ms or longer, LBBB QRS morphology and an LVEF of 35% or less despite optimal medical therapy. (Level of evidence: A)
- Symptomatic patients in sinus rhythm with a QRS duration of 130-149 ms or longer, LBBB QRS morphology and an LVEF of 35% or less despite optimal medical therapy. (Level of evidence: B)
- CRT rather than RV pacing for patients with heart failure with reduced ejection fraction (HFrEF) regardless of NYHA class, including patients with atrial fibrillation who have an indication for ventricular pacing and a high degree AV block. (Level of evidence: A)

CRT should be considered for the following groups[4] :

- Symptomatic patients in sinus rhythm with a QRS duration of 150 ms or longer, non-LBBB QRS morphology and an LVEF of 35% or less despite optimal medical therapy. (Class IIa; level of evidence: B)
- Patients with LVEF of 35% or less in NYHA Class III-IV despite optimal medical therapy, if they are in atrial fibrillation and have a QRS duration of 130 ms or longer provided a strategy to ensure biventricular capture is in place or the patient is expected to return to sinus rhythm. (Class IIa; level of evidence: B)

CRT may be considered for the following groups[4] :

- Symptomatic patients in sinus rhythm with a QRS duration of 130-149 ms, non-LBBB QRS morphology and with an LVEF of 35% or less despite optimal medical therapy. (Class IIb; level of evidence: B)

- Patients with HFrEF who have received a conventional pacemaker or an ICD and subsequently develop worsening heart failure despite optimal medical therapy and who have a high proportion of RV pacing. (Class IIb; level of evidence: B)

CRT is contraindicated in patients with a QRS duration below 130 ms. (Class III; level of evidence: A)

Revascularization Procedures

The American College of Cardiology Foundation/American Heart Association (ACCF/AHA), Heart Failure Society of America (HFSA), and European Society of Cardiology (ESC) guidelines recommend coronary artery bypass graft (CABG) and percutaneous coronary intervention (PCI) revascularization procedures in selected patients with heart failure and coronary artery disease (CAD) to improve symptoms and survival.[3, 4, 5] In patients who are at low risk for CAD, findings from noninvasive tests such as exercise electrocardiography (ECG), stress echocardiography, and stress nuclear perfusion imaging should determine whether subsequent angiography is indicated.

The ACCF/AHA guidelines recommend revascularization procedures for the following heart failure patients[3] :

- CABG or PCI for those on medical therapy with angina and suitable coronary anatomy, especially significant left main stenosis (>50%) or left main equivalent
- CABG to improve survival in patients with mild to moderate left ventricular (LV) systolic dysfunction (ejection fraction [EF] OF 35%-50%) and significant (≥70% stenosis) multivessel CAD or proximal left anterior descending (LAD) artery stenosis in the presence of viable myocardium
- CABG to improve morbidity and survival for patients with an LVEF of 35% or less, heart failure, and significant multivessel CAD
- CABG may also be considered in patients with ischemic heart disease, severe LV systolic dysfunction (EF < 35%), and operable coronary anatomy, regardless of whether or not viable myocardium is present

The ESC guidelines are in general agreement with those of ACCF/AHA, with the choice between CABG and PCI individualized for each patient.[4]

In addition, the ESC points out that the benefit-risk balance of revascularization in patients without angina and without viable myocardium remains uncertain.

Valvular Surgery

The American College of Cardiology Foundation/American Heart Association (ACCF/AHA) recommends aortic valve replacement for patients with critical aortic stenosis and predicted surgical mortality of 10% or less, as well as transcatheter aortic valve replacement for selected patients who are considered to be inoperable.[3] The benefit of transcatheter mitral valve repair or mitral valve surgery for functional mitral insufficiency is unclear and should only be considered after careful candidate selection.

The Heart Failure Society of America (HFSA) indicates that isolated mitral valve repair or replacement for severe mitral regurgitation secondary to ventricular dilatation in the presence of severe left ventricular (LV) systolic dysfunction is not generally recommended.[5]

Although the European Society of Cardiology (ESC) recommends optimized medical treatment for aortic stenosis, it also cautions that vasodilators may cause hypotension and should be used with caution. Surgical decision making should not be delayed. For patients unfit for surgery, transcatheter aortic valve replacement should be considered. Additional valvular surgery recommendations include[4] :

- Aortic valve repair or replacement in all symptomatic patients with severe aortic regurgitation as well as asymptomatic patients with an LV ejection fraction (EF) of 50% or less who are fit for surgery.
- Consider a combination valve and coronary surgery for secondary mitral regurgitation in symptomatic patients with an LVEF below 30% with suitable arteries for revascularization. Surgery is also recommended for those with severe mitral regurgitation with an LVEF over 30% undergoing coronary artery bypass grafting.
- Isolated mitral valve surgery in patients with severe functional mitral regurgitation and severe LV systolic dysfunction (LVEF < 30%) who cannot be revascularized or have non-ischemic cardiomyopathy is questionable; conventional medical and device therapy are preferred.

In selected cases, consider repair to avoid or postpone transplantation.

Mechanical Circulatory Support Devices

The following organizations have released guidelines for the utilization of mechanical circulatory support (MCS):

- Society for Cardiovascular Angiography and Interventions, American College of Cardiology, Heart Failure Society of America, and Society for Thoracic Surgeons (SCAI/ACC/HFSA/STS)
- International Society of Heart and Lung Transplantation (ISHLT)
- American Heart Association (AHA)

Historically, the intra-aortic balloon bump (IABP) and extracorporeal membrane oxygenation (ECMO) devices had been the only MCS devices available to clinicians, but axial flow pumps (eg, Impella) and left atrial to femoral artery bypass pumps (eg, TandemHeart) have more recently entered clinical practice.[82]

The 2015 SCAI/ACC/HFSA/STS clinical expert consensus-based recommendations include the following[82] :

- Percutaneous circulatory assist devices provide superior hemodynamic support (reduce left ventricular [LV] pressures, LV volumes, LV stroke volume) compared with pharmacologic therapy; this is particularly apparent for the Impella and TandemHeart devices.
- In those with cardiogenic shock who fail to stabilize or show signs of improvement after initial interventions, consider early placement of an appropriate MCS.
- For profound cardiogenic shock, IABP is less likely to provide benefit than continuous flow pumps (including the Impella CP and TandemHeart). ECMO may also be beneficial, particularly for patients with impaired respiratory gas exchange.
- Consider MCS for isolated acute right ventricular (RV) failure complicated by cardiogenic shock.

Non pharmacological manganite of chronic heart failure.

- MCS can be beneficial in high-risk percutaneous coronary intervention (PCI) (eg, multivessel, left main, or last patent conduit interventions), particularly if the patient is inoperable or has severely reduced ejection fraction or elevated cardiac filling pressures
- MCS can be utilized when patients fail to wean off of cardiopulmonary bypass.
- Early MCS may benefit patients with acute decompensated heart failure when they continue to deteriorate despite initial interventions.
- MCS can be used in severe biventricular failure via both right- and left-sided percutaneous devices or venoarterial ECMO.

However, there was insufficient evidence to support or refute routine use of MCS as an adjunct to primary revascularization in the setting of large acute MI (myocardial infarction) to reduce reperfusion injury or infarct size.[82]

In its 2013 guidelines for mechanical circulatory support, the ISHLT recommended long-term MCS for the following patients in acute cardiogenic shock (class IIa)[83] :

- Those whose ventricular function is considered unrecoverable or unlikely to recover without long-term device support (level of evidence: C)
- Those considered too ill to maintain normal hemodynamics and vital organ function with temporary MCS, or who cannot be weaned from temporary MCS or inotropic support (level of evidence: C)
- Those with the capacity for meaningful recovery of end-organ function and quality of life (level of evidence: C)
- Those without irreversible end-organ damage (level of evidence: C)
- Those who are dependent on inotropic agents (level of evidence: B)
- Those with end-stage systolic heart failure who do not fall into one of the recommendations: Routine risk stratification at regular intervals to determine the need for and optimal timing of MCS (level of evidence:C)

Additional recommendations for heart failure therapy include[83] :

- Diuretic agents for the management of volume overload during MCS (class I; level of evidence: C)
- An angiotensin-converting enzyme inhibitor (ACEI) or an angiotensin receptor blocker (ARB) for managing hypertension or for risk

reduction in patients with vascular disease and diabetes (class I; level of evidence: C.)
- Beta-blockers for hypertension or for rate control in patients with tachyarrhythmias (class I; level of evidence: C.)
- Mineralocorticoid receptor antagonists to limit the need for potassium repletion in patients with adequate renal function and for potential beneficial antifibrotic effects on the myocardium (class I; level of evidence: C.)
- Digoxin, potentially, for treating atrial fibrillation with rapid ventricular response (class II; level of evidence: C.)

The 2012 AHA guidelines on heart device strategies, patient selection, and postoperative care focuses on risk stratification and early referral of high-risk patients with heart failure to centers that can implant MCS.The specific recommendations for MCS include[84] :

- Consider MCS as a bridge to transplantation (BTT) for eligible patients with end-stage heart failure who are failing optimal medical, surgical, and or device therapies and are at high risk for dying before receiving heart transplantation.
- Early referral for MCS before development of advanced heart failure is preferred.
- Durable, implantable MCS devices is beneficial as permanent or destination therapy for patients with advanced heart failure, high 1-year mortality resulting from HF, and the absence of other life-limiting organ dysfunction; who are failing medical, surgical, and/or device therapies; and who are not heart transplant candidates.
- Consider patients who are ineligible for heart transplantation because of pulmonary hypertension related to heart failure alone for bridge to potential transplant eligibility with durable, long-term MCS.
- Consider urgent nondurable MCS in hemodynamically compromised patients with heart failure and end-organ dysfunction and/or relative contraindications to heart transplantation/durable MCS that are expected to improve with restoration of an improved hemodynamic profile.
- Long-term MCS is not recommended in patients with advanced kidney disease in whom renal function is unlikely to recover despite improved hemodynamics.
- Consider long-term MCS as a bridge to heart-kidney transplantation on the basis of the availability of outpatient hemodialysis.

Non pharmacological manganite of chronic heart failure.

Heart Transplantation

According to the American College of Cardiology Foundation/American Heart Association (ACCF/AHA) and Heart Failure Society of America (HFSA) guidelines, selected patients with refractory end-stage heart failure, debilitating refractory angina, ventricular arrhythmia, or congenital heart disease that cannot be controlled despite pharmacologic, medical device, or alternative surgical therapy should be evaluated for heart transplantation.[3, 5]

The European Society of Cardiology (ESC) guidelines recommend heart transplantation be considered for patients with progressive end-stage heart failure despite maximal medical therapy who have a poor prognosis and no viable alternative form of treatment; these patients must be well informed, motivated, and emotionally stable, and they must be capable of complying with intensive medical treatment.[4]

The ESC considers the following conditions as contraindications for heart transplantation[4] :

- Active infection
- Severe peripheral arterial or cerebrovascular disease
- Current alcohol and/or drug abuse
- Malignancy (collaborate with oncologists for risk stratification of tumor recurrence)
- Irreversible renal dysfunction (creatinine clearance < 30 mL/min)
- Pharmacologically irreversible pulmonary hypertension (consider placing a left ventricular assist device and then reevaluating eligibility)
- Multiorgan systemic disease
- Other serious comorbidity with a poor prognosis
- Pretransplant body mass index above 35 kg/m ^{2}
- insufficient social support in the outpatient setting to achieve compliant care. (Note that the HFSA does not recommend partial left ventriculectomy (Batista operation) to treat nonischemic cardiomyopathy).[5]

References.

1. Ho KK, Pinsky JL, Kannel WB, Levy D. The epidemiology of heart failure: the Framingham Study. J Am Coll Cardiol. 1993 Oct. 22 (4 suppl A):6A-13A. [Medline]. [Full Text].
2. American Heart Association. Classes of heart failure. Available at http://www.heart.org/HEARTORG/Conditions/HeartFailure/AboutHeartFailure/Classes-of-Heart-Failure_UCM_306328_Article.jsp#.WUcGf-vyuHs. Updated: May 8, 2017; Accessed: June 18, 2017.
3. [Guideline] Yancy CW, Jessup M, Bozkurt B, et al, American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. Circulation. 2013 Oct 15. 128(16):e240-327. [Medline]. [Full Text].
4. [Guideline] Ponikowski P, Voors AA, Anker SD, et al, for the Authors/Task Force Members. 2016 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: The task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J. 2016 Jul 14. 37 (27):2129-200. [Medline]. [Full Text].
5. [Guideline] Lindenfeld J, Albert NM, Boehmer JP, et al, for the Heart Failure Society of America. HFSA 2010 comprehensive heart failure practice guideline. J Card Fail. 2010 Jun. 16(6):e1-194. [Medline]. [Full Text].
6. Stiles S. FDA approves heart sympathetic activity imaging agent for HF evaluation. Medscape News from WebMD. March 22, 2013. Available at http://www.medscape.com/viewarticle/781309. Accessed: April 5, 2013.
7. Braunwald E. The pathogenesis of congestive heart failure: then and now. Medicine. 1991 Jan. 70(1):68-79. [Full Text].
8. Braunwald E, Ross J Jr, Sonnenblick EH. Mechanisms of Contraction of the Normal and Failing Heart. 2nd ed. Boston: Little Brown & Co; 1976.
9. Greyson CR. Pathophysiology of right ventricular failure. Crit Care Med. 2008 Jan. 36 (1 suppl):S57-65. [Medline].
10. Haddad F, Doyle R, Murphy DJ, Hunt SA. Right ventricular function in cardiovascular disease, part II: pathophysiology, clinical importance, and management of right ventricular failure. Circulation. 2008 Apr 1. 23 (13):1717-31. [Medline].

11. Onwuanyi A, Taylor M. Acute decompensated heart failure: pathophysiology and treatment. Am J Cardiol. 2007 Mar 26. 99 (6B):25D-30D. [Medline].
12. Ross J Jr, Braunwald E. Studies on Starling's law of the heart. IX. The effects of impeding venous return on performance of the normal and failing human left ventricle. Circulation. 1964 Nov. 30:719-27. [Medline]. [Full Text].
13. [Guideline] Yancy CW, Jessup M, Bozkurt B, et al. 2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. Circulation. 2017 Aug 8. 136(6):e137-e161. [Medline]. [Full Text].
14. [Guideline] Yancy CW, Jessup M, Bozkurt B, et al, for the Writing Committee Members. 2016 ACC/AHA/HFSA focused update on new pharmacological therapy for heart failure: an update of the 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. Circulation. 2016 Sep 27. 134 (13):e282-93. [Medline]. [Full Text].
15. [Guideline] Dickstein K, Vardas PE, Auricchio A, et al al for the Task Force on Acute Heart Failure of the European Society of Cardiology. 2010 Focused Update of ESC Guidelines on device therapy in heart failure: an update of the 2008 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure and the 2007 ESC guidelines for cardiac and resynchronization therapy. Developed with the special contribution of the Heart Failure Association and the European Heart Rhythm Association. Eur Heart J. 2010 Nov. 31(21):2677-87. [Medline]. [Full Text].
16. Groenveld HF, Januzzi JL, Damman K, et al. Anemia and mortality in heart failure patients a systematic review and meta-analysis. J Am Coll Cardiol. 2008 Sep 2. 52 (10):818-27. [Medline].
17. Ronco C, Haapio M, House AA, Anavekar N, Bellomo R. Cardiorenal syndrome. J Am Coll Cardiol. 2008 Nov 4. 52 (19):1527-39. [Medline].
18. Giamouzis G, Butler J, Starling RC, et al. Impact of dopamine infusion on renal function in hospitalized heart failure patients: results of the Dopamine in Acute Decompensated Heart Failure (DAD-HF) Trial. J Card Fail. 2010 Dec. 16 (12):922-30. [Medline].
19. O'Connor CM, Starling RC, Hernandez AF, et al. Effect of nesiritide in patients with acute decompensated heart failure. N Engl J Med. 2011 Jul 7. 365 (1):32-43. [Medline].

20. Konstam MA, Gheorghiade M, Burnett JC Jr, et al, for the Efficacy of Vasopressin Antagonism in Heart Failure Outcome Study With Tolvaptan (EVEREST) Investigators. Effects of oral tolvaptan in patients hospitalized for worsening heart failure: the EVEREST Outcome Trial. JAMA. 2007 Mar 28. 297 (12):1319-31. [Medline].
21. Massie BM, O'Connor CM, Metra M, et al, for the PROTECT Investigators and Committees. Rolofylline, an adenosine A1-receptor antagonist, in acute heart failure. N Engl J Med. 2010 Oct 7. 363 (15):1419-28. [Medline].
22. Badve SV, Roberts MA, Hawley CM, et al. Effects of beta-adrenergic antagonists in patients with chronic kidney disease: a systematic review and meta-analysis. J Am Coll Cardiol. 2011 Sep 6. 14 (11):222-61. [Medline].
23. Wilton SB, Fundytus A, Ghali WA, et al. Meta-analysis of the effectiveness and safety of catheter ablation of atrial fibrillation in patients with versus without left ventricular systolic dysfunction. Am J Cardiol. 2010 Nov 1. 106 (9):1284-91. [Medline].
24. Chen YM, Li ZB, Zhu M, Cao YM. Effects of exercise training on left ventricular remodelling in heart failure patients: an updated meta-analysis of randomised controlled trials. Int J Clin Pract. 2012 Aug. 66 (8):782-91. [Medline].
25. Velazquez EJ, Lee KL, Jones RH, et al, for the STICHES Investigators. Coronary-artery bypass surgery in patients with ischemic cardiomyopathy. N Engl J Med. 2016 Apr 21. 374(16):1511-20. [Medline].
26. Cardiac Rhythm News. FDA approves expanded indication for certain pacemakers and defibrillators used to treat heart failure. Available at https://cardiacrhythmnews.com/fda-approves-expanded-indication-for-certain-pacemakers-and-defibrillators-used-to-treat-heart-failure/. April 15, 2014; Accessed: April 15, 2014.
27. Stiles S. FDA approves Medtronic CRT sevices for mild HF with AV block. Medscape Medical News. Available at http://www.medscape.com/viewarticle/823485. April 10, 2014; Accessed: April 15, 2014.
28. Levy WC, Lee KL, Hellkamp AS, et al. Maximizing survival benefit with primary prevention implantable cardioverter-defibrillator therapy in a heart failure population. Circulation. 2009 Sep 8. 120 (10):835-42. [Medline].
29. Rosanio S, Schwarz ER, Ahmad M, et al. Benefits, unresolved questions, and technical issues of cardiac resynchronization therapy for heart failure. Am J Cardiol. 2005 Sep 1. 96 (5):710-7. [Medline].

30. Giraldi F, Cattadori G, Roberto M, et al. Long-term effectiveness of cardiac resynchronization therapy in heart failure patients with unfavorable cardiac veins anatomy comparison of surgical versus hemodynamic procedure. J Am Coll Cardiol. 2011 Jul 26. 14 (5):483-90. [Medline].
31. Abraham WT, Fisher WG, Smith AL, et al, for the MIRACLE Study Group. Multicenter InSync Randomized Clinical Evaluation. Cardiac resynchronization in chronic heart failure. N Engl J Med. 2002 Jun 13. 346 (24):1845-53. [Medline].
32. Moss AJ, Hall WJ, Cannom DS, et al, for the MADIT-CRT Trial Investigators. Cardiac-resynchronization therapy for the prevention of heart-failure events. N Engl J Med. 2009 Oct 1. 361 (14):1329-38. [Medline].
33. Arshad A, Moss AJ, Foster E, et al, for the MADIT-CRT Executive Committee. Cardiac resynchronization therapy is more effective in women than in men: the MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy) trial. J Am Coll Cardiol. 2011 Feb 15. 57 (7):813-20. [Medline].
34. Ruwald MH, Ruwald AC, Jons C, et al. Effect of metoprolol versus carvedilol on outcomes in MADIT-CRT (multicenter automatic defibrillator implantation trial with cardiac resynchronization therapy). J Am Coll Cardiol. 2013 Apr 9. 61 (14):1518-26. [Medline].
35. Cleland JG, Daubert JC, Erdmann E, et al, for the Cardiac Resynchronization-Heart Failure (CARE-HF) Study Investigators. The effect of cardiac resynchronization on morbidity and mortality in heart failure. N Engl J Med. 2005 Apr 14. 352 (15):1539-49. [Medline].
36. Bristow MR, Saxon LA, Boehmer J, et al, for the Comparison of Medical Therapy, Pacing, et al. Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. N Engl J Med. 2004 May 20. 350 (21):2140-50. [Medline].
37. Curtis AB, Worley SJ, Adamson PB, et al, for the Biventricular versus Right Ventricular Pacing in Heart Failure Patients with Atrioventricular Block (BLOCK HF) Trial Investigators. Biventricular pacing for atrioventricular block and systolic dysfunction. N Engl J Med. 2013 Apr 25. 368 (17):1585-93. [Medline].
38. Veterans Administration Coronary Artery Bypass Surgery Cooperative Study Group. Eleven-year survival in the Veterans Administration randomized trial of coronary bypass surgery for stable angina. N Engl J Med. 1984 Nov 22. 311 (21):1333-9. [Medline].
39. VA Coronary Artery Bypass Surgery Cooperative Study Group. Eighteen-year follow-up in the Veterans Affairs Cooperative Study of

Coronary Artery Bypass Surgery for stable angina. Circulation. 1992 Jul. 86 (1):121-30. [Medline].

40. Caracciolo EA, Davis KB, Sopko G, et al. Comparison of surgical and medical group survival in patients with left main equivalent coronary artery disease. Long-term CASS experience. Circulation. 1995 May 1. 91 (9):2335-44. [Medline].
41. Velazquez EJ, Lee KL, Deja MA, et al, for the STICH Investigators. Coronary-artery bypass surgery in patients with left ventricular dysfunction. N Engl J Med. 2011 Apr 28. 364 (17):1607-16. [Medline]. [Full Text].
42. Elefteriades JA, Morales DL, Gradel C, Tollis G Jr, Levi E, Zaret BL. Results of coronary artery bypass grafting by a single surgeon in patients with left ventricular ejection fractions < or = 30%. Am J Cardiol. 1997 Jun 15. 79 (12):1573-8. [Medline].
43. Kron IL, Flanagan TL, Blackbourne LH, Schroeder RA, Nolan SP. Coronary revascularization rather than cardiac transplantation for chronic ischemic cardiomyopathy. Ann Surg. 1989 Sep. 210 (3):348-52; discussion 352-4. [Medline]. [Full Text].
44. Calafiore AM, Di Giammarco G, Teodori G, et al. Late results of first myocardial revascularization in multiple vessel disease: single versus bilateral internal mammary artery with or without saphenous vein grafts. Eur J Cardiothorac Surg. 2004 Sep. 26 (3):542-8. [Medline].
45. Nishimura RA, Grantham JA, Connolly HM, Schaff HV, Higano ST, Holmes DR Jr. Low-output, low-gradient aortic stenosis in patients with depressed left ventricular systolic function: the clinical utility of the dobutamine challenge in the catheterization laboratory. Circulation. 2002 Aug 13. 106 (7):809-13. [Medline].
46. Carabello BA. Clinical practice. Aortic stenosis. N Engl J Med. 2002 Feb 28. 346 (9):677-82. [Medline].
47. Connolly HM, Oh JK, Schaff HV, et al. Severe aortic stenosis with low transvalvular gradient and severe left ventricular dysfunction:result of aortic valve replacement in 52 patients. Circulation. 2000 Apr 25. 101 (16):1940-6. [Medline].
48. Vaquette B, Corbineau H, Laurent M, et al. Valve replacement in patients with critical aortic stenosis and depressed left ventricular function: predictors of operative risk, left ventricular function recovery, and long term outcome. Heart. 2005 Oct. 91 (10):1324-9. [Medline]. [Full Text].
49. Dujardin KS, Enriquez-Sarano M, Schaff HV, Bailey KR, Seward JB, Tajik AJ. Mortality and morbidity of aortic regurgitation in clinical practice.

A long-term follow-up study. Circulation. 1999 Apr 13. 99 (14):1851-7. [Medline].
50. Chaliki HP, Mohty D, Avierinos JF, et al. Outcomes after aortic valve replacement in patients with severe aortic regurgitation and markedly reduced left ventricular function. Circulation. 2002 Nov 19. 106 (21):2687-93. [Medline].
51. Lancellotti P, Gerard PL, Pierard LA. Long-term outcome of patients with heart failure and dynamic functional mitral regurgitation. Eur Heart J. 2005 Aug. 26 (15):1528-32. [Medline].
52. Patel JB, Borgeson DD, Barnes ME, Rihal CS, Daly RC, Redfield MM. Mitral regurgitation in patients with advanced systolic heart failure. J Card Fail. 2004 Aug. 10 (4):285-91. [Medline].
53. Akasaka T, Yoshida K, Hozumi T, et al. Restricted coronary flow reserve in patients with mitral regurgitation improves after mitral reconstructive surgery. J Am Coll Cardiol. 1998 Dec. 32 (7):1923-30. [Medline].
54. McGee EC, Gillinov AM, Blackstone EH, et al. Recurrent mitral regurgitation after annuloplasty for functional ischemic mitral regurgitation. J Thorac Cardiovasc Surg. 2004 Dec. 128 (6):916-24. [Medline].
55. Srichai MB, Grimm RA, Stillman AE, et al. Ischemic mitral regurgitation: impact of the left ventricle and mitral valve in patients with left ventricular systolic dysfunction. Ann Thorac Surg. 2005 Jul. 80 (1):170-8. [Medline].
56. Yun KL, Sintek CF, Miller DC, et al. Randomized trial comparing partial versus complete chordal-sparing mitral valve replacement: effects on left ventricular volume and function. J Thorac Cardiovasc Surg. 2002 Apr. 123 (4):707-14. [Medline].
57. Feldman T, Kar S, Rinaldi M, et al, for the EVEREST Investigators. Percutaneous mitral repair with the MitraClip system: safety and midterm durability in the initial EVEREST (Endovascular Valve Edge-to-Edge REpair Study) cohort. J Am Coll Cardiol. 2009 Aug 18. 54 (8):686-94. [Medline].
58. Chiarito M, Pagnesi M, Martino EA, et al. Outcome after percutaneous edge-to-edge mitral repair for functional and degenerative mitral regurgitation: a systematic review and meta-analysis. Heart. 2017 Jun 29. [Medline].
59. Yamaguchi A, Ino T, Adachi H, et al. Left ventricular volume predicts postoperative course in patients with ischemic cardiomyopathy. Ann Thorac Surg. 1998 Feb. 65 (2):434-8. [Medline].

60. Mickleborough LL, Carson S, Ivanov J. Repair of dyskinetic or akinetic left ventricular aneurysm: results obtained with a modified linear closure. J Thorac Cardiovasc Surg. 2001 Apr. 121 (4):675-82. [Medline].
61. Ott DA, Parravacini R, Cooley DA, et al. Improved cardiac function following left ventricular aneurysm resection: pre- and postoperative performance studies in 150 patients. Tex Heart Inst J. 1982 Sep. 9 (3):267-73. [Medline]. [Full Text].
62. Athanasuleas CL, Buckberg GD, Stanley AW, et al, for the RESTORE group. Surgical ventricular restoration in the treatment of congestive heart failure due to post-infarction ventricular dilation. J Am Coll Cardiol. 2004 Oct 6. 44 (7):1439-45. [Medline].
63. Pamboukian SV, Tallaj JA, Brown RN, et al. Improvement in 2-year survival for ventricular assist device patients after implementation of an intensive surveillance protocol. J Heart Lung Transplant. 2011 Aug. 30 (8):879-87. [Medline].
64. Daneshmand MA, Rajagopal K, Lima B, et al. Left ventricular assist device destination therapy versus extended criteria cardiac transplant. Ann Thorac Surg. 2010 Apr. 89 (4):1205-9; discussion 1210. [Medline].
65. US National Library of Medicine. Evaluation of the Jarvik 2000 Left Ventricular Assist System with post-auricular connector--destination therapy study. ClinicalTrials.gov. Available at https://clinicaltrials.gov/ct2/show/NCT01627821. Updated: October 16, 2017; Accessed: October 31, 2017.
66. Rose EA, Gelijns AC, Moskowitz AJ, et al, for theRandomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) Study Group. Long-term use of a left ventricular assist device for end-stage heart failure. N Engl J Med. 2001 Nov 15. 345 (20):1435-43. [Medline].
67. Starling RC, Naka Y, Boyle AJ, et al. Results of the post-U.S. Food and Drug Administration-approval study with a continuous flow left ventricular assist device as a bridge to heart transplantation: a prospective study using the INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support). J Am Coll Cardiol. 2011 May 10. 57 (19):1890-8. [Medline].
68. Ventura PA, Alharethi R, Budge D, et al. Differential impact on post-transplant outcomes between pulsatile- and continuous-flow left ventricular assist devices. Clin Transplant. 2011 Jul-Aug. 25 (4):E390-5. [Medline].

69. Kirklin JK, Naftel DC, Kormos RL, et al. Third INTERMACS Annual Report: the evolution of destination therapy in the United States. J Heart Lung Transplant. 2011 Feb. 30 (2):22-23. [Medline].
70. Taylor DO, Edwards LB, Boucek MM, et al. Registry of the International Society for Heart and Lung Transplantation: twenty-second official adult heart transplant report--2005. J Heart Lung Transplant. 2005 Aug. 24 (8):945-55. [Medline].
71. Stevenson LW, Kormos RL, Bourge RC, et al. Mechanical cardiac support 2000: current applications and future trial design. June 15-16, 2000 Bethesda, Maryland. J Am Coll Cardiol. 2001 Jan. 37 (1):340-70. [Medline].
72. Meyer A, Slaughter M. The total artificial heart. Panminerva Med. 2011 Sep. 53 (3):141-54. [Medline].
73. US National Library of Medicine. European clinical evaluation of the Carmat total artificial heart (advance HF). ClinicalTrials.gov. Available at https://clinicaltrials.gov/ct2/show/NCT02962973. Updated: November 25, 2016; Accessed: November 1, 2017.
74. [Guideline] Tracy CM, Epstein AE, Darbar D,et al. 2012 ACCF/AHA/HRS focused update of the 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. [corrected]. Circulation. 2012 Oct 2. 126 (14):1784-800. [Medline]. [Full Text].
75. [Guideline] Rihal CS, Naidu SS, Givertz MM, et al, Society for Cardiovascular Angiography and Interventions (SCAI), Heart Failure Society of America (HFSA), et al. 2015 SCAI/ACC/HFSA/STS clinical expert consensus statement on the use of percutaneous mechanical circulatory support devices in cardiovascular care: endorsed by the American Heart Association, the Cardiological Society of India, & Sociedad Latino Americana de Cardiologia Intervencion; affirmation of value by the Canadian Association of Interventional Cardiology-Association Canadienne de Cardiologie d'intervention. J Am Coll Cardiol. 2015 May 19. 65 (19):e7-e26. [Medline]. [Full Text].
76. [Guideline] Feldman D, Pamboukian SV, Teuteberg JJ, et al., International Society for Heart and Lung Transplantation. The 2013 International Society for Heart and Lung Transplantation Guidelines for mechanical circulatory support: executive summary. J Heart Lung Transplant. 2013 Feb. 32 (2):157-87. [Medline]. [Full Text].
77. [Guideline] Peura JL, Colvin-Adams M, Francis GS, et al. Recommendations for the use of mechanical circulatory support: device

strategies and patient selection: a scientific statement from the American Heart Association. Circulation. 2012 Nov 27. 126 (22):2648-67. [Medline]. [Full Text].

78. [Guideline] Ackerman MJ, Priori SG, Willems S, et al, Heart Rhythm Society (HRS), European Heart Rhythm Association (EHRA). HRS/EHRA expert consensus statement on the state of genetic testing for the channelopathies and cardiomyopathies: this document was developed as a partnership between the Heart Rhythm Society (HRS) and the European Heart Rhythm Association (EHRA). Europace. 2011 Aug. 13 (8):1077-109. [Medline]. [Full Text].
79. Lloyd-Jones D, Adams RJ, Brown TM, et al, for the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Executive summary: heart disease and stroke statistics--2010 update: a report from the American Heart Association. Circulation. 2010 Feb 23. 121 (7):948-54. [Medline].
80. Temporelli PL, Scapellato F, Eleuteri E, Imparato A, Giannuzzi P. Doppler echocardiography in advanced systolic heart failure: a noninvasive alternative to Swan-Ganz catheter. Circ Heart Fail. 2010 May. 3 (3):387-94. [Medline].
81. Miller R. AHA issues mechanical circulatory-support guidance for referring docs. Medscape Medical News. Available at http://www.medscape.com/viewarticle/773806. November 1, 2012; Accessed: November 7, 2012.
82. [Guideline] Bangalore S, Kumar S, Messerli FH. When conventional heart failure therapy is not enough: angiotensin receptor blocker, direct renin inhibitor, or aldosterone antagonist?. Congest Heart Fail. 2013 May-Jun. 19 (3):107-15. [Medline].
83. Cleland JG, Teerlink JR, Senior R, et al. The effects of the cardiac myosin activator, omecamtiv mecarbil, on cardiac function in systolic heart failure: a double-blind, placebo-controlled, crossover, dose-ranging phase 2 trial. Lancet. 2011 Aug 20. 378 (9792):676-83. [Medline].
84. Eklind-Cervenka M, Benson L, Dahlstrom U, Edner M, Rosenqvist M, Lund LH. Association of candesartan vs losartan with all-cause mortality in patients with heart failure. JAMA. 2011 Jan 12. 305 (2):175-82. [Medline].
85. Mozaffarian D, Benjamin EJ, Go AS, et al. Heart disease and stroke statistics—2016 update: a report from the American Heart Association. Circulation. 2016;133(4):e38–e360.