isosorbide dinitrate can be used to reduce morbidity or mortality rates among patients with current or prior symptomatic HFrEF who cannot be given an ACE inhibitor or ARB because of drug intolerance, hypotension, or renal insufficiency, unless contraindicated.

Digoxin

Perhaps the oldest treatment of HF, digoxin works through the inhibition of the sodium-potassium pump to increase intracellular calcium and increase contractility. Unlike the medications previously described, there is no proven mortality benefit from treatment with digoxin, but there may be a reduction in the number of rehospitalizations. Digoxin has been proved to improve symptoms, exercise tolerance, and health-related quality of life in men, but not women. Digoxin has many potential side effects, including nausea, vomiting, induction of ventricular or atrial arrhythmias, and heart block, and it may cause hyperkalemia. It is most famously known for causing visual color disturbances. Caution should be used to avoid toxicity for patients with intrinsic renal disease because digoxin is renally cleared.1

Drugs to Avoid

Nonsteroidal Anti-inflammatory Drugs

Nonsteroidal anti-inflammatory drugs (NSAIDs) cause sodium retention, vasoconstriction, renal impairment, and increased blood pressure. They enhance the toxicity of diuretics, ACE inhibitors, and ARBs.

Calcium-Channel Blockers

Calcium-channel blockers should be avoided in patients with HFrEF. Diltiazem and the nondihydropyridines are contraindicated in patients with an LVEF less than 40% due to their negative inotropic effects and reflex adrenergic system activation.

Antiarrhythmics

Two antiarrhythmic medications are approved for patients with a reduced LVEF. They are amiodarone and dofetilide, and both appear to be mortality neutral in properly selected patients.

Thiazolidinediones

Thiazolidinediones are used in the treatment of diabetes mellitus. They lead to increased sodium reabsorption and ultimately to fluid retention. They are contraindicated for patients with HF.

Hormonal Therapy and Nutritional Supplements

There are no proven benefits for hormonal therapies, unless there is needed replacement due to a specific hormonal deficiency. There are no data to support using nutritional supplements to improve HF symptoms or outcomes. However, some data support the use of omega-3 fatty acids by HF patients

Implantable Cardiac Defibrillators and Cardiac Resynchronization Therapy

Patients with cardiomyopathies of ischemic and nonischemic origins and reduced LVEFs are prone to ventricular arrhythmias. Many studies have demonstrated the survival benefits of implanting a defibrillator for primary prevention of sudden cardiac death. The guidelines recommend implantable cardiac defibrillator (ICD) therapy for patients with nonischemic dilated cardiomyopathy or ischemic heart disease at least 40 days after an MI with an LVEF of 35% or less and NYHA class II or III HF and who have been treated with optimal medical therapy for a minimum of 3 to 6 months and have a life expectancy of more than 1 year. An ICD is also recommended for patients with NYHA class I symptoms and an LVEF less of than 30% 40 days after an MI and who have been treated with optimal medical therapy for 3 to 6 months.

Resynchronization Therapy

Intraventricular conduction delays, demonstrated as a prolonged QRS duration of more than 120 milliseconds by surface ECG, are a common complication in patients with HF. The delay leads to dyssynchronous contraction of the left ventricle and can result in reduced systolic function, decreased cardiac output, and reduced exercise capacity.

Cardiac resynchronization therapy (i.e., biventricular pacing) aims to improve intraventricular synchrony and has been associated with improved cardiac output and LVEF. Biventricular pacing may have a beneficial effect on LV remodeling by reducing LV volume, LV mass, and severity of mitral regurgitation. These hemodynamic and structural changes have translated into a clinical improvement of functional capacity, exercise tolerance, and quality of life.

Biventricular pacing has reduced mortality rates and hospitalization for HF in multiple randomized, controlled trials. A systematic review of 14 randomized trials was published in 2007 by McAlister and colleagues. It evaluated 4420 patients with LVEF values less than 35%, QRS duration longer than 120 msec, NYHA class III and IV HF, and optimal medical therapy. They reported that cardiac resynchronization therapy (CRT) improved LVEF by 3% and improved LV remodeling, quality of life, and exercise capacity; 59% of patients had improvement by at least one NYHA class. Hospitalizations were decreased by 37%, and all-cause mortality was decreased by 22%. CRT was beneficial for patients with NYHA class III and IV symptoms, and there was a mortality benefit for patients with NYHA class I and II symptoms.

One third of patients undergoing biventricular pacemaker placements are found to be nonresponders. Patients with the best response to CRT have a wide QRS in a left bundle branch block pattern. The class I recommendation from the ACC guidelines proposes CRT for patients who have an LVEF of 35% or less, sinus rhythm, left bundle branch block with a QRS duration of 150 milliseconds or greater, and NYHA class II, III, or ambulatory IV symptoms who are receiving optimal medical therapy (Fig. 5-8).

Anticoagulation

Patients with HF; persistent, paroxysmal, or permanent atrial fibrillation; and one other risk factor in the CHADS2 index (i.e., congestive heart failure, hypertension, age 75 years or greater, diabetes mellitus, and stroke) should receive chronic anticoagulant therapy. According to the guidelines, it is reasonable to anticoagulate patients with HF and atrial fibrillation without additional risk factors.