Editorial

End Stage Heart Failure: An Emerging Menace

MA Siddique, M Salman

Department of Cardiology, Bangabandhu Sheikh Mujib Medical University

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Heart failure is a major public health problem, with increasing elderly population. As a consequence of the worldwide increase in life expectancy, and due to improvements in the treatment of heart failure in recent years, the proportion of patients that reach an advanced phase of the disease, so-called end stage, refractory or terminal heart failure, is steadily growing. Patients with end stage heart failure fall into stage D of the ABCD classification of the American College of Cardiology (ACC)/American Heart Association (AHA), and class III–IV of the New York Heart Association (NYHA) functional classification; they are characterized by advanced structural heart disease and pronounced symptoms of heart failure at rest or upon minimal physical exertion, despite maximal medical treatment according to current guidelines.[1,2]

When considering drug therapy Angiotensin-converting enzyme (ACE) inhibitors are recommended as first-line treatment in all patients with reduced left ventricular (LV) systolic function (ejection fraction (EF) 35–40%) independent of clinical symptoms (NYHA I–IV), unless there are contraindications. ACE inhibitors should not be titrated based on symptomatic improvement but should be up-titrated to the target dosages shown to be effective in the large, placebo-controlled heart failure trials, or to the maximal dose that is tolerated.[2]In heart failure patients remaining symptomatic despite optimal medical treatment including ACE inhibitors, administration of ARBs on top of ACE inhibitors leads to an additive reduction in cardiovascular morbidity and mortality.[3,4] A combination treatment of hydralazine and isosorbide dinitrate may improve symptoms and survival in heart failure patients intolerant of both ACE inhibitors and ARBs. As patients with end stage heart failure frequently show signs of fluid retention or have a history of such, inhibitors of the renin-angiotensin system should be co-administered with diuretics, which usually leads to rapid symptomatic improvement of dyspnoea and exercise tolerance while lacking significant effects on survival. In addition to standard treatment with ACE inhibitors and diuretics, patients with symptomatic stable systolic heart failure (NYHA II–IV) should be treated with ß-adrenergic receptor blockers unless there are contraindications.[1,2] ß-adrenergic receptor blocker treatment should be initiated in stable heart failure patients showing no signs of fluid retention at very small doses, and up-titrated to the target doses used in the large clinical heart failure trials, or to the maximal dose that is tolerated.[5] In patients with advanced heart failure (NYHA III–IV), aldosterone receptor antagonists are recommended in addition to ACE inhibitors, ß-adrenergic receptor blockers, and diuretics, unless contraindicated, and have been shown in the RALES and the EPHESUS trials to improve survival and morbidity.[6,7]

Unless there are contraindications, cardiac glycosides are indicated for heart rate control in symptomatic heart failure patients (NYHA I–IV) with tachyarrhythmia due to atrial fibrillation (AF) already treated with adequate dosages of ß-blockers.[1, 2,8] In that respect, a combination therapy of cardiac glycosides with ß-adrenergic receptor blockers seems to be more effective than either agent alone. In patients with systolic LV dysfunction (EF 35–40%) and sinus rhythm remaining symptomatic under treatment with ACE inhibitors, ß-adrenergic receptor blockers, diuretics, and aldosterone receptor antagonists, additional treatment with cardiac glycosides at low serum concentrations (digoxin 0.5–0.8 ng/ml) may improve symptoms and reduce hospitalisations without having an effect on mortality.[1, 2, 9]

Most supraventricular and ventricular arrhythmias in heart failure patients can be effectively treated with the class III antiarrhythmic amiodarone, which may restore and maintain sinus rhythm or improve the success of electrical

cardioversion in heart failure patients with AF.[1, 2, 10]. Anticoagulation is indicated in heart failure patients with AF, a previous thromboembolic event, a mobile LV thrombus or following myocardial infarction.[1]

While repeated or prolonged treatment with positive inotropic agents such as ß-adrenergic agonists (dobutamine) and phosphodiesterase inhibitors (milrinone, enoximone) increases mortality and is not recommended for the treatment of chronic heart failure, intermittent intravenous inotropic treatment may be used in cases of severe cardiac decompensation with pulmonary congestion and peripheral hypoperfusion, or as a bridge to heart transplantation. [1, 2, 11]

In patients with reduced LV function (EF 35%), sinus rhythm, left bundle branch block or echocardiographic signs of ventricular dyssynchrony and QRS width 120 ms, who remain symptomatic (NYHA III–IV) despite optimal medical treatment, cardiac resynchronisation therapy (CRT) using biventricular pacing improves symptoms and exercise capacity while decreasing hospitalisations and mortality.[1, 2,12-14]

For primary prevention of SCD in heart failure patients with optimal pharmacological treatment, ICD therapy is indicated in selected patients with LVEF 30% after myocardial infarction (>40 days) and in patients with ischaemic and non-ischaemic heart failure (NYHA class II–III) with LVEF 35% to reduce mortality.[1,2,12,15,16]

Heart transplantation is a firmly established surgical approach for the treatment of end stage heart failure and has been shown to improve exercise capacity, quality of life, and survival compared with conventional treatment.[1,2,17] The availability of heart transplantation for patients who could benefit from the procedure is limited by the continuing shortage of donor hearts and the increasing number of transplant candidates. Intra-aortic balloon counterpulsation (IABP) can provide short-term haemodynamic support. In patients with end stage heart failure considered too unstable to await a suitable donor organ, biventricular or LV assist devices (LVAD) as well as total artificial hearts can be employed as bridge-to-transplantation therapy.[1, 2,18,19]

In patients with end stage heart failure who are ineligible for heart transplantation, a recently conducted landmark clinical trial has shown that implantation of an LVAD improves survival and quality of life.[1,2,20] These data have led to the use of ventricular assist devices as an alternative to transplantation—so-called destination therapy.

Early clinical studies in patients with heart failure have shown the feasibility of transfer of distinct stem and progenitor cell populations to the heart, and have demonstrated beneficial effects on cardiac function and/or tissue viability.[21] However, due to small study sizes, lack of randomised control groups, poor understanding of the mechanisms of action of transplanted cells, lack of information on procedural issues (that is, optimal cell type, cell dosage, timing of cell transfer, optimal route of application), and safety concerns with some progenitors (such as the arrhythmogenicity associated with skeletal myoblast grafts), further basic research and the initiation of large, double-blind, placebo-controlled, randomised clinical trials with hard end-points (including mortality) are needed.

The new vasodilator agent nesiritide (recombinant human brain natriuretic peptide) has recently been shown to improve symptoms in patients with acute heart failure without affecting clinical outcome; however, effects on morbidity and mortality are not clear from available clinical trials.[1, 2] Ivabradine, a new selective inhibitor of the cardiac pacemaker current I_f that lowers heart rate without negative inotropic effects, is currently being evaluated in a clinical phase III trial involving patients with stable coronary artery disease and systolic heart failure (the BEAUTIFUL study).

Before the condition of patients with end stage heart failure deteriorates so much that they can not actively participate in decisions, patients and their families should be educated about options for formulating and implementing advanced directives and the role of palliative and hospice care services with re-evaluation for changing clinical status.[2] In caring for patients with end stage heart failure during their final days, it may be particularly difficult for the patients, their families and the physicians to define the time point when the patient's treatment goals shift from improving survival to improving quality of life, thus allowing for a peaceful and dignified death.

With the improvement in treatment modalities number of survival of the patients with acute cardiac insult is increasing in our population. Later on these patients present with heart failure, which ultimately leads to end stage heart failure. So that we should formulate a total care policy for our patients that include the multidisciplinary as well as super specialized cardiologist such as expert in heart failure. Hospice care is very important part of the management. Patients and their families should be included in the management plan and regular briefing of outcome and possible options should be discussed.

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