Current Treatments for Heart Failure

Caglar A and Nesligul Y*
Faculty of Medicine Department of Cardiology, Kirikkale University, Turkey
*Corresponding author: Yildirim Nesligul, Faculty of Medicine, Department of Cardiology, Kirikkale University, Turkey, Email: nesligul2004@hotmail.com

Abstract
Heart failure (HF) is a chronic disease associated with significant mortality and morbidity. HF management contains of non-pharmacologic, pharmacologic, and invasive strategies to limit and reverse its manifestations. Despite improvement in the treatment modalities, hospitalizations for HF remain frequent and mortality rates are still high. In this mini-review current treatment strategies are discussed.

Keywords: Heart failure treatment; Cardiac rehabilitation, Device therapy

Abbreviations: HF: Heart failure; HAPPY: Heart Failure Prevalence and Predictors in Turkey; HFrEF: HF with reduced ejection fraction; ACEI: Angiotensin Converting Enzyme Inhibitors; ARB: Angiotensin Receptor Blockers; ICD: Implanted Cardioverter-Defibrillator; VADs: Ventricular Assist Devices.

Introduction
Heart failure (HF) is one of the most important public health problems. It is also one of the most common causes of morbidity and mortality in the world. The worldwide prevalence of HF is estimated to be 23 million [1]. According to HAPPY (Heart Failure Prevalence and Predictors in Turkey) Study, the number of HF patients in Turkey is around 2 million [2]. Despite improvements in treatment strategies, mortality is very high due to the complex nature of the disease. The main goal of HF therapy is to reduce mortality and morbidity and also to improve the quality of life. Pharmacologic therapy, lifestyle modification, cardiac rehabilitation and device therapy are the cornerstones of treatment.

Lifestyle Modification
There is limited evidence that lifestyle modification increases quality of life. Even so it increases motivation for treatment. Lifestyle changes include the following: 1- to stop smoking and taking recreational substances, 2- to avoid excessive fluid intake; fluid restriction of 1.5–2 L/day may be considered in patients with severe HF to relieve symptoms and congestion, 3- to gain healthy eating habits, 4- to avoid excessive salt intake (>6 g/day), while the optimum sodium intake for patients with HF is not known. The 2013 ACC/AHA guidelines suggest that patients should consume less than 3 grams of sodium per day with regular exercise and avoidance of obesity [3].

Cardiac Rehabilitation
The recommended aerobic exercise prescription for HF patients typically does not differ greatly from those with other cardiac diseases, but aerobic interval training is highlighted as being particularly effective [4,5]. Aerobic activities include treadmill walking, cycling and upper body ergometry, dancing and swimming. A published study evaluated the effects of exercise in 37 patients with
HF (New York Heart Association functional class III). After 12 weeks of exercise training; functional class, peak VO2 and left ventricle ejection fraction improved [6]. Exercise training in patients with compensated HF with reduced ejection fraction (HFrEF) reduces symptoms of depression, total and HF-related hospitalization [7,8].

Pharmacologic Therapy
Pharmacologic therapy which reduce mortality in the treatment of systolic HF include angiotensin converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB), beta blockers and mineralocorticoid receptor antagonists. Although digitalis do not affect mortality, they were reported to reduce hospitalization [9]. There are new drugs entering HF guidelines as well as conventional therapy such as angiotensin receptor-neprilysin inhibitor (The combination of sacubitril/valsartan is called ARNI) and ivabradine (a selective sinus node inhibitor). ARNI is a new therapeutic class of agents acting on RAAS and neutral endopeptidase system. In a recent study, long-term effects of sacubitril / valsartan were investigated when compared to ACEI (enalapril) on morbidity and mortality in patients with symptomatic HFrEF. In this population, sacubitril / valsartan was superior to ACEI (enalapril 10), for reducing hospital admissions, cardiovascular mortality and overall mortality [10]. Ivabradine inhibits the If channel in sinus node and slows the heart rate. Ivabradine in HFrEF patients with left ventricle EF ≤35% and in sinus rhythm with a resting heart rate ≥75 bpm, was shown to provide a survival benefit [11].

There are some drugs that were suggested to have benefit in relieving symptoms but do not affect mortality. These are combination of hydralazine and isosorbide dinitrate and intravenous ferric carboxymaltose. The suggestions on the clinical utility of hydralazine and isosorbide combination comes from one relatively small trial conducted exclusively in men and before ACEIs or beta-blockers were used to treat HF [12]. The recently published CVD-REAL (Comparative Effectiveness of Cardiovascular Outcomes in New Users of SGLT-2 Inhibitors) Trial showed lower rates of hospitalization for HF and all-cause death in new users of sodium-glucose co-transporter-2 inhibitors as a group effect in patients with type II diabetes mellitus [13]. Intravenous administration of iron (ferric carboxymaltose) significantly improved exercise capacity and quality of life in patients with proven iron deficiency (ferritin <20%) and HF in the Ferric Carboxymaltose in Patients with Heart Failure and Iron Deficiency (FAIR-HF) Trial [14].

Device Therapy
An implanted cardioverter-defibrillator (ICD) is recommended (class la ) to reduce the risk of sudden death and all-cause mortality in patients who survive a ventricular arrhythmia causing haemodynamic instability [15]. Cardiac resynchronization therapy is recommended (class la) for symptomatic patients with HF in sinus rhythm with a QRS duration ≥150 msec and left bundle branch block QRS morphology and with left ventricle EF≤35% despite optimal medical treatment in order to improve symptoms and reduce morbidity and mortality [16].

Intra-aortic balloon pump (IABP) can be used in patients with cardiogenic shock but there is no good evidence about benefit of IABP. Ventricular assist devices (VADs) are used for bridge to recovery, transplantation and lifetime or destination therapy in HF. VAD types are left ventricular assist device, right ventricular assist device and biventricular assist device.

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