Management of Heart Failure in Elderly Patients

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ABSTRACT

Heart failure is a clinical syndrome, associated with high mortality and frequent as well as long hospitalization duration. Several cohort studies in elderly patients with >80 years of age for 1 year duration demonstrate a very high mortality rate for 3 months and 12 months hospitalization. Major Cardiovascular Events (MACE) observed during follow up is also increased significantly. These findings support the idea that age is a strong predictor and independent concerning mortality in patients with heart failure. There are different factors associated with mortality during hospitalization and follow-up.

Poor ejection fraction, a strong mortality predictor in young people, is not an independent factor in octogenarian population. This owes to the high prevalence of heart failure with normal ejection fraction (preserved ejection fraction), and only one fifth of echocardiography results demonstrate ejection fraction < 30%. The use of ACE-I or ARBs is associated with better one-year-outcome.

Key words: heart failure, cardiovascular, elderly patients.

INTRODUCTION

Heart failure is a clinical syndrome, associated with high mortality and frequent as well as long hospitalization duration. The prevalence of heart failure is increasing with age. Several surveys, e.g. the Euro Heart Failure Survey I (EHFS I), reported poor outcome, especially in elderly patients since the management is frequently complicated due to multiple co-morbidity factors. Moreover, evidence-based therapies are still infrequently applied and under-prescribing, i.e. giving drug less than the recommended dose, is commonly found in elderly patients.

Several cohort studies in elderly patients with >80 years of age for 1 year duration demonstrate a very high mortality rate for 3 months and 12 months hospitalization. Major Cardiovascular Events (MACE) observed during follow up is also increased significantly. These findings support the idea that age is a strong predictor and independent concerning mortality in patients with heart failure.

There are different factors associated with mortality during hospitalization and follow-up. Hospitalization mortality is primarily correlated to acute clinical conditions; while long-term mortality is associated with disability and the presence of other co-morbidities, such as diabetes and kidney dysfunction. Previous study showed that kidney function is a strong predictor for mortality during hospitalization and follow up.

Poor ejection fraction, a strong mortality predictor in young people, is not an independent factor in octogenarian population. This owes to the high prevalence of heart failure with normal ejection fraction (preserved ejection fraction), and only one fifth of echocardiography results demonstrate ejection fraction < 30%. The use of ACE-I or ARBs is associated with better one-year-outcome.
AGE AS PREDISPOSITION FOR HEART FAILURE

Age is one of predisposing factors for the development of heart failure through various mechanisms. First, heart failure is a common outcome for every cardiovascular disease. Thus, patients with cardiovascular diseases (such as hypertension, acute coronary syndrome, heart surgery, etc) tend to develop and experience ventricular remodeling and heart failure in their older age. Second, in spite of cardiovascular diseases, elderly itself is associated with decreasing aortal and left ventricle compliance, and increasing aortal impedance as well as abnormal left ventricle diastolic functions. These conditions lower the threshold of heart failure progression when the heart is exposed to precipitating factors, such as hypertension and/or tachyarrhythmia (mainly, atrial fibrillation). The last mechanism explains why the clinical manifestation of heart failure in elderly patients is basically different from syndromes described and studied on randomized clinical trials.

Heart failure is more frequently found in female patients because of their longer life expectation age; hence, they tend to suffer more risk of having hypertension, normal left ventricular ejection fraction and a great number of co-morbidities. Compared to young people, elderly patients are more frequently experiencing inadequate assessment during hospitalization, and more often received under-prescribing or having treatment less than the recommended dose for life saving therapies. Age is also a predictor of higher mortality and health care.

HEART FAILURE DIAGNOSIS IN ELDERLY PATIENTS

Symptoms of heart failure, such as tiredness and breathing difficulty, may be mistaken as aging process. Delirium, the presence of decreasing functional status, recent peripheral edema, or nocturnal symptoms (cough, dyspnea) calls for further evaluation in regard of heart failure possibility.

The basic examination for heart failure in elderly patients is not significantly different, i.e.: complete blood count, routine biochemistry, including liver and kidney function test, NT-proBNP test, chest x-ray and electrocardiography (ECG). Just as in young patients, objective assessment of left ventricle function should be performed by means of echocardiography. Patients who seem to be having acute pulmonary edema must undergo examination and evaluation to find out the etiology that triggers the development of disease (infection, ischemia, arrhythmia, change of drug regimens or non-compliance to therapy). Other examination depends on whether there is a presumption of the existence of other disease, based on the anamnesis and physical examination.

THE MANAGEMENT OF HEART FAILURE IN ELDERLY PATIENTS

ACC-AHA has recently announced the guideline of heart failure in general (not exclusively for elderly patients). The management of heart failure based on the guideline is shown in figure1.

EXERCISE AND LIFE STYLE MODIFICATION

The benefit of exercise on heart failure includes decreasing neuro-hormonal activity, improving endothelial and physiological function of skeletal muscle and the sensation of improved quality of life. Patients shall have education in regard of dietary modification (low salt and water restriction).

Recommendations

Exercise training is beneficial as an adjunctive approach to improve clinical status in ambulatory patients with current or prior symptoms of heart failure and reduced left ventricular systolic function. (Class I, Level of Evidence: B)

PHARMACOLOGICAL TREATMENT FOR HEART FAILURE IN ELDERLY PATIENTS

Data regarding optimal pharmacological therapy for heart failure in extremely elderly patients (age >80 years) is very limited. Small studies and sub-group analysis on large scale clinical trial demonstrates the safety and efficacy of treatment, especially adjusted for elderly patients with congestive heart failure.

DIURETICS

Diuretics are prescribed to all patients who have evidence of symptoms or signs of pulmonary or systemic congestion. Once daily dose is more preferred. Moreover, renal function and electrolyte balance should be monitored during treatment. Patients who have hypo-perfusion symptoms or exaggerated kidney insufficiency during the titration of neuro-hormonal blockade treatment should reduce their diuretics dose. For long-term treatment, diuretics dose can be altered several times to allow other drugs titration, and to obtain the lowest dose that can stabilize body weight and symptoms.

Recommendation

Diuretics and salt restriction are indicated in patients with current or prior symptoms of heart failure and
reduced left ventricular systolic function who have evidence of fluid retention. (Class I, Level of Evidence: C). 23

ANGIOTENSIN CONVERTING ENZYME (ACE) INHIBITOR

Angiotensin converting enzyme (ACE) inhibitor should be considered for all elderly patients with chronic heart failure, although the data regarding the effectiveness of this drug in elderly patients is still limited. CONSENSUS study24 (enalapril) excludes patients who are over 75 years, and SOLVD study25 (enalapril) and SAVE study26 (captopril) exclude patients who are over 80 years. AIRE study27 (ramipril) does not exclude patients based on age alone, and there is a tendency toward better end-result in population of over 65 years, however, the sample size is not large enough to achieve statistical significance.

When performing ACE inhibitors dose titration in elderly patients, it is important to start with low dose and increase gradually in accordance with the target dose in clinical trial or maximal lower dose that can still be tolerated. Diuretics dose can be reduced if there is no water retention, to maintain stable blood pressure. In several elderly patients, it would be more helpful if the consumption time of ACE inhibitor and diuretics are separated, to prevent peak hemodynamic effect. Blood pressure should be measured in standing, sitting and lying position. The renal function and potassium serum level should be evaluated after altering ACE inhibitors and diuretics dose or if there is any change in clinical condition.

ACE inhibitor study in elderly patients is reported on PEP-HF study28 (Perindopril in Elderly People with Chronic Heart Failure). The incidence of primary endpoint all-cause death or heart failure hospitalization tend to be reduced with perindopril than with placebo in one year time [hazard ratio (HR) 0.69, 95% confidence interval (CI) 0.47 – 1.01; P=0.055]. However, such tendency was not found at the end of this study [HR 0.92, 95% CI 0.70 – 1.21].

Recommendation

Angiotensin converting enzyme inhibitors are recommended for all patients with current or prior symptoms of heart failure and reduced left ventricular systolic function, unless contraindicated. (Class I, Level of Evidence: A)23

ANGIOTENSIN II RECEPTOR BLOCKERS

VAL-HEFT study29 (Valsartan Heart Failure Trial), with mean age of 63±11 years old (47% patients were > 65 years), and CHARM study30 (Candesartan in Heart Failure Assessment of Reduction in Mortality and
Morbidity), with mean age of 66±11 years old (23% patients were >75 years), demonstrate the benefit of ARB on similar outcome in patients <65 years of ≥65 years.

**Recommendation**

Angiotensin II receptor blockers are recommended in all patients with current or prior symptoms of heart failure and reduced left ventricular systolic function, who are ACE inhibitor-intolerant. (Class I, Level of Evidence: A)\(^{23}\)

**BETA BLOCKERS**

Beta blockers are also beneficial for elderly patients, since there is greater role of activation of sympathetic nervous system compared to the renin-angiotensin system. CIBIS II study\(^{31}\), MERIT HF study\(^{32}\), and COPERNICUS study\(^{33}\) demonstrate that beta blockers can increase survival as much as 30-35% and also increase left ventricle systolic function. The mean age of the patients in randomized clinical trial meta-analysis range from 60 to 65 years, and < 30% patients were > 70 years and there were very few patients who were >80 years. Sub-group analysis shows that there is no significant interaction between age and the effect of beta blockers effect on the outcome.\(^{34}\) Beta blockers should be started with the lowest dose, increase gradually in weeks up to months duration. Monitoring shall be performed on heart rate, blood pressure and patients’ complaints.

The role of beta blockers nebivolol in elderly patients who have heart failure (≥ 70 years) with normal left ventricle systolic function (diastolic heart failure) was reported in the SENIORS study.\(^{35}\) There was a decline of primary outcome (all-cause mortality or cardiovascular hospitalization) of lower rate compared to other previous beta blockers studies [HR 0.86; 95% CI 0.74 – 0.99; P=0.039]; and it was also different from previous studies which had young patients as study subjects, since it did not affect the mortality [HR 0.88; 95% CI 0.71 – 1.08; P=0.21]. In sub-group analysis, nebivolol effect on primary outcome was significant in patients <75 years (median value), but it was not significant in patients >75 years.

**Recommendation**

Beta blockers (using 1 from 3 proven to reduce mortality, i.e. bisoprolol, carvedilol and sustained release metoprolol succinate) are recommended for stable patients with current or prior symptoms of heart failure and reduced left ventricular systolic function, unless contraindicated. (Class I, Level of Evidence: A)\(^{23}\)

**SPIRONOLACTONE**

Study on the role of aldosterone antagonist in elderly patients is still lacking. Low- dose spironolactone (mean 26 mg/day) has been researched on RALES study\(^{36}\) (Randomized Aldactone Evaluation Study). Subjects of RALES study were population with mean age of 65 years with severe heart failure (NYHA III-IV, LVEF < 35%), who had been receiving ACE inhibitors and loop diuretics treatment. However, patients with renal dysfunction (creatinine level > 220 μmol/L) or with other significant co-morbidities were excluded. Spironolactone decreases mortality about 30%, as well as hospitalization due to heart failure as much as 35% and significantly improves NYHA functional class. Thus, low dose spironolactone is recommended for patients with severe heart failure, albeit having received optimal medical management. Gynecomastia occurs in 10% male patients. Also have to bear in mind that potassium and renal function were routinely monitored in this study, i.e. on the 1st, 2nd, 3rd, 6th, 9th and 12th month and then 6 months later. With strict monitoring, we expect that hyperkalemia and renal dysfunction will not occur. Oral potassium supplement is not required, unless there is hypokalemia (<3.5 mmol/L).

Sub-group analysis on RALES study demonstrates effect on similar outcome of patients with <67 years and >67 years of age. Moreover, age is associated with increased side effects, particularly hyperkalemia.\(^ {22}\) Spironolactone study in patients who have heart failure and ejection fraction > 45% is currently being conducted and it will evaluate whether spironolactone is effective for heart failure with normal ejection fraction.

**Recommendation**

Addition of aldosterone antagonist is recommended in selected patients with moderately severe to severe symptoms of heart failure and reduced left ventricular systolic function, who can be carefully monitored for preserved renal function and normal potassium level. Creatinine level should be < 2.5 mg/dL for male and <2.0 mg/dL for female and potassium should be < 5 mEq/L. (Class I, Level of Evidence: B)\(^{23}\)

**DIGOXIN**

Study of digitalis on heart failure, which is called DIG (Digitalis Investigation Group) reported the advantages of digoxin for stable heart failure, particularly in patients with left ventricle systolic dysfunction (LVEF < 45%). In addition, the other several small adjunct studies are also evaluating patients with LVEF > 45%. Twenty seven percent subjects were > 70 years. The benefit of treatment in decreasing hospitalization was demonstrated in
all age groups. However, increased age was associated with a higher rate of hospitalization due to assumed digoxin intoxication. Overall, there was no reduced mortality rate. In DIG study, digoxin dose was managed by using an algorithm in accordance with age, sex, weight and renal function. Digoxin should be used cautiously (particularly for those with renal dysfunction). It may alleviate patients’ complaints and decrease hospitalization for patients with severe heart failure symptoms and very poor heart function.

In the sub-study, which was conducted in parallel with the main study, there were almost 1000 patients with had heart failure and normal systolic function, who were usually elderly patients. Digoxin demonstrated a tendency of early advantage on improved outcome, although it is difficult to explain the underlying mechanism.

REFERENCES


