Heart failure in the elderly

Niewydolność serca w wieku podeszłym

INTRODUCTION

Heart failure (HF) is a major clinical and public health problem, with a prevalence of over 23 million worldwide. In 1997, it was singled out as an emerging epidemic (1, 2). HF refers to approximately 1-2% of the adult population in developed countries, with the prevalence rising to ≥ 10% among people in their seventies or older (3).

Early signs and symptoms of HF are usually non-specific and increase as the result of pathophysiologic changes connected with age, such as oxidative stress, inflammation and other cardiovascular (CV) risk factors. The etiology of HF in older adults is considered multifactorial, and includes hypertension, diabetes, coronary artery disease, valvular disease, impaired renal function and chronic obstructive lung disease (3-5).
HF is defined as a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill or to eject blood. As HF is considered a syndrome rather than a disease, its diagnosis relies on combined results of medical, laboratory and imaging examinations. The low physical activity, typical for many older individuals, can mask the development of dyspnea or fatigue. Fatigue at rest in the elderly may suggest depression rather than HF (1, 3, 4). Older people often attribute their HF symptoms to aging, delaying presentation until symptoms become more overt and severe. Cognitive and sensory impairments common in the elderly may additionally delay the diagnosis of HF (4). A clinical course of HF is usually characterized by periodic acute exacerbations. Acute decompensated HF is defined as a gradual or rapid change in heart failure signs and symptoms resulting in a need for urgent therapy. This definition comprises worsening chronic HF, new onset HF and advanced HF. Periodic exacerbations require intensification of treatment, most often in the hospital, and they are considered most frequent cause of hospitalization for people aged 65 years or older. Although HF incidence and prevalence increase disproportionately among the elderly aged ≥ 80 years, optimal management of this group of patients remains not firmly established, and standards of care developed for younger adults often fail to achieve beneficial outcomes for the very old HF population (1, 4).

HEART FAILURE DIAGNOSTICS

There is no single test or procedure that can definitively confirm the diagnosis of HF. Similarly, there are many diagnostic criteria for HF to be used in clinical and population settings, and none of them is universally accepted (4). Several criteria were proposed to diagnose HF, e.g. the Framingham criteria, Boston criteria, Gothenburg criteria, and the European Society of Cardiology criteria. All of them rely on similar signs and symptoms, and combine data from the medical history, physical examination and chest X-ray (1). It was found that the specificity of the Framingham criteria and their predictive value were lower than those of the Boston score for definite HF, but they provided greater sensitivity to diagnose possible HF (6). The Boston criteria have been recommended over other criteria for older adults due to their construct validity and improved prediction of adverse outcomes (7).

Most clinical symptoms of heart failure overlap with manifestations of other conditions that often occur in elderly people. Symptoms such as exertional dyspnea, orthopnea, paroxysmal nocturnal dyspnea, fatigue and weakness have both poor sensitivity and specificity. Signs of fluid retention and sympathetic activation (tachycardia) as well as pulmonary venous hypertension found with chest X-ray can be supportive for the diagnosis (8).

The current classification of HF includes the parameters of left ventricular function. The left ventricular ejection fraction (EF) enables classifying HF as the one with preserved or reduced EF. Different thresholds have been suggested as a diagnostic value of decreased EF. The threshold of 55% was recommended by the American Society of Echocardiography, 50% was the result of Framingham Heart Study, while the Organized Program to Initiate Lifesaving Treatment for Hospitalized Patients with Heart Failure Registry, and the Acute Decompensated Heart Failure National Registry recommended the value of 40% as the cut-off point (9-11). For the very old adults, both HF with preserved EF (HFPEF) and HF with reduced EF (HFREF) are common, however occurrence of HFPEF increases more distinctly in relation to aging, especially in women (12). Several population-based studies, such as the Framingham Heart Study and the Olmsted County Study revealed that more than half of older HF patients demonstrated a form with preserved EF. The factors that particularly predispose older adults to HFPEF are arterial and myocardial stiffening. In elderly women augmented myocardial growth responses were observed that could additionally prone them to impaired diastolic physiology (13, 14).

Essential examinations that are considered to be helpful to diagnose HF include an electrocardiogram (ECG), chest X-ray and transthoracic echocardiography. The ECG is sensitive but non-specific test. Normal ECG, however, virtually rules out heart failure (15). A chest X-ray may demonstrate cardiac enlargement with or without pulmonary hemostasis, pulmonary venous hypertension, and/or interstitial pulmonary edema. The echocardiogram is the definitive test in the diagnosis of heart failure. This exam provides information on ventricular size and function as well as the prior occurrence of myocardial infarction such as areas of hypocontractility. All these examinations can be also useful in determining whether the underlying etiology is of ischemic or non-ischemic origin. Additionally, assessment of valvular structure and function, assessment of pulmonary pressure, and the presence or absence of pericardial disease may be useful in guiding therapy (4). Echocardiography-Doppler is considered the approach of choice to assess the diastolic function in routine practice. It was found, however, that the relationships between standard Doppler parameters and left ventricular diastolic pressures were uniformly poor. It was concluded that the diagnosis of diastolic HF could not be made on the basis of a single echo-Doppler parameter but, rather, all parameters had to be examined in concert and used in combination with clinical observations (16-18).

No single biochemical test is considered pathognomonic for heart failure, but plasma levels of B-type natriuretic peptide (BNP) and N-terminal pro-BNP (NT-pro-BNP) can be used to facilitate diagnosis. Both peptides are neurohormones that are secreted by the failing ventricle in response to increased myocardial wall stress. Although multiple studies showed that elevated BNP or NT-pro-BNP may assist
in the diagnosis of HF, their utility in older adults remained less clear as age itself was associated with modest increases of serum concentrations of these hormones. It was suggested that higher cut-off points are needed for older patients (19). Moreover, other conditions associated with heart failure, e.g. atrial fibrillation as well as female sex are also associated with increased plasma BNP level, whereas obesity is characterized by decreased serum BNP concentrations. It should be emphasized that low levels of BNP have a very high negative predictive value, making it an extremely useful rule-out test for heart failure (20).

In people with confirmed diagnosis of HF, the mortality rate of 50% at 5-10 years was estimated. Fortunately, the proportion of cardiovascular deaths was found to be reduced from 69% in 1979-1984 to 40% in 1997-2002 (p = 0.007) among subjects with preserved EF contrasting with only a modest change among those with reduced EF (77 to 64%, p = 0.08) (21-23).

**NON-PHARMACOLOGICAL THERAPY**

The comprehensive treatment of the HF patients includes individualized physical activity, exercises under the supervision of a physiotherapist, reduction of body mass in overweight patients and modification of the lifestyle factors such as cigarette smoking, alcohol consumption, and diet. Patients with HF should be encouraged to undertake physical activity compatible with their cardiovascular tolerance, to achieve a healthy weight (BMI 20-25 kg/m²) as well as stop smoking and reduce alcohol consumption (4). It is extremely important to avoid malnutrition of elderly HF patients as it is associated with significantly increased mortality rate. Several small and moderately-sized trials have shown that exercise-training programs in older individuals with HF and reduced EF were able to improve functional capacity at a similar degree as in younger persons. In a study of 200 individuals about the age of 72 years, 24 weeks of combined aerobic and low-resistance strength training improved NYHA class, health-related quality of life and increased 6-minute walk distance (24).

Reduced sodium intake to 2 g per day, corresponding to 5 g of sodium chloride has been well established practice. Recent studies suggest, however, that it may not be necessary. It was found that sodium intake of 2.7 g/day reduced the rate of death or hospitalization by 25% compared to an intake of 1.8 g/day (25).

Patients should be encouraged to consume an adequate but restricted amount of sodium-free fluids. This recommendation is critical in patients who have low serum sodium levels, which is often seen in the setting of heart failure due to the activation of neurohormones such as vasopressin (8). Since exacerbations of HF are preceded by fluid retention the patients should be suggested to weigh themselves every morning after urinating. If they notice weight gain of 2.5 kg or more they should increase the diuretic dose temporarily and contact their doctor (4).

**PHARMACOLOGICAL THERAPY**

The treatment of patients at high risk for the development of HF should be aimed at reducing significant risk factors by aggressive treatment of hypertension, diabetes, hyperlipidemia and obesity. It was shown that long-term control of hypertension may reduce the risk of an HF incident by more than 50% (26).

Activation of the renin-angiotensin-aldosterone system (RAAS) and sympathetic nervous system (SNS) plays a pivotal role in pathogenesis and progression of heart failure and was found to increase mortality rate (27, 28). Blockade of these systems is considered a cornerstone in the management of HF. Angiotensin converting enzyme inhibitors (ACE-Is) or angiotensin receptor blockers (ARBs) as well as beta-blockers are the main drugs in the treatment of systolic heart failure. Therapy with these agents should be initiated at low doses and gradually up-titrated to the target maximal tolerated doses. With all above drug classes blood pressure (measured in supine and standing positions), heart rate, renal function and serum potassium concentration should be regularly monitored (8, 29, 30).

In the Studies Of Left Ventricular Dysfunction (SOLVD) – the largest randomized control trial on efficacy and safety of ACE-Is in HFREF patients, only 36% of included individuals were > 65 years of age and none was 81 years or older. The study revealed that the rate of sudden death that was a major mode of death in HF patients was only slightly influenced by ACE-Is. It was found that augmentation of ACE-Is doses was not beneficial and could result in increased risks of dizziness, falling and impaired renal function (31). It needs to be remembered that ARBs may be considered for patients who do not tolerate ACE-Is and that iatrogenic effects are more often and more severe when drugs of both groups are used in combination (4).

β-adrenergic blockers differ in their clinical efficacy in older HF patients. Based on clinical trials data bisoprolol, carvedilol, and metoprolol are indicated in patients with reduced EF while metoprolol tartrate and atenolol should be avoided (4). Some of beta-blockers e.g. carvedilol and nebivolol possess vasodilating properties, that can be useful in the treatment of hypertensive individuals but make them more difficult to initiate therapy in patients with borderline-low blood pressure. In studies that included patients with severe HF, carvedilol was very well tolerated, even though a baseline systolic blood pressure cut-off was 85 mmHg (32). Highly selective beta-blockers such as nebivolol, bisoprolol, and metoprolol should be preferred in HF patients with chronic obstructive pulmonary disease (8).

The effectiveness of aldosterone receptor antagonists are questioned despite clear evidence of their efficacy in randomized clinical trials. It was found in 1999 that spironolactone decreased total mortality in patients with chronic HF, New York Heart Class III and IV (33). Recently patients with HF at New York Heart Class II with reduced EF have been shown to benefit from the aldosterone antagonist, eplerenone at...
The use of antiplatelet and anticoagulant therapy in HF patients is controversial. In patients with known ischemic heart disease, aspirin and other antiplatelet agents should be continued. Warfarin can be considered in patients with chronic HF and atrial fibrillation (8).

**DEVICE-BASED THERAPY**

The two main device-based therapies used in patients with HF are: implantable cardioverter defibrillator (ICD) and cardiac resynchronization therapy (CRT). ICDs are indicated in high-risk patients to reduce the incidence of sudden death. This device is recommended in patients with low EF (≤ 30% after myocardial infarction or ≤ 35% in other patients) (26). The Multicenter Automatic Defibrillator Implantation Trial II (MADIT-II) revealed that therapy with ICD reduced absolute risk in all-cause death by 5.6% over the mean of 20 months of follow-up (39). CRT is indicated in patients with the New York Heart Class III and IV symptoms of HF with sinus rhythm and evidence of ventricular dyssynchrony, with a QRS duration of ≥ 120 ms on ECG. The Cardiac Resynchronization-Heart Failure trial (CARE-HF) has shown benefit with CRT added to the pharmacological therapy in patients who met the above criteria with reduction in absolute mortality risk by 7.1% over 2 years (40).

**CONCLUSIONS**

The Kaiser Permanente system comparing the incidence of HF in 1970 to 1974 and in 1990 to 1994 among people aged ≥ 65 indicated that the age-adjusted incidence of HF increased by 14% over time and was greater for older age groups and for men (41). The Framingham and Olmsted County studies reported similar trends towards increasing HF incidence among older people. Available data indicate that lifetime risks of HF are very high regardless of gender, race and geographical location, emphasizing the importance of population-wide efforts to reduce the burden of HF. The proper therapy of HF in the elderly remains a very important way to improve both life expectancy and quality.

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