Symposium: Editorial

Multifactor heart failure in the elderly: a proposal for cooperative research

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Chronic heart failure (CHF) is a clinical syndrome as a common pathway at the end stage of cardiac diseases of different etiologies, and it is currently the only cardiovascular disease with an increasing prevalence in the developed countries. In the United States, the prevalence of CHF at age 50 years is 1.0%, whereas it reaches 7.5% at age 80 years. In the United Kingdom, the prevalence of CHF is 5.0% at age 60-70 years, and 10-20% at age 80 years. The situation is similar in Italy and Portugal. Despite being a developing country in Asia, China has experienced rapid progress in acquiring medical knowledge and advancing techniques in recent years. Due to the markedly declined mortality of acute myocardial infarction (AMI) as well as the aging of Chinese population, about four million Chinese have CHF with a prevalence of 0.9%, most of whom are 60 years of age and older.

As a new clinical entity, multifactor heart failure in the elderly (MHFE) is defined as heart failure caused by cardiac impairment with two or more concomitant etiologies in the elderly. MHFE has its unique pathogenesis, pathophysiology, clinical manifestation, and needs particular management as compared to heart failure caused by a single etiology during the whole process of heart failure. We proposed the concept of MHFE in 2003 and then initiated a research program which was supported by the Beijing Medicine Development Foundation in 2004. The first training course of MHFE was held in Kunming, China in 2005. After that, MHFE was recognized as an important new clinical entity by many other Chinese distinguished medical professionals. The common causes of MHFE include coronary heart disease, hypertension, and concomitant valvular disease, idiopathic cardiomyopathy, uremia, congenital heart disease, obesity, hyperthyroid cardiomyopathy, anemic heart disease and diabetic cardiomyopathy, etc. Multifactor heart failure has its own characteristics which make it distinct from heart failure in younger population in that (1) heart failure resulted from collaborative effects of multiple co-existent diseases, (2) concomitance of cardiac aging and multiple diseases, (3) high prevalence in the elderly population, (4) unstable condition and prone to exacerbation, (5) low compliance to therapy, and (6) many contradictions in the medication.

Recently, we carried out a retrospective study at the Institute of Geriatric Cardiology (IGC), Chinese PLA General Hospital. The objective of this study was to investigate the etiological characteristics of CHF in old patients. A total of 1,372 CHF patients at 60 years of age and older hospitalized from January 1993 to June 2006 were enrolled in this study. The results showed that: (1) The percentage of CHF patients with two or three causes increased with age. Of all the CHF patients, those with two causes accounted for 33%, and those with three causes accounted for 25%. In CHF patients aged 80 years and older, those with three causes account for 50.3%. (2) The leading three causes were coronary heart disease (63.8%), hypertension (47.7%) and cor pulmonale (33.9%). Other common causes of CHF in the elderly were diabetes mellitus, idiopathic cardiomyopathy, myocardiitis, uremic cardiomyopathy, rheumatic heart disease, degenerative calcified valvular disease, and congenital heart disease.

The Framingham CHF study, Italy CHF study, and Fukuoka CHF study laid emphasis on the variety of causes of CHF and its changes with age; however, the concept of MHFE was not explicitly proposed in these studies. Our retrospective study showed that ten or more diseases might contribute to the pathogenesis to CHF in the elderly, and the common types of causes of MHFE were listed as follows:

(1) 2-factor CHF:
- hypertension-coronary heart disease
- hypertension-diabetic cardiomyopathy
- idiopathic cardiomyopathy-hypertension
- coronary heart disease-cor pulmonale
- rheumatic heart disease-coronary heart disease

(2) 3-factor CHF:
- hypertension-coronary heart disease-calcified valvular disease
- hypertension-coronary heart disease-rheumatic heart
disease
hypertension-coronary heart disease-idiopathic cardiomyopathy

(3) 4-factor CHF:
hypertension-coronary heart disease-diabetic cardiomyopathy-renal anemia
idiopathic cardiomyopathy-hypertension-cor pulmonale-congenital heart disease

(4) 5-factor CHF:
hypertension-coronary heart disease-cor pulmonale-idiopathic cardiomyopathy-anemia

(5) 6-factor CHF:
hypertension-coronary heart disease-diabetic cardiomyopathy-congenital heart disease-uremic heart disease-anemia

Here we presented a case of an elderly CHF patient with 6 causes. The 86-year-old man was admitted to the IGC on August 10, 2006 because of heart failure. He has had hypertension for 30 years, diabetes mellitus for 26 years, coronary heart disease (old myocardial infarction) for 12 years, cor pulmonale for 15 years (a heavy smoker for 40 years), and degenerative calcified valvular heart disease (aortic regurgitation and 3 valves calcification) for more than 20 years. He had been hospitalized in our hospital more than dozen times in the recent 10 years. His electrocardiography showed atrial fibrillation and nonsustained ventricular tachycardia. His echocardiography suggested patent foramen ovale. He was diagnosed MHFE, and died of ventricular fibrillation on September 4, 2006. Autopsy examination verified the clinical diagnosis of patent foramen ovale.

The most common cause of CHF in the elderly is coronary heart disease. The severity and extent of coronary atherosclerosis increase with age, which is generally presumed as a result of prolonged exposure to risk factors of coronary heart disease. Compared with young patients, the elderly patients with coronary heart disease are more often to have multivessel disease, lower left ventricular ejection fraction (LVEF), non-Q-wave myocardial infarction (MI) and unrecognized MI. Hypertension is another common cause of CHF in old patients. The long-term uncontrolled hypertension may result in heart failure in old patients, which often presented with preserved left ventricular systolic function and impaired diastolic function, that is, diastolic heart failure. Diabetes mellitus alone may lead to or aggravate CHF. In patients with diabetes mellitus, glycermia and free fatty acid, through increased reactive oxygen species and advanced glycation end products, which may induce myocardial toxicity and subsequent cardiomyocyte apoptosis, or even lead to diabetic cardiomyopathy. In patients with chronic renal dysfunction, inflammatory mediators and cytokines may aggravate the injury of myocardial cells; furthermore, increased blood volume due to sodium and liquid retention, may augment the left ventricular preload and exacerbates CHF. Of note, chronic anemia is importantly involved in the pathogenesis of CHF. Chronic anemia is commonly seen in the elderly population due to malnutrition and other chronic diseases. Chronic anemia may worsen myocardial ischemia, increase myocardial hibernation and induce cardiomyocyte apoptosis. In patients with chronic anemia, the hearts has to pump more blood in compensation for tissue ischemia, thus increasing cardiac workload and oxygen consumption, ultimately precipitating or aggravating heart failure.

In summary, the elderly population is more likely to have various kinds of diseases with aging. These age-related diseases may be involved in the pathogenesis of CHF, which makes the etiology of CHF more complicated. Drug therapy for patients with MHFE is challenging because of drug-drug interaction, effects of medications to the hepatic and renal function, as well as the influence of drugs to many kinds of metabolism. Thus, it is crucial to identify the pathogenesis of MHFE as a guide to clinical care and improve the prognosis of elderly CHF patients.

Considering that MHFE has gathered much more attention in the cardiology community, we would like to develop clinical and basic research on MHFE in cooperation with 10-15 hospitals or medical centers in the next 3-5 years. The clinical research program may include: (1) epidemiological study on CHF in the elderly population, especially the age-related structure of CHF etiology; (2) the diagnostic and therapeutic characteristics of MHFE and single-factor CHF; (3) the therapy for subclinical MHFE; (4) different treatment for MHFE according to different etiology; (5) prognosis of MHFE; (6) rehabilitation of MHFE. The basic research may involve: (1) animal model of MHFE; (2) the correlation between animal model and patients with MHFE; (3) ventricular remodeling in MHFE; (4) pathophysiology of MHFE.

Through the above research on MHFE, we hope to shed some light on the pathogenesis and clinical characteristics of MHFE, and establish a practical guideline for its diagnostic criteria, therapeutics and prevention. We hope that medical professionals both in China and other countries will join us in the research team, to overcome the worldwide health problem by our hard work and harmonious cooperation. I hope everybody will enjoy the challenge, and be prepared for the "silver society".