## **EDITORIAL**

## Clinical characteristics of elderly patients with heart failure: what else do we need to know?

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Despite contemporary therapeutic options, heart failure (HF) is a growing public health problem, especially in elderly population.

In an article by Ozieranski et al,¹ the authors made an attempt at assessing the clinical profile and 1-year outcomes of 765 elderly patients hospitalized for HF decompensation and participating in the Polish ESC-HF Long-Term Registry. Patients aged 65 years or older were compared with those younger than 65 years of age. An additional subanalysis sought to determine the clinical differences among elderly patients aged from 65 to 74 years and the very elderly, aged 75 years or older.¹

Nowadays, it is particularly important to investigate the clinical characteristics of elderly patients as well as the effects of contemporary therapies on the outcomes of these patients. This is because most clinical trials on HF excluded this population, especially persons over 75 years of age.<sup>2,3</sup>

Except more frequent comorbidities such as hypertension, coronary artery disease [CAD], or atrial fibrillation[AF], aging is associated with specific changes to cardiac structure and function, which may explain a number of pathophysiological and phenotypic features typical for the elderly.2 Among these, particularly important is the greater predisposition of these patients to develop HF, especially HF with preserved ejection fraction (HF-PEF).<sup>4,5</sup> These changes involve the reduction in the number of myocytes and regenerative capacity of cardiac progenitor cells, which occurs even in individuals without evidence of cardiovascular disease.<sup>5</sup> The loss of functioning cardiomyocytes is compensated by hypertrophy of the remaining cells.<sup>5,6</sup> Alterations in the function of myocytes associated with older age also include impaired calcium metabolism and regulation, as well as secondary less efficient adenosine triphosphate ATP utilization, which reflects changes in the processes of contraction and relaxation of the heart muscle. 1 The shortening of telomeres has been suggested as a marker of

biological and cellular aging and has been associated with the development of HF.<sup>7</sup> The severity of myocardial fibrosis is another abnormality observed in elderly patients, and is associated with increased susceptibility to HF.<sup>8</sup>

In the study by Ozieranski et al,1 most of the patients with HF under the age of 75 years were male, but over the age of 75 years, the sex distribution was almost equal because of the increase in the number of women with HF. In the Polish ESC-HF Long-Term Registry, the risk of death or rehospitalization was shown to increase with age over 75 years old, which is consistent with the findings of other studies.<sup>2,4,9</sup> However, the study lacks data on the sex distribution of patients with HF-PEF and the number of patients with acute HF. This information would verify the results of some studies which revealed that elderly patients hospitalized for acute HF are more likely to be female and to have higher ejection fraction and a higher prevalence of HF-PEF compared with younger patients. 2,10,11 These patients also have an increased prevalence of comorbidities including AF, hypertension, cerebrovascular disease, anemia, and renal failure. 10-12 On the other hand, CAD and diabetes are less common in very elderly patients (>75 years old).<sup>2,9-12</sup> This may be explained by the longer survival of patients without these diseases, which, on the other hand, causes systolic dysfunction and HF at a younger age. 13

In contrast to younger patients with HF, elderly patients with acute decompensation of HF more often present with acute pulmonary edema and hypertension, which is consistent with a significant vascular contribution to the underlying pathophysiology. Conversely, elderly persons with chronic HF may present with a gradual onset of symptoms and atypical findings, including loss of appetite, tiredness, and global weakness, whereas traditional HF symptoms may be absent or difficult to interpret due to the lack of specificity.

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There is also little known on the response to pharmacological treatment in elderly patients. Ozierański et al,¹ in their analysis of the Polish ESC-HF Long-Term Registry, demonstrated that treatment with  $\beta$ -blockers results in a 50% reduction of the risk of death at 1 year, but only in patients younger than 75 years old.¹ This finding has not been unequivocally confirmed in the study, but the authors provided a possible explanation: it might be due to a decreasing use of appropriate doses of  $\beta$ -blockers and a worse response to  $\beta$ -adrenergic blockade in the elderly population. In addition, possible cognitive impairment and financial problems may affect treatment adherence.²

Data from recent trials investigating the effects of  $\beta$ -blockers in elderly patients are still insufficient. Admittedly, in the SENIORS study with nebivolol and the CIBIS-ELD study with bisoprolol, which were cited by Ozieranski et al<sup>1</sup> in their research, the mean age of patients was over 73 years, but in other studies with  $\beta$ -blockers, like COPERNICUS or BEST, the participants were much younger (mean age, about 60 years).<sup>2</sup>

The lack of evidence-based therapies in the elderly represents a major challenge because the management of a medical therapy is a complex process for several reasons. First of all, drug pharmacokinetics changes during the aging process because of a reduction in lean body mass and total body water, reduction in the metabolic capacity of the liver, and a decrease in renal function.<sup>14</sup> Furthermore, treatment comorbidities often accompanying old age require polypharmacy, which results in a higher risk of drug interactions and side effects.<sup>2,14</sup> Some comorbidities and their treatments may by themselves contribute to the worsening of HF.15 By contrast, invasive strategies of HF treatment, such as cardioverter--defibrillator implantation or cardiac resynchronization therapy, are performed less frequently in patients over 75 years of age because of shorter life expectancy, so our knowledge on this subject is still insufficient.<sup>2</sup>

In conclusion, although the definition of old age is 65 years or older, the elderly population is extremely diverse in terms of health condition and prognosis. In addition, increased life expectancy may make this age cut-off too low. Elderly patients represent the majority of the population with HF and have worse prognosis compared with the younger HF cohort. Target treatment strategies have been insufficiently developed for elderly patients, and a multidisciplinary approach and further research on this population (especially individuals over 75 years of age) are necessary.

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