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EDITORIAL POINT OF VIEW

Chronic Heart Failure with Normal Contractility

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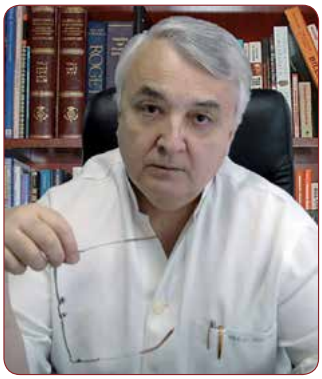

It is properly called Heart Failure with Preserved Ejection Fraction (HFpEF) (1).

Heart failure (HF) appears when the heart cannot supply the proper flow to the organs. This occurs under two conditions: when the myocardial contractility is not good and/or when the ventricles (especially the left one) do not fill adequately. The two conditions generally coexist. However, there are many situations in which only the heart does not fill properly due to myocardial reasons. Other non-myocardial conditions of improper filling, such as pericardial constriction, mitral stenosis or others, are not excluded from the guideline as causes of HF, but the real problem is when the bad filling is caused by a myocardial reason (1). Today it is believed that the isolated improper filling of the ventricles accounts for about half of the total number of heart failure cases, but this estimate is expected to be exceeded in the future.

The definition of chronic heart failure is based on symptoms, evaluation of heart performance (either systolic or diastolic) and biomarkers (1). A heart condition responsible for the condition (either etiologically related to it or as a comorbidity) should also be identified.

It is well known that the symptoms or signs of congestion are not specific for HF and they have to be evaluated with care by an experienced clinician. The echocardiographic evaluation of the heart performance is also a complicated approach, with many gaps in defining systolic performance, but even more for the diastolic function. Among biomarkers, BNP and/or NT-proBNP are the most frequently used today, but there are numerous conditions with demonstrated HF and normal BNP and NT-proBNP (1). In these conditions, the diagnosis of HFpEF may be difficult and many errors may occur at the first clinical evaluation.

To put a good diagnosis is important for both therapy and prognosis. A few years ago, the prognosis of HFpEF was considered to be as bad as that of HF with reduced contractility (HFrEF), which means a generally bad prognosis. The therapy of HFpEF is regarded as non-specific. Even if today the prognosis of HFpEF is deemed to be better than that of HFrEF (2) and some specific therapies are described, these therapies are more effective for special subgroups in clinical trials (3). Under these circumstances, the rapid, correct and detailed diagnosis of HFpEF is mandatory.

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In this respect, the ESC has very recently established a new algorithm for the detailed and secure diagnosis of HFpEF (4). Therefore, the significance of some biomarkers which are modified in this condition has to be analyzed (5).

The ESC's proposed algorithm consists in four steps, P, E, F1 and F2, and is therefore called PEFF (4). The first step, P, includes detailed clinical examination and search of comorbidities, ECG, detailed standard echocardiography, BNP and the six-minute walk test. The second step, E, progresses to a comprehensive echocardiographic examination and a detailed analysis of the natriuretic peptides. It is important to note the various conditions in which BNP or NT-proBNP become non-diagnostic for heart failure (5). The third step, F1, comes to a diastolic stress test and the beginning of invasive hemodynamic measurements. The fourth step is the most complicated one, including magnetic resonance imaging (MRI), genetic tests, different biopsies and other approaches.

From this perspective, HFpEF becomes one of the most difficult diagnoses in cardiology. And for what? For a prognosis which is better than that of HFrEF and the lack of a global specific therapy.

In my opinion, just to simplify the matter, some of the many existing biomarkers which are currently described as modified in HFpEF will become more useful. In the detailed paper of Carnes and Gordon (5), the presence and significance of various markers is discussed:

- troponins (linked to myocardial damage);
- soluble ST2 (sST2) and galectin-3 linked to fibrosis;
- pentraxin 3 and von Willebrand factor – some of the markers related to inflammation;
- GDF-15, which parallels the diastolic dysfunction.

The evaluation of such markers goes even more profoundly to the metabolomics range, and a review of this domain has been recently presented (6). The profile of the multiple analysed markers was different in HFpEF in comparison with HFrEF. Patients with new onset of HF had higher levels of cyclic GMP, cyclic AMP and serine, indicating more oxidative stress. Other markers which were shown to be increased in HFpEF revealed endothelial dysfunction, hypoxia and inflammation. All these suggest an important involvement of microvascular dysfunction in HFpEF as compared to HFrEF.

In this respect, the direction of cardiology towards the evaluation of heart failure goes into two directions. One is to complicate the diagnosis by pathophysiological markers to detail the particular mechanism which is more involved in the common clinical form of HFpEF. The other one promotes a more practical medical attitude which enables to sort patients with heart failure, from the beginning, into three categories: according to the mechanism, according to the activity of the pharmaceutical pathway and according to the signature of different subgroups (7).

In this way, even the general classification of heart failure could be modified and better linked to therapy. ❑

References

1. **Ponikowski P, Voors AA, Anker SD, et al.** 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *European Heart Journal* 2016;37:2129-2200 https://doi.org/10.1093/eurheartj/ehw128.
2. **Dunlay SM, Roger VL, Redfield MM.** Epidemiology of heart failure with preserved ejection fraction. *Nat Rev Cardiol* 2017;10:591-602. doi: 10.1038/nrcardio.2017.65.
3. **Solomon SD, McMurray JJV, Anand IS, et al for the PARAGON-HF.** Investigators and Committees. Angiotensin–Neprilysin Inhibition in Heart Failure with Preserved Ejection Fraction. *N Engl J Med* 2019 September 1. doi: 10.1056/NEJMoa1908655.
4. **Pieske B, Tschope C, deBoer RA, et al.** How to diagnose heart failure with preserved ejection fraction: the HFA-PEFF diagnostic algorithm: a consensus recommendation from the Heart Failure Association (HFA) of the European Society of Cardiology (ESC). *Eur Heart J* 2019 Aug 31. pii: ehz641. doi: 10.1093/eurheartj/ehz641.
5. **Carnes J, Gordon G.** Biomarkers in Heart Failure With Preserved Ejection Fraction: An Update on Progress and Future Challenges. *Heart, Lung and Circulation* 2019. https://doi.org/10.1016/j.hlc.2019.05.180
6. **Hage C, Lofgren L, Michopoulos F, et al.** Metabolomic profile of patients with new onset of heart failure – more microvascular dysfunction in patients with preserved ejection fraction compared to reduced ejection fraction – the PREFERS Study. *ESC Congress 2019 abstract and presentation* FP – 217.
7. **Triposkiadis F, Butler J, Abboud FM, et al.** The continuous heart failure spectrum: moving beyond an ejection fraction classification. *Eur Heart J* 2019;26:2155-2163. doi: 10.1093/eurheartj/ehz158.