

Heart Failure with Preserved Ejection Fraction and Pulmonary Hypertension a Common but Ugly Combination

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Abstract

This short review aims to provide some assistance in decision making for patient who present with reduced exercise tolerance mainly by breathlessness. In clinical praxis this would frequently meet patients with heart failure but preserved ejection fraction (HFpEF). At first glance the left heart contracts correct whereas the right ventricle may be enlarged. However, the underlying filling problem of the right ventricle because of disturbed relaxing and stiffness is not easy to detect. The recent development of a HFpEF score makes the diagnosis now easier and more accurate. Therefore, a strategical approach may help to promptly find the right diagnosis and could avoid overtreatment in patients who have a surprisingly bad prognosis.

Keywords: Heart Failure; Ejection Fraction; Pulmonary Hypertension

Introduction:

Heart failure with preserved ejection fraction (HFpEF) is at least as frequent as heart failure with reduced ejection fraction (HFrEF) [1]. Pulmonary hypertension (PH) is very common in HFpEF patients with a reported occurrence of 70 to 83% [2] unfavorably influencing prognosis in these patients [3]. Nowadays HFpEF seems to be the most common cause of PH in the elderly. However, a validated gold standard diagnosing HFpEF is still missing [4].

In contrast to patients with HFrEF there is a fundamental difference in clinical decision- making regarding patients with HFpEF. First, HFpEF is not easy to diagnose. Second, there is a high frequency of coincident pulmonary hypertension which may confuse the clinician as to be of precapillary origin since the left ventricle contracts normally [5]. Third, HFpEF seems to be a common end organ dysfunction of many syndromes like overweight - especially in the context of the metabolic syndrome, diabetes, renal diseases, hypertension, chronic obstructive lung disease [6,7] obstructive sleep disorders [8] and others more. And fourth, despite intensive research there is no proven effective medical therapy for patients with HFpEF. Up to now only exercise training seems to have a positive clinical effect on patients with HFpEF [9]. Unfortunately, the prognosis in patients with HFpEF is as bad as in HFrEF [10].

Irrespective of HFrEF or HFpEF signs and symptoms are commonly identical in heart failure patients. However, the leading symptom of HFpEF is exercise intolerance mostly through dyspnea [7]. So, when it comes to treat patients with exertional dyspnea clinician often stand before a dilemma not to know where exactly the dyspnea comes from: Is it pure exercise intolerance because of overweight and a sedentary life style or is it solely HFpEF or HFpEF with other comorbidities like COPD or DM for example? [11].

A strategical approach may help to find the right diagnosis and could avoid overtreatment.

Biomarkers

The most used and best validated biomarker in heart failure will be natriuretic peptides especially NTproBNP and BNP. Natriuretic peptides are very sensitive to cardiac dysfunction and the 2016 European society of cardiology (ESC) Heart failure guidelines set a cut off for NTproBNP of < 125 pg/ml or BNP < 35 pg/ml especially in the nonacute setting to exclude heart failure with high probability. Nevertheless, NTproBNP and BNP will be weight dependent and overweight do decrease these natriuretic peptides disproportionately [12]. Furthermore, the ECG in patients with HFpEF of disclose left ventricle hypertrophy, repolarization abnormalities and or atrial fibrillation. Especially in the absence of the with HFpEF aligned frequently co-morbidities a normal ECG and low natriuretic peptide levels, dyspnea is probably not related to heart failure.

Echocardiography

If the abovementioned approach does not rule out heart failure imaging will be the next step, whereas echocardiography is the most useful tool to do it. Right ventricle enlargement is very common in patients with heart failure and preserved ejection fraction. Therefore, a precise echocardiographic work up is necessary to correctly relate the diverse morphologic phenotypes in this setting.

There are some helpful clinical and morphologic combinations which almost certain give a direct answer that right ventricle enlargement or dysfunction will be related to HFpEF and the underlying cause is post capillary pulmonary hypertension. Several pathophysiologic mechanisms are involved in left ventricular hypertrophy. First female sex and aging and second features of the metabolic syndrome and renal dysfunction. In the case of this clinical presentations a concentric hypertrophic left ventricle with atrial enlargement needs no further functional measurements. HFpEF is almost always the correct diagnosis. These observations are now used in new H2FPEF score combining simple echocardiographic and clinical measures [13]. In this score (0-9) weight and atrial fibrillation scores most. (Hypertension, Heavy, Atrial Fibrillation, Signs of Pulmonary Hypertension, Elder, Filling pressure) (Figure 1). A score of 7 points gives a probability of about 95% to deal with HFpEF [14].

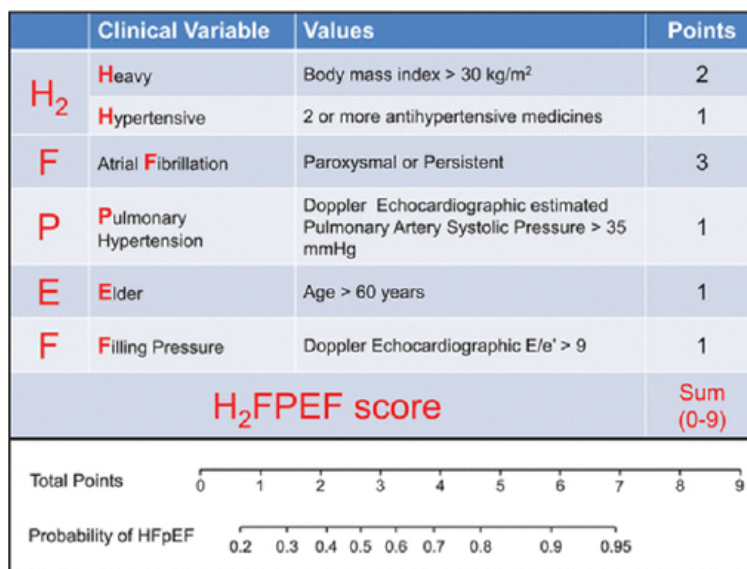


Figure 1: Published from Yogesh N.V. Reddy in Circulation Volume 138; Issue:9; 2018.

With respect pulmonary hypertension in HFpEF the right ventricle over a long period stays compensated by adapting through muscle contractility and wall thickness [15]. In this case there is full coupling of the right ventricle with the pulmonary artery system. Furthermore, the pulmonary artery pressure would be proportionally elevated in relation to the left ventricle end-diastolic pressure. A simple sign for this correlation will be found in the right shifted intra atrial septum, which denotes a higher pressure in the left atrium in comparison to the right atrium. This means the driving force for the pulmonary hypertension is the left ventricular filling pressure and the origin of the pulmonary hypertension therefore lies in the post capillary system. This is an immense important clinical observation, since invasive testing of the pulmonary pressure in these cases is not meaningful - it just would verify the post capillary origin of the right ventricle pressure increase. And as a matter of fact there will be no other treatment options as for left ventricle heart failure with preserved ejection fraction.

However, as soon as we find a flattened intraventricular septum or a D-shaping of the left ventricle we need to assume an out of proportion pulmonary hypertension or even an additional pathogenic process to the pulmonary vasculature irrespective of HFpEF.

There are several large studies which addressed pulmonary hypertension as a consequence of HFpEF and as generally with HFpEF there seems to be no treatment option neither with HFpEF alone nor with HFpEF and postcapillary pulmonary hypertension [16,17]. However, there are rare cases of patients which may have combined post and pre-capillary pulmonary hypertension. These patients have an even worse prognosis than patients with HFpEF and post-capillary hypertension but otherwise could have some benefit from pulmonary vasodilating medications like sildenafil [18]. That means, if echocardiography suggests out of proportion pulmonary hypertension either by high tricuspidal regurgitation velocity or by severe structural abnormalities of the right ventricle (enlargement and or D-shaping) invasive hemodynamic measurements by Swan Ganz catheterization should be performed. Only with invasive measurements an exact clarification and discrimination of post- and or pre-capillary pulmonary hypertension is possible. Whenever possible, treatment options for patients with HFpEF and pre-capillary pulmonary hypertension should be tested in randomized trials.

Conclusion

In summary, heart failure with preserved ejection fraction is very common and often combined with pulmonary hypertension. There is a direct association with worse prognosis as pressures are chronically and quantitatively increased - beginning in the left atrium (post-capillary with pulmonary venous congestion) and finally but rarely - independent from the left heart filling pressures - leading to an out of proportion pre-capillary pulmonary artery hypertension. In most cases echocardiography is sufficient to discriminate pulmonary hypertension as post-capillary origin because of elevated left ventricle filling pressure. For these patients there are no specific treatment options and no further hemodynamic measurement of the pulmonary circulation need to be done.

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