Proceedings of Anticancer Research, 2021, Volume 5, Issue 5
http://ojs.bbwpublisher.com/index.php/PAR
ISSN Online: 2208-3553
ISSN Print: 2208-3545

Progress in the Pathogenesis and Treatment of Heart Failure with Preserved Ejection Fraction

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Abstract: Heart failure with preserved ejection fraction (HFpEF) is a special and common clinical heart failure with left ventricular diastolic dysfunction. It has attracted much attention at home and abroad in recent years because of its high heterogeneity and complex pathogenesis. Compared with heart failure with reduced ejection fraction (HFrEF), HFpEF has complex clinical manifestations, many complications, limited clinical treatment, and poor prognosis. In recent years, the research on the pathogenesis and treatment of HFpEF has made certain progress, but there are no specific guidelines for clinical practice. By combing the latest research at home and abroad, the pathogenesis and treatment of HFpEF are systematically reviewed in order to provide a relevant basis for reference its clinical treatment.

Keywords: Heart failure with preserved ejection fraction; Pathogenesis; Treatment progress

Publication date: September 2021; ***Online publication:*** September 30, 2021

1. Introduction

Heart failure (HF) is a series of clinical manifestations of multiple factors, such as ventricular ejection and/or filling damage, lack of cardiac output, circulatory congestion, and insufficient blood perfusion, manifested as dyspnea, physical activity limitations, fluid retention, and so on [1]. Heart failure with preserved ejection fraction (HFpEF), as a special type of heart failure, is defined as heart failure with left ventricular ejection fraction (LVEF) ≥ 50% [2]. The pathophysiology of heart failure with preserved ejection fraction is complex and its pathogenesis has not been fully clarified. In addition, its signs and symptoms are nonspecific, and its treatment is passive without any recognized treatment plan that can change the clinical course of HFpEF at present. Therefore, this article reviews the pathogenesis and treatment progress of heart failure with preserved ejection fraction.

2. Pathogenesis of HFpEF

Borlaug Ba and another researcher [3] believe that HFpEF involves entricular diastolic delay, elevated end diastolic pressure, abnormal filling, and ventricular dysfunction. Studies have shown that the compliance of HFpEF patients' arteries and ventricles at the end of systole is significantly reduced, resulting in high ventricular ejection resistance and myocardial oxygen consumption. This in turn leads to poor contraction and myocardial hypertrophy [4]. It has been mentioned in a literature that left ventricular concentric hypertrophy and subsequent diastolic dysfunction have been considered as an important pathogenesis of HFpEF for a long time [5]. The prevalence of non-cardiac complications in HFpEF patients is high. Research have found that obesity and metabolic abnormalities are closely related to the pathogenesis of HFpEF and abnormal cardiac metabolism is a characteristic change of HFpEF [6,7]. Among the patients, 52% are

associated with diabetes, 62% with hyperlipidemia, and 70% with obesity. Upadhya B believes that HFpEF is a systemic syndrome involving multiple organ systems caused by inflammation, which is closely related to aging, lifestyle, genetic susceptibility, and other factors [8].

3. Treatment of HFpEF

3.1. Diuretics

Borlaug BA believes that diuretics have the capacity of playing a key role in reducing central congestion in HFpEF patients [9]. In this way, fluid retention and edema in HFpEF patients can be ameliorated by the use of diuretics along with alleviating pulmonary congestion and improving cardiac function [10]. Therefore, for all patients with HFpEF, low sodium diet and diuretic treatment are recommended.

3.2. Angiotensin-converting enzyme inhibitor (ACEI) and angiotensin receptor blocker (ARB)

Research has found that because the pathogenesis of HFpEF involves multiple systems, the treatment depends on the potential complication [11]. Since complexity is considered to be the cause of inflammation and multiple organ dysfunction, it is very important to correctly manage those diseases that are known to cause HFpEF [9]. In regard to that, ACEIs and ARBs play an important role in the treatment of HFpEF complicated with hypertension, coronary heart disease, diabetes, and chronic respiratory diseases [12]. It has been suggested that ARBs or ACEIs should be considered to reduce the rate of hospitalization of HFpEF patients.

3.3. *β*-blocker

Current studies have not fully demonstrated the mechanism of *β*-blockers in HFpEF, and it is not recommended to treat HFpEF based on current evidence [13,14]. However, *β*-blockers can improve the symptoms of heart failure, which may have a positive effect on the prognosis of patients with atrial fibrillation combined with HFpEF. The large-scale research results by Pauluswj and another researcher [15] showed that *β*-blockers, renin-angiotensin-aldosterone system inhibitors, and other treatment strategies are proven to have little or no effect on the prognosis of HFpEF. In addition, drugs with definite clinical benefits to HFrEF have not been proven to reduce the hospitalization rate, mortality, or exercise tolerance of patients with HFpEF, and have not achieved satisfactory results in improving their prognosis.

3.4. New drugs

As a new hypoglycemic drug, sodium-glucose cotransporter 2 inhibitor (SGLT2i) has good efficacy in the treatment of heart failure. The ongoing EMPEROR-Preserved trial would reveal its efficacy in the treatment of HFpEF in the future [16]. Sacubitril-valsartan is a new drug for the treatment of heart failure, where both European experts and Chinese experts have agreed that the drug plays an excellent role in improving the pathophysiological process of HFpEF and it can be recommended. Studies have shown that dose-dependent sacubitril-valsartan can reduce hospitalization and death rates from heart failure [17]. In addition, the hypothesis of its treatment in HFpEF has been proposed. However, due to its high cost and clinical limitations, it is expected to be confirmed by further research in the future.

4. Conclusion and prospect

As a complex clinical syndrome, HFpEF has gained much attention due to its high prevalence and rehospitalization rate, poor prognosis, and limited treatment. The reason for this is because the pathogenesis and pathology are complex. At present, the understanding of the pathogenesis and treatment of HFpEF is

still improving.

Disclosure statement

The authors declare that there is no conflict of interest.

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