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Predictive Role of Diastolic Echocardiographic Findings in the Outcome of Heart Failure with Preserved Ejection Fraction

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ABSTRACT

The main predictors of Heart Failure with preserved Ejection Fraction (HFpEF) are increased systolic blood pressure, atrial fibrillation, and female gender. Heart Failure (HF) with reduced Ejection Fraction (EF) is associated with prior myocardial infarction and left bundle-branch block QRS morphology. This study aimed to evaluate the effect of diastolic echocardiographic findings on the outcome of patients with HFpEF.

This systematic review was conducted via searching in databases such as Cochrane Library and MEDLINE until September 2015, and articles with available abstracts published in English were included in the study. Manual search was performed within the reference lists of the articles. Moreover, two reviewers independently assessed the inclusion criteria, quality and extracted data of the selected articles.

In total, four articles were evaluated in this systematic review, with the earliest study published in 2007 and the most recent article published in 2015. According to the results of this review, Doppler echocardiography plays a pivotal role in the assessment of diastolic left ventricular filling dynamics. However, this technique is restricted by the confounding effects of the changes in the heart rate and loading conditions.

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Introduction

This systematic review was conducted in order to evaluate the effect of diastolic echocardiographic findings on the outcome of patients with Heart Failure with preserved Ejection Fraction (HFpEF). Comparison of the differences in the risk factors and underlying diseases between HFpEF patients and those with Heart Failure (HF) and reduced Hjection Fraction (EF) has been a major concern among medical researchers (1-4).

In one study, Framingham examined the clinical characteristics and risk factors of HF patients at the onset of the disease. Moreover, long-term survival rate of the patients was evaluated based on the preserved or reduced EF. According to the findings, the main predictors for HFpEF were increased systolic blood pressure, atrial fibrillation, and female sex, whereas HF with reduced EF was associated with prior myocardial infarction and left bundle-branch block QRS morphology (5).

In the community-based population of the study by Framingham, long-term prognosis was equally poor in both types of HF, as well as both genders, with a median survival of 2.1 years. Therefore, it was concluded that although these syndromes have some common risk factors, there are significant differences in the prediction of these factors, which is indicative of the need for distinct preventive strategies. Controversy continues regarding the prevalence of the exact abnormities associated with myocardial diastolic function in patients with HFpEF syndrome (6-8).

In comprehensive invasive and non-invasive monitoring of patients with hemodynamically confirmed HFpEF, Prasad reported that unlike age-matched control referents, increased static ventricular stiffness was not a universal finding in patients with HFpEF. On the other hand, assessment of the Left Ventricular (LV) relaxation by tissue Doppler was consistently abnormal (9).

Special attention has been given to the role of cardiac interstitium in the pathophysiology of HFpEF. In this regard, previous research has indicated that patients with HFpEF have similar LV masses and left atrial volumes compared to patients with LV hypertrophy without HF symptoms. Despite the fact that one measure of the left atrial strain reduced, the left atrial

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stiffness was used to discriminate patients with HFpEF from those with LV hypertrophy without HF symptoms.

HFpEF is associated with diastolic LV dysfunction, which leads to reduced LV relaxation and increased LV stiffness with a relatively normal EF of 50% or more (10).

A consistent and unexplained finding in population-based studies in this regard is that HFpEF syndrome is more prevalent among women compared to men, with an impressive ratio of 2:1. It is noteworthy that natriuretic peptide levels may be normal in HFpEF patients, especially during the early phases of the disease, when the patient has not exercised for the past few days, and in the absence of the signs of water and salt retention (11).

In the open population aged 65 years and older, the overall prevalence of HFpEF has been estimated at 3-5%, accounting for 4-6% of male and 8-10% of female patients aged 80 years and above (12). In the elderly female population, HFpEF is a growing epidemic with limited treatment options, which could lead to disabling HFpEF in these individuals.

This systematic review aimed to evaluate the effect of diastolic echocardiographic findings on the outcome of patients with HFpEF syndrome.

Materials and Methods

Literature search strategy

This systematic review was conducted via searching in databases such as Cochrane Library and MEDLINE until September 2015. Related articles were found using key words in medical subject headings (MESH) with broad terms, such as “diastolic echocardiographic findings”, “outcome” and “heart failure with preserved ejection fraction". Moreover, reference lists of the retrieved articles were assessed to identify additional related studies. Full-text articles with available abstracts published in English were included in this study, and manual search was also performed within the reference lists of the selected articles.

Critical appraisal

Initially, abstracts of the selected articles were reviewed by two researchers independently, and 40 abstracts were screened twice for relevancy. Following that, 12 articles were excluded from the review due to the lack of relevancy. The remaining 28 abstracts were fully assessed by two reviewers. With respect to the type of articles, disqualified studies included one review and 22 irrelevant full-text articles.

In this review, we used the Consolidated Standards of Reporting Trials (CONSORT) quality appraisal to evaluate the quality of the selected studies. Two reviewers independently scored the quality criteria of each study, and another reviewer resolved the discrepancies. In addition, a structural data extraction tool was used for this purpose. However, no meta-analysis was performed due to the heterogeneity of the main outcome measures.

Results

The flow diagram of the literature review is presented in Figure 1.

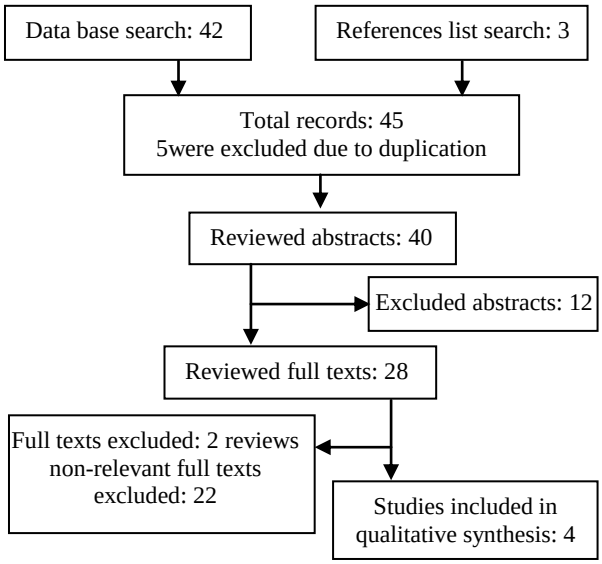

Figure1: The flow diagram of literature search.

According to our search results, the earliest article in the literature was published in 2007, and the most recent paper was published in 2015. All the selected studies were conducted on patients with HF. General characteristics of the selected studies are shown in Table 1.

Table1: Summary of Reviewed Studies

Reference Number	Target Population	Sample Size	Final Results
12	Decompensated Heart Failure	95	E/DT* produced independent and incremental prognostic data in patients with heart failure.
13	HFpEF**	935	Structural heart disease, including left ventricular hypertrophy and left atrial enlargement, in addition to pulmonary hypertension, were associated with adverse outcomes in HFpEF.
1	HFpEF	402	Eccentric hypertrophy was associated with reduced left ventricular contractility compared to CH (lower LVEF*** and ratio of systolic blood pressure to end-systolic volume)
15	HFpEF	312	Moderate and severe diastolic dysfunction were significant predictors for adverse patient outcomes.

*HFpEF: Heart failure with preserved ejection fraction; **E/DT: Velocity/deceleration time; ***LVEF: Left ventricular ejection fraction

Discussion and Conclusion

According to the results of this review, approximately half of the patients with clinical HF had Preserved LV Systolic Function (HF-PSF), which indicates that Diastolic Dysfunction (DD) may be responsible for the clinical manifestations in these patients (8). In this regard, recent studies have suggested that patients with HF and EF of >40% have relatively higher mortality and hospitalization rates. Therefore, Doppler echocardiography is considered as the method of choice in the routine clinical evaluation of DD. However, Doppler assessment of DD is a complex process requiring expert clinical interpretation (4). Furthermore, loading conditions have been shown to affect mitral inflow pulsed-wave Doppler parameters, making the differentiation between normal and pseudo-normal diastolic function particularly difficult. Therefore, in addition to mitral inflow parameters, pulmonary venous flow by Doppler echocardiography and changes in mitral inflow parameters during Valsalva maneuver are commonly used to distinguish between pseudo-normal and normal diastolic function (6). Our findings regarding a favorable intermediate-term prognosis in patients with mild DD might seem inconsistent with previous studies. This discrepancy could be due to the longer duration of follow-up in population-based studies.

Findings of the current review confirmed an insignificant link between echocardiographically determined relaxation abnormality and HF; however, this does not undermine the role of this parameter as a predictor for long-term mortality (3). According to the other results of the present review, moderate and severe DD were the most significant predictors for adverse outcomes in patients with HFpEF, which has been confirmed in population-based studies suggesting a graded relationship between the severity of DD and clinical outcomes, especially in HF patients.

Our definition of diastolic function is more reflective of diastolic filling rather than intrinsic parameters of diastolic function (15). Although Doppler echocardiography plays a pivotal role in the assessment of diastolic filling dynamics of LV, this technique is restricted by the confounding influences of changes in the heart rate and loading conditions.

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