Original Article

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Echocardiographic Evaluation of Diastolic Dysfunction among Menopausal Women: A Cross-sectional Study

Others Section

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ABSTRACT

Introduction: Heart Failure with Normal Ejection Fraction (HFNEF), also known as Diastolic Heart Failure (DHF), has been well-studied since the past two decades. The signs of HFNEF are signs of heart failure and abnormal ventricular filling pressure with normal systolic function. A Metabolic Syndrome (MS) is a clustering of metabolic risk factors. Cardiovascular disease caused by metabolic syndrome includes vascular and myocardial abnormalities such as diastolic dysfunction and relaxation abnormalities.

Aim: To study the assosciation between the timing of menopause and Left Ventricular Diastolic Dysfunction (LVDD) in those with and without MS.

Materials And Methods: This cross-sectional study was conducted in the period between December 2021 to June 2022 at the Department of Cardiology in A.C.S Medical College and Hospital, Chennai, Tamil Nadu, India. All female patients that underwent a medical examination were selected for the study. Postmenopausal women without overt heart diseases (such as a history of heart valve disease or myocardial infarction, or a prior LV ejection fraction > 50%) were included. This study included 80 patients grouped into two: those with and without MS. The MS group included 30 subjects divided into two subgroups: those who experienced menopause at or before 50 years of age (early menopause group) and those who experienced menopause at or after 50 years of age (late menopause group). Out of 80, 50 participants were divided into early menopause and late menopause groups among women without MS. This study analyse the evolution of left ventricular diastolic dysfunction (LVDD), assessed by transthoracic echocardiography (TTE), in 80 postmenopausal women with and without MS. Independent t-tests was applied to assess the association between the timing of menopause and LVDD.

Results: The mean age was 60±7.3 years in women with MS and 62±8.8 years in women without MS. There were no significant differences in the duration since menopause between the postmenopausal women with and without MS. No significant difference was found between the two groups (early vs. late menopause group) with respect to any diastolic parameter, including Early (E) and Late (A), E/A ratio, and E/e in women with MS. In postmenopausal women without MS, there was a significant difference in diastolic parameters including the A, early diastolic annular velocity (e'), ratio of early diastolic transmitral flow velocity to annular flow velocity was calculated (E/e') between the two groups (early vs. late menopause group). In comparison to patients with MS, patients without the condition had significantly lower early peak mitral inflow velocity (E, p-value=0.019), early diastolic mitral annulus motion velocity (e'-septal, p-value=0.05), late peak mitral inflow velocity ratio (E/A, p-value=0.07), and LV filling pressure values (E/e, p-value=0.02).

Conclusion: Early menopause impacts diastolic function in postmenopausal women and LVDD progression in women without MS. LVDD progression in women with MS was unaffected by early menopause.

Keywords: Diastolic heart failure, Early menopause, Late menopause, Metabolic syndrome, Postmenopausal women

INTRODUCTION

Due to the stiffening of cardiac muscles, Diastolic Heart Failure (DHF) is characterised by a reduction in the volume of the ventricles and an inability to relax them. Age, gender, hypertension, diabetes mellitus, and cardiomyopathy contribute to a greater prevalence of Heart Failure with Preserved Ejection Fraction (HFpEF). The risk of cardiovascular disease associated with hypertension rises sharply with age. Clinically, the diastolic function of the LV may be defined as its capacity to receive LV filling volume with sufficient stroke volume. Heart failure with normal ejection fraction (HFNEF), also called DHF, has become increasingly well-known over the last two decades. The clinical features of HFNEF include symptoms of heart failure and signs of elevated ventricular filling pressure and impaired relaxation in spite of normal systolic function [1]. The Helsinki ageing study showed that DHF is common in older adults. DHF was present in 50% of patients with clinical heart failure aged 75-86 years. However, a definitive diagnosis is still elusive [2]. The risk of DHF is higher in women than in men, particularly in postmenopausal women [3]. The diastolic function of the LV was found to be significantly reduced in women after 50-60 years of age compared to men, suggesting that menopause leads to the condition [4]. The mechanisms of estrogen's cardioprotective effects have been extensively studied. Through the renin-angiotensin system, estrogen regulates gene expression, sympathetic tone, and heart function [5,6]. The natural cessation of menstruation that occurs during menopause is accompanied by a sharp drop in ovarian hormone production, particularly estrogen. Estrogen has a cardioprotective effect. The loss of estrogen's cardioprotective function after menopause may be a major factor in the progression of LVDD in elderly women. [7]. LVDD and age at menopause (early or late) have been studied in healthy postmenopausal women [8]. Menopausal age (early or late) may influence the development of LVDD in postmenopausal women [9]. The present study was undertaken to assess the association between the timing of menopause and LVDD in those with and without MS, with the hypothesis that women who experienced early menopause may have more advanced LVDD due to the loss of estrogen's cardioprotective effect.

MATERIALS AND METHODS

The cross-sectional study was conducted in the Department of Cardiology at ACS Medical College and Hospital, Chennai, Tamil Nadu, India, from December 2021 to June 2022. Written informed consent was obtained from each participant before the commencement of the study. The study was approved by the Institutional Ethical Committee (No.474/2022/IEC/ACSMCH).

Inclusion criteria: Postmenopausal women without overt heart diseases (such as a history of heart valve disease or myocardial infarction, or a prior LV ejection fraction >50%) were included in the study.

Exclusion criteria: Patients with an LV ejection fraction of less than 50%, atrial fibrillation, and poor echocardiography were excluded from the study.

Sample size calculation: The sample size was calculated based on the following formula [10]

$$n = \frac{2\,(Z_{1-\alpha/2} + Z_{1-\beta})^2\,\alpha^2}{d^2}$$

$Z_{1-\alpha/2}$ = 2.24 (5% Level of significance after Bone ferroni correction for 4 comparsions)

$z_{1-\beta}$ = 0.84 (for 80% power valve), α=2.5(SD)

d= 2 (expected clinically significant difference between any two comparison)

$$n = \frac{2\,(2.24 + 0.84)^2\,(2.5)^2}{2^2} = 30\ (\text{Pregroup}) = 60\ (\text{Total})$$

The final sample size calculated was 60.

Procedure

This study included 80 patients grouped into two: those with and without MS. The MS group included 30 subjects divided into two subgroups: those who experienced menopause at or before 50 years of age (early menopause group) and those who experienced menopause at or after 50 years of age (late menopause group). Out of total, 50 participants were divided into early menopause and late menopause groups among women without MS.

A complete clinical assessment was conducted, including height, weight, diastolic and systolic blood pressure measurements, heart rate, and Basal Metabolic Index (BMI). Furthermore, the subjects were asked when they experienced menopause as the natural cessation of bleeding, as well as the duration after menopause. Additionally, a questionnaire was used to obtain information concerning the subjects' pregnancy status, delivery history, treatment of hypertension, diabetes, dyslipidemia, and smoking status.

An echocardiographic examination was conducted using commercially available equipment (E95, Phillips) and included both two-dimensional and Doppler imaging. Two-dimensional echocardiography was performed to quantify the left atrial and left ventricular chambers following the guidelines of the American Society of Echocardiography (ASE). The Teichholz formula was used to calculate the LV ejection fraction. The mitral annular motion at the septum was measured using tissue Doppler imaging. An apical 4 four-chamber view of pulsed wave Doppler imaging measured the peak velocity of Early (E) and Late (A) diastolic flow and the deceleration time of early diastolic flow. Using tissue Doppler imaging, early diastolic annular velocity (e') was measured at the septum in an apical four-chamber view. The ratio of early diastolic transmitral flow velocity to annular flow velocity was calculated (E/e'). The diastolic function of all subjects was also classified into 1 of 4 categories (normal, grade I, grade II, or grade III) [11].

STATISTICAL ANALYSIS

Statistical Package for the Social Science (SPSS) software was used for the statistical analysis. The descriptive variables are presented as means and standard deviations. Independent t-tests were performed to compare echocardiographic parameters (peak E, peak A, E/A, e', E/e', and DCT) between the two groups. A p-value of less than 0.05 was considered significant.

RESULTS

In this study, 80 patients were enrolled into two categories: postmenopausal women with and without MS. The mean age was 60±7.3 years in women with MS and 62±8.8 years in women without MS. There were no significant differences in the duration since menopause, between the postmenopausal women with and without MS [Table/Fig-1].

Variables	Postmenopausal women with MS	Postmenopausal women without MS	p-value
Mean age (years)	60±7.3	62±8.8	0.31
Duration since menopause (years)	Late-59.9±6.4 Early-41.4±2.7	Late-54.4±3.9 Early-46.8±1.2	0.66
Overall duration (years)	50.6±10.6	51.3±4.8	

[Table/Fig-1]: Comparison of basic characteristics between postmenopausal women with and without MS.

In postmenopausal women without MS, there was a significant difference in diastolic parameters including the A, e', E/e' between the two groups (early vs. late menopause group) [Table/Fig-2].

ECHO parameters	Postmenopausal women without MS (n=50)		
	Early menopause (n=20)	Late menopause (n=30)	p-value
E	0.58±0.13	0.64±0.20	0.26
A	0.70±0.08	0.81±0.17	0.01
E/A	0.84±0.20	0.78±0.17	0.27
e'	0.12±0.21	0.10±0.01	0.02
E/e'	5.02±1.33	6.32±2.91	0.05
DT	210.0±88.0	201.7±70.3	0.71

[Table/Fig-2]: Comparison of echocardiographic parameters in two groups of postmenopausal women without MS (early vs. late).
p-value of less than 0.05 was considered significant

The echocardiographic parameters of the two groups (early vs late) were compared in the MS group, as shown in [Table/Fig-3]. No significant difference was found between any diastolic parameter. Despite a large difference in e' between the two groups (p-value=0.04), e' was higher in the late menopause group than in the early menopause group.

ECHO parameters	Postmenopausal women with MS (N=30)		
	Early menopause (n=15)	Late menopause (n=15)	p-value
E	0.67±0.15	0.66±0.14	0.83
A	0.80±0.26	0.77±0.16	0.69
E/A	0.91±0.26	0.88±0.28	0.78
e'	0.09±0.31	0.11±0.02	0.04
E/e'	8.79±5.66	6.30±1.20	0.10
DT	226.6±75.6	188.7±42.3	0.10

[Table/Fig-3]: Comparison of echocardiographic parameters in two groups of postmenopausal women with MS (early vs. late).
p-value of less than 0.05 was considered significant

The echocardiographic parameters of the two groups (women with and without MS) are compared in [Table/Fig-4]. In

ECHO Parameters	Postmenopausal women without MS (N=50)	Postmenopausal women with MS (N=30)	p-value
E	0.62±0.18	0.67±0.14	0.19
A	0.76±0.15	0.79±0.21	0.58
E/A	0.80±0.18	0.89±0.26	0.07
e'	0.10±0.19	0.11±0.02	0.05
E/e'	5.80±2.47	7.55 ±4.22	0.02
DT	205.0±77.1	207.7±63.2	0.87

[Table/Fig-4]: Echocardiographic parameter comparison between postmenopausal women with and without MS.
p-value of less than 0.05 was considered significant

comparison to patients with MS, patients without the condition had significantly lower early peak mitral inflow velocity (E, p-value=0.019), early diastolic mitral annulus motion velocity (e'-septal, p-value=0.05), late peak mitral inflow velocity ratio (E/A, p-value= 0.07), and LV filling pressure values (E/e, p-value=0.02).

DISCUSSION

In postmenopausal women, estrogen secretion decreases as a result of metabolic changes and the accumulation of abdominal fat. It is important to lower postmenopausal women's risk of cardiovascular disease. It implies that among postmenopausal women, monitoring blood sugar, blood pressure, and lipid profiles as well as altering their lifestyle can result in weight loss by diet [12]. The progression of LVDD has been demonstrated to expose patients to a high risk of developing future DHF, which is associated with ageing even in a healthy population [13]. Even though there is a strong association between a high prevalence of DHF and an increased progression of LVDD in older women, the underlying pathogenesis is unclear. Literature has examined the mechanism underlying the cardioprotective effects of estrogen [14,15]. Through the renin-angiotensin system, estrogen regulates gene expression, sympathetic tone, and heart function [5,6].

According to a recent study by Rahman I et al. [16], the age of natural menopause and the risk of HF are significantly related. However, the study did not evaluate LV diastolic function. The mean age or early menopause cutoff of the current study was similar to that in the Hirokawa M et al. study of 115 elderly women patients and found that LVDD progression was not influenced by early menopause in healthy postmenopausal women [8]. According to the present study hypothesis, early menopausal women would incur an advanced LVDD. This study provides evidence that early menopause impacts postmenopausal women's LV diastolic function and LVDD progression in patients without metabolic syndrome.

Chung JW et al. studied 190 women and found that the MS group had a significantly lower mean E, E', and E/A ratios than the normal group [17]. This study provides evidence that the women without metabolic syndrome had a significantly lower early peak mitral inflow velocity (E, p-value=0.019), early diastolic mitral annulus motion velocity (e'-septal, p-value=0.05), late peak mitral inflow velocity ratio (E/A, p-value=0.07), and LV filling pressure values (E/e, p-value=0.02) than those with metabolic syndrome.

The pathophysiological mechanism underlying the rapid progression of LVDD in older women is likely multifactorial and not mainly influenced by the loss of estrogen's cardioprotective effects [18]. Increased LV afterload produced by higher blood pressure and vascular tone is linked to the occurrence of LVDD [20]. LVDD is exacerbated by an increase in body weight and alterations to the body's fat distribution [20]. Further study is necessary to overcome these challenges.

Limitation(s)

The study was conducted in a single centre. Diabetes and hypertension are risk factors for DHF, and may have an effect on LV diastolic function, which could influence study findings further.

CONCLUSION(S)

According to the results of the present study, menopause, particularly early menopause, impacts diastolic function and LVDD progression in women without metabolic syndrome. On the other hand, this study shows that early menopause had no impact on the progression of LVDD in women with metabolic syndrome. Consequently, women with MS experiences diastolic dysfunction more than women without it.

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