# The relation between hormonal changes and myocardial deformation parameters as determined by speckle-tracking echocardiography in women with preserved ejection fraction

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## Abstract

In the era of technological modernization, new preventive and therapeutic strategies have been developed for cardiovascular diseases. Speckle tracking studies are no exception.

**Study objective.** To evaluate the values of speckle tracking echocardiography parameters in the diagnosis of left ventricular myocardial dysfunction in perimenopausal women.

**Materials and methods.** This study had a prospective design with a one-year follow-up period. The study included 150 female patients, aged 47 to 53 years, with known hormonal levels, corresponding to the perimenopausal period. The study was conducted at the Clinical Medical Center of the Presidential Administration of the Republic of Kazakhstan, Department of Functional Diagnostics. All tests were performed using IBM SPSS Statistics 20 (IBM, USA) with a 95% confidence level.

**Study results.** All 150 subjects underwent routine echocardiography, after which they were divided into two main groups: 90 women (60%) constituted the cohort of individuals with existing LV diastolic dysfunction, while the remaining 60 women, or 40%, were individuals without existing LV diastolic dysfunction. Speckle-tracking echocardiography was performed.

In the study, of the 90 patients with LV diastolic dysfunction based on routine echocardiography, 85 had basal segment systolic dysfunction. This constituted 94.5% of patients. In the remaining 5 patients (5.5%), no regressive changes in systole were detected. In the second cohort of sixty women with no LV diastolic dysfunction on routine cardiac ultrasound, only 50 (83.4%) had normal systolic function on the basal plane. The remaining 16.6% (10 patients) with normal diastolic function on routine echocardiography showed abnormal systole and pre-diastolic pathology on speckle-tracking echocardiography.

**Conclusions.** Routine echocardiography in our study demonstrated that it can often serve as a prognostic tool for the development of systolic myocardial dysfunction in individuals with existing left ventricular diastolic dysfunction. A direct correlation was found between the presence of decreased basal plane indices on speckle-tracking echocardiography. This means it is mandatory and recommended to implement speckle tracking in routine echocardiography as an informative predictor of future adverse cardiovascular events.

## 1. Introduction

Speckle tracking, a current echocardiographic study, is a popular and promising technique for assessing myocardial structural and functional changes. Its estimated global longitudinal myocardial strain is more sensitive to early changes in left ventricular contractility than ejection fraction and other parameters.

Attention is paid in detail to diastolic dysfunction, which has become increasingly important for assessing pathological conditions characterized by elevated left ventricular filling pressure without overt left ventricular (LV) dysfunction. In fact, assessment of diastolic function is recommended for every echocardiographic examination. Therefore, new indices have been investigated for sensitive and reliable quantitative assessment of diastolic dysfunction, particularly for the early diagnosis of cardiovascular events. Assessment of global left ventricular strain has demonstrated its role in the diagnostic and prognostic evaluation of cardiac pathologies [1]. The diagnostic capabilities of speckle-tracking echocardiography are reflected in the clinical guidelines of the European Society of Cardiology (2016–2018), the European Association of Cardiovascular Imaging (EACVI), and the American Society of Echocardiography (2016–2018). Currently, considerable attention is being paid to the use of speckle-tracking echocardiography in various cardiac pathologies, oncologic pathologies, and hormonal and metabolic disorders [2]. Importantly, speckle-tracking echocardiography can be used not only for diagnosis but also for assessing the prognosis of cardiovascular events [3].

According to the WHO, cardiac pathology is one of the most common non-specific diseases, accounting for 30% of all deaths.

Gender differences in cardiovascular diseases, particularly heart failure (HF), have been noted in several recent publications. Although sex differences in age-related cardiovascular changes are well described, little is known about how female menopause and sex hormones relate to myocardial mechanics and function [4].

Women's cardiovascular disease risk increases later in life, often coinciding with their menopausal transition. Previous studies have identified key changes associated with menopause, including changes in endogenous sex hormone levels, body fat distribution, and cardiometabolic health. Although the menopause transition is not formally recognized as a cardiovascular risk factor in guidelines, there are compelling adverse cardiometabolic changes that accompany midlife and menopause [5].

Taken together, these maladaptive changes at menopause are potentially associated with worsening myocardial function, i.e., greater left ventricular diastolic dysfunction [7,9], increased LV concentric remodeling [6,12], and altered cardiac strain indices [8,13], potentially making postmenopausal women susceptible to heart failure with preserved ejection fraction [14,18]. However, to date, no study has comprehensively examined the relationship between menopause, circulating estradiol levels, and left ventricular and left atrial myocardial strain indices. Previous studies have been relatively small and have not included comparisons between hormonal status and advanced echocardiographic techniques [9,10,14,18]. Therefore, we used a chamber-specific speckle tracking method to examine the relationship between menopause stages and cardiac geometry and mechanics (left atrium and left ventricle) in an asymptomatic population.

## 2. Methods

This study had a prospective design with a 12-month follow-up period. The study included 150 female patients, aged 47 to 53 years, with known hormonal levels, consistent with their perimenopausal stage. The study was conducted at the Functional Diagnostics Department of the Clinical Medical Center of the Presidential Administration of the Republic of Kazakhstan.

According to electrocardiography results, all study participants had sinus rhythm, with a heart rate of 60-90 bpm.

Exclusion criteria included congenital and acquired heart defects, coronary artery disease, atrial fibrillation, heart failure with an ejection fraction of less than 50%, chronic kidney disease, and liver and thyroid dysfunction.

Upon recruitment, all participants underwent a thorough medical history, laboratory data, electrocardiography, echocardiography with tissue Doppler, and speckle - tracking echocardiography. Hormonal status was determined by estradiol and follicle - stimulating hormone (FSH) levels, and obstetric gynecological examination was performed.

Left ventricular longitudinal strain was measured globally and regionally (basal, mid, and apical) in all patients using speckle-tracking echocardiography. Left atrial longitudinal strain was also assessed in all patients. Normal left ventricular speckle - tracking echocardiography was defined as ≤ - 18%, and for the left atrium, - 35%.

The study protocol was approved by the LEC of the NAO MUA in 2022, Protocol N 1. All subjects signed informed consent before inclusion in the study.

**Echocardiographic examination**

Full two-dimensional and Doppler echocardiography was performed by two experienced physicians at rest (GE Vivid E9 with a 1–5 MHz transducer) in accordance with the ASE guidelines. Left ventricular end-diastolic volume, left ventricular end-systolic volume, and ejection fraction were calculated from apical two- and four-chamber views using a modified Simpson method. Diastolic parameters, including mitral inflow velocity (E and A waves), mitral annular Doppler velocity (septal and lateral e'), left atrial volume index (LAVI), and peak tricuspid regurgitation velocity, were measured by averaging over three

consecutive cardiac cycles to assess diastolic function. Isovolumic relaxation time (IVRT) and myocardial performance index (MPI) were also measured using tissue Doppler. All patients then underwent echocardiography to assess longitudinal myocardial strain in 16 segments and determine the circulation type. Speckle-tracking echocardiography of the left atrium with determination of reservoir, conduit, and pump functions [7,9].

### Statistical analysis

Results for quantitative variables with a normal distribution were expressed as mean ± standard deviation, while numerical variables with a non-normal distribution were expressed as median with interquartile range. Qualitative variables were presented as number and percentage. The Student's t-test and Mann-Whitney U-test were used to compare numerical variables with and without a normal distribution, respectively. In addition, the chi-square test was used to compare nominal variables. All tests were performed using IBM SPSS Statistics 20 (IBM, USA) with a 95% confidence level.

**Diagram 1**
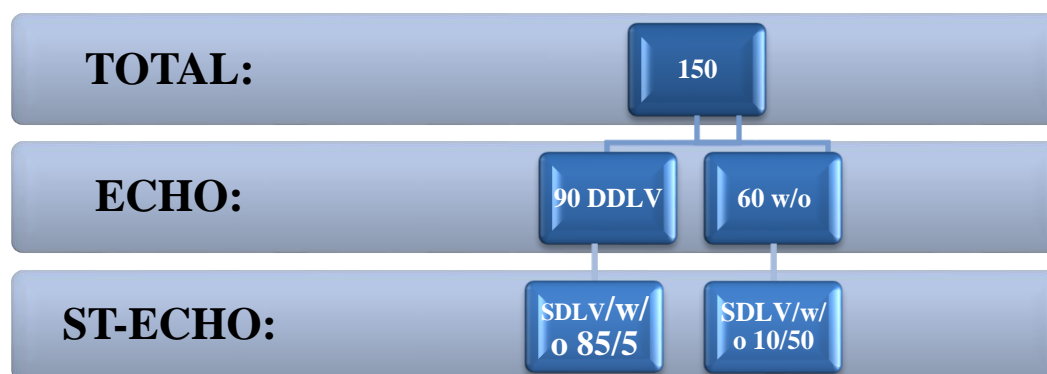


## 3. Results

All 150 subjects underwent routine echocardiography, after which we divided them into two main groups: 90 women (60%) formed a cohort of individuals with existing LV diastolic dysfunction, the remaining 60 women were individuals without existing LV diastolic dysfunction. During the speckle tracking study in individuals with LVEDD according to the results of routine echocardiography, 85 out of 90 patients had a decrease in basal segment indices. This amounted to 94.5% of patients. In the remaining 5 patients (5.5%), regressive changes in myocardial dysfunction were not detected. In the second cohort of sixty women without LVEDD on routine echocardiography, only 50, or 83.4%, had no impairment in the reduction of speckle tracking echocardiography indices in the basal section. The remaining 16.6% (10 patients) with no changes in diastolic dysfunction on routine echocardiography showed decreased speckle-tracking echocardiography parameters (Tables 1 and 2).

**Table 1 - Echocardiography parameters**

| Group statistics of routine echocardiography | | | | | |
|---|---|---|---|---|---|
| | **Factor** | **N** | **Mean** | **Standart deviation** | **Standard error of the mean** |
| **E/e** | DDLV | 90 | 11.10 | 1.050 | 0.111 |
| | w/o DDLV | 60 | 6.78 | 0.666 | 0.086 |
| **LV MMI** | DDLV | 90 | 101.00 | 6.106 | 0.644 |
| | w/o DDLV | 60 | 83.75 | 5.488 | 0.709 |
| **RWT** | DDLV | 90 | 31.54 | 1.664 | 0.175 |
| | w/o DDLV | 60 | 25.70 | 1.522 | 0.196 |
| **SPAP** | DDLV | 90 | 36.96 | 1.669 | 0.176 |
| | w/o DDLV | 60 | 25.68 | 3.322 | 0.429 |
| **EF** | DDLV | 90 | 54.71 | 2.536 | 0.267 |
| | w/o DDLV | 60 | 60.77 | 2.205 | 0.285 |

**Table 2** - **ST-Echocardiography parameters**

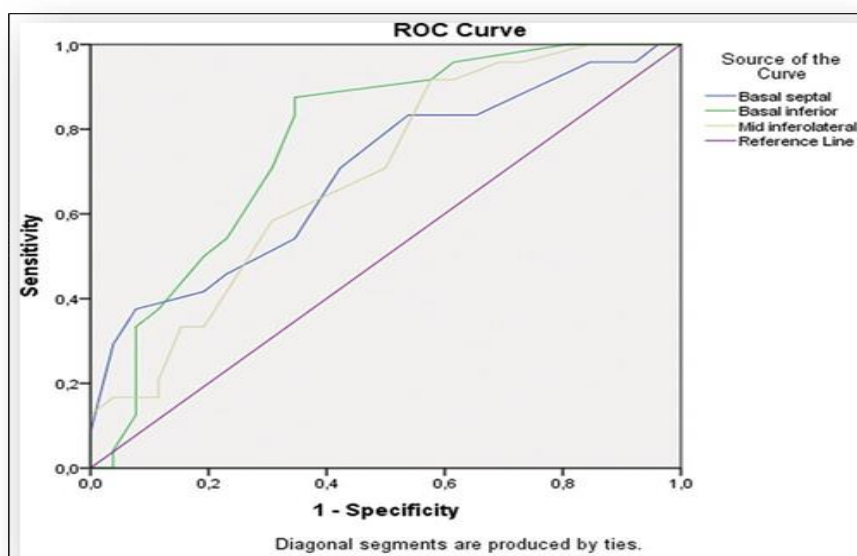| Group statistics of ST-Echocardiography | | | | | |
|---|---|---|---|---|---|
| | **Factor** | **N** | **Mean** | **Standart deviation** | **Standard error of the mean** |
| **Global ST** | DDLV | 90 | -16.89 | 0.827 | 0.087 |
| | w/o DDLV | 60 | -20.07 | 1.572 | 0.203 |
| **LA** | DDLV | 90 | -31.89 | 1.869 | 0.197 |
| **ST** | w/o DDLV | 60 | -35.60 | 0.978 | 0.126 |



**Figure 1** - **ROC curve of the relationship between LV diastolic dysfunction and echocardiography segments by speckle tracking**

According to Figure 1, the area under the receiver operating characteristic (ROC) curve for the correlation between the presence of left ventricular diastolic dysfunction and the basal septal segment of the left ventricle was 0.696 ± 0.075 (95% CI: 0.549–0.842, p = 0.018).

The cutoff value for the basal septal segment was -19.50. When the basal septal segment was equal to or greater than this value, a high risk of left ventricular diastolic dysfunction was predicted. The sensitivity and specificity of the method were 70.8% and 57.7%, respectively.

The area under the receiver operating characteristic (ROC) curve for the correlation between the presence of left ventricular diastolic dysfunction and the basal inferior segment was 0.772 ± 0.068 (95% CI: 0.639–0.904, p = 0.001). The cutoff value for the basal inferior

segment was - 21.50. When the basal inferior segment was equal to or greater than this value, a high risk of left ventricular diastolic dysfunction was predicted. The sensitivity and specificity of the method were 87.5% and 65.4%, respectively. The area under the ROC curve for the correlation between the presence of LV diastolic dysfunction and the mid-lateral segment was AUC 0.692 ± 0.074 (95% CI: 0.547–0.838, p = 0.020). The cutoff value for the mid-lateral segment was - 20.50. When the mid-lateral segment was equal to or greater than this value, a high risk of left ventricular diastolic dysfunction was predicted. The sensitivity and specificity of the method were 70.8% and 50.0%, respectively. The area under the receiver operating characteristic (ROC) curve was 0.806 ± 0.065 (95% CI: 0.679-0.933, p < 0.001), indicating "very good" predictive performance of the model.

## 4. Discussion

According to the scientific article on the role of speckle-tracking echocardiography in the diagnosis and treatment of cardiovascular diseases by E.G. Nesukai and A.A. Danilenko, speckle-tracking echocardiography is a new technique for assessing myocardial function [15]. Global longitudinal strain is the most clinically used parameter in speckle-tracking echocardiography. Routine sonographic methods have a place in the diagnosis of existing clinical signs of pathology. This study examines left ventricular diastolic dysfunction as a model for assessing deformation, contractility, and other cardiac muscle functions, including left ventricular remodeling and hypertrophic processes. Atria involvement cannot be ruled out [11,12].

Relevant data continues to emerge due to the intensive use of speckle-tracking echocardiography in various patient groups with various pathologies [15,16]. For future guidelines and research, the question of supplementing left atrial data and a full examination of right ventricular function remains open, focusing on the usefulness of the results. In this study, using speckle tracking for a comprehensive assessment of myocardial function in an asymptomatic population, women had varying indicators of diastolic function. Female

menopause and declining estradiol levels were associated with greater left ventricular remodeling combined with reduced left ventricular longitudinal strain. Furthermore, among postmenopausal women, decreased speckle tracking echocardiography parameters were independently associated with clinical outcomes. Taken together, these data contribute to our understanding of hormonal differences in heart failure and the predominance of postmenopausal women among heart failure patients with preserved LV function. Our findings of smaller LV dimensions, greater LV sphericity and concentricity, larger LA dimension, and worse LV diastolic function, despite better LV systolic function in women compared with men, are consistent with previous studies [15,16]. Our results extend previous data showing that, regardless of age and cardiovascular risk factors, female menopause is associated with greater LV and LA structural remodeling in tandem with a modest decrease in LV and LA longitudinal strain, despite preserved LVEF. Notably, while LV longitudinal function decreased, LV torsional function increased in postmenopausal women. Chinese American women in early menopause are at higher risk of cardiac remodeling compared with other ethnic

groups [20]. Menopause and a shorter reproductive period due to early menopause are proposed to be risk factors for the development of HF with EF in women [9,13,14,20]. Importantly, speckle tracking echocardiography is a highly sensitive and relatively afterload-independent measure of left atrial and left ventricular function, respectively. Our data suggest that strain indices and the LA stiffness index, with cutoff values of 31.6% and 18.2%, respectively, may be more sensitive for detecting subclinical kinetic changes, even when traditional left atrial (e.g., LA emptying fraction) and left ventricular (e.g., LV ejection fraction, or E/e') markers remain unchanged.

## 5. Conclusion

Routine echocardiography in our study demonstrated that it can often serve as a prognostic tool for the development of systolic myocardial dysfunction in individuals with pre-existing left ventricular diastolic dysfunction. A direct correlation was found between the presence of decreased basal layer indices on speckle tracking. This suggests that speckle tracking should be incorporated into routine echocardiography as an informative predictor of subsequent adverse cardiovascular events.

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# Аластау фракциясы сақталған әйелдердегі спекл-трекинг эхокардиографиясының деректері бойынша гормоналды өзгерістер мен миокард деформациясының параметрлері арасындағы байланыс

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## Түйіндеме

Технологиялық жаңғыру дәуірінде жүрек-қан тамырлары ауруларына қарсы жаңа профилактикалық және емдік стратегиялар жасалды. Дақты бақылау зерттеулері де ерекшелік емес.

**Мақсаты.** Перименопаузадағы әйелдерде сол жақ қарынша миокард дисфункциясын диагностикалауда дақты бақылау эхокардиографиясы параметрлерінің мәндерін бағалау.

**Материалдар мен әдістер.** Бұл зерттеу бір жылдық бақылау кезеңімен перспективалық дизайнға ие болды. Зерттеуге перименопауза кезеңіне сәйкес келетін белгілі гормоналды деңгейі бар, 47 жастан 53 жасқа дейінгі 150 әйел пациент қатысты. Зерттеу Қазақстан Республикасы Президенті Әкімшілігінің Медициналық орталығының функционалдық диагностика бөлімінде жүргізілді. Барлық сынақтар IBM SPSS Statistics 20 (IBM, АҚШ) көмегімен 95% сенімділік деңгейімен жүргізілді.

**Зерттеу нәтижелері.** Барлық 150 субъектіге жоспарлы эхокардиография жасалды, содан кейін біз оларды екі негізгі топқа бөлдік: 90 әйел (60%) сол жақ қарыншаның диастолалық дисфункциясы бар адамдардың когортасын құрады, ал қалған 60 әйел немесе 40% сол жақ қарыншаның диастолалық дисфункциясы жоқ адамдар болды. Дақтарды бақылау эхокардиографиясы жүргізілді.

Зерттеуде, әдеттегі эхокардиографияға негізделген сол жақ қарыншаның диастолалық дисфункциясы бар 90 науқастың 85-інде базальды сегменттің систолалық дисфункциясы болды. Бұл науқастардың 94,5%-ын құрады. Қалған 5 науқаста (5,5%) систолада регрессивті өзгерістер анықталмады. Әдеттегі жүрек ультрадыбысында сол жақ қарыншаның диастолалық дисфункциясы жоқ алпыс әйелден тұратын екінші когортада тек 50-інде (83,4%) базальды жазықтықта қалыпты систолалық функция болды. Әдеттегі

эхокардиографияда қалыпты диастолалық функциясы бар қалған 16,6%-да (10 науқас) дақтарды бақылау эхокардиографиясында қалыптан тыс систола және диастолалыққа дейінгі патология байқалды.

**Қорытынды.** Біздің зерттеуіміздегі әдеттегі эхокардиография сол жақ қарыншаның диастолалық дисфункциясы бар адамдарда систолалық миокард дисфункциясының дамуының болжамдық құралы ретінде қызмет ете алатынын көрсетті. Дақтарды бақылау эхокардиографиясында базальды жазықтық индекстерінің төмендеуі арасында тікелей корреляция анықталды. Бұл болашақтағы жағымсыз жүрек-қан тамырлары оқиғаларының ақпараттық болжаушысы ретінде күнделікті эхокардиографияда дақтарды бақылауды енгізу міндетті және ұсынылғанын білдіреді.

**Түйін сөздер:** дақтарды бақылау эхокардиографиясы, сол жақ қарыншаның диастолалық дисфункциясы, сол жақ жүрекше.

# Связь гормональных изменений и параметров деформации миокарда по данным спекл-трекинг эхокардиографии у женщин с сохранной фракцией выброса

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**Резюме**

В эпоху модернизирования технологий были разработаны новые профилактические и терапевтические стратегии и для сердечно-сосудистых заболеваний. Спекл-трекинговое исследование тому не исключение.

**Цель исследования.** Оценить значения параметров спекл трекинг эхокардиографии при диагностике дисфункций миокарда левого желудочка у лиц женского пола в период перименопаузы.

**Материалы и методы.** Данное исследование имело проспективный дизайн с продолжительностью периода наблюдения в год. В исследовании участвовало 150 пациенток женского пола, в возрасте от 47 до 53 лет, с известным гормональным уровнем, в соответствии с переменопаузальным периодом. Исследование проводилось в Больница Медицинского Центра Управления Делами Президента Республики Казахстан, отделении функциональной диагностики. Все тесты проводились с использованием IBM SPSS Statistics 20 (IBM, США) с доверительной вероятностью 95%.

**Результаты исследования.** Всем 150 исследуемым было воспроизведено рутинное эхокардиографическое исследование, после которого мы разделили их на две основные группы: 90 женщин

(60%) составили когорту лиц с имеющейся диастолической дисфункцией ЛЖ, оставшиеся 60 женщин, а это 40%, явились лицами без имеющейся диастолической дисфункции ЛЖ. Произвели спекл-трекинг ЭХОКГ.

В ходе исследования у когорты лиц с наличием диастолической дисфункции ЛЖ по результатам рутинного ЭХОКГ, из 90 пациенток, у 85 пациенток имелась систолическая дисфункция базального сегмента. Это составило 94,5 % пациенток. У оставшихся 5 пациенток (5,5%) регрессивные изменения со стороны систолы выявлены не были. У второй когорты шестидесяти женщин с отсутствием диастолической дисфункции ЛЖ на рутинном узи сердца, лишь у 50 , а это 83,4%, систолическая функция на базальном срезе нарушена не была. Оставшиеся 16,6 % - 10 пациенток, без изменений диастолической функции на ЭХОКГ рутинном, выдали показатели нарушения систолы и пред диастолической патологии при исследовании на спекл-трекинг ЭХОКГ.

**Выводы.** Рутинный метод эхокардиографии в рамках нашего исследования показал, что он зачастую может выступать как прогностический метод развития систолической дисфункции миокарда у лиц, с уже имеющейся диастолической дисфункцией миокарда левого желудочка. Выявлена прямая связь наличия снижения показателей базальных слоев на спекл-трекинг. Это означает обязательным и рекомендованным внедрить спекл-трекинг к рутинному обследованию ЭХОКГ, как информативный метод-предиктор дальнейших неблагоприятных сердечно-сосудистых событий.

**Ключевые слова:** спекл-трекинг эхокардиография, диастолическая дисфункция миокарда левого желудочка, левое предсердие.