

# Reliability of two-dimensional speckle tracking echocardiography in assessment of left atrial function in postmenopausal hypertensive women

M. Yu. Kolesnyk, M. V. Sokolova

Zaporizhzhia State Medical University, Ukraine, Educational and Scientific Medical Center "University Clinic"

Left atrium (LA) state reflects the severity of cardiovascular remodeling and indicates the degree of compensation in many cardiovascular diseases, including arterial hypertension (AH). Transthoracic echocardiography determines linear and volumetric parameters of LA, but it has limitations in early stages of AH. Speckle tracking echocardiography is a new technique which can identify early subclinical dysfunction of cardiac chambers.

**The purpose** of the study was 1) to assess feasibility, intra- and inter-observer reproducibility of LA longitudinal strain (LS) derived by both P- and R-wave triggering method; 2) to compare LA strain values obtained by P- and R-wave synchronization in hypertensive postmenopausal women.

**Material and methods.** The study involved 65 post-menopausal hypertensive women (mean age –  $56.8 \pm 8.15$  years). All patients underwent a standard transthoracic and two-dimensional speckle tracking echocardiography using Vivid E9 XDClear Console 4D Expert 100 (General Electric, USA). Apical four- and two-chamber views images were obtained during breath hold with ECG synchronization. All statistical analyses were performed using SPSS 20 for Windows (SPSS, Inc., Chicago, IL).

**Results.** Initial feasibility of echocardiographic data for performing LA strain analysis was 93.85 %. Adequate tracking quality was achieved in 96.93 % of segments by P-triggering and in 96.35 % by R-wave as initial point of analysis. The intra-class correlation (ICC) coefficient for R-triggering was 0.96 (95 % CI 0.89–0.98) for intra-observer and 0.94 (95 % CI – 0.52–0.97) for inter-observer variability. The ICC coefficients for P-triggering were higher 0.97 (95 % CI 0.92–0.99) and 0.96 (95 % CI – 0.9–0.98), respectively. The Bland-Altman statistic confirmed absence of bias in both variants of ECG-triggering. Values of LA LS calculated by R-triggering method were significantly higher than those ones by P-triggering ( $P < 0.001$ ).

**Conclusions.** Speckle tracking echocardiography is a reliable technique, which provides quantitative assessment of LA physiology. The P-wave triggering method of LA strain analysis is more reproducible compared with R-wave triggering variant. The LA LS values differ significantly depending on ECG-triggering type (P- or R wave), providing higher values by R-wave triggering method.

## Key words:

speckle tracking echocardiography, left atrium, women, hypertension, menopause.

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E-mail:  
zsmumk@gmail.com

## Надійність двовимірної спекл-трекінг ехокардіографії при оцінюванні функції лівого передсердя в жінок у стані менопаузи з гіпертонічною хворобою

М. Ю. Колесник, М. В. Соколова

Стан лівого передсердя (ЛП) показує тяжкість серцево-судинного ремоделювання та вказує на ступінь компенсації багатьох серцево-судинних захворювань, у тому числі гіпертонічної хвороби (ГХ). Трансторакальна ехокардіографія визначає лінійні та об'ємні параметри ЛП, але має обмеження на ранніх стадіях ГХ. Спекл-трекінг ехокардіографія – це нова методика, що дає змогу ідентифікувати ранню субклінічну дисфункцію камер серця.

**Мета роботи** – оцінити технічну можливість визначення, а також внутрішньо- та міждослідницьку відтворюваність поздовжнього стрейна ЛП, синхронізованого з Р- та R-зубцями ЕКГ; порівняти значення деформації ЛП, що отримані за допомогою Р- і R-хвильової ЕКГ-синхронізації, в жінок із гіпертонічною хворобою у стані менопаузи.

**Матеріали та методи.** У дослідження включили 65 жінок із ГХ у стані менопаузи (середній вік –  $56,8 \pm 8,15$  року). Усім пацієнтам здійснили стандартну трансторакальну ехокардіографію та двовимірну спекл-трекінг ехокардіографію на ультразвуковому сканері Vivid E9 XDClear Console 4D Expert 100 (General Electric, USA). Апікальні дво- та чотирикамерні зображення отримали під час затримки дихання та синхронізовані з ЕКГ. Статистичний аналіз виконали з використанням SPSS 20 для Windows (SPSS, Inc., Chicago, IL).

**Результати.** Технічна можливість аналізу деформації ЛП становила 93,85 %. Адекватна якість відстеження досягнута у 96,93 % сегментів за допомогою Р-синхронізації та 96,35 % із зубцем R як початкова точка аналізу. Коефіцієнт інтракласової кореляції для R-синхронізації становив 0,96 (95 % ДІ 0,89–0,98) для внутрішньодослідницької і 0,94 (95 % ДІ – 0,52–0,97) для міждослідницької варіабельності. Коефіцієнти інтракласової кореляції при аналізі від Р-зубця ЕКГ були ще вищими: 0,97 (95 % ДІ 0,92–0,99) і 0,96 (95 % ДІ – 0,9–0,98) відповідно. Статистика Bland-Altman підтвердила відсутність системної похибки при обох варіантах аналізу. Значення поздовжнього стрейна ЛП, що розраховані методом R-синхронізації, були вірогідно вищими, ніж при Р-синхронізації ( $p < 0,001$ ).

**Висновки.** Спекл-трекінг ехокардіографія – надійна методика, що забезпечує кількісне оцінювання фізіології ЛП. Аналіз деформації ЛП від початку зубця Р ЕКГ є більш відтворюваний порівняно з варіантом аналізу від зубця R. Показники поздовжньої деформації ЛП вірогідно різняться залежно від варіанта аналізу деформації (від Р- або R-зубця ЕКГ). Вищі значення стрейна ЛП визначаються під час побудови кривих деформації від зубця R ЕКГ.

## Ключові слова:

спекл-трекінг ехокардіографія, ліве передсердя, жінки, гіпертонічна хвороба, менопауза.

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**Ключевые слова:**

спекл-трекинг  
эхокардиография,  
левое предсердие,  
женщины,  
гипертоническая  
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## Надежность двухмерной спекл-трекинг эхокардиографии при оценке функции левого предсердия у женщин в состоянии менопаузы с гипертонической болезнью

М. Ю. Колесник, М. В. Соколова

Состояние левого предсердия (ЛП) отражает тяжесть сердечно-сосудистого ремоделирования и указывает степень компенсации многих сердечно-сосудистых заболеваний, в том числе и гипертонической болезни (ГБ). Трансторакальная эхокардиография определяет линейные и объемные параметры ЛП, но имеет ограничения на ранних стадиях ГБ. Спекл-трекинг эхокардиография – это новая методика, которая позволяет идентифицировать раннюю субклиническую дисфункцию камер сердца.

**Цель работы** – оценить техническую возможность выполнения, а также внутри- и межисследовательскую воспроизводимость стрейна ЛП, синхронизированного с P- и R-зубцами ЭКГ; сравнить значения деформации ЛП, полученные с помощью P- и R-волновой ЭКГ-синхронизации, у женщин с гипертонической болезнью в состоянии менопаузы.

**Материалы и методы.** В исследование включены 65 женщин с гипертонической болезнью в состоянии менопаузы (средний возраст – 56,8 ± 8,15 года). Всем пациентам была проведена стандартная трансторакальная и двухмерная спекл-трекинг эхокардиография на ультразвуковом сканере Vivid E9 XDClear Console 4D Expert 100 (General Electric, USA). Апикальные двух- и четырехкамерные изображения получены во время задержки дыхания и синхронизированы с ЭКГ. Статистический анализ выполнен с использованием SPSS 20 для Windows (SPSS, Inc., Chicago, IL).

**Результаты.** Техническая возможность проведения анализа деформации ЛП составила 93,85 %. Адекватное качество отслеживания достигнуто в 96,93 % сегментов посредством P-синхронизации и 96,35 % с зубцом R в качестве начальной точки анализа. Коэффициент интраклассовой корреляции для R-синхронизации составил 0,96 (95 % ДИ 0,89–0,98) для внутриисследовательской и 0,94 (95 % ДИ – 0,52–0,97) – для межисследовательской вариабельности. Коэффициенты интраклассовой корреляции при анализе от R-зубца ЭКГ были еще выше: 0,97 (95 % ДИ 0,92–0,99) и 0,96 (95 % ДИ – 0,9–0,98) соответственно. Статистика Bland-Altman подтвердила отсутствие системной ошибки при обоих вариантах анализа. Значения продольного стрейна ЛП, рассчитанные методом R-синхронизации, были достоверно выше, чем при P-синхронизации ( $p < 0,001$ ).

**Выводы.** Спекл-трекинг эхокардиография является надежной методикой, которая обеспечивает количественную оценку физиологии ЛП. Анализ деформации ЛП от начала зубца P ЭКГ является более воспроизводимым в сравнении с вариантом анализа от зубца R. Показатели продольной деформации ЛП достоверно различаются в зависимости от варианта анализа деформации (от P- или R-зубца ЭКГ). Более высокие значения стрейна ЛП определяются при построении кривых деформации от зубца R ЭКГ.

### Introduction

Quantification of left atrium (LA) provides important information about heart remodeling in patients with arterial hypertension (AH). LA index volume (LAVI) is one of echocardiographic markers to be evaluated according to European Society of Cardiology (ESC) guidelines for the management of AH [1]. The LAVI predicts mortality risk, independent of left ventricular (LV) geometry, in patients with preserved ejection fraction [2]. The cut-off value more than 34 ml/m<sup>2</sup> considered to be pathological both in men and women. However, volumetric measures of LA function may be limited by lower sensitivity in early disease stages [3].

LA plays an important role in LV filling by its contractile, reservoir and conduit function. LAVI only indirectly reflects this three-phasic LA physiology. Speckle-tracking echocardiography is a promising diagnostic tool for detailed LA function evaluation [4,5]. This technique was successfully tested in various pathological conditions [6–8]. However, the methodology of LA strain analysis needs standardization. The choice of zero reference point (P- or R-wave on ECG) for building LA deformation curves is still under discussion [9].

### Purpose

The aim of the study was 1) to assess feasibility, intra- and inter-observer reproducibility of LA strain derived by both P- and R-wave triggering method; 2) to compare LA strain values obtained by P- and R-wave synchronization in hypertensive postmenopausal women.

### Materials and methods

The study involved 65 post-menopausal hypertensive women (mean age – 56.8 ± 8.15 years) hospitalized to the cardiological department of University Clinic. Postmenopausal period was defined as at least 12 months of amenorrhea. The exclusion criteria were diabetes, heart failure, history of coronary artery disease, moderate or severe valvular disease, atrial fibrillation, conduction disorders, use of hormone replacement therapy as well. All participants gave informed written consent.

All patients underwent a standard transthoracic echocardiography using Vivid E9 XDClear Console 4D Expert 100 (General Electric, USA) ultrasound system equipped with a matrix M5S phase array transducer. Left ventricular end-diastolic (LV-EDD) and end-systolic diameters (LV-ESD), LA maximum anterior-posterior (A-P) diameter, thickness of the interventricular septum (IVS) and thickness of the LV posterior wall (LVPW) were measured from the internal dimensions obtained from parasternal long axis view in B-mode. LV mass was calculated by the American Society of Echocardiography formula and then indexed to body surface area (BSA). LV mass in grams was calculated from B-mode echocardiograms according to the formula:

$$LV \text{ mass} = 0.8 \times (1.04 \times \{ \{LV - EDD + LVPW + IVS\}^3 - \{LV - EDD\}^3 \}) + 0.6;$$

[10]. LV hypertrophy was defined as a LV mass index more

than 95 g/m<sup>2</sup>. Relative wall thickness (RWT) was calculated according to the formula:

$$RWT = (2 \times LVPW) / LV - EDD.$$

LV ejection fraction was measured using the modified biplane Simpson's rule.

LA area and volume were measured using the biplane method of disks (modified Simpson's rule), in the apical 4- and 2-chamber view on the frame before mitral valves opening. LA volume was indexed to BSA. LAVI was used to estimate LA dilation with cut-off value more than 34 ml/m<sup>2</sup>.

Pulsed spectral Doppler echocardiography was performed using a 5-mm sample volume placed at the tips of the mitral leaflets as parallel as possible to inflow. Tissue Doppler measurements were sampled at the level of the mitral annulus over the septal (e' sept) and lateral (e' lat) wall. The ratio of the transmitral Doppler E wave velocity and the composite mean of e' were then used to calculate the E/e' ratio. All parameters were measured three times and then averaged.

**Speckle tracking echocardiography.** Apical four- and two-chamber views images were obtained during breath hold with ECG synchronization. One of three standard leads (I, II or III) was chosen to get stable ECG trace with clear P- and R-wave. Particular attention was given to

obtain non-foreshortened LA view with clear delineation of myocardial tissue. The frame rate was set between 60 and 80 per second. The three cardiac cycles were recorded and averaged. All images and cine-loops were stored for off-line analysis on Echopac (version 113) using software package 2D Strain. First, the atrial endocardial border was traced by a point-and-click method. Then, LA wall was divided into six segments in every view by automatic creation of a region of interest (ROI). The nomenclature of 12 LA segments is not standardized. We used the nomenclature proposed by R. Yasuda et al. [11]. After manual adjustment of ROI width and shape the tracking quality for each segment was automatically analysed. Segments with inadequately tracking were removed from further analysis. Finally, the software generates strain curves for each atrial segment. Strain is defined as the percentage change in object's dimension in comparison to its initial dimension.

The analysis was performed using two variants of ECG-triggering:

1) Onset of P wave as reference point (Fig. 1). The strain curve has biphasic view with first negative part reflecting LA contraction (LA LS<sub>cont'</sub>) and second positive part which mirrors conduit function (LA LS<sub>cond'</sub>). The sum of these peaks equals reservoir (total) strain (LA LS<sub>tot'</sub>). LA LS<sub>cont'</sub>, LA LS<sub>cond'</sub> and their summation LS<sub>tot'</sub> values were obtained by

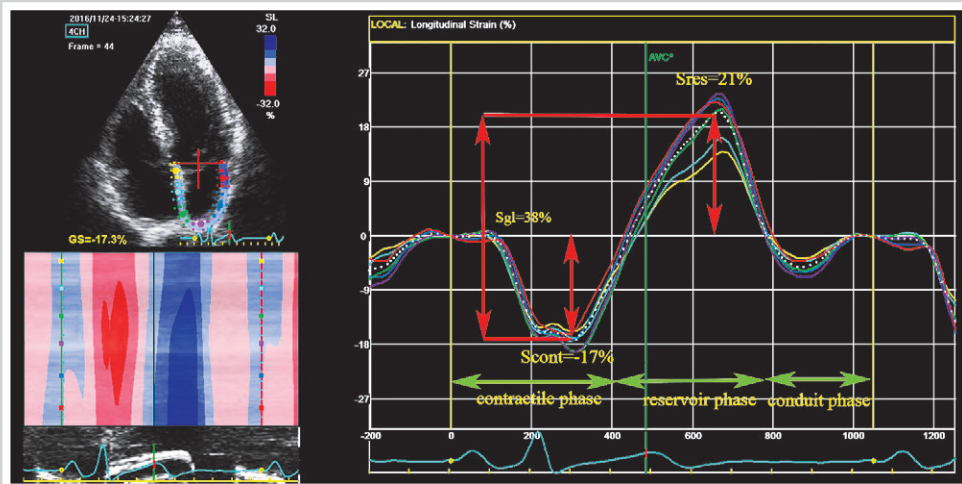


Fig. 1. The normal graph of LA longitudinal deformation by P-wave triggering method of analysis. Scont – strain in the contractile phase; Sres – strain in the reservoir phase; Sgl – global strain.

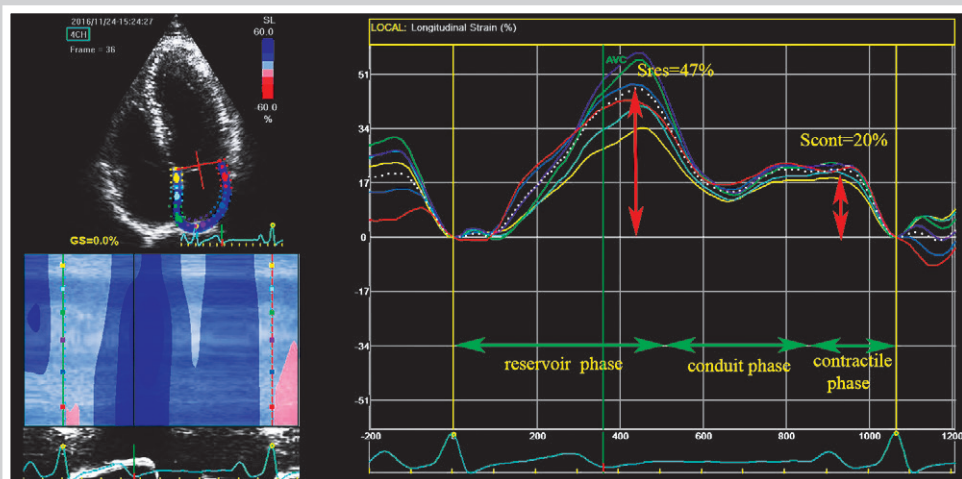


Fig. 2. The normal graph of LA longitudinal strain by P-wave triggering method of analysis.

**Table 1.** Clinical characteristics of the patients

Parameter	Value
Age, years	56.8 ± 8.15
AH duration, years	8 (3–15)
Menopause duration, years	7.5 (3–11)
Smoking, n (%)	9 (13.84 %)
Body mass index, kg/m <sup>2</sup>	30.03 ± 6.01
Office SBP, mm Hg	143 ± 21
Office DBP, mm Hg	92 ± 10
24-hour SBP, mm Hg	128 ± 15
24-hour DBP, mm Hg	74 ± 9
Heart rate, beats/min	71 ± 9

**Table 2.** Standard echocardiography data of the patients

Parameter	Value
LV-EDD, cm	4.9 (4.13–4.65)
LV-ESD, cm	2.66 (2.43–2.81)
LV mass index, g/m <sup>2</sup>	88.67 ± 17.78
RWT	0.46 (0.38–0.495)
LV EF, %	66.38 ± 5.85
LAA-P diameter, cm	3.92 ± 0.55
LAVI, ml/m <sup>2</sup>	32.52 ± 7.03
e' sept, cm/s	7.46 ± 1.66
e' lat, cm/s	9.44 ± 2.52
E/e' ratio	9.25 (7.94–10.84)

**Table 3.** Feasibility of LA segments for longitudinal strain analysis

	Segments	P-triggering	R-triggering
4-chamber view	Septal base	2 (9.5 %)	1 (4 %)
	Septal mid	0	2 (8 %)
	Septal roof	1 (4.8 %)	3 (12 %)
	Lateral roof	1 (4.8 %)	1 (4 %)
	Lateral mid	1 (4.8 %)	0
	Lateral base	2 (9.5 %)	3 (12 %)
2-chamber view	Inferior base	5 (23.8 %)	6 (24 %)
	Inferior mid	1 (4.8 %)	0
	Inferior roof	4 (19 %)	2 (8 %)
	Anterior roof	1 (4.8 %)	1 (4 %)
	Anterior mid	0	1 (4 %)
	Anterior base	3 (14.3 %)	5 (20 %)

**Table 4.** Values of left atrial longitudinal strain by speckle tracking

	P-triggering	R-triggering	P
LA LS tot 2CH	28.60 (24.96–31.99)	35.58 (30.22–44.40)	P < 0.001
LA LS tot 4CH	29.09 (24.35–34.69)	37.30 (29.72–46.83)	P < 0.001
LA LS global	29.38 (24.59–34.90)	36.77 (31.21–44.68)	P < 0.001

averaging individual values from 12 LA segments. Global peak atrial longitudinal strain (PALS) was calculated by averaging values observed in all LA segments, and by separately averaging values measured in 4- and 2-chamber views (4- and 2-chamber average PALS).

2) R-wave as initial point of analysis (Fig. 2). All strain values are positive, and there are two peaks that correspond to reservoir function (first peak between R wave and T wave) and atrial contractile function (starting on the P wave). We measured the first peak only which equals LA LS<sub>tot</sub>.

**Reproducibility.** We analysed the intra- and inter-ob-

server variability on 20 randomly selected subjects. For the intra-observer variability assessment, one observer (M. K.) measured LA deformation parameters on a separate occasion 1 month apart. For the inter-observer variability, the second sonographer (M. S.) repeated the analysis.

**Statistics.** The distribution of variables was tested by Shapiro–Wilk test. Continuous variables were presented as “mean ± standard deviation” or as “median and interquartile range” when data was non-parametric. Categorical variables were presented as absolute values and percentages. Intra- and inter-observer reproducibility was assessed by intraclass correlation coefficient (ICC) and its 95 % confidence interval (CI). The ICC values refer to the thresholds suggested by Vincent et al., indicating <0.8 as poor agreement, 0.80–0.90 as moderate agreement, ≥0.9 as excellent agreement [12]. Mean differences and limits of agreement (LoA) were calculated and visualized as Bland–Altman plots for descriptive purposes [13]. A P value < 0.05 was considered statistically significant. All statistical analyses were performed using SPSS 20 for Windows (SPSS, Inc., Chicago, IL).

## Results and discussion

The clinical characteristics of the study participants are presented in Table 1. Almost half of post-menopausal women (47.69 %) had increased BMI. The vast majority of patients (63.08 %) had the 1<sup>st</sup> and 2<sup>nd</sup> degree of AH. 84.62 % of study patients were never smokers. The 24 hour blood pressure monitoring was performed under antihypertensive treatment.

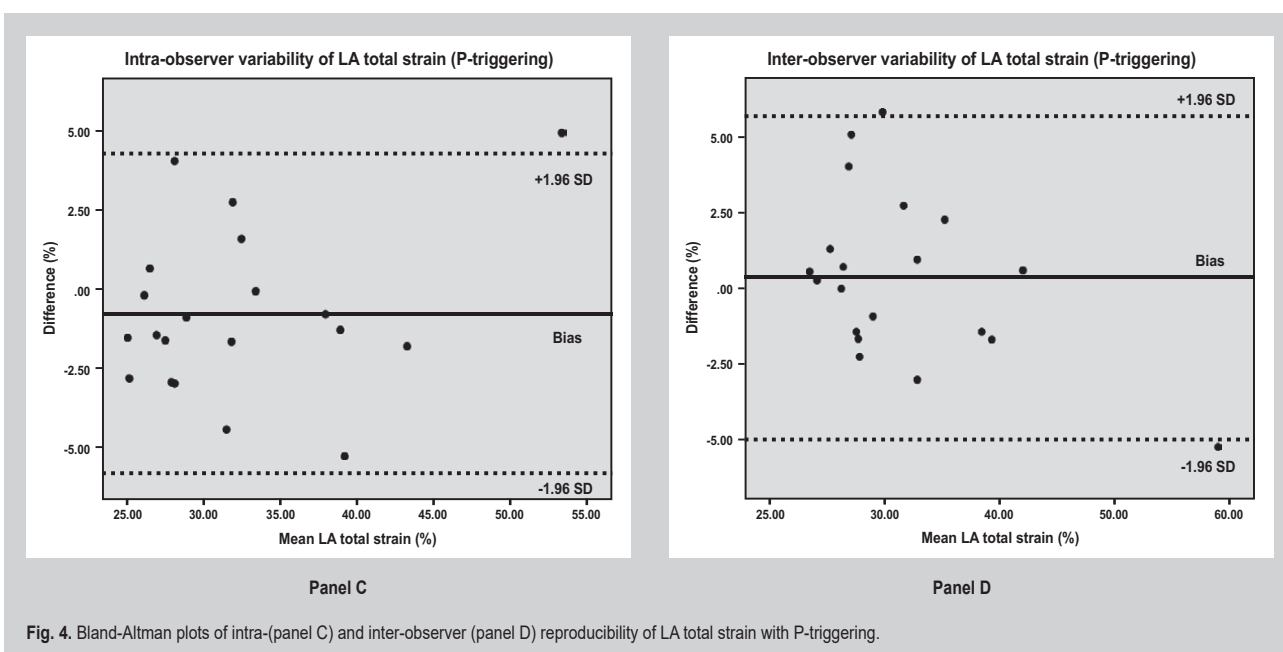
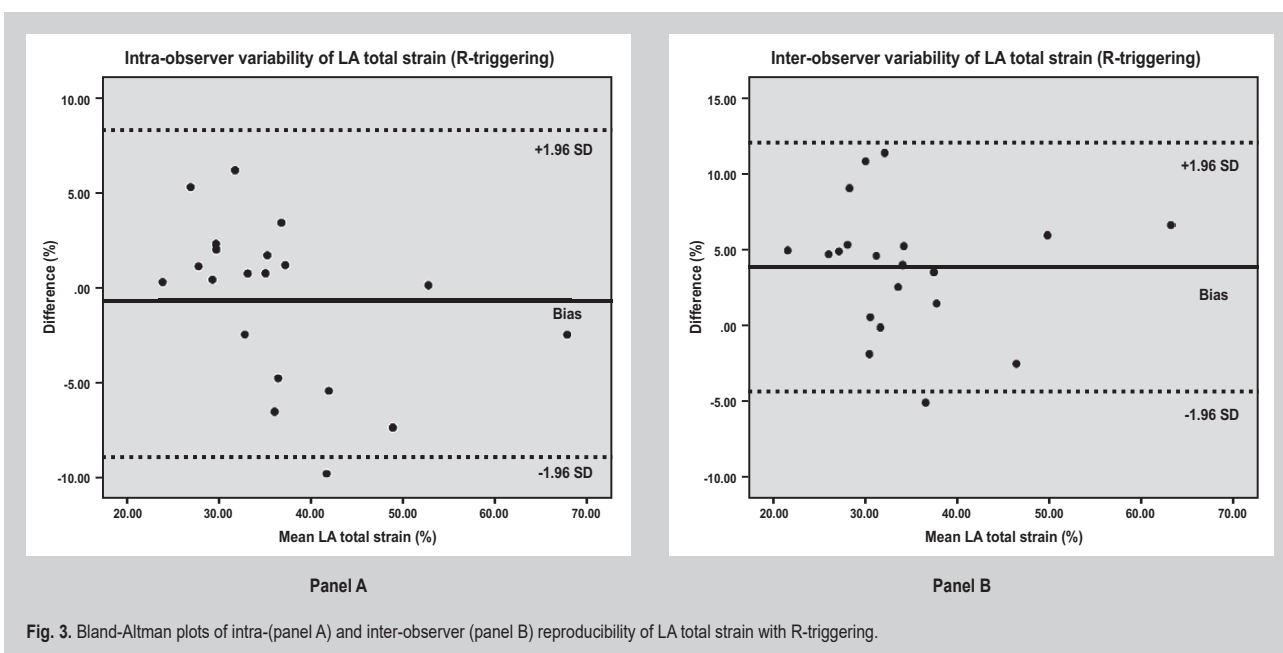
Table 2 details standard echocardiography data of post-menopausal hypertensive women. The percentage of women with LAVI >34 ml/m<sup>2</sup> was 38.46 %. Percentage of left ventricle hypertrophy was 36.92 % among surveyed hypertensive women. All of patients had preserved ejection fraction. Diastolic dysfunction of the left ventricle was identified in 23.08 % of the study participants.

It was impossible to obtain enough quality images in 4 (615 %) patients. So, initial feasibility of echocardiographic data for performing LA strain analysis was 93.85 %.

A total of 682 segments were analysed both in 2- and 4-chamber views. Adequate tracking quality was achieved in 96.93 % by P-triggering and in 96.35 % by R-triggering way. The software wasn't able to track 21 (3.07 %) segments by P-wave method and 25 (3.65 %) segments by R-triggering method. Average post-processing time per patient was 2 ± 1 min. “Inferior base” segments had been more often excluded because of the impossibility of achieving adequate tracking both by P- and R-triggering: 23.8 % and 24 %, respectively (Table 3). 20 % of excluded segments in R-wave trigger method were “Anterior base”.

It was established an excellent reliability of LA longitudinal strain analysis. The ICC coefficient for R-triggering was 0.96 (95 % CI 0.89–0.98) for intra-observer and 0.94 (95 % CI – 0.52–0.97) for inter-observer variability. The ICC coefficients for P-triggering were even higher – 0.97 (95 % CI 0.92–0.99) and 0.96 (95 % CI – 0.9–0.98), respectively.

The Bland–Altman statistics confirmed absence of bias in both variants of ECG-triggering (Fig. 3, 4). Reproduc-



cibility of PALS measurements was reached in 19 from 20 randomly selected subjects.

Median and interquartile range of global, 4-chamber, and 2-chamber observed in the study population are reported in Table 4. Notably, our research has shown values of LA LS calculated by R-triggering method were significantly higher than such ones by P-triggering ( $P < 0,001$ ).

To our knowledge, it is the first study to describe the ranges for LA strain and all its components in the population of postmenopausal hypertensive women. Rimbas et al. also have found out significantly higher LA strain values from R-R gating compared with P-P gating [14].

This phenomenon can be explained by the fact that R-wave is the electrical signal of LV contraction. LA phases on R-wave peak can differ among patients. Thus, the LA

myocardium at R-wave peak may be in contraction or relaxation, which indicates that the LA area or volume at R-wave peak is not always the minimum volume. If one defines the initial length of the LA myocardium at R-wave peak and if the LA myocardium has already started relaxation at that instance, then the initial length for LA strain calculation will be greater than the minimum LA length, causing an error in the calculated LA strain value [9]. Consequently, LA strain in any phase should be analysed from P-wave initial point rather than from R-wave peak, which is used in analytical software developed to define LV strain.

According to our results, there was no difference between 2- and 4-chamber average LA LS within the same measurement technique ( $p = 0.69$ ). However, some previous studies have described differences in mean LA

strain ranges between 2-chamber (37.6 %–44.3 %) and 4-chamber (33.8 %–40.1 %) views [15–17]. The lower values for the latter may be due to the insertion of pulmonary veins.

LA assessment of reservoir, conduit, and contractile function has previously shown no difference between men and women. Similarly, Morris et al. did not demonstrate a relationship between gender composition of the study and LA strain [18]. Boyd et al. showed a decline of LA strain with age describing significant changes in strain values after the sixth decade [19]. Furthermore, studies have shown that menopause, characterized by markedly decreased levels of estrogen, leads to significant increases in cardiovascular mortality and morbidity. In a few studies, menopause has been shown to have an impact on cardiovascular structure and functions, but only LV functions were evaluated and compared in pre- and postmenopausal women [20]. Study results demonstrated that with the development of menopause in asymptomatic individuals, LV functions assessed by speckle tracking echocardiography were impaired, even in cases with normal conventional echocardiography parameters.

## Conclusions

1. Speckle tracking echocardiography is a reliable technique, which provides quantitative assessment of LA three-phasic physiology (contraction, reservoir and conduit function).

2. The feasibility of LA strain analysis is 93.85 % in cohort of postmenopausal hypertensive women.

3. The P-wave triggering method of LA strain analysis is more reproducible compared with R-wave triggering variant.

4. The LA longitudinal strain results differ significantly depending on ECG-triggering type (P- or R wave), providing higher values by R-wave triggering method.

**The perspectives of further scientific research** are the study of the LA function features in hypertensive women, depending on the type of menopause.

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## Information about authors:

Kolesnyk M. Yu., MD, PhD, DSc, Associate Professor of the Department of Family Medicine, Therapy and Cardiology, Faculty of Postgraduate Education, Zaporizhzhia State Medical University, Ukraine.  
Sokolova M. V., MD, Post-Graduate Student (PhD-Student), Department of Family Medicine, Therapy and Cardiology, Faculty of Postgraduate Education, Zaporizhzhia State Medical University, Ukraine.

## Відомості про авторів:

Колесник М. Ю., д-р мед. наук, доцент каф. сімейної медицини, терапії і кардіології ФПО, Запорізький державний медичний університет, Україна.

---

Соколова М. В., аспірант каф. сімейної медицини, терапії і кардіології ФПО, Запорізький державний медичний університет, Україна.

**Сведения об авторах:**

Колесник М. Ю., д-р мед. наук, доцент каф. семейной медицины, терапии и кардиологии ФПО, Запорожский государственный медицинский университет, Украина.

Соколова М. В., аспірант каф. семейной медицины, терапии и кардиологии ФПО, Запорожский государственный медицинский университет, Украина.

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