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Echocardiographic Predictors of Undiagnosed Heart Failure with Preserved Ejection Fraction in Hospitalized Atrial Fibrillation Patients with Dyspnea

Davletova M.A.¹, Stavtseva Y.V.^{1,2}, Safarova A.F.¹, Timofeeva T.M.^{1,2}, Kobalava Zh.D.¹

¹ Peoples' Friendship University of Russia named after Patrice Lumumba (RUDN University)
6 Miklouho-Maclay St., 117198 Moscow, Russian Federation

² Vinogradov City Clinical Hospital, RUDN University
61 Vavilov St., 117292 Moscow, Russian Federation

ABSTRACT

The aim was to evaluate the prevalence and echocardiographic predictors of previously undiagnosed heart failure with preserved ejection fraction (HFpEF) in patients with atrial fibrillation (AF) and chronic dyspnea.

Material and methods. This prospective observational study included 85 patients hospitalized for cardioversion with paroxysmal or persistent AF and chronic dyspnea. All participants underwent transthoracic speckle-tracking echocardiography of left atrial longitudinal strain (LAS). HFpEF probability was assessed using the HFA-PEFF algorithm. Dynamic follow-up of diastolic function was performed at three predefined time points: during AF paroxysm, 24 hours post-cardioversion, and one-month post-cardioversion.

Results. High probability of HFpEF was identified in 78.7% of patients (67 out of 85). These patients exhibited significantly higher NT-proBNP levels, greater CHA₂DS₂-VASc score, as well as more impaired LAS parameters and elevated left atrial stiffness index compared to low-intermediate HFpEF probability groups. At one-month follow-up after cardioversion ($n = 55$), while NT-proBNP levels significantly declined, overall HFpEF probability remained unchanged. Left atrial stiffness index demonstrated the strongest independent predictive value in verifying high probability HFpEF, with remarkable discriminative capacity both during AF (OR = 34.5; 95% CI 2.5–478.7) and after sinus rhythm restoration (OR = 193.1; 95% CI 7.3–1,207).

Conclusion. This study reveals high prevalence of undiagnosed HFpEF among AF patients undergoing cardioversion, with disease probability persisting despite rhythm control during one-month follow-up. The left atrial stiffness index is as a valuable diagnostic marker for HFpEF detection in this population, potentially enhancing standard HFA-PEFF algorithm.

Keywords: atrial fibrillation, heart failure with preserved ejection fraction, cardioversion, left atrial strain, HFA-PEFF score

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✉ Davletova Marianna A., maridavletova@mail.ru

Эхокардиографические предикторы недиагностированной сердечной недостаточности с сохраненной фракцией выброса у госпитализированных пациентов с фибрилляцией предсердий и жалобами на одышку

Давлетова М.А.¹, Ставцева Ю.В.^{1,2}, Сафарова А.Ф.¹, Тимофеева Т.М.^{1,2}, Кобалава Ж.Д.¹

¹ Российский университет дружбы народов (РУДН) им. Патриса Лумумбы
Россия, 117198, г. Москва, ул. Миклухо-Маклая, 8

² Университетская клиническая больница (УКБ) им. В.В. Виноградова (филиал) Российского университета дружбы народов (РУДН) им. Патриса Лумумбы
Россия, 117292, г. Москва, ул. Вавилова, 61

РЕЗЮМЕ

Цель: оценить частоту встречаемости и эхокардиографические предикторы ранее недиагностированной сердечной недостаточности с сохраненной фракцией выброса (СНсФВ) у пациентов с фибрилляцией предсердий (ФП) и хронической одышкой.

Материалы и методы. В проспективное наблюдательное исследование включены 85 пациентов с пароксизмальной или персистирующей формой ФП и хронической одышкой, госпитализированных для проведения кардиоверсии. Всем участникам выполнялась трансторакальная эхокардиография в сочетании с методом спекл-трекинга для анализа продольной деформации левого предсердия (ПД ЛП). Вероятность СНсФВ оценивалась с помощью алгоритма HFA-PEFF. Для динамического наблюдения за пациентами были выделены три временные точки: во время фибрилляции предсердий, через 24 ч после кардиоверсии и через 1 мес наблюдения.

Результаты. Высокая вероятность СНсФВ была выявлена у 78,7% пациентов (67 из 85). В этой группе зарегистрированы статистически значимо более высокие уровни NT-proBNP, более высокие баллы по шкале CHA₂DS₂-VASc, а также более низкие показатели ПД ЛП, более высокий индекс жесткости ЛП по сравнению с пациентами с низкой и промежуточной вероятностью СНсФВ. При динамическом наблюдении через 1 мес после кардиоверсии ($n = 55$) количество баллов по алгоритму HFA-PEFF оставалось неизменным, несмотря на статистически значимое снижение уровня NT-proBNP. Наибольшую прогностическую значимость для выявления пациентов с высокой вероятностью сердечной недостаточности продемонстрировал индекс жесткости ЛП, с отношением шансов 34,5 (95%-й доверительный интервал (ДИ) 2,5–478,7) во время ФП и 193,1 (95% ДИ 7,3–1207) при синусовом ритме.

Заключение. Полученные данные свидетельствуют о высокой распространенности ранее недиагностированной СНсФВ среди пациентов с ФП, госпитализированных для кардиоверсии. Вероятность СНсФВ существенно не изменялась в течение месяца после восстановления синусового ритма. Индекс жесткости ЛП обладает высокой диагностической ценностью для верификации СНсФВ у данной категории пациентов и может рассматриваться как дополнительный критерий при использовании стандартного алгоритма HFA-PEFF.

Ключевые слова: фибрилляция предсердий, сердечная недостаточность с сохраненной фракцией выброса, кардиоверсия, деформация левого предсердия, шкала HFA-PEFF

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

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INTRODUCTION

Verification of the diagnosis of heart failure with preserved ejection fraction (HFpEF) in patients with atrial fibrillation (AF) and complaints of dyspnea can be significantly challenging, as both conditions are highly prevalent in the elderly, have similar symptoms, and may directly cause each other [1–5]. At present, questions regarding the reversibility of heart failure after cardioversion as left atrial (LA) function normalizes and, consequently, the appropriateness of diagnosing HFpEF during hospitalization for cardioversion remain insufficiently studied.

Moreover, this patient population often have comorbid conditions (such as chronic obstructive pulmonary disease, anemia, and obesity), which complicate the accurate interpretation of the underlying cause of dyspnea. Given the abovementioned, optimizing the detection of HFpEF in this patient group is critically important to enable timely adjustments in pharmacological therapy [1, 2, 6].

Patients with HFpEF are often characterized by cardiac fibrosis, remodeling, overload, and impaired LA function. These changes can be assessed using parameters already widely employed in clinical practice and metrics whose role requires further investigation. Among these, the evaluation of LA longitudinal strain (LAS) via speckle-tracking echocardiography is of particular interest [7–10].

LAS is a promising echocardiographic marker that reflects not only LA function but also left ventricular (LV) filling pressure. It may serve as a complementary parameter to validated clinical tools, such as the H2FPEF and HFA-PEFF scores, which are used for diagnosing HFpEF [11, 12]. Moreover, LAS is likely a more sensitive marker of diastolic dysfunction compared to conventional parameters assessing LA and LV morphology [3, 13]. For instance, some studies have demonstrated high accuracy of LAS in differentiating between HFpEF and other causes of dyspnea in patients with sinus rhythm [14–16]. However, data on the utility of this method in patients with AF remain limited and require further investigation.

The aim of this study was to assess the prevalence and echocardiographic predictors of previously undiagnosed HFpEF in patients with atrial fibrillation and chronic dyspnea.

MATERIALS AND METHODS

After screening 171 patients, this prospective observational study included 85 patients aged ≥ 55 years with paroxysmal or persistent AF

and complaints of chronic dyspnea, who were consecutively admitted to the Cardiac Intensive Care Unit at Vinogradov City Clinical Hospital (a branch of RUDN University) for cardioversion between March 2023 and May 2024. The final analysis included 55 patients who underwent a one-month follow-up. The method for sinus rhythm restoration (either pharmacological or electrical cardioversion) was selected according to current clinical practice guidelines of the Russian Ministry of Healthcare.

The main exclusion criteria were previously diagnosed heart failure, inability to restore and maintain sinus rhythm during follow-up (AF episodes requiring repeat cardioversion), left ventricular systolic dysfunction, presence of potentially reversible causes of AF (such as electrolyte disturbances or thyrotoxicosis), and severe comorbidities (including severe anemia, chronic obstructive pulmonary disease, or active malignancy). A follow-up visit was scheduled one month after discharge to assess changes in laboratory and echocardiographic parameters.

The study database recorded the main clinical and demographic characteristics of the study sample. Additional parameters included duration of medical history and AF type, along with presence of comorbidities. Dyspnea severity was classified according to NYHA criteria. Standard laboratory parameters were documented at hospital admission, and changes in NT-proBNP were reported at admission, next day, and one month post-cardioversion. All patients underwent thromboembolic and bleeding risk assessment using CHA₂DS₂-VASc and HAS-BLED scales, respectively, based on clinical and laboratory parameters.

Electrocardiography (ECG) was used to assess QRS complex morphology and basic interval durations (PQ, QRS, and QT). Transthoracic echocardiography was performed using expert-class equipment (GE Vivid E90, GE Healthcare, Horten, Norway) with standard imaging planes ensuring optimal visualization and recording of required parameters. The method for assessing global LV contractility (the Teichholz method or Simpson's method) was selected based on visualization quality and presence of regional LV wall motion abnormalities, following the clinical practice adopted at the institution.

Diastolic function was evaluated using tissue Doppler imaging in apical four-chamber view by measuring peak mitral inflow E-wave velocity (E) and averaging lateral and septal mitral annular early

diastolic velocities (e'), with subsequent calculation of E/e' ratio. Automated strain analysis was conducted using specialized software. For LV global longitudinal strain (LVGLS) assessment, automatic tracking between endocardial and epicardial borders was performed followed by bull's eye diagram generation and GLS calculation. Left atrial strain was evaluated using ECG-gated images from apical 4- and 2-chamber views. The zero-reference point for atrial strain curves was set at the ECG R-wave followed by analysis of reservoir (LASr), conduit (LAScd), and contractile (LASct) phases, with the latter parameter assessed only during sinus rhythm [17]. Left atrial stiffness index was calculated as E/e' divided by LASr.

The likelihood of HFpEF was assessed using the HFA-PEFF score. In cases of intermediate HFpEF probability, a diastolic stress test (DST) was performed according to protocols outlined in current Russian and international guidelines [12, 18, 19]. DST was positive if: 1) there was an increase in E/e' ratio ≥ 15 (2 points), or 2) there was an increase in E/e' ratio ≥ 15 with a peak tricuspid regurgitation velocity ≥ 3.4 m/s (3 points).

Statistical analysis was performed using IBM SPSS Statistics software (v. 27.0). Quantitative data are presented as median and interquartile range Me [IQR], while qualitative variables are expressed as absolute numbers and percentages n [%]. To assess statistical significance of intergroup differences, we used the Mann–Whitney U test for independent samples, Wilcoxon signed-rank test for two related samples, and Friedman test with subsequent post-hoc pairwise comparisons (with Bonferroni correction) for three related samples. Differences were considered statistically significant at $p < 0.05$ (with Bonferroni correction at $p < 0.017$).

To identify independent predictors of persistent high HFpEF probability at one-month follow-up, we performed logistic regression analysis separately for parameters recorded during AF episodes and after cardioversion. Variables showing statistical significance at $p < 0.1$ were included in the multivariate analysis. For each independent predictor, ROC analysis was performed. The predictive value of variables was assessed based on the area under the curve (AUC), with optimal cutoff values determined using the Youden index.

All patients provided a written informed consent to participate in the study. The study protocol was approved by the Ethics Committee of the Medical

Institute at RUDN University (Minutes No. 16 dated March 16, 2023).

RESULTS

High probability of HFpEF according to the HFA-PEFF score was identified in 67 patients (78.7%), including 47 patients with initially high HFpEF probability and 20 patients with intermediate probability and positive diastolic stress test (DST). Intermediate and low HFpEF probabilities were recorded in 16 and 2 cases, respectively. At one-month follow-up, AF episodes were documented in 30 patients (35.3%), including 25 from the group with high HFpEF probability and 5 from the group with low/intermediate probability. Thus, the final analysis included 55 patients (42 with high HFpEF probability, including those with positive DST – Group 1; and 13 with low/intermediate HFpEF probability – Group 2). Group 1 patients demonstrated higher NT-proBNP levels (both at admission and during follow-up) and higher CHA_2DS_2 -VASc scores (Table 1).

Data on the dynamics of HFA-PEFF score components and LA strain parameters in patients with HFpEF are presented in Table 2. Over the one-month follow-up period, the median HFA-PEFF score remained unchanged (5→5 points, $p > 0.05$). Transition from high to intermediate HFpEF probability occurred in only three patients, driven exclusively by reductions in NT-proBNP levels. During follow-up, we noted statistically significant positive changes in some algorithm parameters (NT-proBNP, lateral e') and in all LA strain parameters.

Statistically significant differences: * – for FU-1 vs. FU-2 and FU-3; FU-2 vs. FU-3; # – for FU-2 vs. FU-3; ** – for FU-1 vs. FU-2; ## – for FU-1 and FU-2 vs. FU-3.

Logistic regression analysis demonstrated that the left atrial stiffness index (E/e' /LASr) was the only independent predictor of HFpEF persistence at one-month follow-up in AF patients undergoing cardioversion, showing significant associations both during the AF episode (odds ratio (OR) = 34.5 [95% CI 2.5–478.7; $p = 0.008$]) and after sinus rhythm restoration (OR = 193.1 [95% CI 7.3–1207; $p = 0.008$])

ROC analysis identified the following cutoff values for the left atrial stiffness index (see Figure): > 1.10 (area under the curve [AUC] 0.83; sensitivity 49.1%; specificity 100%) during AF and > 0.48 (AUC 0.86; sensitivity 91.2%; specificity 66.7%) during sinus rhythm.

Table 1

Baseline Clinical and Demographic Parameters of Study Participants at the Time of Inclusion			
Parameter	Group 1 (n = 42)	Group 2 (n = 13)	p
Age, Me [IQR], years	75.5 [68;82]	73 [67;75]	0.18
Female sex, n (%)	29 (69.0)	6 (46.1)	0.24
Smoking, n (%)	3 (7.1)	0 (0)	0.77
<i>Heart Failure Characteristics</i>			
HFA-PEFF, Me [IQR], points	6.0 [5.0;6.0]	4.0 [3.0;5.0]	<0.0001
NYHA FC, n (%)			
– II	29 (69)	11 (84.6)	0.46
– III	13 (31)	2 (15.4)	
NT-proBNP, Me [IQR], pg/ml	1,225 [568; 2,225]	226 [171;694]	<0.0001
<i>Atrial Fibrillation Characteristics</i>			
AF subtype, n (%)			
– newly diagnosed (paroxysmal or persistent);	9 (21.4)	4 (30.8)	0.75
– paroxysmal;	34 (81.0)	11 (84.6)	0.91
– persistent;	8 (19.0)	2 (15.4)	
Duration of AF history (including patients with newly diagnosed AF), n (%)			
– less than 1 year;	11 (26.2)	5 (38.5)	0.95
– 1–3 years;	13 (31.0)	5 (38.5)	
– more than 3 years	18 (42.8)	3 (23.0)	
AF paroxysm duration ≥48 hours, n (%)	17 (40.5)	2 (15.4)	0.18
CHA ₂ DS ₂ -VASc, Me [IQR], points	4.0 [3.0;5.0]	3.0 [2.0;3.0]	0.014
HAS-BLED, Me [IQR], points	2.0 [1.0;2.0]	2.0 [1.0;2.0]	0.66
<i>Comorbidities</i>			
Hypertension, n (%)	42 (100.0)	13 (100)	0.87
Coronary artery disease, n (%)	7 (16.6)	1 (7.7)	0.73
Obesity, n (%)	17 (40.5)	3 (23.1)	0.42
Diabetes mellitus, n (%)	6 (14.3)	0 (0)	0.3
Stroke, n (%)	4 (9.5)	1 (7.7)	0.73
CKD (GFR-EPI <60 ml/min/1.73 m ²), n (%)	24 (57.1)	4 (30.8)	0.18
<i>Pharmacological Therapy</i>			
ACEI/ARBs, n (%)	28 (66.7)	9 (69.2)	0.87
Beta-blockers, n (%)	13 (31.0)	7 (53.8)	0.24
MRAs, n (%)	2 (4.8)	1 (7.7)	0.77
Thiazide diuretics, n (%)	5 (12.0)	3 (23.1)	0.58
Loop diuretics, n (%)	6 (14.3)	0 (0)	0.35
CCBs, n (%)	9 (21.4)	4 (30.8)	0.75
AAD, n (%)	18 (42.9)	4 (30.8)	0.65
Anticoagulants, n (%)	25 (59.5)	7 (53.8)	0.97

Note. AAD – antiarrhythmic drugs; ACEI – angiotensin-converting enzyme inhibitors; AF – atrial fibrillation; ARB – angiotensin II receptor blockers; CCB – calcium channel blockers; CKD- chronic kidney disease; FC – functional class; GFR – glomerular filtration rate; HFA-PEFF – Heart Failure Association score for HFpEF diagnosis; MRA – mineralocorticoid receptor antagonists; NT-proBNP – N-terminal pro-brain natriuretic peptide; NYHA – New York Heart Association functional classification. The results were considered statistically significant at $p < 0.05$.

Table 2

Longitudinal Changes in Laboratory and Echocardiographic Parameters				
Parameter	FU-1	FU-2	FU-3	p
NT-proBNP, Me [IQR], pg/ml	1,225 [560; 2,297]	899.0 [330.5; 412.5]	374 [133; 1,099]	<0.001*
LAVI, Me [IQR], ml/m ²	40.0 [31.9;45.2]	40.8 [33.7;44.2]	37.0 [34.0; 43.0]	0.03 [#]
IVSd, Me [IQR], cm	1.3 [1.1;1.4]	–	1.2 [1.1;1.3]	0.01
LVPWd, Me [IQR], cm	1.1 [1.0;1.2]	–	1.1 [1.0;1.2]	NS
LVMI, Me [IQR], g/m ²	96.9 [82.3;108.5]	–	96.0 [77.5;108.5]	0.02
RWT, Me [IQR]	0.48 [0.43;0.55]	–	0.48 [0.42;0.55]	NS
PASP, Me [IQR], mm Hg	35.0 [28.7;41.2]	–	35.5 [28.7;41.2]	H3
TRV, Me [IQR], m/s	2.8 [2.1;3.6]	–	3.0 [2.4;3.5]	NS
Lateral e', Me [IQR], cm/s	0.06 [0.05; 0.09]	0.07 [0.06; 0.09]	0.07 [0.05; 0.08]	<0.001**

End of table 2

Parameter	FU-1	FU-2	FU-3	<i>p</i>
Septal <i>e'</i> , <i>Me</i> [IQR], cm/s	0.06 [0.05; 0.08]	0.07 [0.05; 0.08]	0.05 [0.04; 0.06]	<0.001 ^{##}
<i>E/e'</i> ratio, <i>Me</i> [IQR]	11.4 [9.0;14.0]	12.0 [9.3;14.5]	11.6 [9.0; 14.5]	NS
GLS, <i>Me</i> [IQR], %	16 [14;18]	–	–	–
LASr, <i>Me</i> [IQR], %	11.5 [8.0;14.0]	15.5 [11.7;21.2]	21.0 [17.0;24.0]	<0.001*
LAS cd, <i>Me</i> [IQR], %	-7.0 [-10.0; -4.0]	-10.5 [-13.0; -8.0]	-13.0 [-14.5; -10.5]	<0.001*
LAS ct, <i>Me</i> [IQR], %	–	-5.0 [-8.0; -3.0]	-7.0 [-12.0; -4.5]	0.006
<i>E/e'</i> / LASr, <i>Me</i> [IQR]	1.0 [0.68;1.7]	0.70 [0.52;1.0]	0.53 [0.41;0.78]	<0.001*

Note. FU – follow-up; FU-1, FU-2, and FU-3 represent time points corresponding to parameter measurements at admission (during AF episode – FU-1), 24 hours post-cardioversion – FU-2, and 30 days post-cardioversion – FU-3, respectively. LVMMI – left ventricular mass index; LA – left atrium; NS – not significant; PASP – pulmonary artery systolic pressure; TRV – peak tricuspid regurgitation velocity; LVPWd – left ventricular posterior wall thickness; IVSd – interventricular septum thickness; *E/e'* – ratio of early diastolic mitral inflow velocity to average mitral annular tissue Doppler velocity; *E/e'*/LASr – left atrial stiffness index; LV GLS – left ventricular global longitudinal strain; LAScd – left atrial conduit strain; LASct – left atrial contraction strain (assessed in sinus rhythm only); LASr – left atrial reservoir strain.

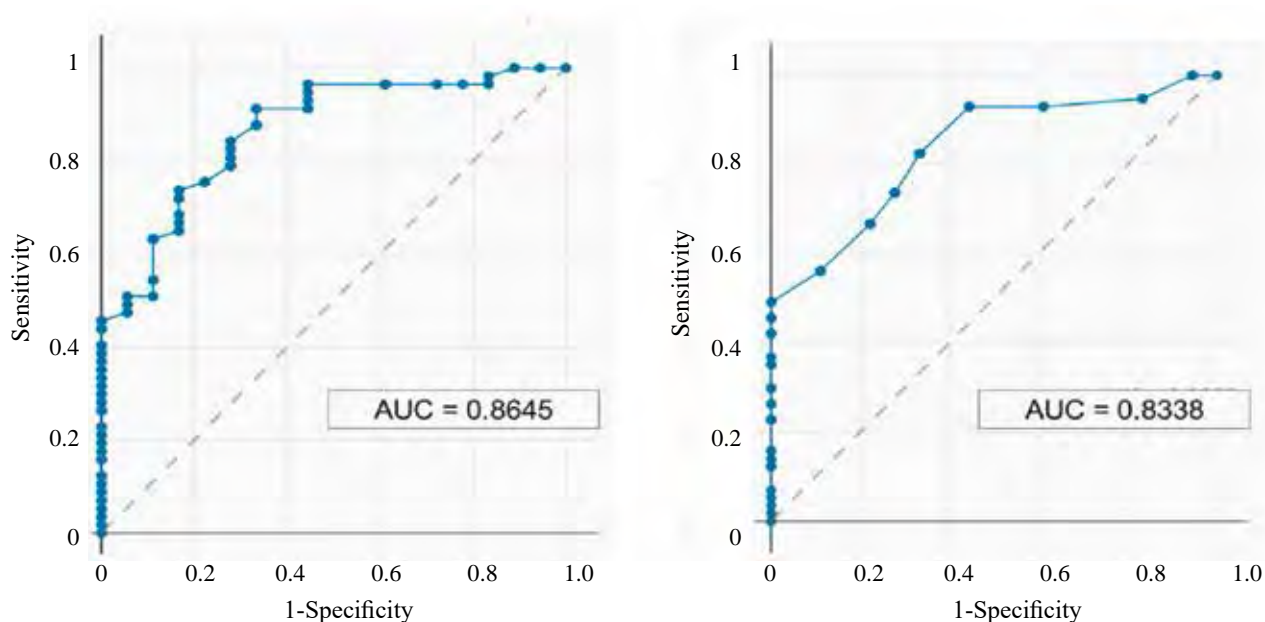


Figure. ROC curve for the left atrial stiffness index measured during: *a* – sinus rhythm; *b* – atrial fibrillation episodes

DISCUSSION

HFpEF often remains underdiagnosed in AF patients, since in clinical practice dyspnea, which is the cardinal symptom of heart failure, may be attributed solely to AF [20, 21]. Specifically, J.A.Naser et al. et al. (2023) reported high HFpEF probability in 62% of patients with this arrhythmia, yet only 5% had corresponding ICD-10 codes in medical records at enrollment [20].

Y.N.V. Reddy et al. (2018) demonstrated hemodynamic evidence of HFpEF via right heart catheterization in 64% of AF patients with unexplained dyspnea [21]. Our study identified high HFpEF probability using HFA-PEFF score in most elderly AF patients without prior heart failure history but with

chronic dyspnea, aligning with invasive diagnostic data. Indeed, when using the mainstay – exercise stress right heart catheterization – HFpEF can be detected in 65–94% of AF patients [21–23]. Furthermore, AF is associated with a 2.5-fold increased risk of developing clinically significant LV diastolic dysfunction (with 3.4% annual incidence) during follow-up compared to sinus rhythm [20]. These findings together underscore the imperative for active HFpEF screening in AF patients with chronic dyspnea [20–24].

HFpEF in AF patients may be the sole thromboembolic risk factor requiring anticoagulant therapy and itself constitutes an indication for prognosis-modifying medications [11, 12, 25]. Moreover, AF episodes can induce changes that promote the

development and progression of heart failure [24, 26]. Consequently, post-cardioversion changes in both individual HFpEF markers and overall HFpEF probability are of particular interest.

Indeed, sinus rhythm restoration may be accompanied by reverse remodeling of cardiac chambers [27–29], where functional improvements in LA and LV (E/e' and LASr) along with reductions in HF biomarkers typically precede morphological changes (LA volume index), which may require months of maintained sinus rhythm. Some studies have demonstrated restored atrial mechanical synchrony [30] and increased LASr shortly after cardioversion [29, 31]. The latter rarely normalizes completely, likely due to atrial myocardial stunning whose duration varies depending on AF episode characteristics, atrial size, and underlying structural heart disease [32, 33].

In our study, despite successful sinus rhythm restoration in all cases (main inclusion criterion), only three patients (4.5%) showed reduced HFpEF probability (from high to intermediate) based on NT-proBNP reduction. The overall study population exhibited bidirectional changes in medial/lateral mitral annular velocities alongside improvements in LA reservoir, conduit, and contractile functions. These findings supported by existing evidence [24–33] suggest limited short-term reversibility of HFpEF parameters post-cardioversion and highlight the need for early initiation of prognosis-modifying therapies (anticoagulants, SGLT2 inhibitors, and non-steroidal MRAs) [11, 12]. Improved LA function following rhythm control supports the early rhythm control strategy demonstrated in EAST-AFNET 4 [34], where HF hospitalizations were part of the primary endpoint.

Among echocardiographic markers of HFpEF, the stiffness index ($E/e'/\text{LASr}$) deserves special attention as it represents an integrated measure of left heart diastolic function [6, 35–42]. Several studies have demonstrated in HFpEF patients associations of this parameter both with AF recurrence after cardioversion or catheter ablation [35, 36] and with long-term prognosis [37–39]. Furthermore, the stiffness index has been investigated for HFpEF screening as a potential adjunct to currently used diagnostic probability models [6, 40, 41]. While standardized reference values are lacking, this index typically does not exceed 0.3 in healthy individuals.

HFpEF leads to increased stiffness index values, with additional contribution from impaired LA reservoir function during AF episodes, explaining the varying cutoff values identified by ROC analysis

in our study [31, 42]. Although this parameter showed slightly greater accuracy immediately after cardioversion, its potential utility during AF is particularly clinically relevant, as Russian practice typically involves only a single pre-cardioversion echocardiogram. In our study, the stiffness index was the sole predictor of persistent HFpEF during follow-up. Consequently, this indicator may be valuable both as an adjunct to other HFpEF probability assessment methods and as a potential alternative to diastolic stress testing in cases of intermediate HFpEF probability. However, the precise role of the stiffness index in contemporary HFpEF diagnostic algorithms requires further investigation.

Study limitations include the relatively small sample size, short follow-up period (one month), and lack of a control group with permanent AF. A promising direction for future research involves investigating the long-term effects of cardioversion combined with HFpEF-targeted therapy on left atrial remodeling and clinical outcomes.

CONCLUSION

In this study, the majority of elderly patients with atrial fibrillation and chronic dyspnea demonstrated high probability of HFpEF according to the HFA-PEFF score, which persisted during follow-up after cardioversion. The limited reverse remodeling of cardiac chambers observed despite maintained sinus rhythm supports the importance of active HFpEF screening in this population to enable early initiation of prognosis-modifying therapies. The stiffness index appears particularly valuable in this context as a potential adjunct to current guideline-recommended diagnostic algorithms for early HFpEF detection.

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Author Contribution

Stavtseva Yu.V., Kobalava Zh.D. – conception and design. Stavtseva Yu.V., Davletova M.A., Timofeeva T.M. – analysis and interpretation of data. Stavtseva Yu.V., Safarova A.F. – justification of the manuscript or critical revision for important intellectual content. Safarova A.F., Kobalava Zh.D. – final approval of the manuscript for publication.

Author Information

Davletova Marianna A. – Postgraduate Student, Assistant, Department of Internal Medicine with the Course of Cardiology and Functional Diagnostics Named after Academician V.S. Moiseev, RUDN University, Moscow, maridavletova@mail.ru, <https://orcid.org/0009-0006-0025-6091>

Stavtseva Yulia V. – Cand. Sci. (Med.), Associate Professor, Department of Internal Medicine with the Course of Cardiology and Functional Diagnostics Named after Academician V.S. Moiseev, RUDN University; Doctor, Cardiology Unit, Vinogradov City Clinical Hospital, RUDN University, Moscow, y.stavtseva@gmail.com, <https://orcid.org/0000-0001-9323-4444>

Safarova Ayten Fuad Kyzy – Dr. Sci. (Med.), Professor, Department of Internal Medicine with the Course of Cardiology and Functional Diagnostics Named after Academician V.S. Moiseev, RUDN University, Moscow, aytensaf@mail.ru, <https://orcid.org/0000-0003-2412-5986>

Timofeeva Tatyana M. – Cand. Sci. (Med.), Assistant, Department of Internal Medicine with the Course of Cardiology and Functional Diagnostics Named after Academician V.S. Moiseev; Doctor, Functional Diagnostics Unit, Vinogradov City Clinical Hospital, RUDN University, Moscow, timtan@bk.ru, <https://orcid.org/0000-0001-6586-7404>

Kobalava Zhanna D. – Dr. Sci. (Med.), Professor, Corresponding Member of the RAS, Head of the Department of Internal Medicine with the Course of Cardiology and Functional Diagnostics Named after Academician V.S. Moiseev, RUDN University, Moscow, zkobalava@mail.ru, <https://orcid.org/0000-0002-873-1768>

(✉) **Davletova Marianna A.**, maridavletova@mail.ru

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