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Determining The Risk of Atrial Fibrillation Paroxysm in Patients With Chronic Heart Failure With Intact and Reduced Ejection Fraction

Aim — To determine predictors for the development of atrial fibrillation (AF) in patients with chronic heart failure (CHF) with preserved and reduced ejection fraction by echocardiography (EchoCG) according to an extended protocol with determination of diastolic function and left atrial global strain.

Material and methods — Data of 168 patients with stage I–III CHF without a history of AF were analyzed. All patients underwent echocardiography according to an extended protocol with the determination of diastolic dysfunction (DD), left atrial ejection fraction (LA EF), and left atrial global strain (LA GS). Tissue Doppler imaging (TDI) was used to evaluate the early (E) and late (A) LV filling velocity and the early (E') and late (A') diastolic mitral annular velocity. In all patients, Holter ECG monitoring (HM ECG) of heart rhythm was performed for 3 days, and ECG monitoring with telemedicine technologies was performed for 7 days, 3 times a day for 3 minutes. The follow-up period was 3 months or until an AF episode.

Results — During the study, paroxysmal AF (pAF) was detected in 41 (24.4%) patients using various methods of heart rhythm monitoring. Complaints of palpitations were noted for 10 (24.4%) patients during pAF, which was recorded using a CardioQVARK® device, HM ECG or a 12-lead ECG. In 5 (12.2%) patients, daily ECG monitoring revealed pAF without associated complaints. HM ECG detected 8, 2, 4 (19.5%, 4.8%, and 9.7%) cases during 24, 48 and 72 hours, respectively; a single-channel CardioQVARK® detected 30 (73.2%) cases when used 3 times a day for 7 days. These results showed that AF frequently develops in CHF without accompanying symptoms. The method for detecting pAF with CardioQVARK® showed good results: it was twice more effective than HM ECG and three times more effective than 12-lead ECG. Also, according to ultrasound data, significant changes in the following parameters were noted in patients with AF: LA EF <36% (OR 1.04, 95% CI: 1.02–1.08), p=0.003; LA GS <9.9% (OR 1.16, 95% CI: 1.02–1.38), p<0.001; TDI E med <5.7 cm/s (OR 0.97, 95% CI: 0.94–1.00), p=0.026. Grade 2 DD did not show statistically significant results (OR 1.1, 95% CI: 0.7–1.5, p=0.54). However, it was detected more frequently in patients with AF, in 34% of cases, compared to 29% of cases in patients without AF, which requires further study on a larger patient sample.

Conclusion — Patients with CHF have a high risk of developing pAF (24.4%). 75% of patients with AF do not feel the development of paroxysm. All CHF patients should undergo EchoCG with assessment of LA EF, TDI E med and LA GS to identify a group at risk for the development of AF. Heart rhythm remote monitoring with CardioQVARK® devices can be considered a reliable method for early detection of pAF and timely initiation of anticoagulant therapy in patients with CHF.

Keywords — Atrial fibrillation; chronic heart failure; telemedicine; myocardial strain; left atrium

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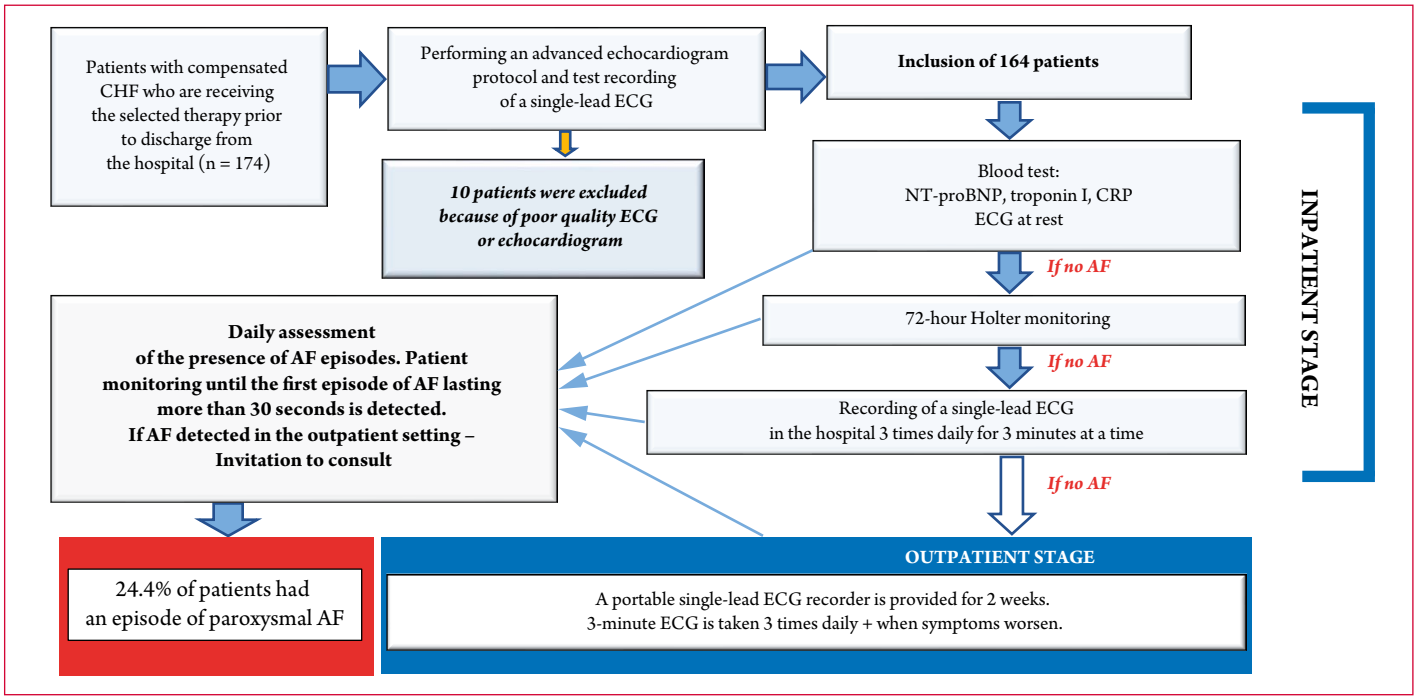
Introduction

Chronic heart failure (CHF) and atrial fibrillation (AF) are two common cardiovascular diseases (CVDs) that together represent a significant socioeconomic problem associated with multiple comorbidities and adverse outcomes [1, 2].

CHF affects 3% of the total population in developed countries, reduces the quality of life of patients and increases the risk of sudden cardiac death [3-6]. 25-49% of patients with CHF are at risk of developing AF, depending on the stage of heart failure and the dimensions of the left atrium (LA) [7].

Central illustration. Determining The Risk of Atrial Fibrillation Paroxysm in Patients With Chronic Heart Failure With Intact and Reduced Ejection Fraction



AF, atrial fibrillation; CHF, chronic heart failure; ECG, electrocardiography; NT-proBNP, N-terminal pro-brain natriuretic peptide; CRP, C-reactive protein.

AF is the most common form of heart arrhythmia [8–12]. It is considered an independent negative prognostic factor in patients with heart failure, increasing the risk of death by 36% compared to those without AF [13–15]. The likelihood of developing AF increases with age, reaching 8–9 % in the elderly population [16]. The pathophysiology of AF and CHF share common risk factors: advanced age, hypertension, diabetes mellitus, structural heart diseases, and coronary artery disease, which cause hemodynamic, electrophysiological, and neurohormonal changes in the myocardium and lead to its remodeling [11, 17, 18].

Given the increasing number of patients with CHF and AF associated with the development of acute care medicine and the aging of the population, there is a growing interest in the search for predictors of the development of AF in patients with CHF, allowing the identification of a risk group for close monitoring of arrhythmias [19].

Patients with CHF develop diastolic dysfunction with an increase in left ventricular (LV) filling pressure, which subsequently leads to LV dilatation. This is associated with an increased risk of developing AF and is a factor in exacerbating the clinical picture in patients with CHF [20–22]. Chronic elevation of pressure in the heart's chambers leads to cardiac remodeling, which causes the progression of AF and CHF [2–24].

LV dilation in response to high pressure leads to disruption of ion channels and myocardial calcium metabolism, which is mainly regulated by ryanodine receptors and sarcoplasmic reticulum calcium ATPase [23, 24]. Neurohumoral activation causes structural remodeling of the heart with the development of interstitial fibrosis of both the atria and ventricles, predisposing patients with CHF to the development of AF by disrupting normal atrial conduction [2, 25].

Verifying AF in patients is relatively simple - a documented ECG protocol recorded during an AF episode is enough to verify AF. [26]. In clinical practice, however, there is an asymptomatic or mildly symptomatic form of AF that goes unnoticed by the patient [27, 28]. Long-term monitoring of heart rhythm with Holter monitors or loop recorders is used to address this problem [26]. Studies are actively underway to determine the efficacy of telemedicine-based long-term rhythm monitoring devices such as smartwatches, smartphones with the appropriate software installed, and single-channel ECG recording devices [29–31].

According to the recommendation of the Russian Society of Cardiology (RSC), patients with CHF are divided into groups according to left ventricular ejection fraction (LVEF) based on echocardiographic findings [17]. In this group of patients, the determination of NT-proBNP and diastolic cardiac function is an important diagnostic step [32–35]. Studies are also underway to determine the relationship between global longitudinal strain (GLS) of the myocardium and various cardiovascular diseases, including AF [36–43].

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Objective

Determine predictors of atrial fibrillation (AF) in patients with chronic heart failure (CHF) with preserved and reduced ejection fraction by echocardiography using an enhanced protocol with determination of diastolic function and global left atrial longitudinal strain.

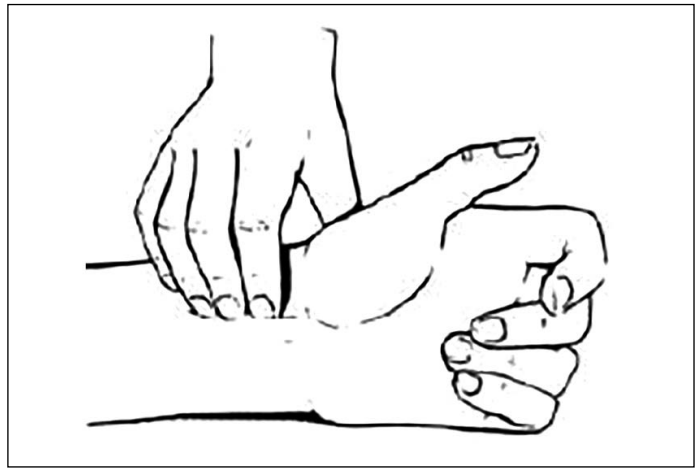
Tasks of the study

Perform echocardiography to determine the dependence of AF development on diastolic dysfunction and globoidal left atrial strain; determine the number of asymptomatic episodes of paroxysmal atrial fibrillation (PAF); compare the effectiveness of Holter monitoring and remote ECG recording with a single-channel portable device in detecting episodes of paroxysmal AF.

Material and methods

The clinical observational cohort study was conducted in the Cardiology Department of Sechenov Training Clinical Hospital No. 1 after approval by the Ethics Committee. A total of 168 patients with CHF of varying degrees were enrolled in the study. All patients had a documented history of CHF and symptoms and signs of its decompensation on admission, according to the RSC clinical guidelines [17]. The stage and functional class of CHF were assessed using classifications according to the guidelines [17]. This was followed by a series of tests including a 12-lead ECG to confirm sinus rhythm, echocardiogram to determine EF, diastolic dysfunction and LA GLS. The patient was trained to detect arrhythmia using the finger method (Figure 1).

Figure 1. Finger method of pulse wave monitoring



Method description: Place the fingers of the right hand around the wrist of the left hand in the area of the wrist joint. Feel the radial artery with fingers II and III. Gently press the artery against the radius and feel for a pulse. Determine pulse rate and rhythm. If an irregular pulse is detected, visit a medical facility or call an ambulance to record the irregular rhythm with a 12-lead ECG and notify the investigator the same day.

During hospital stay, patients were monitored daily with a 12 lead ECG until discharge or detection of PAF. Heart rate was also monitored using 24-, 48-, and 72-hour Holter monitoring to determine the frequency of detection of PAF episodes in patients with CHF. Patients received a CardioQVARK® single-channel remote ECG monitor after the tests. This device is a personal portable ECG recorder in the form of a smartphone case with the necessary software pre-installed. Patient data are entered: sex, height, and weight, then ECG is recorded with analysis of R-R interval, which makes it possible to register PAF. The standard I-lead ECG is recorded with two sensors on which the index fingers of the hands are placed (Figure 2). Patients performed three-minute recordings 3 times a day for 7 days and when there was a worsening/change in their condition or an irregular heartbeat. Experts at the Sechenov University remote monitoring center analyzed the ECG recordings.

Echocardiography was performed according to standard protocol with additional assessment of LA GLS: chamber size and volume, wall thickness, Simpson's EF, assessment of valvular heart apparatus and LV outflow tract velocity time integral (VTI) were determined (normal - over 16 cm) [35, 44].

Determination of GLS by speckle tracking: images were acquired using two-dimensional electrocardiography, images were acquired in three apical views: four-chamber, two-chamber, and three-chamber views with LV, LA, LVOT, and aorta outlined. The endocardial surface was automatically determined, and the degree of deformation was calculated for each myocardial segment, providing a value for the segmental and global change in myocardial thickness. We analyzed 17 LV segments with bull's-eye plotting and further software data analysis [35, 44].

Myocardial diastolic function and degree of deterioration were assessed by echocardiography. For this purpose, tissue Doppler echocardiography (TDI) was used to measure LV early (E) and atrial (A) filling velocities and mitral annular velocity in early diastole (E') and atrial phase (A'). TDI E'<10 cm/s at the LV lateral wall and<8 cm/s at the interventricular septum with an LV volume index>34 mL/m2 was considered a criterion for diastolic dysfunction. The American Society of Cardiology recommendations were used to determine the degree of LV diastolic dysfunction [35, 44].

During the study, patients were divided into two groups: patients with documented CHF and detected AF and CHF patients without AF.

Inclusion criteria were the following (Figure 3):

- Age>18 years;
- Documented CHF;
- Signed informed consent to participate in the study.

Exclusion criteria:

- implanted pacemaker,
- cardiac resynchronization therapy device
- or cardioverter defibrillator;
- History of myocardial infarction
- for up to 6 months;
- History of AF;
- Patients with a history of newly diagnosed cancer for up to 12 months.

Withdrawal criteria:

- Willingness to discontinue participation at any time during the study;
- Failure to follow instructions.

Statistical analysis was performed using the R programming language, version 4.2. The distribution pattern of the quantitative variables was evaluated using the Shapiro–Wilk test. Comparative analysis was performed using Welch's t-test for normally distributed quantitative variables (2 groups) and Mann–Whitney U-test for non-normally distributed quantitative variables (2 groups).

Regression analysis with univariate equations was used to assess the influence of factors on outcomes. Significant factors were included in a single multivariate regression equation to find independent endpoint predictors using a stepwise factor selection procedure. The quality of the final model was assessed using ROC analysis with calculation of the area under the curve; sensitivity, specificity, positive and negative predictive values were calculated for the optimal Youden index cut-off point.

Results

A total of 168 patients admitted to the cardiology department with decompensated pre-existing CHF were enrolled in the clinical cohort study. Dyspnea during exercise or at rest, edema of the lower extremities, and decreased exercise tolerance were the most common complaints. On examination, all patients met the study criteria: pulmonary rales, edema of the lower 1/3 of the leg, dilated jugular veins, documented diagnosis of CHF [17]. Patients were between 48 and 86 years of age, had no history of AF, 83 were female and 85 were male. Body mass index was 25.2 ± 6.0. All patients received conventional CHF therapy [17]. At examination, 124 (73.8 %) patients were diagnosed with stage IIA or IIB CHF and 35 (20.8 %) with stage III CHF. Medical history included diabetes mellitus in 23.7 % of patients, hypertension in 90.2 %, myocardial infarction in 30.4 %, and coronary artery disease (CAD) in 62.8 %.

During the study, PAF was detected in 41 (24.4 %) patients using various rhythm monitoring techniques. Only 10 patients noted the onset of palpitations, increasing dyspnea, consistent with PAF recorded by 12 lead ECG,

Figure 2. Recording an electrocardiogram with CardioQVARK®, designed as a smartphone case

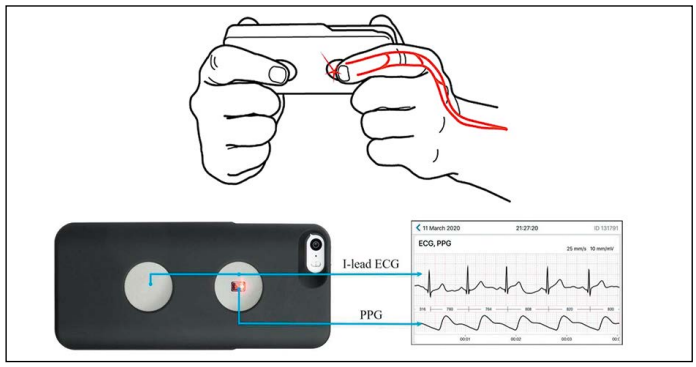
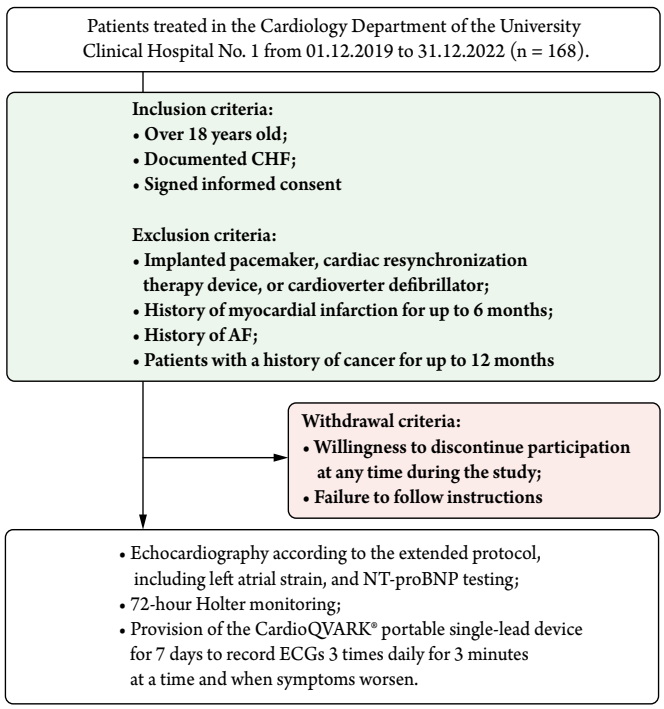


Figure 3. Patient enrollment plan



CHF, chronic heart failure; AF, atrial fibrillation; ECG, electrocardiography; NT-proBNP, N-terminal pro-brain natriuretic peptide.

Figure 4. Paroxysmal AF episode recorded with the CardioQVARK® device

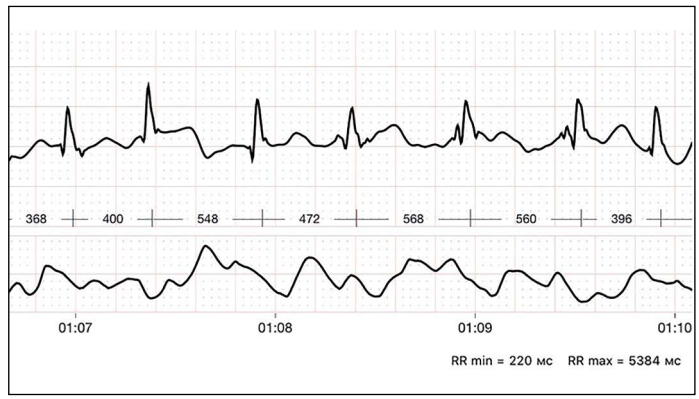


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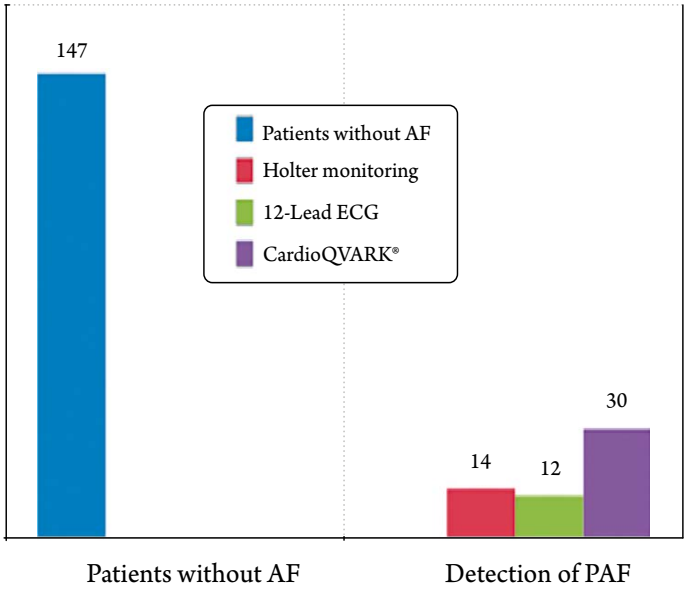
Figure 5. Frequency of AF detection by different methods; there is a recurrence of AF detection by different examination methods



AF, atrial fibrillation; ECG, electrocardiography; PAF, paroxysmal atrial fibrillation.

Holter monitoring, or the CardioQVARK® single-lead device (Figure 4).

Using 24-, 48-, and 72-hour Holter monitoring, 8, 2, and 4 (19.5 %, 4.8 %, and 9.7 %) cases were detected, respectively, for a total of 14 (34.1 %) cases; using the CardioQVARK® single-lead device 3 times daily for 7 days, 30 (73.2 %) cases were detected; 12-lead ECG detected PAF in 10 (24.4 %) patients (Figure 5).

These results suggest that there is a high prevalence of asymptomatic AF. Only 24.4% of patients reported experiencing symptoms of palpitations or worsening dyspnea during the study.

The CardioQVARK® device had good results in the detection of PAF. Specifically, the single-lead device was 2 times more effective than Holter monitoring and 3 times more effective than 12 lead ECG.

The study included 20 (11.9 %) patients with reduced LVEF, 41 (24.4 %) patients with mid-range LVEF and 107 (63.7 %) patients with preserved LVEF. Data analysis revealed that 26 (24.2 %) of 107 patients with preserved EF had paroxysmal AF, representing 63.4% of all patients with known AF. AF was detected in 9 (21.9 %) of 41 patients with mid-range EF, representing 21.9% of all patients with AF. PAF was detected in 6 (30%) of 20 patients with reduced EF, representing 14% of the sample of patients with known AF (Table 1).

Diastolic dysfunction was detected in 94 (55.9%) patients, including 50 (29.8 %) with preserved LVEF, 30 (17.9 %) with mid-range LVEF, and 14 (8.3 %) with reduced LVEF.

The diagnosis of CHF was confirmed in patients with preserved LVEF and without diastolic dysfunction by a level of NT-proBNP>125 pg/mL or the presence of myocardial hypertrophy confirmed by echocardiography.

PAF was found in 26 of the 94 patients with impaired diastolic function, which corresponds to 27.7 % of the patients. Among them, 12 patients had grade 1 diastolic dysfunction and 14 patients had grade 2 diastolic dysfunction.

Grade 2 diastolic dysfunction was detected in 51 of 168 patients: 14 patients with AF (34.1 % of the total sample of patients with AF) and 37 patients without AF (29.1 % of the total sample of CHF patients without AF) (OR 1.4, 95 % CI: 0.8–1.8), p=0.54; LVEF<36 % was detected statistically significantly more often in patients with PAF (OR 1.24, 95 % CI: 1.02–1.48), p=0.003; LA GLS<9.9 % was statistically significantly more frequent in patients with PAF (OR 1.16, 95 % CI: 1.02–1.38), p<0.001; TDI E med<5.7 cm/s was more frequent in patients with paroxysmal AF (OR 1.27, 95 % CI: 1.04–1.82; p=0.026) (Table 2).

A composite prediction model was constructed from the obtained thresholds of echocardiographic indicators associated with PAF: LAEF<36 %, OR 1.24, 95 % CI: 1.02–1.48, p=0,003; LV GLS<9.9 %, OR 1.16, 95 % CI: 1.02–1.38), p<0.001; TDI E med <5.7 cm/s, OR 1.27, 95 % CI: 1.04 – 1.82, p=0.026. Diastolic dysfunction grade 2 (OR 1.1, 95 % CI: 0.7–1.5, p=0,54) was also included in the model to improve its quality. Blood test results were not included in the multivariate model due to a non normal distribution of indicators.

The predictive value of the model is quite high, 94 % for a negative outcome and 72 % for a positive outcome (Table 3), which is confirmed by the ROC analysis. The area under the curve (AUC) was 0.88 (Figure 6).

Discussion

Currently, the problem of identifying AF risk factors in patients with CHF remains relevant. The number of patients with CHF and AF tends to increase every year [13]. The data obtained on the incidence of AF and the number of asymptomatic cases is consistent with global statistics [28, 45]. This suggests that the issue needs to be addressed more vigorously and that reliable methods to detect PAF in this population need to be developed.

This study confirms the predictive properties of echocardiography, particularly speckle tracking in assessing CVD progression [46]. Abnormal LV GLS is associated with myocardial hypertrophy in patients with hypertension and also increases the risk of CAD, decompensated CHF, and cardiac arrest [47]. The 2022 study found that decreased LV GLS in patients with cardiomyopathies of various origins is a predictor of an adverse arrhythmic event [48].

According to our findings, reduced LV GLS increases the risk of developing AF in patients with CHF independent of LVEF.

Clinical practice is increasingly turning to technologies that allow remote monitoring of a patient's health. There was a great demand for such technologies during the Covid-19 pandemic [49]. According to the study results, cardiac rhythm monitoring devices significantly increase the detection rate of cardiac dysfunction and are suitable screening methods for patients with cardiovascular pathology [29–31]. Some conditions are already included in the RSC for monitoring heart rhythm in patients at increased risk of developing AF [17].

This study demonstrates the advantages of the CardioQVARK® portable device over standard cardiac rhythm monitoring methods.

The CardioQVARK® single-lead device detected PAF 2 times more frequently than Holter monitoring and 3 times more frequently than 12-lead ECG. This is explained by the fact that the ECG recording was longer when using a portable device, and therefore the likelihood of detecting asymptomatic PAF was higher. PAF was most commonly detected on day 4.3 after hospital discharge and was likely associated with the omission of prescribed therapy and the resumption of the daily routine.

It is worth noting that the use of the CardioQVARK® portable device by a patient is an easy and reliable way to identify paroxysmal AF. This method eliminates the need to visit a healthcare facility to detect PAF and allows for long-term monitoring without invasive or inconvenient wearable devices.

Figure 6. ROC curve for the composite prediction model

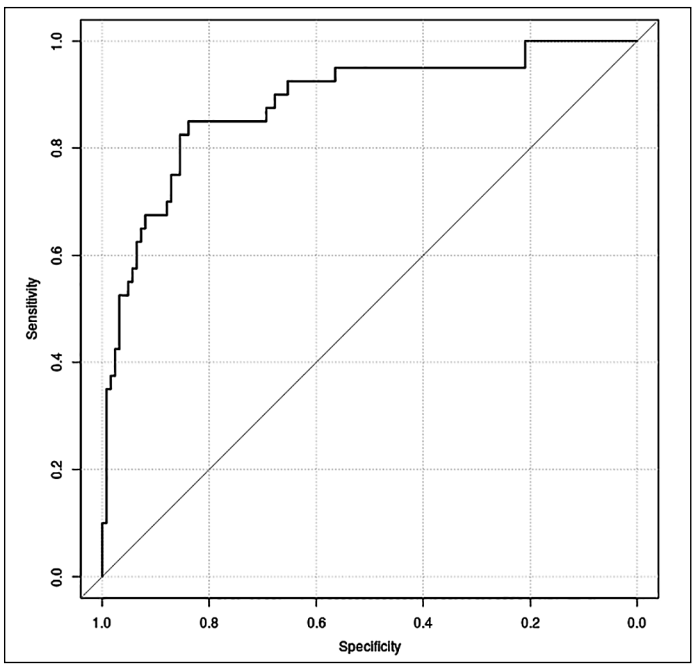


Table 1. Distribution of patients into subgroups by LVEF

Group characteristics	EF>50 %	EF 40–49 %	EF<40 %
Number	107	41	20
Patients with AF, n (%)	26 (24.2)	9 (21.9)	6 (30)
Diastolic dysfunction			
Total, n (%)	50 (46.7)	30 (73)	14 (70)
Grade 1	21 (19.6)	8 (19.5)	2 (10)
Grade 2	24 (22.4)	18 (43.9)	8 (40)
Grade 3	5 (4.6)	4 (9.7)	4 (20)

Data are presented as number of patients (n (%));
AF, atrial fibrillation; EF, ejection fraction.

Table 2. Comparative characteristics of patients with and without AF

Comparative characteristics	Patients without AF, n=127	Patients with AF, n=41	(p)
Age, years	65.4 ± 9.3	65.8 ± 9.3	0.992
Creatinine, μg/mL	98.75 ± 35.25	110.63 ± 42.66	0.036
Potassium, μmol/L	4.5 ± 0.7	4.5 ± 0.8	0.948
Hb, g/L	131.6 ± 16.9	128.7 ± 20.2	0.427
NT-proBNP, pg/mL	469.67 ± 354.65	1057 ± 548.54	0.009
LVEF, %	53.3 ± 11.1	53.7 ± 13.2	0.761
LV GLS, %	17.1 ± 4.3	15.1 ± 3.6	0.006
LVEF, %	38.9 ± 7.1	35.7 ± 7.9	0.003
LA GLS, %	11.4 ± 1.8	9.9 ± 1.8	< 0.001
A VTI, cm	17.0 ± 4.9	16.7 ± 6.1	0.506
TDI E med, cm/s	6.3 ± 1.9	5.7 ± 1.9	0.026
TDI E lat, cm/s	8.3 ± 2.1	7.8 ± 2.4	0.058
TDI A, cm/s	9.0 ± 1.5	8.4 ± 1.3	0.016
Diastolic dysfunction grade 2	29.1 %	34.1 %	0.54

AF, atrial fibrillation; Hb, hemoglobin; LVEF, left ventricular ejection fraction; LAEF, left atrial ejection fraction; LV GLS, left ventricular global longitudinal strain; LA GLS, left atrial global longitudinal strain; NT-proBNP, N-terminal pro-brain natriuretic peptide; A VTI, left ventricular outflow tract velocity time integral; TDI E med, early diastolic septal mitral annular velocity; TDI E lat, early diastolic lateral mitral annular velocity; TDI A, late diastolic mitral annular velocity

Table 3. ROC curve indicators

Parameter	Point estimate, 95 % CI
AUC	0.88 [0.81; 0.95]
Se	0.86 [0.73; 0.95]
Sp	0.86 [0.76; 0.93]
NPV	0.94 [0.90; 0.98]
PPV	0.72 [0.53; 0.78]

AUC, area under curve; Se, sensitivity; Sp, specificity;
PPV, positive prognostic value; NPV, negative prognostic value.

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The obtained results allow us to say that it is necessary during echocardiography in patients with CHF to determine LAEF, LV GLS and TDI E to determine the group with increased risk of developing AF. Long-term telemedicine ECG monitoring is required in this group. The role of grade 2 diastolic dysfunction in assessing the risk of developing AF requires further study in a larger sample of patients.

Conclusions

The study in the group of patients with CHF showed an increased risk of developing PAF when the following characteristics were combined: LAEF<36 %, TDI E med <5.7 cm/s and LA GLS<9.9 %, which can be considered as predictors of AF in patients with CHF and which is confirmed by statistical analysis.

In patients with CHF, the CardioQVARK® single-lead device is the preferred method for assessing rhythm with 7-day ECG monitoring. This method has proven superior to Holter monitoring and routine 12-lead ECG because it is easy for the patient to use and allows for unlimited long-term use.

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