Hüseyin Aykaç , Cihan Aydın, Aykut Demirkıran, Nurullah Uslu, Şeref Alpsoy
Tekirdağ Namık Kemal University, Department of Cardiology, Faculty of Medicine, Tekirdağ, Turkey

Natriuretic Peptide Concentrations and Echocardiography Findings in Patients with Micro-atrial Fibrillation

Aim	Atrial fibrillation (AF) is a rhythm disorder characterized by very rapid and disorganized atrial-derived electrical activations with uncoordinated atrial contractions. Very short periods of AF-like activity (micro-AF) may be precursors of undetected, silent episodes of atrial fibrillation. Here, we examined the relationship between natriuretic peptide concentrations and echocardiography findings in patients with micro-AF.
Material and methods	The electrocardiograms (ECGs) of patients complaining of palpitations were recorded with a 24-hour Holter monitor, and the patients were consecutively included in the study. Micro-AF was defined as sudden, irregular atrial tachycardia lasting less than 30 sec with episodes of ≥5 consecutive supraventricular depolarizations with the absolute absence of p-waves. After a G-power test, patients were consecutively included in the study: 45 patients in the micro-AF group and 45 patients in the control group. Laboratory parameters, ECG and echocardiographic findings of the two groups were compared.
Results	N-terminal pro B-type natriuretic peptide (Pro-BNP) and serum troponin T concentrations were higher in the micro-AF group, (375.5±63.6 pg/ml vs. 63.1±56.8 pg/ml, p<0.001; 13±11.4 ng/dl vs. 4.4±2.4 ng/dl, p<0.001 respectively.) Each 1 pg/ml increase in serum Pro-BNP increased the risk of micro-AF by 1.8%. In the ROC analysis, the cut-off value of Pro-BNP for the diagnosis of micro-AF was 63.4 pg/ml, with a sensitivity of 91.1% and a specificity of 73.3%. Atrial electro-mechanical delay durations were significantly higher in the micro-AF group. To predict micro-AF, the inter-annulus plane electromechanical delay time (inter-annulus plane AEMD) had a cut-off value of 18.5 sec, with a sensitivity of 93.3% and a specificity of 91.1%. Left intra-annulus plane electro-mechanical delay time (intra-annulus AEMD LEFT) had a cut-off value of 11.5 sec with a 95.6% sensitivity and 75.6% specificity. In the ECG evaluation, maximum P wave duration (Pmax) (113.±10.2 ms vs. 98±10.4 ms; p<0.001), minimum P wave duration (Pmin) (73.8±5.5 ms vs.70±6.3 ms; p<0.001) and P wave dispersion (PWD) (39.1±7.9 ms vs.28±7.6 ms; p<0.001) were longer in the micro-AF group.
Conclusions	Micro-AF in patients may be predicted by evaluating ECG, echocardiographic, and serum natriuretic peptide data.

Keywords	Atrial fibrillation; micro-atrial fibrillation; atrial electro-mechanical delay time; electrocardiography; natriuretic peptide
For citations	Hüseyin Aykaç , Cihan Aydın, Aykut Demirkıran, Nurullah Uslu, Şeref Alpsoy. Natriuretic Peptide Concentrations and Echocardiography Findings in Patients With Micro-atrial Fibrillation. Kardiologiia. 2024;64(8):56–63. [Russian: Хусейн Айкач, Джихан Айдын, Айкут Демиркыран, Нурулла Услу, Шереф Алпсой. Концентрация натрийуретических пептидов и данные эхокардиографии у пациентов с микро-фибрилляцией предсердий. Кардиология. 2024;64(8):56–63].

Corresponding author	Cihan Aydın. E-mail: drcihanaydin@hotmail.com

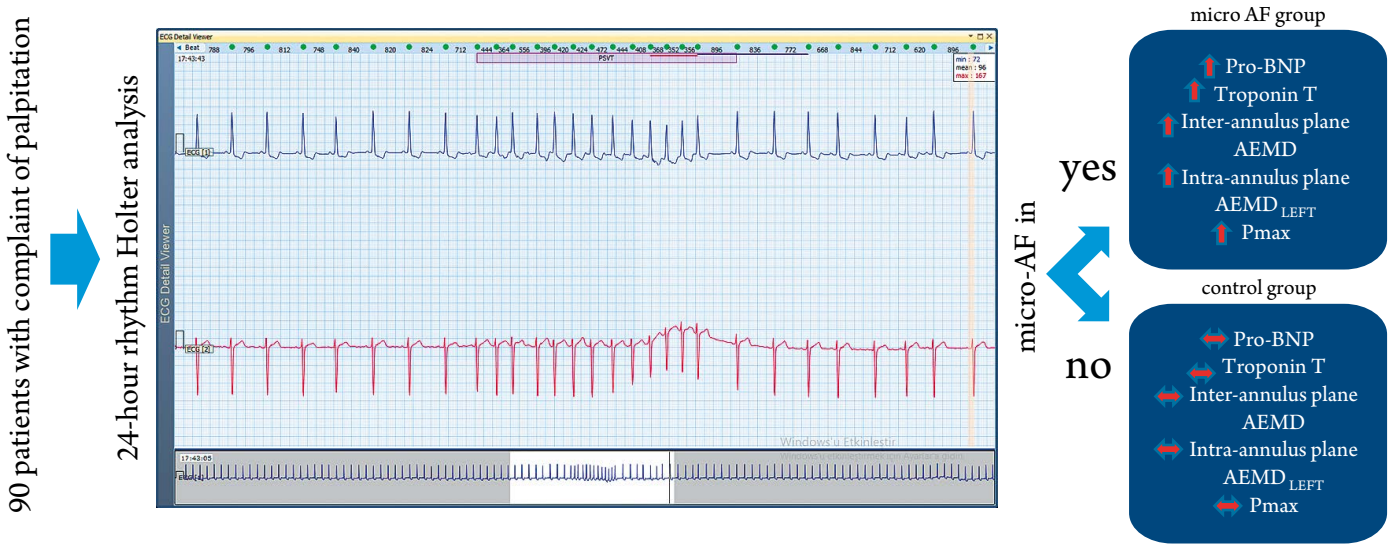
Introduction

Atrial fibrillation (AF) is a cardiac rhythm disorder characterized by very rapid and irregular depolarizations of the atria and irregular activation of the ventricles [1]. Surface electrocardiography (ECG) shows irregular R-R intervals (when atrioventricular conduction is not impaired), absence of prominent, repetitive P waves, and irregular, fast AF waves [2]. AF is the most common rhythm disorder in clinical practice [3]. While AF is seen in 3% of adults, this rate increases to 4.8–17% in the elderly and up to 79% in mitral valve patients [4]. As the elderly population increases, the total number of patients diagnosed with AF also increases. Clinically, symptomatic or asymptomatic AF is documented by ECG. The minimum duration of ECG monitoring required to make a clinical diagnosis of AF is at least 30 sec or the entire 12-lead ECG.

Atrial fibrillation is common in patients with hypertensive heart disease and coronary artery disease. In developing countries, the frequency of AF has increased due to the increased incidence of rheumatic mitral valve disease [4]. Heart failure, acute myocardial infarction, cardiomyopathies, myocarditis, congenital heart disease, post-cardiac surgery, and Wolf Parkinson – White Syndrome are other cardiac conditions that increase the frequency of AF [5]. Advanced

ISSN 0022-9040. Кардиология. 2024;64(8). DOI: 10.18087/cardio.2024.8.n2633

Central illustration. Natriuretic Peptide Concentrations and Echocardiography Findings in Patients with Micro-atrial Fibrillation



patient age, excessive alcohol consumption, diabetes mellitus (DM), obesity, chronic kidney failure, hyperthyroidism, chronic obstructive pulmonary diseases, sleep apnea syndrome, smoking, and genetic factors are non-cardiac factors that increase the frequency of AF [6]. Micro-AF is observed as brief, rapid, irregular atrial activity on ECG or rhythm recorders. Micro-AF describes the abrupt onset of irregular tachycardia attacks with ≥5 consecutive episodes of supraventricular beats lasting less than 30 sec that do not meet the criteria for clinical definition of AF and with complete absence of P waves.

In a long-term, randomized, controlled atrial fibrillation screening study conducted in Sweden, the risk of developing AF was higher patients with micro-AF than in those without micro-AF [7]. When patients with and without micro-AF (the subgroups of the STROKESTOP trial [7]), were recalled after two weeks of follow-up, AF was observed in 26 of 196 patients in the micro-AF group and only in 7 out of 250 patients in the control group [8]. Otherwise healthy patients with supraventricular tachycardia attacks longer than 20 beats and supraventricular ectopic beats greater than 30 beats per hour were followed for an average of 6.3 years in healthy individuals by Binici et al [9]. Compared to the control group, patients with supraventricular tachycardia or supraventricular ectopic beats had an increased frequency of atrial fibrillation and stroke.

In the current cardiology guidelines, there are no clear recommendations for the management of patients with micro-AF. All the cited studies show the importance of early recognition of micro-AF patients and starting anticoagulant and antiarrhythmic treatment to preventing stroke due to atrial fibrillation. In many studies, prolonged inter-annulus plane electromechanical delay time (AEMD) durations and increased natriuretic peptide concentrations were found in patients with AF [10]. However, there are few studies in the literature on patients with micro-AF. In this study, we aimed to examine the relationship between natriuretic peptide concentrations and echocardiographic findings in patients with micro-AF.

Material and methods

Study population

Patients who presented to the Cardiology Polyclinic of Tekirdağ Namık Kemal University Hospital between June 2021 and October 2022 with the complaint of palpitation and were fitted with a 24-hour rhythm Holter monitor and were consecutively included in the study. A G-power analysis indicated that there should be 45 patients in the micro-AF group and 45 patients in the control group.

Following 24-hour rhythm Holter analysis, patients with micro-AF were included in Group 1, and patients with no supraventricular tachycardia attacks in their Holter records were included in Group 2, the control group. The study was conducted according to the principles outlined in the Declaration of Helsinki and approved by the local ethics committee.

Patients included in the study were over 18 yrs of age, without heart failure or heart valve disease, and were diagnosed with micro-AF following 24-hour rhythm Holter monitoring. Patients who were diagnosed with paroxysmal AF following Holter monitoring, who used oral anticoagulants or warfarin before monitoring, and patients with structural valve disease, heart failure, thyroid hormone disorder, or severe coronary artery disease were excluded from the study. The medical histories of all patients included in the study were recorded, including their age, gender,

presence of hypertension, DM, peripheral artery disease, previous history of coronary artery disease, or previous history of cerebrovascular disease.

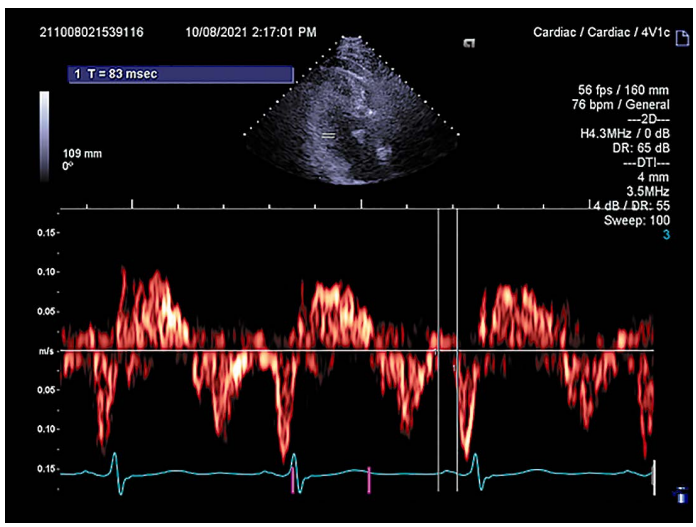
Detailed physical examinations were performed. The BMI was calculated by dividing weight in kilograms by height in metres squared. ECG and echocardiography was performed on all patients. All blood samples were taken after a 12 hr fast following the Holter monitoring..

The presence of hypertension was defined as systolic blood pressure >140 mmHg or diastolic blood pressure >90 mmHg, or by the patient using blood pressure- lowering medication. The presence of DM was defined as a fasting blood glucose level of 126 mg/dl, a spot blood glucose level of 200 mg/dl, and/or using oral antidiabetic medication and/or insulin. The presence of peripheral artery disease was defined as the presence of plaque in an artery other than the coronary arteries, with or without stenosis, as identified by an imaging method. The presence of coronary artery disease was defined by imaging coronary disease by invasive coronary angiography or by coronary computed tomography angiography. The history of cerebrovascular disease was defined as the presence of a previously diagnosed transient ischemic attack, stroke, or intracranial hemorrhage.

Transthrocacic Echocardiography

Echocardiography was performed on all patients in the lateral decubitus position with a Siemens Acuson SC2000 echocardiography device (Siemens Medical Solutions USA, Inc.) with single-lead ECG monitoring. For the tissue Doppler echocardiographic examination, a transducer with a frequency of 3.5–4.0 MHz was used. The monitor flow velocity was set to 50–100 mm/sec. In an apical 4-chamber view, a 3 mm sample volume pulse wave Doppler was positioned at the mitral leaflet tips, and the peak E and A waves were measured. Tissue Doppler imaging (TDI) was performed in the apical 4-chamber view at the septal and lateral mitral, tricuspid valve annulus, and atrial walls. The time interval between the start of the P wave on the ECG to the start of the late diastolic wave (Am) was assessed for atrial electromechanical delay (AEMD) from the atrial wall and valve annulus levels (Figure 1). AEMD durations were identified as follows: lateral mitral annulus (mitral lateral AEMD), medial mitral annulus (mitral medial AEMD), lateral tricuspid annulus (tricuspid lateral AEMD), lateral left atrium wall (LA lateral AEMD), interatrial septum (LA medial AEMD) and lateral right atrium wall (RA lateral AEMD).

Figure 1. Measuring left atrium lateral wall atrial electromechanical delay (83 ms) by echocardiography with accompanied by electrocardiography monitoring



The differences between the following time intervals, respectively, were expressed as: inter-atrial electromechanical delay time (inter-AEMD) = LA lateral wall AEMD – RA lateral wall AEMD. Inter-annulus plane electromechanical delay time (inter-annulus plane AEMD) =mitral lateral AEMD – tricuspid lateral AEMD. Left intra-atrial electromechanical delay time (intra-AEMD LEFT) =LA lateral wall AEMD–LA medial wall AEMD. Left intra-annulus plane electromechanical delay time (intra-annulus AEMD LEFT) = mitral lateral AEMD – mitral medial AEMD. Right intra-atrial electromechanical delay time (intra-AEMDRIGHT) = LA medial wall AEMD – RA lateral wall AEMD. Right intra-annulus plane electromechanical delay time (intra-annulus AEMDRIGHT) = mitral medial annulus AEMD – tricuspid lateral annulus AEMD.

Measurement of P-wave duration and P-wave dispersion

12 lead ECGs of all patients were taken in the supine position (EDAN SE-601 PC ECG system, EDAN Instruments, Inc., China). ECG recording speed was standardized as 50 mm/sec and amplitude as 20 mm/mV. Measurement values were calculated by taking the average of three consecutive waves recorded in each lead. The point where the P wave left the isoelectric line of the first deflection and intersected with the isoelectric line again was accepted as the duration of the P wave. The maximum P wave duration (Pmax) was measured as the duration of the longest P wave in any of the 12 leads, and the minimum P wave duration (Pmin) was measured as the shortest P wave duration in any of the 12 leads. The time between Pmax and Pmin was recorded as P wave dispersion (PWD).

Statistical Analysis

All patient data were analyzed using the SPSS 27.0 statistics package (SPSS Inc, Chicago, III, USA). Continuous variables with a normal distribution are reported as mean±standard deviation (SD), and non-normally distributed continuous variables are presented as median (interquartile range [IQR])) Categorical variables are

ISSN 0022-9040. Кардиология. 2024;64(8). DOI: 10.18087/cardio.2024.8.n2633

reported as percentages and numbers. The student's t-test was used to compare means of normally distributed data, and the Mann-Whitney U test was to compare non-normally distributed data. Categorical variables were compared using the Chi-square test or Fisher's exact test as appropriate. Univariate and multivariate logistic regression analyses were used to determine significant factors affecting micro-AF status. The sensitivity and specificity of the Pro-BN levels and the AEMD durations to predict micro-AF were analyzed by receiver operating characteristics (ROC) analysis. Pearson statistical correlation analysis was performed to evaluate the relationship between LA diameter and inter-annulus plane AEMD. P values less than 0.05 were considered significant.

Results

This prospective study enrolled a total of 90 consecutive patients. Baseline characteristics of the patients are summarized in Table 1. In Group 1, stroke rates and CHA2DS2-VASc scores were significantly higher [11]. Pro-BNP and troponin T were significantly higher in group 1 (375.5±63.6 pg/ml vs. 63.1±56.8 pg/ml, p<0.001; 13±11.4 ng/dl vs. 4.4±2.4 ng/dl, p<0.001), respectively. There was no difference between the two groups in terms of other demographic data and biochemical parameters. B-blocker use was higher in Group 1.

Electrocardiographic examinations showed that the maximum and minimum durations of the p wave and the dispersion of the p wave were longer in Group 1 (Table 2). Echocardiographic examinations showed that the LA diameters were larger and that the durations measured by tissue Doppler from the valve annulus and atrial walls were longer in Group 1. Also, in Group 1, tissue Doppler measurements from all regions showing diastolic dysfunction had low e' wave and high E/e' ratios (Table 3).

In the ROC analysis the inter-annulus plane AEMD predicted micro-AF with a cut-off value of 18.5 ms with a sensitivity of 93.3% and a specificity of 91.1% (area under the curve (AUC) =0.977; 95% confidence interval (CI) 0.953–1.000, p<0.001). The left intra-annulus plane electromechanical delay time (intra-annulus AEMD LEFT) predicted micro-AF with a cut-off value of 11.5 ms and a 95.6% sensitivity and 75.6% specificity (AUC=0.921; 95% CI 0.866–0.976, p<0.001). The ROC analysis of Pro-BNP and P max values for predicting micro-AF were as follows: Pro-BNP cut-off ≥63.4 pg/ml, AUC: 0.860; 95% CI (0.783–0.936) with 91.1% sensitivity and 73.3% specificity, p<0.001; P max cut-off ≥102.5 ms, AUC: 0.852; 95% CI (0.773–0.931)) with 80% sensitivity and 73.3% specificity, p<0.001.

When the P max value increased by 1 ms, the risk of micro-AF increased by 15.7% (odds ratio (OR) = 1.1595% CI (1.086–1.231). When the PRO-BNP value increased by 1 unit, the risk of micro-AF increased by 1.8% (OR=1.01; 95% CI (1.009–1.028). In the micro-AF group, a positive, weak, and statistically significant correlation was found between LA diameter and inter-annulus plane AEMD (r=0.324; p=0.030). In multivariate logistic regression analysis, LA, P max, Pro-BNP, intra-annulus plane AEMD RIGHT were independent predictors of micro-AF, (OR=2.62; 95% CI (1.490–4.628), p=0.001; OR=1.29; 95% CI (1.107–1.522), p=0.001; OR=0.97; 95% CI (0.963–0.993), p=0.004; OR=0.79; 95% CI (0.664–0.945, p=0.01, respectively.

Table 1. Baseline characteristics of the study participants

Characteristic	Group 1, Micro-AF	Group 2, Control	p value
Age (yrs)	62.8±8.2	60.3±10	0.273
Body mass index (kg/m²)	29.7±4.3	28.7±5.1	0.228
Male	22 (48.9)	23 (51.1)	0.833
Diabetes	13 (28.9)	12 (26.7)	0.814
Hypertension	34 (75.6)	28 (62.2)	0.172
Coronary artery disease	8 (17.8)	9 (20)	0.788
Stroke	23 (51.1)	6 (13.3)	<0.001
CHA2DS2-VASc Score	3 (0-6)	2 (0-6)	0.004
Laboratory parameters			
Creatinine (mg/dl)	0.8±0.2	0.7±0.1	0.390
Hemoglobin(g/dl)	13.3±1.5	13.5± 1.7	0.125
Pro-BNP(pg/ml)	375.5±63.6	63.1±56.8	<0.001
ANP(ng/ml)	160.1±8.4	152±7.9	0.789
Troponin T(ng/dl)	13±11.4	4.4±2.4	<0.001
CRP(mg/l)	3.02±2.6	4.2±13.1	0.190
TSH	1.52±1.15	1.81±0.94	0.071
Medication use			
ACEI	9 (20)	16 (35.6)	0.099
ARB	20 (44.4)	11 (29.3)	0.076
βeta-Blocker	23 (51.1)	9 (20)	0.002
Ca–channel blocker	9 (20)	10 (22.2)	0.796
Diuretic	22 (48.9)	13 (28.9)	0.052
Oral antidiabetic	13 (28.9)	11 (24.4)	0.634
Insulin	6 (13.3)	3 (6.7)	0.292
Statin	13 (28.9)	9 (20)	0.327

Data are mean±SD or number (percent). ACE-I, angiotensin-converting enzyme inhibitors, ARB, angiotensin receptor blocker; TSH, thyroid stimulating hormone; Pro-BNP, B-type natriuretic peptide precursor, ANP; atrial natriuretic peptide.

Discussion

The results of this study showed that, while troponin T, Pro-BNP levels were higher in the micro-AF group, Pmax, Pmin, and PWD durations were longer. In the echocardiographic evaluation, LA diameters were larger and electromechanical delay times were longer in all foci of the tissue Doppler, and stroke rate was more frequent in the micro-AF group.

Table 2. Comparison of electrocardiographic and echocardiographic data

Variable	Group 1, Micro-AF	Group 2, Control	p value
Pmax (ms)	113±10.2	98±10.4	<0.001
Pmin (ms)	73.8±5.5	70±6.3	0.009
PWD (ms)	39.1±7.9	28±7.6	<0.001
LVEF (%)	61.6±4.8	61.5±5	0.934
LA (mm)	35.9±1.3	34.6±1.7	<0.001
E (cm/s)	0.76±0.1	0.74±0.1	0.683
Mitral lateral AEMD (ms)	108.4±9.6	89±6.5	<0.001
Mitral medial AEMD (ms)	92.4±7.9	79.1±6.7	<0.001
Tricuspid lateral AEMD (ms)	82.7±6.7	74.8±6.5	<0.001
LA lateral AEMD (ms)	98.7±7.9	83.6±6.1	<0.001
LA medial AEMD (ms)	85.3±6.4	75.5±6.	<0.001
RA lateral AEMD (ms)	76.9±6	70.7±6.25	<0.001
Inter-AEMD (ms)	22±5.9	12.7±3	<0.001
Inter-annulus plane AEMD (ms)	25.8±5.6	14.1±3.3	<0.001
Intra-AEMD LEFT (ms)	13.9±5.3	8.1±2.4	<0.001
Intra-annulus plane AEMD LEFT (ms)	16±3.6	9.8±2.7	<0.001
Intra-AEMDRIGHT (ms)	8.1±2.9	4.6±1.5	<0.001
Intra-annulus plane AEMDRIGHT (ms)	9.6±3.1	4.3±1.3	<0.001

Data are mean±SD. LA, left atrium;
RA, right atrium; AEMD, atrial electromechanical delay.

Table 3. Univariate and multivariate logistic regression analysis of the independent predictors of micro-AF

Variable	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p value	OR (95% CI)	p value
Pmax (ms)	1.15 (1.086-1.231)	<0.001	1.29 (1.107-1.522)	0.001
Pmin (ms)	1.11 (1.035-1.206)	0.005	0.79 (0.627-1.010)	0.06
PWD (ms)	1.20 (1.111-1.296)	<0.001	1.09 (0.968-1.232)	0.152
Left atrium (mm)	1.79 (1.285-2.495)	0.001	2.62 (1.490-4.628)	0.001
A (cm/s)	30.25 (1.708-536.116)	0.020	22.39 (0.04-32.042)	0.332
Pro-BNP (pg/ml)	1.01 (1.009-1.028)	<0.001	0.97 (0.963-0.993)	0.004
Intra-annulus plane AEMDRIGHT (ms)	5.98 (2.550-14.05)	<0.001	0.79 (0.664-0.945)	0.01

OR, odds ratio; CI, confidence interval;
AEMD, atrial electromechanical delay.

The term micro-AF, as used in this study, refers to ≥5 consecutive episodes of supraventricular beats during less than 30 sn and sudden onset, irregular atrial activity with the complete absence of P waves in ECG or rhythm recording devices. Current guidelines do not include clear treatment recommendations for micro-AF, so treatment recommendations for this patient group have remained at the level of expert opinion. When these patients were followed up for a long time, it was observed that permanent AF developed more frequently than healthy people [12]. Thus, it is important to find ways to early detect additional risk factors for the development of AF in these patients along with long-term follow-up by comparing AF patients with the healthy population. The present prospective study addressed this problem by investigating natriuretic peptide concentrations and echocardiography findings in patients with micro-AF.

Although atrial fibrillation is more common in men in all age groups, the number of men and women with atrial fibrillation is equal [12]. In our study, the patient group (n=45) consisted of 23 females (51.1%) and 22 males (48.9%) There was no significant difference in terms of gender in the micro-AF and control groups. Apart from stroke, the groups were similar in terms of other risk factors. The reason why CHA2DS2-VASc scores were higher in Group 1 in our study was that the number of patients who had a stroke was higher in the micro-AF group. The two groups were similar in terms of other risk factors. While 23 patients (51.1%) in the micro-AF group had a history of previous ischemic stroke, 6 patients (13.3%) in the control group had a history of previous ischemic stroke.

Pro-BNP is a biomarker of volume overload and myocardial distension. Pro-BNP plays an important role in cardiovascular remodeling, volume homeostasis, and ischemia response. Previous studies have described the relationship between circulating NT-pro BNP and the risk of developing AF, and, thus, provided evidence of the value of NT-pro -BNP measurements to predict AF [10].

In a study by Richards et al, patients with AF were found to have a statistically significant increase in Pro-BN when compared to patients without AF and patients with AF at Pro-BNP in patients who presented to the emergency department with shortness of breath (p<0.001) [10]. In another study by Ellinor et al., when 150 patients with AF alone were compared with the control group, Pro-BNP concentrations were found to be significantly higher in patients with AF (166 vs. 133 fmol/ml, p=0.003) [13, 14].

Atrial natriuretic peptide (ANP) is a cardiac hormone with pleiotropic cardiovascular and metabolic properties, including vasodilation, natriuresis, and suppression of the renin-angiotensin-aldosterone system [15]. Plasma ANP concentrations increase secondary to volume overload

ISSN 0022-9040. Кардиология. 2024;64(8). DOI: 10.18087/cardio.2024.8.n2633

CSL Vifor

феринжект®
железа карбоксимальтозат

Железная защита полноценной жизни

ВЫСОКОДОЗНЫЙ внутривенный препарат железа[1]

ВЫСОКОСТАБИЛЬНЫЙ комплекс железа[1]

НЕДЕКСТРАНОВЫЙ состав[1]

1. **Быстрый гематологический ответ[1–4]**
2. **Благоприятный профиль переносимости и безопасности[1, 2, 4–6]**
3. **Убедительная доказательная база[50]**
4. **Может уменьшать симптомы СН[7, 8], улучшать функциональные возможности[7, 8], переносимость физических нагрузок[8, 51] и качество жизни пациентов[8, 52] с СН**
5. **Может снижать частоту госпитализаций[10] и увеличивать время до первой госпитализации пациентов с СН[52]**

1. Funk F., et al. Arzneim. Forsch. 2010; 60 (6a): 345–53;2. Neiser S., et al. Int. J. Mol. Sci. 2016; 17: 1185 ; 3. Beshara S., et al. Br. J. Haematol. 2003;4. Инструкция по медицинскому применению лекарственного препарата Феринжект®, раствор для внутривенного введения 50 мг/мл, регистрационное удостоверение: ЛСР-008848/10 от 30.08.2010;5. Toblli J.E., et al. Nephrol. Dial. Transplant. 2010; 25: 3631–40 ;6.Tobli J.E. et al. Drug Res (Stuttg) 2015; 65: 354–60; 7. Anker SD et al. NEJM. 2009;361:2436–2448; 8. Ponikowski P et al. Eur Heart J. 2015;36:657–668; 9. Van Veldhuisen DJ et al. Circulation. 2017;136:1374–1383; 10. Ponikowski P et al. The Lancet. 2020;396(10266):1895–1904; 11. Clinical Study Report FER-CARS-01; 12. Clinical Study Report FER-CARS-03 (EFFICACY-HF); https://classic.clinicaltrials.gov/ct2/show/NCT00821717; 13. Kulnigg S et al. Am J Gastroenterol. 2008;103:1182–1192; 14. Evstatiev R et al. Clinical Gastro Hepatol. 2013;11:269–277; 15. Evstatiev R et al. Gastroenterol. 2011;141(3):846–853; 16. Kulnigg-Dabsch S et al. Inflamm Bowel Dis. 2013;19:1609–1616; 17. Clinical Study Report 1VIT13035; https://classic.clinicaltrials.gov/ct2/history/NCT02086968?V_7=View; 18. Qunibi WY et al. Nephrol Dial Transplant. 2011;26:1599–1607; 19. Charytan C et al. Nephrol Dial Transplant. 2013;28:953–964; 20. Onken JE et al. Nephrol Dial Transplant. 2014;29:833-842; 21. Macdougall IC et al. Nephrol Dial Transplant 2014;29(11):2075–2084; 22. Clinical Study Report VIT-IV-CL-015; https://clinicaltrials.gov/study/NCT02826681; 23. Ikuta K. et al. Int J Hematol. 2019;109(1):41–49; 24. Van Wyck DB et al. Obstet Gynecol. 2007;110:267–278; 25. Breymann C et al. J Perinat Med. 2017;45:443–453; 26. Seid MH et al. Am J Obstet Gynecol. 2008;199(4):435.e1–7; 27. Van Wyck DB et al. Transfusion. 2009;49:2719–2728; 28. Favrat B et al. PLoS ONE. 2014;9(4):e94217; 29. Breymann C et al. Int J Gynaecol Obstet 2008; 101: 67–73; 30. Seid MH et al. Anemia. 2017;Article ID:9642027; 31. Clinical Study Report 1VIT08022 ; https://classic.clinicaltrials.gov/ct2/show/NCT01290315; 32. Allen RP et al. Sleep Med. 2011;12(9):906–913; 33.Trenkwalder C et al. Mov Disord. 2017;32(10):1478–1482; 34. Boomershine CS et al. Rheumatol Ther. 2018 Jun;5(1):271-281 ; 35. Bae H. et al, Sleep Med. 2021 Aug:84:179-186; 36. Clinical Study Report VIT-RLS-2012-013; https://classic.clinicaltrials.gov/ct2/show/NCT01382901; 37. Hedenus M et al. Med Oncol. 2014;31(12):302; 38. Clinical Study Report FER-AOC-MM; https://classic.clinicaltrials.gov/ct2/show/NCT01100879; 39. Clinical Study Report 1VIT-14039 IRON CLAD https://clinicaltrials.gov/study/NCT02453334?term=IRON%20CLAD&rank=1; 40. Bailie GR et al. Hemodialysis Int. 2010;14:47–54; 41. Geisser P and Banké-Bochita J. Arzneim Forsch. 2010;60(6a):362–372; 42. Barish CF et al. Anemia. 2012;Article ID:172104; 43. Hussain I et al. Anemia. 2013;Article ID:169107; 44. Onken JE et al. Transfusion. 2014;54:306–315; 45. Clinical Study Report VIT-IRON-2011-003 ; https://classic.clinicaltrials.gov/ct2/show/NCT03591406; 46. Clinical Study Report VIT-IRON-2011-004; https://classic.clinicaltrials.gov/ProvidedDocs/06/NCT03591406/Prot_000.pdf; 47. Clinical Study Report 1VIT13032;https://classic.clinicaltrials.gov/ct2/show/NCT01950247;48. Clinical Study Report 1VIT08021;https://classic.clinicaltrials.gov/ct2/show/NCT00704353;49. Clinical Study Report 1VIT08019;https://classic.clinicaltrials.gov/ct2/show/NCT00703937; 50. Clinical Study Report 1VIT17044; https://classic.clinicaltrials.gov/ProvidedDocs/17/NCT03523117/Prot_000.pdf51. Van Veldhuisen D.J., et al. Circulation 2017; 136: 1374-83. 52. Jankowska E.A., et al. Eur Heart J. 2021;42:3011-3020.

Краткая инструкция по медицинскому применению лекарственного препарата ФЕРИНЖЕКТ® / FERINJECT®*

Регистрационный номер: ЛСР-008848/10. Торговое наименование: ФЕРИНЖЕКТ® / FERINJECT®. Группировочное (химическое) наименование: железа карбоксимальтозат. Лекарственная форма: раствор для внутривенного введения 50 мг/мл. Показания к применению: Лечение дефицита железа (включая железодефицитную анемию) в том случае, когда пероральные препараты железа неэффективны или не могут быть использованы; диагноз должен быть подтвержден лабораторными исследованиями. Лечение дефицита железа при необходимости быстрого восполнения уровня железа. Противопоказания: Повышенная чувствительность к комплексу железа карбоксимальтозата, раствору железа карбоксимальтозата или к любому из компонентов препарата; анемия, не связанная с дефицитом железа, например, другая микроцитарная анемия; признаки перегрузки железом или нарушение утилизации железа; беременность (I триместр); дети в возрасте от 1 до 13 лет с хроническим заболеванием почек, требующим проведения гемодиализа; детский возраст до 1 года. С осторожностью: Препарат Феринжект® следует применять с осторожностью у пациентов с печёночной и почечной недостаточностью, острой или хронической инфекцией, астмой, экземой или атопическими аллергиями. Рекомендуется контролировать применение препарата Феринжект® у беременных женщин (II–III триместр). Побочное действие: Нежелательные реакции, сообщения о которых были получены в ходе проведения клинических исследований, а также в постмаркетинговый период, встречающиеся часто (≥ 1/100 и < 1/10): гипофосфатемия, головная боль, головокружение, «приливы» крови к лицу, артериальная гипертензия, тошнота, реакции в области инъекции/инфузии. Наименование и адрес юридического лица, на чьё имя выдано регистрационное удостоверение / Компания, осуществляющая выпускающий контроль качества: Вифор (Интернэшнл) Инк., Рехенштрассе 37, 9014 Ст. Галлен, Швейцария. Организация, принимающая претензии потребителей: Представительство АО «Вифор (Интернэшнл) Инк.» (Швейцария); 125047, г. Москва, ул. Бутырский Вал, д.10, здание А, этаж 15, офис 36а, БЦ «Белая Площадь»; телефон +7 (495) 766–25–25; электронная почта: info.mo@viforpharma.com; Интернет: www.viforpharma.ru *Полная информация содержится в инструкции по применению. Дата утверждения краткой инструкции: 23 апреля 2024 г.

МАТЕРИАЛ ПРЕДНАЗНАЧЕН ДЛЯ СПЕЦИАЛИСТОВ ЗДРАВООХРАНЕНИЯ. ИМЕЮТСЯ ПРОТИВОПОКАЗАНИЯ. ПЕРЕД НАЗНАЧЕНИЕМ ОЗНАКОМЬТЕСЬ С ПОЛНОЙ ИНСТРУКЦИЕЙ ПО МЕДИЦИНСКОМУ ПРИМЕНЕНИЮ ЛЕКАРСТВЕННОГО ПРЕПАРАТА.

115054, Москва
Космодамианская наб., 52, стр. 5
Тел.: +7 (495) 788 52 89
E-mail: inforussia@cslbehring.com

RU-FCM-2200030 август 2024. Реклама

and/or increased atrial pressure [16]. Studies on ANP and atrial fibrillation have shown contradictory results [15, 16]. ANP concentrations were similar in our groups as well. All of these studies revealed that, in contrast to ANP, Pro-BNP concentrations are significantly higher in patients with AF [15, 16]. In our study, Pro-BN concentrations were higher in the micro-AF group, which supports previous studies.

On the ECG, the P wave represents the depolarization of the atria. P wave anomalies are associated with deterioration in the structure of the atria, and most of these anomalies are directly related to AF. An increase in Pmax and PWD time are non-invasive electrocardiographic findings for atrial remodeling and for scar tissue. In a study by Chen et al., three-dimensional voltage mapping of the left atrium was performed, and the patients with scar tissue and those without scar tissue were compared [17]. The P wave duration was significantly longer in patients with scar tissue (122.9±18.5 and 116.9±28.0 ms, respectively, p:0.01). Some clinical studies in which increased Pmax and PWD times were also associated with an increased risk of AF [18, 19]. In a study by Aytemur et al., when patients with paroxysmal AF were compared with the control group in terms of Pmax and PWD durations, Pmax was found significantly higher in patients with a history of paroxysmal AF compared to controls (116±17ms vs 101±1 ms; p<0.001). PWD was also significantly higher in patients with a history of paroxysmal AF compared to controls (44±15 ms vs 27± 10 ms, p <0.001) [19]. In our study, Pmax, Pmin, and PWD durations were significantly longer in the micro-AF group.

Diastolic dysfunction and atrial electromechanical delay are considered independent risk factors for AF. The e' velocities and s' velocities measured in the micro-AF group were significantly lower than the control group. The e/e' ratio was higher in the micro-AF group than in the control group. Cha et al. followed up patients with and without diastolic dysfunction after AF ablation [20]. In patients with diastolic dysfunction, recurrence of AF was observed more frequently after 1 yr of follow-up. After AF ablation, 30% of patients with diastolic dysfunction had at least 1 degree improvement in the diastolic dysfunction stage. All of these data show that AF may be commonly found along with diastolic dysfunction, that prolongation of atrial fibrillation duration will impair diastolic function, and that shortening of atrial fibrillation duration will improve diastolic function. The atrial electromechanical delay time is defined as the time between the onset of the P wave in the single-lead, surface ECG and the onset of the late diastolic A wave measured in tissue Doppler imaging. AEMD has been observed to be prolonged in many systemic diseases and in paroxysmal atrial fibrillation. In a study by Çalık et al., it was observed that prolongation of AEMD durations was associated with AF independent of left atrial area and volume [21]. A study by Hasan et al. in patients with paroxysmal AF found that the duration of LA lateral AEMD was longer in patients with AF [22]. In our study, inter-annulus plane AEMD and intra-annulus AEMD LEFT durations were longer in the micro-AF group. All the studies in the literature and our study showed that there are similar changes in the structure of the atrium in micro-AF, in paroxysmal AF, and in permanent AF. Along with these changes, an increase in the Pro-BN concentration, prolongation of the P wave duration, prolongation of AEMD durations in echocardiography, and deterioration in diastolic function were observed.In order to include micro AF patients in the definition of AF in the guidelines and to determine treatment indications, studies involving a large number of patients need to be conducted. In this way, uncertainties about treatment can be eliminated.

Study limitations

The study has some limitations. First, it was a single center study with a small number of patients. The duration of rhythm Holter recordings could be extended in patients with micro-AF. In this way, paroxysmal AF events in these individuals could be recognized. Large-scale multicenter studies are needed to confirm the results of this study. B-blocker use was higher in the micro-AF group included in the study. This may have affected the measured AEMD durations.

Conclusion

Early diagnosis and treatment of Micro-AF could be possible with data that can be obtained in routine clinical practice. Pro-BNP measurement, Pmax and Pdd times on ECG, and checking atrial electromechanical delay times in the echocardiography laboratory, can help us to predict Micro-AF.

No conflict of interest is reported.

The article was received on 23/12/2023

REFERENCES

1. Westerman S, Wenger N. Gender Differences in Atrial Fibrillation: A Review of Epidemiology, Management, and Outcomes. Current Cardiology Reviews. 2019;15(2):136–44. DOI: 10.2174/1573403X15666181205110624
2. Steinberg JS, O'Connell H, Li S, Ziegler PD. Thirty-Second Gold Standard Definition of Atrial Fibrillation and Its Relationship With Subsequent Arrhythmia Patterns: Analysis of a Large Prospective Device Database. Circulation: Arrhythmia and Electrophysiology. 2018;11(7):e006274. DOI: 10.1161/CIRCEP.118.006274
3. Benjamin EJ, Muntner P, Alonso A, Bittencourt MS, Callaway CW, Carson AP et al. Heart Disease and Stroke Statistics – 2019 Up-

date: A Report From the American Heart Association. Circulation. 2019;139(10):e56–528. DOI: 10.1161/CIR.0000000000000659
4. Aronow WS, Banach M. Atrial Fibrillation: The New Epidemic of the Ageing World. Journal of Atrial Fibrillation. 2009;1(6):154. DOI: 10.4022/jafib.154
5. Rodriguez F, Stefanick ML, Greenland P, Soliman EZ, Manson JE, Parikh N et al. Racial and ethnic differences in atrial fibrillation risk factors and predictors in women: Findings from the Women's Health Initiative. American Heart Journal. 2016;176:70–7. DOI: 10.1016/j.ahj.2016.03.004
6. Seyed Ahmadi S, Svensson A-M, Pivodic A, Rosengren A, Lind M. Risk of atrial fibrillation in persons with type 2 diabetes and the excess risk in relation to glycaemic control and renal function: a Swedish cohort study. Cardiovascular Diabetology. 2020;19(1):9. DOI: 10.1186/s12933-019-0983-1
7. Svennberg E, Friberg L, Frykman V, Al-Khalili F, Engdahl J, Rosenqvist M. Clinical outcomes in systematic screening for atrial fibrillation (STROKESTOP): a multicentre, parallel group, unmasked, randomised controlled trial. The Lancet. 2021;398(10310):1498–506. DOI: 10.1016/S0140-6736(21)01637-8
8. Fredriksson T, Gudmundsdottir KK, Frykman V, Friberg L, Al-Khalili F, Engdahl J et al. Brief episodes of rapid irregular atrial activity (micro-AF) are a risk marker for atrial fibrillation: a prospective cohort study. BMC cardiovascular disorders. 2020;20(1):167. DOI: 10.1186/s12872-020-01453-w
9. Binici Z, Intzilakis T, Nielsen OW, Køber L, Sajadieh A. Excessive Supraventricular Ectopic Activity and Increased Risk of Atrial Fibrillation and Stroke. Circulation. 2010;121(17):1904–11. DOI: 10.1161/CIRCULATIONAHA.109.874982
10. Richards M, Di Somma S, Mueller C, Nowak R, Peacock WF, Ponikowski P et al. Atrial Fibrillation Impairs the Diagnostic Performance of Cardiac Natriuretic Peptides in Dyspneic Patients: results from the BACH Study (Biomarkers in ACute Heart Failure). JACC: Heart Failure. 2013;1(3):192–9. DOI: 10.1016/j.jchf.2013.02.004
11. Camm AJ, Kirchhof P, Lip GYH, Schotten U, Savelieva I, Ernst S et al. Guidelines for the management of atrial fibrillation. EP Europace. 2010;12(10):1360–420. DOI: 10.1093/europace/euq350
12. Feinberg WM, Blackshear JL, Laupacis A, Kronmal R, Hart RG. Prevalence, age distribution, and gender of patients with atrial fibrillation. Analysis and implications. Archives of Internal Medicine. 1995;155(5):469–73. PMID: 7864703
13. Ellinor PT, Low AF, Patton KK, Shea MA, MacRae CA. Discordant atrial natriuretic peptide and brain natriuretic peptide levels in lone atrial fibrillation. Journal of the American College of Cardiology. 2005;45(1):82–6. DOI: 10.1016/j.jacc.2004.09.045
14. Abe H, Kosugi S, Ozaki T, Mishima T, Date M, Ueda Y et al. Prognostic Impact of Echocardiographic Congestion Grade in HFpEF With and Without Atrial Fibrillation. JACC: Asia. 2022;2(1):73–84. DOI: 10.1016/j.jacasi.2021.10.012
15. Cannone V, Cabassi A, Volpi R, Burnett JC. Atrial Natriuretic Peptide: A Molecular Target of Novel Therapeutic Approaches to Cardio-Metabolic Disease. International Journal of Molecular Sciences. 2019;20(13):3265. DOI: 10.3390/ijms20133265
16. Nakagawa Y, Nishikimi T, Kuwahara K. Atrial and brain natriuretic peptides: Hormones secreted from the heart. Peptides. 2019;111:18–25. DOI: 10.1016/j.peptides.2018.05.012
17. Chen Q, Mohanty S, Trivedi C, Gianni C, Della Rocca DG, Canpolat U et al. Association between prolonged P wave duration and left atrial scarring in patients with paroxysmal atrial fibrillation. Journal of Cardiovascular Electrophysiology. 2019;30(10):1811–8. DOI: 10.1111/jce.14070
18. Achmad C, Tiksnadi BB, Akbar MR, Karwiky G, Sihite TA, Pramudya A et al. Left Volume Atrial Index and P-wave Dispersion as Predictors of Postoperative Atrial Fibrillation After Coronary Artery Bypass Graft: A Retrospective Cohort Study. Current Problems in Cardiology. 2023;48(3):101031. DOI: 10.1016/j.cpcardiol.2021.101031
19. Aytemir K, Özer N, Atalar E, Sade E, Aksöyek S, Övünç K et al. P Wave Dispersion on 12-Lead Electrocardiography in Patients with Paroxysmal Atrial Fibrillation. Pacing and Clinical Electrophysiology. 2000;23(7):1109–12. DOI: 10.1111/j.1540-8159.2000.tb00910.x
20. Cha Y-M, Wokhlu A, Asirvatham SJ, Shen W-K, Friedman PA, Munger TM et al. Success of ablation for atrial fibrillation in isolated left ventricular diastolic dysfunction: a comparison to systolic dysfunction and normal ventricular function. Circulation. Arrhythmia and Electrophysiology. 2011;4(5):724–32. DOI: 10.1161/CIRCEP.110.960690
21. Çalık AN, Özcan KS, Çağdaş M, Güngör B, Karaca G, Gürkan U et al. Electromechanical delay detected by tissue Doppler echocardiography is associated with the frequency of attacks in patients with lone atrial fibrillation. Cardiology Journal. 2014;21(2):138–43. DOI: 10.5603/CJ.a2013.0106
22. Ari H, Ari S, Akkaya M, Aydin C, Emlek N, Sarigül OY et al. Predictive value of atrial electromechanical delay for atrial fibrillation recurrence. Cardiology Journal. 2013;20(6):639–47. DOI: 10.5603/CJ.2013.0164