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# Predictors of 5-year arrhythmia recurrence after treatment of typical atrial flutter in patients with coronary artery disease

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## ABSTRACT

***BACKGROUND:*** There is no consensus on the predictors of arrhythmia recurrence following treatment for typical atrial flutter.

***AIM:*** The study aimed to identify the factors associated with arrhythmia recurrence in patients with coronary artery disease and typical atrial flutter after cardioversion.

***METHODS:*** The study included 165 patients who underwent different treatment modalities, including pharmacological cardioversion with amiodarone (61 patients), electrical cardioversion (20 patients), transesophageal atrial pacing (48 patients), and radiofrequency ablation (36 patients). Patients underwent a 5-year follow-up at intervals of 6, 12, 24, 36, 48, and 60 months. The predictors of arrhythmia recurrence were determined by analyzing correlation coefficients using Pearson's (r) and Spearman's (R) tests, depending on data distribution, followed by multiple regression analysis and receiver operating characteristic (ROC) analysis, including area under the curve (AUC) calculation. The statistical analysis assessed the influence of sex, age, height, weight, body mass index, body surface area, smoking status, arrhythmia characteristics, and comorbidities (atrial flutter type, arrhythmia duration, time since last recurrence, history of atrial fibrillation, symptom severity using the EHRA scale, $CHA_2DS_2$-VASc and HAS-BLED scores, presence of silent myocardial ischemia and ventricular arrhythmias based on 24-hour Holter ECG monitoring, lipid profile, functional class of angina and heart failure, prior percutaneous coronary intervention with stenting, and history of coronary artery bypass grafting). Structural and functional parameters of the atria and left ventricle were assessed using transthoracic echocardiography. Statistical significance was set at $p < 0.05$.

***RESULTS:*** The success rates in restoring sinus rhythm were as follows: 54.1% with pharmacological cardioversion, 87.5% with transesophageal atrial pacing combined with amiodarone, 95.0% with electrical cardioversion, and 100% with radiofrequency ablation with cryoisolation of the pulmonary vein ostia. Arrhythmia recurrence was identified in 62.42% of patients. Significant predictors of atrial flutter recurrence included obesity grade ⩾2 (AUC = 0.655; $p = 0.0117$), regular-type atrial flutter (AUC = 0.736; $p < 0.0001$), and a history of coronary angioplasty with stenting (AUC = 0.687; $p < 0.0001$). Following conservative cardioversion, a history of atrial fibrillation was the primary predictor of atrial fibrillation recurrence. After ablation, recurrence was predicted by age >62 years (AUC = 0.703; $p = 0.0211$) and left ventricular diastolic diameter >5.3 cm (AUC = 0.703; $p = 0.0305$). Predictors of atrial flutter-to-fibrillation recurrence included a history of atrial fibrillation (AUC = 0.702; $p = 0.0193$), left atrial dilation (AUC = 0.714; $p = 0.0439$), and left ventricular hypertrophy (AUC = 0.703; $p = 0.0121$).

***CONCLUSION:*** The five-year recurrence of atrial flutter is associated with the severity of underlying cardiovascular pathology, whereas atrial fibrillation recurrence is linked to a history of atrial fibrillation, patient age, and structural remodeling of the left heart chambers.

**Keywords:** typical atrial flutter; conservative treatment; surgical treatment; predictors of arrhythmia recurrence.

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# Предикторы 5-летнего рецидивирования аритмии после лечения типичного трепетания предсердий у пациентов с ишемической болезнью сердца

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## АННОТАЦИЯ

**Актуальность**. Отсутствует единый взгляд на предикторы рецидива аритмии после лечения типичного трепетания предсердий.

**Цель**. Выявить факторы рецидива аритмии у пациентов с ишемической болезнью сердца с типичным трепетанием предсердий после кардиоверсии.

**Материал и методы**. Лечение проводили 165 больным: медикаментозную кардиоверсию амиодароном составил 61 пациент, электроимпульсную терапию — 20 пациентов, чреспищеводную электрокардиостимуляцию — 48 пациентов и радиочастотную абляцию — 36 больных. Пациенты находились под наблюдением на протяжении 5 лет (через 6, 12, 24, 36, 48 и 60 мес). Предикторы рецидива аритмии устанавливали путём оценки корреляционных отношений с использованием критериев Пирсона (r) и Спирмена (R) в зависимости от вида распределения с последующим множественным регрессионным и ROC-анализом с построением ROC-кривой и указанием площади под ней (AUC). В качестве предикторов в ходе статистического анализа устанавливали: влияние на рецидив аритмии пола, возраста, роста, веса, индекса массы тела, площади поверхности тела пациентов, статуса курения, клинических характеристик аритмии и фоновой патологии (форма трепетания предсердий, длительность существования аритмии, давность конкретного рецидива, наличие фибрилляции предсердий в анамнезе, выраженность симптомов по шкале EHRA, количество баллов по шкалам $CHA_2DS_2$-VASc и HAS-BLED, присутствие безболевой ишемии миокарда и желудочковых аритмий по данным суточного холтеровского мониторирования электрокардиограммы, липидный профиль пациентов, функциональный класс стенокардии напряжения и сердечной недостаточности, наличие чрескожной коронарной ангиопластики со стентированием и аортокоронарного шунтирования в анамнезе), структурно-функциональных параметров миокарда предсердий и левого желудочка по данным трансторакальной эхокардиографии, сопутствующей патологии. Данные считали статистически значимыми при $p$ <0,05.

**Результаты**. Частота достижения синусового ритма путем медикаментозной кардиоверсии составила 54,1%, чреспищеводной электрокардиостимуляции с болюсом амиодарона — 87,50%, электроимпульсной терапии — 95,00%, радиочастотной абляции с криоизоляцией устьев лёгочных вен — 100%. Рецидив аритмии наблюдали у 62,42% всех обследованных пациентов. Предикторами рецидива трепетания предсердий являются: ожирение 2-й степени и выше (AUC=0,655; $p$=0,0117), правильная форма трепетания предсердий (AUC=0,736; $p$ <0,0001), наличие коронарной ангиопластики со стентированием в анамнезе (AUC=0,687; $p$ <0,0001). После консервативной кардиоверсии универсальным предиктором рецидива фибрилляции предсердий считается наличие фибрилляции предсердий в анамнезе, а после абляции — возраст >62 лет (AUC=0,703; $p$=0,0211) и диастолический размер левого желудочка >5,3 см (AUC=0,703; $p$=0,0305). Для рецидива по типу трепетания-фибрилляции предсердий имели значение наличие фибрилляции предсердий в анамнезе (AUC=0,702; $p$=0,0193), дилатация левого предсердия (AUC=0,714; $p$=0,0439) и гипертрофия левого желудочка (AUC=0,703; $p$=0,0121).

**Заключение**. Пятилетний рецидив трепетания предсердий зависит от тяжести фоновой патологии, а рецидив фибрилляции предсердий — от её наличия в анамнезе, возраста пациента и структурного ремоделирования левых отделов сердца.

**Ключевые слова**: типичное трепетание предсердий; консервативное лечение; хирургическое лечение; предикторы рецидива аритмии.

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## BACKGROUND

Atrial flutter (AFl) accounts for approximately 10% of all supraventricular arrhythmias, second only to atrial fibrillation (AF) in terms of prevalence [1]. A twofold increase in the incidence of both isolated AFl and AFl combined with AF in the population is predicted to occur by 2050 [1]. The most frequent underlying cause of both paroxysmal and chronic forms of AFl is coronary artery disease (CAD) (>80%) [1–3]. Furthermore, the presence of AFl, according to the Framingham Heart Study (2016), is associated with a 10-year increased risk of developing AF, myocardial infarction, stroke, heart failure, and mortality from all causes [4].

The initial stage of AF treatment generally involves the use of more accessible conservative methods for restoring sinus rhythm (SR), such as pharmacological cardioversion (PCV), transthoracic electrical cardioversion (TEC), and transesophageal atrial pacing (TEAP) [5, 6–8].

Despite the high periprocedural effectiveness (85%–100%) of radiofrequency ablation of the cavotricuspid isthmus (RFA CTI), the main challenge in the interventional treatment of typical AFl remains the occurrence of post-ablation AF, which showed a recurrence rate of up to 60% during a 5-year follow-up, irrespective of its presence in the patient's medical history [9].

To date, there exists no unified view on the potential predictors of recurrence of AFl and AF after conservative and surgical treatment of typical AFl [4, 10–14].

**The study aimed** to identify the predictors of recurrence of AFl/AF/AFl-AF in patients with CAD and typical AFl following different methods of cardioversion.

## METHODS

A comparative non-randomized prospective study was conducted from 2010 to 2020 at the Nizhny Novgorod Regional Clinical Hospital and the City Clinical Hospital No. 5 (Nizhny Novgorod).

All study patients were diagnosed with typical AFl on a 12-lead electrocardiogram (ECG) at rest and had a history of chronic CAD. The criteria for verifying CAD included a history of myocardial revascularization, clinical symptoms of typical exertional angina pectoris, or a positive stress test (treadmill exercise test or stress echocardiography). The study was approved by the local ethics committee (protocol No. 73, dated September 21, 2010).

Patient follow-up continued until the end of 2023, and the interim results were published in the *Journal of Clinical Medicine* in 2020 [5] and in the *Journal of Medical Almanac* in 2024 [15].

The inclusion criteria for the enrolled patients in the study were as follows [5, 15]:

- documented typical AFl (newly diagnosed, paroxysmal, or persistent);
- duration of paroxysm of up to 1 year;
- complete adherence to the study protocol;
- age of >18 years;
- signed informed consent;

The exclusion criteria for the patient participation in the study was as follows [5, 15]:

- duration of AFl for ⩾1 year;
- presence of scar tissues in the left or right atrium;
- active myocarditis or pericarditis;
- acute coronary syndrome;
- intracardiac thrombi;
- a history of systemic thromboembolic events;
- cardiomyopathies;
- congenital and acquired heart defects;
- uncontrolled stage 3 hypertension; chronic heart failure, functional class IV;
- severe pulmonary hypertension;
- hyperthyroidism;
- severe liver and kidney dysfunction;
- obesity, grade 3;
- malignant neoplasms of any localization;
- pregnancy and lactation.

The study included 165 patients (115 [69.7%] men and 50 [30.3%] women) with an average age of 57.51 ±7.42 years (range: 42–75 years). During the screening, the duration and nature of AFl, the presence of AF in the medical history, and any comorbidities were recorded. Further clinical examination was performed, which included the assessment of hemostasis, lipid profile, and thyroid hormone levels.

All patients underwent electrocardiography with 12 standard leads using the six-channel Cardisuny C-300 BX (Fucuda M-E, Japan), as well as 24-h Holter ECG monitoring with the Astrokard HS-200 018 (Meditex, Russia) and MYOCARD-HOLTER 8.13 (NIMP ESN LLC, Russia) devices to detect paroxysms of AFl, episodes of silent myocardial ischemia and other arrhythmias (AF, ventricular arrhythmias); they were also monitored for the preservation of SR after successful treatment and any recurrences of AFl, AF, and their combination (AFl-AF) were identified.

Transthoracic echocardiography was performed using GE Vivid 7 (GE Healthcare, GE Medical Systems, GE VINGMED ULTRASOUND A/S, Norway) and Philips iE33 xMatrix (Philips Ultrasound Inc., USA) devices using two-dimensional echocardiography in pulsed-wave and continuous-wave modes with color Doppler imaging. The following parameters were assessed:

- linear dimensions, areas, and volumes of the atria with volume indices adjusted to the body surface area ($m^2$) and height;
- left ventricular wall thickness and the left ventricular myocardial mass indexed to the body surface area ($m^2$) and height ($m^{2.7}$);
- end-systolic and end-diastolic dimensions and volumes of the left ventricle, along with left ventricular ejection fraction.

In all the patients, symptom severity of AFl was evaluated with reference to the modified European Heart Rhythm

Association (EHRA) scores, the thromboembolic risk was assessed by using the $CHA_2DS_2$-VASc scores and the bleeding risk by using the HAS-BLED scores [16–18].

Table 1 presents the standard therapy for CAD considering concomitant hypertension and chronic heart failure.

Anticoagulant therapy for patients with AFl and CAD was administered in accordance with the Russian guideline stating that "For patients with AFl, the same approach to anticoagulant therapy is recommended as for AF" [17].

Before cardioversion (including elective procedures) and surgical interventions the patients received only β-adrenergic receptor blockers. Antiarrhythmic therapy to prevent recurrence after SR restoration was performed with the same β-adrenergic receptor blocker (metoprolol) as that used for the treatment of the primary disease. In case of arrhythmia recurrence, amiodarone (maintenance dose up to 200 mg/day) was additionally prescribed [17].

All patients were categorized into four groups based on the method of SR restoration:

• Group 1 (PCV group) included 61 (36.97%) patients with SR that was restored using PCV with intravenous amiodarone administered at a standard dosage of 5–7 mg/kg over 1–2 h (15 mg/min), followed by 50 mg/h for 1–2 days [17]. Owing to amiodarone inefficacy, 28 (46.67%) patients underwent electrical cardioversion: TEC in 20 (71.43%) patients or TEAP in 8 (28.57%) patients [5].

• Group 2 (TEC group) included 20 (12.12%) patients with SR that was restored via TEC in the intensive care unit under anesthesia by using the PRIMEDIC™Defi-B (METRAX GmbH, Germany) and CardioLife ActiBiphasic™ Defibrillator TEC-5631 (Nihon Kohden, Japan). A monophasic shock was applied with an initial energy of 100 J, with subsequent increments up to 360 J, if required. Biphasic shocks were delivered starting at 50 J, with increases up to 150 J, if required [5].

• Group 3 (TEAP Group) included 48 (29.09%) patients with SR that was restored using TEAP with a SP-5E transesophageal cardiac stimulator (OBREAM Zabrze/ITAM Zabrze, Poland) and a bipolar electrode EP2 (DMS Advanced Technologies, Russia). Stimulation was performed in an overdrive pacing mode, with burst stimulation at 15%–25% above the FF′ wave rate for 5–10 s, but not exceeding 320 bpm [19, 20]. If AFl persisted, intravenous amiodarone 150 mg was administered over 5–7 min, and the TEAP procedure was repeated after 10–15 min using the same protocol [5].

• Group 4 (RFA/surgical treatment group) included 36 (21.82%) patients who underwent interventional treatment of typical AFl by using RFA CTI with intracardiac electrophysiological mapping in the catheterization laboratory. The procedure was performed using an irrigated Therapy™ Cool Flex™ Quadripolar Ablation Catheter (St. Jude Medical, USA). Procedure success was defined as a bidirectional conduction block across the CTI [2]. If AF was recorded previously, the RFA CTI procedure was supplemented with cryoisolation of the pulmonary vein ostia.

Patients from groups 1–3 were conditionally combined into the conservative treatment group.

After SR restoration, all patients underwent a 5-year follow-up to assess rhythm stability, detect arrhythmia recurrence, and evaluate treatment adherence with reference to the Morisky–Green Medication Adherence Scale (MMAS-8) [21]. Visits were scheduled at 6, 12, 24, 36, 48, and 60 months, with 12-lead resting ECG, echocardiography, and 24-h Holter ECG monitoring. Visits could also be preponed upon the appearance of arrhythmia recurrence symptoms. Thus, the study accounted for symptomatic arrhythmia recurrences and all episodes of arrhythmia recorded during the 5-year follow-up, including short-term, mildly symptomatic, and asymptomatic episodes.

Data were processed using Statistica 13.0 (StatSoft Inc., USA), MedCalc 22.014 (MedCalc Software Ltd., Belgium) and Microsoft® Excel 2019 for Windows 10 (Microsoft Corp., USA). The distribution of quantitative variables was assessed

**Table 1**. Treatment of underlying cardiovascular pathology in all study patients

| Medications | Total group, n (%) |
|---|---|
| Anti-ischemic therapy: | |
| – β-adrenergic receptor blocker (metoprolol succinate) | 165 (100) |
| – β-adrenergic receptor blocker and dihydropyridine calcium channel antagonist (metoprolol succinate + amlodipine) | 82 (49.70) |
| – prolonged-release organic mono- and dinitrates (monosan/monochinkwe/cardiket) + short-acting organic nitrates (nitroglycerin) as needed | 65 (39.39) |
| Lipid-lowering therapy: | |
| – atorvastatin | 115 (69.70) |
| – rosuvastatin | 50 (30.30) |
| – atorvastatin/rosuvastatin + ezetimibe | 86 (52.12) |
| ACE inhibitors (enalapril/perindopril/ramipril) | 78 (47.27) |
| ARBs (losartan/valsartan) | 56 (33.94) |
| Thiazide (hydrochlorothiazide) or thiazide-like diuretics (indapamide) | 94 (56.97) |
| Mineralocorticoid receptor antagonists (spironolactone/eplerenone) | 62 (37.58) |

Note: ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker

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**Table 2**. Clinical and demographic characteristics of patients in the groups of conservative and surgical treatment of typical atrial flutter

| Indicators | Total group | Conservative treatment group | Surgical treatment group | *p* |
|---|---|---|---|---|
| Number of patients, n (%) | 165 (100) | 129 (78,18) | 36 (21.82) | 0.1240 |
| Sex- Male, n (%)<br>Female, n (%) | 115 (69.70)<br>50 (30.30) | 87 (67,44)<br>42 (32,56) | 28 (77.78)<br>8 (22.22) | 0.4208;<br>0.3554 |
| Mean age, years | 57.51±7,42 | 56.22±6,96 | 62.13±7.26 | 0.0020 |
| First-diagnosed AFl, n (%) | 53 (32.12) | 44 (34.11) | 9 (25.00) | 0.07942 |
| Paroxysmal AFl, n (%) | 28 (16.97) | 28 (21.71) | 18 (50.00) | 0.1541 |
| Persistent AFl, n (%) | 119 (72.12) | 101 (78.29) | 18 (50.00) | 0.0769 |
| Re-entry wave direction— counterclockwise, n (%) | 149 (90.30) | 116 (89.92) | 33 (91.67) | 0.1671 |
| Re-entry wave direction— clockwise, n (%) | 16 (9.70) | 13 (10.08) | 3 (8.33) | 0.5330 |
| Regular form AFl, n (%) | 113 (68.48) | 87 (67.44) | 26 (72.22) | 0.4533 |
| Irregular form AFl, n (%) | 52 (31.52) | 42 (32.56) | 10 (27.78) | 0.2531 |
| Tachysystolic AFl, n (%) | 85 (51.52) | 69 (53.49) | 16 (44.44) | 0.2870 |
| Normosystolic AFl, n (%) | 66 (40.00) | 51 (39.53) | 15 (41.67) | 0.3147 |
| Bradyarrhythmic AFl, n (%) | 14 (8.48) | 9 (6.98) | 5 (13.89) | 0.7412 |
| EHRA Class I, n (%) | 8 (4.85) | 5 (3.88) | 3 (8.33) | 0.8152 |
| EHRA Class IIa, n (%) | 40 (24.24) | 27 (20.93) | 13 (36.11) | 0.1360 |
| EHRA Class IIb, n (%) | 53 (32.12) | 41 (31.78) | 12 (33.33) | 0.1098 |
| EHRA Class III, n (%) | 54 (32.73) | 46 (35.66) | 8 (22.23) | 0.1143 |
| EHRA Class IV, n (%) | 10 (6.06) | 10 (7.75) | 0 | 0.0514 |

Note: AFl, atrial flutter; AF, atrial fibrillation; EHRA, European Heart Rhythm Association classification.

using the Shapiro–Wilk test (for n < 30) and the Kolmogorov–Smirnov test (for n ⩾ 30). For the normally distributed variables, the mean (M) and standard deviation (±SD) were calculated. For non-normally distributed variables, the median (Me) and quartiles ($25^{th}$ quartile; $75^{th}$ quartile) were determined. The comparison of two independent groups based on quantitative variables was performed using Student's *t*-test (for normally distributed data) or the Mann–Whitney U-test (for non-normally distributed data). Categorical variables were compared using the Chi-square test ($\chi^2$) with Yates' correction for continuity. Factors influencing arrhythmia recurrence were determined using correlational analysis to assess the strength of associations between variables (with Pearson's correlation coefficient [r] for normally distributed variables and Spearman's rank-correlation coefficient [R] for non-normally distributed data), followed by multiple regression analysis and receiver operating characteristic (ROC) analysis. The sensitivity and specificity of the developed 5-year recurrence models for AFl and AF were determined using ROC curve analysis, with the calculation of the area under the curve (AUC) for each model. The differences between the groups and the correlations between parameters were considered to be statistically significant at $p < 0.05$.

## RESULTS AND DISCUSSION

The analysis of clinical and demographic characteristics revealed a statistically significant predominance of male patients (2.3 times more, $\chi^2 = 16.58$; $p = 0.0001$) with the regular ($\chi^2 = 14.52$; $p = 0.0001$) tachy- or normosystolic form of AFl ($\chi^2 = 38.71$ and $\chi^2 = 26.34$, respectively; $p = 0.00001$) and a counterclockwise macro re-entry wave pattern ($\chi^2 = 75.30$; $p = 0.00001$) (Table 2). These findings align with a previously established 2–5-fold higher prevalence of AFl in men and the predominant regular form of the arrhythmia with a counterclockwise macro re-entry wave circulation [3, 6–8].

In 28 (16.97%) patients, the duration of AFl episodes was up to 7 days, with 13 patients (7.88%) experiencing episodes lasting for <48 h. The duration of AFl paroxysms was documented in 147 (89.09%) patients. A history of AF was present in 54 (32.73%) patients, which aligns with previous reports of AF in 27%–55% of patients with typical AFl [10, 11].

All patients presented with stable angina pectoris, functional class II or III (50.30% vs. 49.70%, respectively). Prior to their enrollment, 142 (86.06%) patients underwent selective coronary angiography, with myocardial revascularization performed in 53.33% of the cases (42.42% with percutaneous

**Table 3**. Main echocardiographic parameters of the atria and left ventricle in the in the groups of conservative and surgical treatment of typical atrial flutter

| Indicators | Total group | Conservative treatment group | Surgical treatment group | *p* |
|---|---|---|---|---|
| Number of patients, n | 165 | 129 | 36 | — |
| RA area, $cm^2$ | 22.78 ± 3.91 | 23.31 ± 4.04 | 20.89 ± 2.72 | 0.0009 |
| LA area, $cm^2$ | 23.31 ± 4.46 | 23.90 ± 4.51 | 21.21 ± 3.59 | 0.0010 |
| RA volume, mL | 57.84 ± 9.03 | 60.00 (55.00; 64.00) | 55.69 ± 6.55 | 0.0120 |
| LA volume, mL | 58.76 ± 9.40 | 59.52 ± 9.60 | 56.03 ± 8.19 | 0.0480 |
| RA volume index, $mL/m^2$ | 35.78 ± 7.28 | 35.97 ± 7.49 | 35.10 ± 6.51 | 0.0562 |
| RA volume index, $mL/m^2$ ($height^2$) | 19.38 ± 3.47 | 19.60 ± 3.63 | 18.59 ± 2.72 | 0.0612 |
| LA volume index, $mL/m^2$ (BSA) | 36.33 ± 7.51 | 36.66 ± 7.68 | 35.16 ± 6.86 | 0.2995 |
| LA volume index, $mL/m^2$ ($height^2$) | 19.71 ± 3.77 | 19.99 ± 3.89 | 18.67 ± 3.13 | 0.1491 |
| LV EDD, cm | 5.21 ± 0.42 | 5.25 ± 0.44 | 5.07 ± 0.30 | 0.0180 |
| LV ESD, cm | 3.62 (3.30; 4.00) | 3.70 (3.40; 4,00) | 3.45 ± 0.36 | 0.1433 |
| LV MI, $g/m^{2,7}$ ($height^{2,7}$) | 59.14 ± 12.91 | 59.41 ± 13.05 | 58.17 ± 12.53 | 0.1176 |
| LV MI $g/m^2$ (BSA) | 152.49 (138.83; 180.02) | 158.85 ± 32.89 | 159.67 ± 31.20 | 0.1645 |
| LV EF, % | 51.00 (47.00; 54.00) | 50.00 (46.00; 53.00) | 53.50 ± 5.47 | 0.0020 |

Note: RA, right atrium; LA, left atrium; LV EDD, left ventricular end-diastolic diameter; LV ESD, left ventricular end-systolic diameter; LV MI, left ventricular mass index; LV EF, left ventricular ejection fraction; BSA, body surface area.

coronary intervention and stenting; 10.91% with coronary artery bypass grafting). Chronic heart failure was observed in all patients, with a statistically significant predominance of the preserved ejection fraction form over the mildly reduced and reduced ejection fraction forms (64.24% vs. 31.52% and 4.24%; $\chi^2 = 11.95$ and $\chi^2 = 66.17$, $p = 0.005$ and $p = 0.00001$, respectively), which is consistent with previously reported data [9–11, 13]. No significant differences were recorded in comorbidities or baseline characteristics across the study groups.

Transthoracic echocardiography results (Table 3) demonstrated an increase in both atrial sizes, which directly correlated with the duration of AFl episodes (R = 0.309 and R = 0.424; $p < 0.05$).

SR was restored using:

- PCV with amiodarone (54.1%)
- TEAP, enhanced by a single bolus of amiodarone (87.5%)
- TEC (95.0%)
- RFA with cryoisolation of pulmonary vein ostia in AF cases (100%).

During the subsequent 5-year follow-up, all patients exhibited moderate to high adherence to prescribed therapy, as assessed using MMAS-8 [21]: 6 points in 89 (53.94%) patients, 7 points in 54 (32.73%) patients, and 8 points in 22 (13.33%) patients. Most patients effectively regulated their blood pressure (104 [63.03%] patients maintained values within the target range of 120–130/70–80 mmHg) and heart rate (HR; 115 [69.70%] patients exhibited regulated HR at 55–60 bpm). In the remaining cases, office blood pressure fluctuations remained ⩽150/90 mmHg, whereas the HR remained at <75 bpm.

Atrial arrhythmia recurrence was identified in 103 (62.42%) patients within 5 years of cardioversion, regardless of the treatment method: PCV 90.91%, TEC 89.47%, TEAP 85.71%, RFA 55.56%. The recurrence pattern in all the patients with typical AFl included AFl, AF, and mixed AFl-AF [46 (27.88%), 31 (18.79%), and 26 (15.76%) patients, respectively]. Correlation analysis identified a set of risk factors for AF, AFl, and mixed AFl-AF recurrence within the next 5 years, both in the entire cohort and across different cardioversion methods. These factors were subsequently evaluated using multiple regression analysis.

The resulting multiple regression model for 5-year Afl-recurrence risk after PCV included two components: obesity severity and the presence of the regular AFl form. The model's coefficient of determination ($R^2$) was 0.3141 (adjusted $R^2 = 0.2905$, standard error of the estimate = 0.415, $p < 0.00002$):

$$\text{5-year Afl-recurrence risk} = -0.001 + 0.128*(X_{\text{obesity degree}}) + 0.472*(X_{\text{regular AFl form}})$$

where: $X_{\text{obesity degree}}$, obesity degree in patients with typical AFl (0, none; 1, grade I obesity; 2, grade II obesity); $X_{\text{regular AFl form}}$, the presence of the regular AFl form (0, absent; 1, present).

ROC curve analysis further confirmed the model's statistical significance (AUC = 0.803; 95% confidence interval [CI]: 0.681–0.894; $p < 0.0001$; Youden index = 0.4865; model sensitivity = 100%; specificity = 48.65%; cut-off threshold >0.255; Fig. 1).

For TEC, a two-component multiple regression model was developed to predict the 5-year-recurrence risk of AFl, based

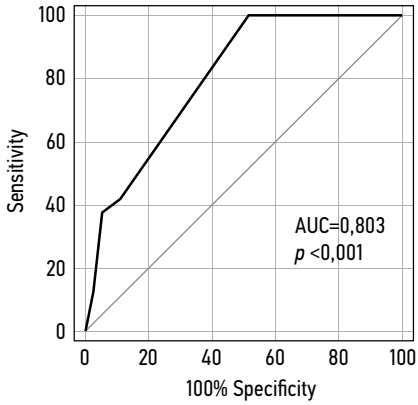


**Fig. 1**. ROC curve for the probability of 5-year atrial flutter recurrence after drug cardioversion with amiodarone (the regression model).

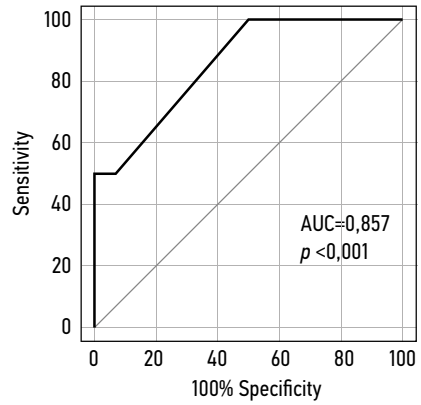


**Fig. 2**. ROC curve for regression model of the probability of 5-year atrial flutter recurrence after electrical impulse therapy.

on the presence of type 2 diabetes mellitus and the regular form of AFl. The model's determination coefficient was $R^2 = 0.4571$ (adjusted $R^2 = 0.3933$; standard error of the estimate = 0.366; $p < 0.0056$):

$$\text{5-year Afl-recurrence risk} = -0.06 + 0.48*(X_{\text{diabetes mellitus}}) + 0.44*(X_{\text{regular AFl form}})$$

where: $X_{\text{diabetes mellitus}}$, type 2 diabetes mellitus (0, none; 1, present); $X_{\text{regular AFl form}}$, the presence of the regular AFl form (0, absent; 1, present).

The ROC curve for this model indicates high prognostic significance (AUC = 0.857; 95% CI: 0.630–0.971; $p < 0.0001$; Youden index = 0.5000; sensitivity = 100%; specificity = 50.00%; cut-off point >–0.06; Fig. 2).

Following TEAP and RFA, no statistically significant multiple regression models were obtained for predicting the 5-year AFl recurrence.

The ROC analysis identified the following significant predictors of 5-year AFl recurrence: obesity grade ⩾2 (AUC = 0.655; 95% CI 0.522–0.772; $p = 0.0117$), regular AFl form (for PCV: AUC = 0.736; 95% CI 0.607–0.841; $p < 0.0001$; for TEC: AUC = 0.786; 95% CI 0.548–0.935; $p < 0.0001$), and history of percutaneous coronary intervention with stenting (for TEAP: AUC = 0.687; 95% CI 0.537–0.813; $p = 0.087$). The literature provides limited data regarding factors influencing the recurrence rates of AFl after conservative treatment of typical AFl in the long-term follow-up [10–14, 19, 22, 23]. These results highlight the relationship between arrhythmia recurrence and the presence of AFl, along with the severity of the underlying CAD.

According to multiple regression analysis, the risk of 5-year AF recurrence following PCV for typical AFl was associated with a history of AF, tachysystolic AFl form, and irregular AFl form. The data indicating that a history of AF is a predictor of AF recurrence during long-term follow-up after PCV aligns with findings from the LADIP study [22]. However, the impact of electrocardiographic characteristics of AFl on AF detection after amiodarone-based PCV has not been previously reported [19, 22]. A three-component multiple regression model was developed with a determination coefficient $R^2 = 0.4375$ (adjusted $R^2 = 0.4079$; standard error of the estimate = 0.275; $p < 0.0001$):

$$\text{5-year-recurrence risk of AF} = -0.147 + 0.339*(X_{\text{AF history}}) + 0.201*(X_{\text{tachysystolic AFl}}) + 0.287*(X_{\text{irregular AFl}})$$

where, $X_{\text{AF history}}$, AF history (0, absent; 1, present); $X_{\text{tachysystolic AFl}}$, tachysystolic AFl typical form (0; absent, 1, present); $X_{\text{irregular AFl}}$, typical AFl irregular form (0, absent, 1, present).

The ROC curve for this model indicates high predictive significance (AUC = 0.943; 95% CI: 0.853–0.986; $p < 0.0001$; Youden index = 0.7543; model sensitivity = 88.89%; specificity = 86.54%; cut-off >0.192; Fig. 3).

For the 5-year recurrence of AF following electrical cardioversion methods, no statistically significant multiple regression models were identified.

Age and left ventricular end-diastolic dimension (LVEDD) were found to be predictors of 5-year AF recurrence after typical AFl RFA. A two-component multiple regression model was developed with a coefficient of determination $R^2 = 0.2670$ (adjusted $R^2 = 0.2226$; standard error of the estimate = 0.436; $p < 0.0059$):

$$\text{5-year AF-recurrence risk} = -4.310 + 0.026*(X_{\text{age}}) + 0.603*(X_{\text{LVEDD}})$$

where $X_{\text{age}}$, age (years); $X_{\text{LVEDD}}$, left ventricular end-diastolic dimension (cm).

The ROC curve for this regression model demonstrated a high prognostic value (AUC = 0.805; 95% CI 0.639–0.918; $p < 0.0001$, Youden index = 0.5325; model sensitivity = 71.43%; specificity = 81.82%; cut-off threshold >0.448; Fig. 4).

When applying the developed multiple regression models, it was essential to consider certain limitations associated with the study design, as some of the exclusion criteria may independently act as predictors of 5-year arrhythmia recurrence (e.g., severe arterial hypertension, renal dysfunction, grade 3 obesity, NYHA class IV chronic heart failure, and significant pulmonary hypertension).

ROC analysis identified a universal predictor of 5-year AF recurrence in patients with typical AFl following conservative cardioversion methods — a history of AF:

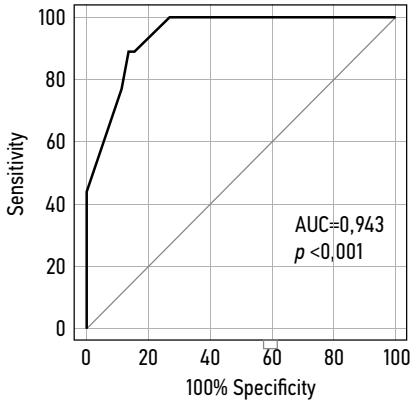


**Fig. 3**. ROC curve for a regression model of the probability of 5-year atrial fibrillation recurrence after drug cardioversion.

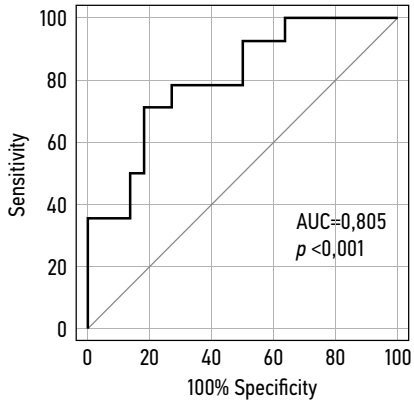


**Fig. 4**. ROC curve for regression model of the probability of 5-year atrial fibrillation recurrence after radiofrequency ablation.

- for PCV: AUC = 0.868; 95% CI 0.756–0.941; $p < 0.0001$;
- for TEC: AUC = 0.882; 95% CI 0.661–0.981; $p < 0.0001$;
- for TEAP: AUC = 0.860; 95% CI 0.730–0.943; $p < 0.0001$.

The predictors of AF recurrence after RFA included: age >62 years (AUC = 0.703; 95% CI 0.528–0.843; $p = 0.0211$) and enlargement of LVEDD >5.3 cm (AUC = 0.703; 95% CI 0.528–0.843; $p = 0.0305$). Age >75 years was recognized as a risk factor for AF recurrence after interventional treatment of typical AFl using the HATCH scores [24]. The earlier threshold (>62 years) observed in this study may be attributable to the underlying disease (i.e., CAD). LVEDD enlargement as a risk factor for post-ablation AF recurrence has also been previously reported in similar studies [10].

ROC analysis revealed that, among the examined patients with typical AFl, the primary predictor of AFl-AF recurrence following PCV and TEC was a history of AF. For patients in the PCV group, additional predictive factors for this type of arrhythmia recurrence included left atrial transverse diameter >4.5 cm (AUC = 0.702; 95% CI 0.571–0.812; $p = 0.0193$) and left atrial volume index (normalized to the body surface area) >38.88 mL/m$^2$ (AUC = 0.714; 95% CI 0.584–0.822; $p = 0.0439$), left ventricle myocardial mass index (normalized to height) >54.89 g/m$^{2.7}$ (AUC = 0.724; 95% CI 0.594–0.830; $p = 0.0121$). These findings underscore the significant role of structural cardiac changes, particularly in the left heart chambers, as a basis for post-ablation AFl-AF development. The current literature describes factors influencing AF occurrence during long-term follow-up after successful conservative or surgical treatment [9, 10–14, 19, 22–24]. However, these reports do not separately assess the predictors based on the specific arrhythmia type diagnosed (i.e., whether AFl, AF, or AFl-AF).

## CONCLUSION

In patients with typical AFl against the background of chronic CAD, the predictors of 5-year AFl recurrence were grade ⩾2 obesity, the regular form of AFl (for PCV and TEC), and a history of percutaneous transluminal coronary angioplasty with stenting (for TEAP). For the development of isolated AF or AFl-AF recurrence, irrespective of the cardioversion method, the most significant factors for 5-year recurrence were a history of AF, patient age, and structural remodeling of the left heart chambers.

## ADDITIONAL INFORMATION

**Authors' contribution**. K.V.P. — methodology, investigation, formal analysis, writing — original draft; V.P.N. — conceptualization, writing — review and editing, supervision; L.Yu.K. — writing — review and editing. Thereby, all authors made a substantial contribution to the conception of the work, acquisition, analysis, interpretation of data for the work, drafting and revising the work, final approval of the version to be published and agree to be accountable for all aspects of the work.

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**Competing interests**. The authors declare that they have no competing interests.

## ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

**Вклад авторов**. Все авторы подтверждают соответствие своего авторства международным критериям ICMJE (все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией). Наибольший вклад распределён следующим образом: К.В.П. — методология, исследование, анализ, создание черновика; В.П.Н. — концептуализация, редактирование рукописи, общее руководство; Л.Ю.К. — редактирование рукописи.

**Источник финансирования**. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

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

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