https://doi.org/10.35336/VA-1510

# EFFICIENCY OF CARDIOVERSION IN PERSISTENT ATRIAL FIBRILLATION AND MAINTENANCE OF SINUS RHYTHM IN THE LONG-TERM PERIOD IN PATIENTS WITH MYOCARDITIS

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**Aim.** To compare the immediate and long-term efficacy of cardioversion in patients with persistent atrial fibrillation (AF) in the setting of active myocarditis versus those without myocardial inflammation.

**Methods.** The study included 80 patients with persistent atrial AF (mean age 58.39±14.3 years; 56.2% male), of whom 40 had biopsy- or magnetic resonance imaging-confirmed myocarditis, elevated antimyocardial antibody titers, and ≥3 points on a non-invasive myocarditis diagnostic algorithm (main group). The control group (n=40) consisted of patients with non-inflammatory cardiovascular diseases (coronary artery disease, hypertension). All patients with myocarditis received standard anti-inflammatory therapy. Following pre-treatment with amiodarone for 10-12 days, electrical cardioversion (ECV) was performed. The efficacy of ECV, the need for radiofrequency ablation (RFA), the incidence of persistent AF, and adverse outcomes were evaluated. Differences were considered statistically significant at $p<0.05$.

**Results:** Patients in the myocarditis group were characterized by a higher proportion of males (80.0% vs. 32.5%), younger age (49.1±12.0 vs. 67.7±9.5 years), lower left ventricular ejection fraction (LVEF) (37% [30;41] vs. 56% [52;59]), and larger left ventricular end-diastolic volume (152 ml [119;184] vs. 89 ml [76;106]), all with $p<0.001$. The duration of AF history and left atrial size did not differ significantly between groups. Only in the myocarditis group did spontaneous sinus rhythm (SR) restoration occur during amiodarone loading, observed in 17.5% of cases. ECV was successful on the first attempt in all patients of the control group and in 57.5% of patients with myocarditis; an additional 15% achieved SR with a second ECV attempt ($p<0.001$). Reversible recurrences of AF, terminated by intravenous amiodarone, were observed in 20% of myocarditis patients versus 5% in the control group ($p=0.012$). By the end of the one-week observation period, irreversible recurrences were recorded in two patients in each group. LVEF improved more significantly in the myocarditis group (to 42% [33;49], $p<0.001$). At six months post-ECV, SR was maintained in 50% of patients with myocarditis and 66.5% in the control group ($p=0.530$). Rhythm control was discontinued in 15% of patients with myocarditis and in 5% of the control group ($p=0.547$), and radiofrequency ablation was performed in 10% and 5% of patients, respectively ($p=0.509$). All-cause mortality was documented in 12.5% (n=5) of myocarditis patients. No thromboembolic events or heart transplantations were reported in either group.

**Conclusion:** AF in the context of myocarditis more commonly affects individuals of working age and worsens LV systolic dysfunction. The immediate and long-term efficacy of ECV was non-significantly lower in patients with myocarditis; however, successful restoration and maintenance of SR were associated with a more pronounced improvement in LVEF, supporting the rationale for a rhythm control strategy. Further research is planned to identify predictors of sustained SR in this population.

**Key words:** persistent atrial fibrillation; myocarditis; electropulse therapy; electrical cardioversion; antiarrhythmic therapy; left ventricular systolic dysfunction.

**Conflict of Interest**: none.
**Funding:** none.
**Received:** 19.04.2025 **Revision received:** 26.09.2025 **Accepted:** 26.09.2025
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**For citation:** Panin DS, Blagova OV, Katasonova SA. Efficiency of cardioversion in persistent atrial fibrillation and maintenance of sinus rhythm in the long-term period in patients with myocarditis . *Journal of Arrhythmology.* 2025;32(4): 5-12. https://doi.org/10.35336/VA-1510.

According to the definition proposed by N.R. Paleev (1997), myocarditis is an inflammatory disease of the myocardium caused by the direct or immune-mediated effects of infection, parasitic or protozoal invasion, chemical or physical factors, as well as myocardial involvement occurring in allergic and autoimmune diseases [1]. In the definition provided by Russian experts in the 2023 Ministry of Health clinical guidelines, particular emphasis is placed on the wide spectrum of clinical manifestations of myocarditis, ranging “from an asymptomatic course, mild dyspnoea, and non-intense chest pain resolving spontaneously, to heart failure, cardiogenic shock, life-threatening arrhythmias, and sudden cardiac death” [2]. Among the typical complications of myocarditis, atrial fibrillation (AF) occupies a prominent place.

The same clinical guidelines state that the development of AF - either persistent or paroxysmal - in the ab-

sence of ischaemic heart disease, a history of arterial hypertension, or valvular heart disease allows myocarditis to be suspected with a high degree of probability [2]. While the available literature includes studies assessing the incidence of arrhythmias, including AF, in the setting of active myocarditis, none specifically address the efficacy of cardioversion in this patient population.

A multicentre retrospective study conducted in the United States in 2019 demonstrated that AF was documented in 602 patients (9%) out of 6,642 individuals with acute myocarditis, with a predominance of male patients (61.3%). In this cohort, AF was associated with significantly prolonged hospitalisation, a higher incidence of acute heart failure, and increased mortality [3].

A 2021 review encompassing 65 studies showed that AF is the most common cardiac arrhythmia in patients with COVID-19, sepsis, or acute respiratory distress syndrome. Among patients with a prior history of AF, arrhythmia recurrence was observed in 23–33%, while approximately 10% developed AF for the first time [4]. Management strategies depended on the patient's clinical condition, in line with current guidelines: haemodynamically unstable patients underwent urgent cardioversion. However, in the context of coronavirus infection, myocarditis is only one of several potential mechanisms contributing to the onset or exacerbation of AF.

Since AF occurring in the setting of active myocarditis makes a significant contribution to left ventricular (LV) systolic dysfunction, aggravates the course of heart failure, and leads to recurrent hospitalisations, a rhythm-control strategy using electrical cardioversion (ECV) may be justified in this patient population. The relative simplicity of the ECV procedure and its safety, provided that the established protocol is followed, make it an attractive method for AF termination [5]. At the same time, it is essential to protect patients from unjustified attempts at cardioversion in clinical situations where the risk of early AF recurrence is predictably high.

The first attempts to predict unfavourable factors for maintenance of sinus rhythm date back to the 1960s. A.V.

***Table 1.***

***Clinical and functional parameters of patients in the main group and the comparison group at admission***

| | Main group | Comparison group | p |
|---|---|---|---|
| Follow-up duration, months | 22 [7;50] | 6 [6;7] | <0.001 |
| Age, years | 49.1±12.0 | 67.7±9.5 | <0.001 |
| Male sex, n (%) | 32 (80) | 13 (32.5) | <0.001 |
| Body mass index, kg/m$^2$ | 27 [26;32] | 31 [27;36] | 0.010 |
| Grade of arterial hypertension | 0[0;2] | 3[2;3] | <0.001 |
| NIMDA score (points) | 7[6;8] | 1[1;2] | <0.001 |
| Duration of AF history, weeks | 26 [8;58] | 24 [4;57] | 0.370 |
| Time since last AF episode, weeks | 10 [4;30] | 8 [4;16] | 0.380 |
| Number of AF episodes per year | 1 [1;2] | 1 [1;2] | 0.970 |
| History of LAA thrombosis, n (%) | 8 (20.0) | 3 (7.5) | 0.105 |
| HR on admission (AF), bpm | 104.5±23.6 | 99.8±22.6 | 0.360 |
| PVCs per 24 h | 213 [55;1300] | 44 [1;91] | 0.021 |
| Low QRS voltage, n (%) | 5 (12.5) | 0 | 0.021 |
| Low RV1-V6 amplitude, n (%) | 30% (n=12) | 0 | <0.001 |
| QRS duration, ms | 96.5[90;111] | 92.5[83;101] | 0.360 |
| Corrected QT interval (QTc), ms | 450[422;469] | 450[429;461] | 0.710 |
| LVEDD, cm | 5.9±0.7 | 4.9±0.4 | <0.001 |
| LVEDV, mL | 152 [119;184] | 89 [76;106] | <0.001 |
| LVEDV/BSA, mL/m$^2$ | 70 [59;86] | 51[44;58] | 0.013 |
| LVESV, mL, мл | 89 [66;137] | 39 [30;47] | <0.001 |
| LVEF, % | 37 [30;41] | 56 [52;59] | <0.001 |
| VTI, см | 11.2±3.1 | 16.7±3.8 | <0.001 |
| LA diameter, cm | 4.56±0.67 | 4.39±0.50 | 0.280 |
| LA volume, mL | 92 [79;104] | 84 [72;92] | 0.073 |
| LA volume/BSA, mL/m$^2$ | 42 [39;56] | 38 [45;39] | 0.370 |
| RA volume, mL | 74 [56;88] | 65 [60;79] | 0.360 |
| RV diameter, cm | 3[2.9;3.6] | 3[2.8;3.5] | 0.440 |
| Mitral regurgitation grade | 1 [1;2] | 1 [1;1.5] | 0.280 |
| mPAP, mmHg | 30 [25;40] | 33 [29;38] | 0.318 |
| Leukocytes, ×10$^9$/L | 7.1±1.9 | 6.75±1.7 | 0.350 |
| Hemoglobin, g/L | 151.7 ±2.56 | 143 ±14.8 | 0.007 |
| CRP, mg/mL | 3 [1.3;5.6]. | 2.4 [1.3;4.2] | 0.400 |
| Fibrinogen, g/L | 3.5 [3.1;4.0] | 3.0 [2.6; 3.3] | 0.011 |
| ESR, mm/h | 6.5 [5;10] | 10 [6;20] | 0.012 |
| TSH, μIU/mL | 2.5[1.8;3.5] | 2[1.8;3.2] | 0.117 |

Notes: NIMDA - non-invasive myocarditis diagnostic algorithm; AF - atrial fibrillation; LAA - left atrial appendage; LA - left atrium; HR - heart rate; PVCs - premature ventricular contractions; LVEDD - left ventricular end-diastolic diameter; LVEDV - left ventricular end-diastolic volume; BSA - body surface area; LVESV - left ventricular end-systolic volume; LVEF - left ventricular ejection fraction; VTI - velocity time integral; RA - right atrium; RV - right ventricle; mPAP - mean pulmonary artery pressure; CRP - C-reactive protein; ESR - erythrocyte sedimentation rate; TSH - thyroid-stimulating hormone.

Nedostup et al. proposed selection criteria for electroimpulse therapy of AF, in which a substantial role was assigned to anamnestic factors, including the duration of sinus rhythm maintenance during previous episodes, the number of AF paroxysms in the medical history, and other parameters [6]. Almost all contraindications to ECV identified at that time-factors reducing its effectiveness or rendering the procedure impractical or unsafe-have retained their clinical relevance to this day. Among these factors, active inflammatory processes (predominantly rheumatic in origin at that time) were considered particularly important.

Since then, the spectrum of myocarditis aetiologies has changed considerably. However, no studies have evaluated the course of AF, the appropriateness, or the efficacy of cardioversion in myocarditis in comparison with AF associated with other forms of heart disease. Moreover, there are no studies assessing long-term maintenance of sinus rhythm after ECV in patients with myocarditis or identifying its predictors. These gaps in evidence underscore the high clinical relevance of the present study.

The aim of this study is to assess the efficacy of cardioversion and long-term maintenance of sinus rhythm in patients with persistent AF and myocarditis, compared with patients with persistent AF associated with non-inflammatory heart diseases.

## MATERIALS AND METHODS

A retrospective and prospective study included 80 patients (mean age 58.39 ± 14.3 years; 43.8% women and 56.2% men) admitted to the V.N. Vinogradov Faculty Therapy Clinic of Sechenov University with persistent AF between 2017 and 2024. Patients were divided into a main group (40 patients with myocarditis) and a comparison group (40 patients with non-inflammatory heart diseases).

Inclusion criteria for the main group were age ≥18 years, persistent AF scheduled for electrical cardioversion, and a diagnosis of active myocarditis, established on the basis of:

- endomyocardial biopsy (EMB) with myocarditis diagnosed according to the Dallas morphological criteria, supplemented by immunohistochemical criteria; or
- non-invasive diagnostic criteria, including a diagnostically significant ≥3-fold increase in anticardiac antibody (ACA) titres in combination with the 2018 Lake Louise criteria for cardiac magnetic resonance imaging (MRI) and a score of ≥3 points according to the non-invasive myocarditis diagnostic algorithm (excluding ACA titres) [7-9].

Exclusion criteria for the main group included a history of acute coronary syndrome or myocardial infarction, infective endocarditis within the preceding 6 months, acquired valvular heart disease, hypertrophic, restrictive, non-compaction, or arrhythmogenic cardiomyopathy, a history of thyrotoxicosis, prior open-heart surgery of any duration, verified cardiac sarcoidosis, lymphoproliferative disorders, and prior anthracycline-based chemotherapy.

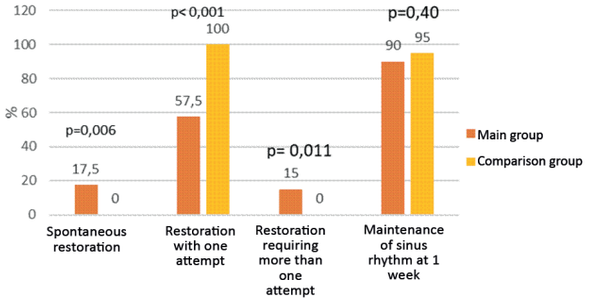


***Figure 1. Immediate efficacy of electrical cardioversion.***

Patients aged ≥18 years with persistent AF scheduled for cardioversion and non-inflammatory heart diseases were included in the comparison group. Non-inflammatory conditions comprised idiopathic AF, arterial hypertension, and coronary artery disease, excluding myocardial infarction within the preceding 6 months.

Patients were excluded from the comparison group if myocarditis was diagnosed on the basis of EMB and/or the 2018 Lake Louise MRI criteria for myocarditis, in combination with a score of ≥4 pointsaccording to the non-invasive myocarditis diagnostic algorithm (including elevated ACA titres), as well as in cases of exudative pericarditis or the presence of any of the exclusion criteria defined for the main group.

General exclusion criteria for both groups also included established contraindications to ECV, such as intracardiac thrombosis, duration of the current AF episode exceeding 3 years, thyrotoxicosis, a history of sick sinus syndrome or second- or third-degree atrioventricular block, as well as patient refusal to undergo ECV.

Non-inclusion criteria were refusal to participate in the study, pregnancy, breastfeeding, intellectual disability, legal incapacity, and decompensated psychiatric disorders.

All patients underwent clinical interview and physical examination, standard laboratory testing, assessment of thyroid hormone levels, 12-lead electrocardiography with calculation of the QTc interval, transthoracic echocardiography, and 24-hour Holter ECG monitoring. In addition, coronary angiography or multislice computed tomography (MSCT) of the heart was performed in 30 patients (37.5%).

For verification of myocarditis, ACA levels were measured using indirect immunofluorescence, cardiac magnetic resonance imaging was performed in 19 patients (47.5%), and morphological examination of myocardial tissue was carried out in 15 patients with myocarditis (37.5%), including one post-mortem specimen and EMB samples in the remaining cases.

After assessment of inclusion and exclusion criteria in both groups, patients underwent preparation for planned ECV. Amiodarone was prescribed at a loading dose of 600 mg/day. If atrial fibrillation persisted by day 10-12 of therapy, electrical cardioversion was performed, with assessment of its immediate effectiveness and the number of shocks required to restore sinus rhythm (SR).

The maintenance of sinus rhythm was evaluated at the end of the first week of treatment and at 6 months after discharge, which was considered the measure of long-term cardioversion efficacy, in both groups. In cases of early AF recurrence, intravenous amiodarone infusion was administered.

Patients in the myocarditis group additionally received background therapy for myocarditis. Methylprednisolonewas prescribed to 29 patients (72.5%) at a median dose of 16 [14; 24] mg/day, including 13 patients (32.5%)

who received combination therapy with azathioprine at 150 [88; 150] mg/day or mycophenolate mofetil (n = 3, 7.5%) at 2000 mg/day. Hydroxychloroquine was administered to 9 patients (22.5%) at a dose of 200 mg/day, including two cases in combination with corticosteroids.

Follow-up in the myocarditis group was continued beyond the initial 6 months. At the end of follow-up (mean duration 22 months [7; 50]), the incidence of long-term outcomes was assessed. The primary endpoint was death or heart transplantation. Secondary endpoints included the need for radiofrequency catheter ablation, the development of sustained forms of AF (persistent or permanent), and the incidence of thromboembolic events.

**Statistical analysis**

Data analysis was performed using IBM SPSS Statistics, version 25.0 (IBM Corp., USA). Normality of data distribution was assessed using the Shapiro–Wilk test. Continuous variables are presented as mean ± standard deviation for normally distributed data and as median with interquartile range (Me [Q25; Q75]) when the distribution deviated from normality.

Comparisons of continuous variables were performed using the Student's t-test, Mann–Whitney U test, or Wilcoxon signed-rank test, as appropriate. Categorical variables were analyzed using the $\chi^2$ test or Fisher's exact test, with construction of 2×2 contingency tables where applicable. Differences were considered statistically significant at $p < 0.05$.

The study protocol was approved by the Local Ethics Committee (Protocol No. 02-24, dated 29 January 2024). All patients provided written informed consent for participation in the study, diagnostic procedures, and interventions.

## RESULTS

Clinical characteristics at admission and after cardioversion, as well as the immediate and long-term effectiveness of cardioversion, were analysed. The main clinical characteristics of patients in both groups are presented in Table 1. Patients with myocarditis were characterised by younger age and a predominance of male sex compared with the control group. The duration of atrial fibrillation (AF) history and the time since the last AF episode did not differ between groups. In the myocarditis group, the duration of myocarditis history was 20 [10; 60] weeks.

Patients with myocarditis also demonstrated a higher prevalence of ventricular arrhythmias, low QRS voltage in standard ECG leads, and reduced left ventricular (LV) systolic function parameters prior to ECV, including left ventricular ejection fraction (LVEF) and LV outflow tract velocity–time integral (VTI). Atrial dimensions and volumes did not differ significantly between groups, whereas LV dimensions were significantly largerin the myocarditis group.

No significant differences were observed between groups in leukocyte count, leukocyte differential, or C-reactive protein levels. A higher fibrinogen level was noted in the myocarditis group; however, mean values remained within the normal range. Immunological activity of myocarditis was assessed by circulating anticardiac antibody (ACA) titres. The highest titres were observed for antibodies against smooth muscle antigens and conduction system fibres, with a mean titre of 1:160 [80; 160]. Antibodies to cardiomyocyte nuclear antigens (specific antinuclear factor) were detected in 52.5% (n = 21) of patients, with a mean titre of 1:40 [0; 80].

According to cardiac MRI, late gadolinium enhancement in patients with non-ischaemic AF was detected in 73.7% (n = 14). Myocardial oedema was identified in 2 patients (10.5%), and increased trabeculation not meeting criteria for non-compaction cardiomyopathy was observed in 2 patients (10.5%).

During amiodarone loading as preparation for ECV, spontaneous restoration of SR occurred in 7 patients (17.5%) in the myocarditis group. No association was found between spontaneous SR restoration and AF recurrence within one week after ECV (r = 0.166, p = 0.145). In the control group, spontaneous SR restoration during amiodarone loading was not observed.

If AF persisted after 10–12 days of amiodarone loading, planned ECV was performed. In the myocarditis group, SR was restored with a single 200-J shock in 57.5% (n = 23) of patients, whereas in the control group ECV was successful on the first attempt in all patients (100%). More than one shock was required in 6 patients in the myocarditis group (mean 2.7 attempts). In one of these patients SR was not restored immediately, but spontaneous restoration occurred after 2 months on continued amiodarone therapy. In another patient, ECV was ineffective with persistent AF during follow-up (Figure 1).

The number of reversible AF recurrences within the first week after ECV or spontaneous SR restoration was higher in the myocarditis group (8 cases), 2 of which required repeat ECV (Figure 2). In the control group, one episode of sustained AF paroxysm was recorded and successfully terminated with intravenous amiodarone.

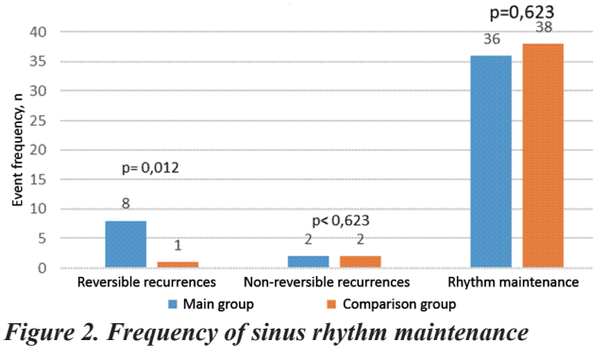


***Figure 2. Frequency of sinus rhythm maintenance one week after electrical cardioversion or spontaneous restoration of sinus rhythm.***

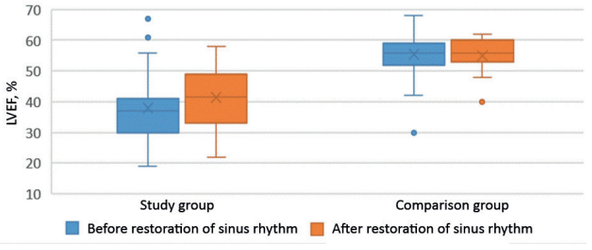


***Figure 3. Changes in left ventricular ejection fraction (LVEF) in the study groups one week after electrical cardioversion or spontaneous restoration of sinus rhythm (SR).***

Within the first week after cardioversion or spontaneous SR restoration, the number of irreversible AF recurrences at discharge did not differ between groups and amounted to 2 cases in each group. Thus, the overall rate of SR maintenance at one week was 36 patients in the myocarditis group and 38 patients in the control group.

One week after cardioversion, LVEF increased in both groups. In the myocarditis group, LVEF increased from 37 [30; 41]% to 42 [33; 49]% ($p < 0.005$), which was clinically significant, while in the control group it increased from 56 [52; 59]% to 57 [52; 60]% ($p = 0.085$) (Figure 3). In the myocarditis group, a significant reduction in LV end-systolic volume was also observed, from 89 [66; 137] to 85 [65; 136] mL ($p = 0.025$).

Long-term outcomes at 6 months after cardioversion were assessed in all patients in the myocarditis group and in 27 patients in the control group. The rate of SR maintenance was 50% (n = 20) in patients with myocarditis and 66.5% (n = 18) in the control group ($p = 0.45$). Radiofrequency ablation was performed more frequently in the myocarditis group. In the control group, rhythm-control strategy was discontinued in two cases. No thromboembolic events were recorded in either group (Table 2).

The follow-up duration in the myocarditis group exceeded 6 months and averaged 22 [7; 50] months. One year after cardioversion, atrial fibrillation (AF) recurrences were documented in 32 patients (80%) with myocarditis. In five of these patients, recurrence was associated with self-discontinuation of therapy, while in two cases it was related to documented amiodarone-induced thyrotoxicosis.

In six patients (15%) from the myocarditis group, a decision was made to abandon an active rhythm-control strategy. Radiofrequency ablation (RFA) for arrhythmia management was performed at any time during follow-up in eight patients (20%). No thromboembolic events were recorded during the long-term follow-up period.

There were no cases of heart transplantation throughout the entire follow-up period. All-cause mortality occurred in 12.5% (n = 5) of patients with myocarditis. The immediate causes of death were end-stage chronic heart failure in three cases, myocardial infarction due to late stent thrombosis in one case, and septic complications of immunosuppressive therapy in one patient.

## DISCUSSION

Atrial fibrillation (AF) is frequently a complication and, in some cases, the sole clinical manifestation of myocarditis. Both the clinical guidelines of the Ministry of Health of the Russian Federation and the multicentre study by A. Subahi et al. report a younger age and predominance of male patients among individuals with myocarditis, which is fully consistent with our findings and underscores the relevance of the present study [3].

A distinctive feature of this work was the application of maximally stringent inclusion criteria, including the exclusion of other primary myocardial diseases, toxic myocardial injury, thyrotoxicosis, as well as the active exclusion of myocarditis in the comparison group using a minimal score according to the non-invasive myocarditis diagnostic algorithm.

Analysis of baseline clinical characteristics revealed no significant differences in atrial size or volume between the two groups. In both groups, the atria were moderately enlarged, slightly more so in patients with myocarditis, but did not reach threshold values traditionally considered a contraindication to ECV or significantly reducing its clinical justification. In both early and subsequent studies, A. V. Nedostup et al. proposed a left atrial linear diameter of 5.5–6.0 cm as a critical threshold [6]. Numerous later studies have repeatedly confirmed the prognostic value of left atrial size for cardioversion outcomes in AF. Nevertheless, in our study, moderate atrial enlargement did not preclude ECV [10]. The absence of intergroup differences in this key parameter increased group comparability by eliminating the influence of one of the most extensively studied predictors of AF recurrence, although full matching of the groups was not pursued, as the primary comparison was based on AF aetiology.

A significantly larger LV volume was observed in the myocarditis group, reflecting inflammatory myocardial dysfunction and correlating with reduced LV contractility, as evidenced by lower LVEF and LV outflow tract velocity-time integral (VTI). Notably, despite a comparable degree of tachysystole (mean heart rate 100–105 bpm), similar AF history duration, and comparable duration of the current AF episode, patients in the comparison group (without myocarditis) demonstrated minimal LV dilatation and preserved systolic function. This finding further emphasizes the necessity of actively searching for the underlying aetiology of AF in patients with LV dysfunction and highlights the inadequacy of attributing LV impairment solely to “tachycardia-induced cardiomyopathy”.

The present study provides an answer to the clinically important question of the appropriateness of cardioversion in patients with persistent AF in the setting of active myocarditis. To our knowledge, no prior studies have specifically addressed this issue. Earlier investigations evaluating ECV outcomes suggested that not only high (grade II–III) activity of rheumatic inflammation, but even minimal (grade I) activity, reduced the efficacy of cardioversion and worsened prognosis [6]. In contrast, despite pronounced morphological and immunological activity of myocarditis in our cohort, the immediate success rate of

***Table 2.***

***Achievement of study endpoints at 6 months of follow-up***

| | Main group | Comparison group | p |
|---|---|---|---|
| Death, n (%) | 2 (5) | 0 | 0.376 |
| Heart transplantation, n (%) | 0 | 0 | - |
| Radiofrequency ablation, n (%) | 4 (10) | 2 (5) | 0.509 |
| Discontinuation of rhythm control strategy, n (%) | 0 | 2 (5) | 0.152 |
| Thromboembolic complications, n (%) | 0 | 0 | - |

ECV and the rate of sinus rhythm maintenance one week after cardioversionwere relatively high and comparable to those observed in patients with AF due to non-inflammatory cardiac diseases.

In addition, in patients with myocarditis and baseline left ventricular (LV) dysfunction, we observed a rapid and statistically significant increase in left ventricular ejection fraction (LVEF) within the first days following successful cardioversion, a phenomenon that was not observed in the comparison group. This finding confirms the substantial contribution of atrial fibrillation (AF) to the aggravation of LV dysfunction specifically in patients with myocarditis and provides a strong argument in favour of a rhythm-control strategy with restoration of sinus rhythm (SR).

Multicentre studies have demonstrated that elimination of AF in patients with LV dysfunction leads to a greater improvement in LVEF compared with a passive rate-control approach; however, in those studies the aetiology of heart failure was not specifically analysed, or was oversimplified as being solely a consequence of tachysystole [11]. In our cohort, following cardioversion in patients with myocarditis, LVEF increased but remained reduced, which was primarily attributable to the underlying inflammatory myocardial disease and necessitated continued cardiotropic and disease-modifying therapy.

A characteristic feature of patients with myocarditis was markedly greater rhythm instability compared with the control group. This was reflected both in a high rate of spontaneous restoration of sinus rhythm (17.5%), which was not observed in the comparison group, and in a higher number of reversible AF recurrences, most of which were successfully terminated with intravenous amiodarone. It is likely that myocardial inflammation creates a state of electrical instability and plays a central role in arrhythmogenesis in myocarditis. Among the key mechanisms of arrhythmia development in myocarditis are direct cytopathic injury with cardiomyocyte membrane lysis, myocardial ischaemia due to coronary microvasculitis, and abnormal calcium channel function, the latter bringing myocarditis closer to arrhythmogenic cardiomyopathy in terms of electrophysiological substrate [12].

Nevertheless, rhythm stabilisation was achieved in the majority of patients. During six months of follow-up, the rate of sinus rhythm maintenance in patients with myocarditis was somewhat lower than in the comparison group, and the need for radiofrequency catheter ablation (RFA) was higher (performed after suppression of inflammatory activity), which may be explained by the development of irreversible atrial myocardial fibrosis. Importantly, in a subset of patients with myocarditis, AF recurrences were related to premature and unjustified discontinuation of amiodarone, including cases where regression of LV dysfunction created a false impression of recovery. Such recurrences may potentially be prevented by more cautious long-term rhythm management.

It should also be noted that with standard preparation for planned electrical cardioversion—including transoesophageal echocardiography and anticoagulant therapy according to general principles—no thromboembolic events were observed in patients with myocarditis, as in the group with non-inflammatory heart disease. This is noteworthy given the presumed prothrombotic potential of active myocarditis, possibly related to inflammatory involvement of the mural endocardium.

Analysis of long-term outcomes in the myocarditis group revealed that heart transplantation, predefined as a study endpoint, was not required in any case. This may be explained by the arrhythmic clinical phenotype of myocarditis in a subset of patients, the reversibility of LV systolic dysfunction following restoration of sinus rhythm, and the use of comprehensive cardiotropic and immunosuppressive therapy. In cases where transplantation was considered due to therapy resistance, it was not performed because of weight-related limitations; fatal outcomes were predominantly associated with end-stage heart failure.

It is likely that specific predictors exist that allow forecasting long-term cardioversion efficacy in patients with myocarditis complicated by sustained forms of AF. Identification of such factors represents one of the objectives of the ongoing study.

## CONCLUSION

In patients with myocarditis and persistent atrial fibrillation (AF), a rhythm-control strategy aimed at restoration of sinus rhythm yields more heterogeneous outcomes than in patients with non-inflammatory heart disease. During amiodarone loading, spontaneous restoration of sinus rhythm was observed in 17.5% of patients, whereas 15% required more than one defibrillation shock, and in 5% of patients electrical cardioversion proved ineffective.

The overall rate of sinus rhythm restoration in patients with myocarditis and persistent AF reached 95%, compared with 100% first-shock cardioversion success in patients with non-inflammatory heart disease (with no cases of spontaneous sinus rhythm restoration in the comparison group).

One week after spontaneous or electrical cardioversion, sinus rhythm was maintained in 90% of patients with myocarditis (including 95% of those in whom sinus rhythm had been successfully restored) and in 95% of patients with non-inflammatory heart disease, with no statistically significant difference between groups. However, during the first week of follow-up, reversible AF recurrences were significantly more frequent in the myocarditis group than in the comparison group (21% vs 2.5%).

Six months after successful cardioversion, sinus rhythm was preserved in 53% of patients with myocarditis and 67% of patients in the comparison group ($p = 0.45$). At that time point, 62.5% and 40.7% of patients, respectively, continued amiodarone therapy. One case of spontaneous sinus rhythm restoration during ongoing amiodarone therapy was documented following ineffective electrical cardioversion. Radiofrequency catheter ablation was used more frequently in the myocarditis group, although the difference did not reach statistical significance (10% vs 5%). No thromboembolic complications were recorded in either group.

Electrical cardioversion of persistent AF in patients with myocarditis appears justified even before the full effect of disease-modifying and cardiotropic therapy becomes evident. Despite greater rhythm instability compared with patients without myocarditis, the rates of sinus

rhythm restoration and maintenance are comparable, while allowing for a rapid and statistically significant improvement in left ventricular systolic function, which is initially impaired in myocarditis. Specifically, left ventricular ejection fraction increased from 37 [30; 41]% to 42 [33; 49]% ($p < 0.05$.

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