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## EFFICACY OF SECONDARY PREVENTION AND REHABILITATION PROGRAMS WITH DISTANT SUPPORT IN PATIENTS WITH ATRIAL FIBRILLATION AFTER INTERVENTIONAL PROCEDURES: IMPACT ON PSYCHOLOGICAL STATUS

|                             |  |
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| <i>Aim</i>                  | To evaluate the effectivity of secondary prevention/rehabilitation programs with remote support for the psychological condition of patients with paroxysmal atrial fibrillation (AF) following interventional procedures (radiofrequency catheter ablation and cryoablation).  |
| <i>Material and methods</i> | This prospective, controlled, randomized clinical study was performed in three parallel groups. Each group consisted of 45 patients with AF after interventional procedures. In groups 1 and 2, secondary prevention/rehabilitation programs with remote support were performed, including a single individual in-hospital counseling (on risk factors of AF and their control and on major aspects of the disease, treatment and prevention of complications) and three months of remote support (by phone in group 1 and by e-mail in group 2). Patients of group 3 (control group) received standard recommendations at discharge from the hospital. The psychological status was evaluated using the Hospital Anxiety and Depression Scale, the PHQ-9 questionnaire, the Spielberg-Hanin scale for reactive and personal anxiety, and the visual analogue scale for stress assessment. The follow-up duration was 12 months.       |
| <i>Results</i>              | At the end of the follow-up period, the proportion of patients with anxiety symptoms considerably decreased in both intervention groups ( $p < 0.001$ for each group) and was significantly less than in the control group ( $p < 0.001$ for both comparisons). Also, in intervention group 1, the proportion of patients with clinically pronounced anxiety symptoms was significantly decreased. For 12 months of follow-up, the severity of depressive symptoms significantly decreased in all three groups. However, in both intervention groups, this decrease was significantly greater than in the control group ( $p < 0.001$ for group 1 and $p = 0.020$ for group 2). In both intervention groups at 12 months, the stress level was significantly reduced whereas in the control group, it remained practically unchanged. The greatest (50% on average) decrease in the stress level was observed in intervention group 2. |
| <i>Conclusion</i>           | Secondary prevention and rehabilitation programs with remote support during a 12-month follow-up resulted in improvement of the psychological status in patients with AF after interventional procedures.  |
| <i>Keywords</i>             | Atrial fibrillation; catheter ablation; stress; anxiety symptoms; depressive symptoms; secondary prevention/rehabilitation programs; remote support  |
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Atrial fibrillation (AF) is the most common abnormal cardiac rhythm in clinical practice [1]. It significantly increases the risk of cardioembolic stroke, chronic heart failure, and death [2–4]. AF worsens the quality of life (QoL), and produces negative psychological effects: many patients become more stressed, develop anxiety and depression [5, 6]. Cardiac factors play a

leading role in the development of AF. However, a particular significance is attributed to the peculiarities of patient's personality and psycho-emotional state [7]; psychological distress may be the main mechanism of AF development in some patients.

Psycho-emotional disorders are common in patients with AF. According to foreign studies [8, 9], the pre-

valence of anxiety and depression ranges from 25% to 50%. The presence of symptoms of anxiety and depression is associated in patients with AF with increased all-cause and cardiovascular mortality, and the severity of the symptoms correlate with QoL [10].

Psycho-emotional disorders (mainly anxiety and depression) occurring in AF are usually associated with the expectation of AF attacks, often accompanied by fear of death, limited physical activity, reduced work capacity, or disability due to the development of complications [11, 12].

Interventional treatment, such as radiofrequency catheter ablation or cryoablation, is an effective treatment for AF that allows eliminating attacks in most patients. There is evidence that catheter ablation reduces the severity of anxiety/depression symptoms or even completely eliminates them in patients with AF [13]. At the same time, negative post-intervention psycho-emotional state increases the risk of AF recurrence, which is why it is expected that psychological correction aimed at reducing the severity of or eliminating anxiety, depression, and increased stress or can increase the efficacy of treatment and improve long-term outcomes, prognosis, and QoL of patients [11, 14].

## Objective

Evaluate the efficacy of two secondary prevention/rehabilitation programs of remote psychological support designed specifically for patients with paroxysmal AF who underwent interventional treatment based on the 12-month follow-up.

## Material and methods

A prospective randomized controlled clinical trial was conducted in three parallel groups.

### *Inclusion criteria:*

- 1) Age > 18 years;
- 2) Paroxysmal AF;
- 3) Interventional treatment for AF (radiofrequency ablation or cryoablation of pulmonary vein) during hospital stay;
- 4) Ability to use a mobile phone or email.

*Exclusion criteria:* acute coronary syndrome or cerebral stroke within the previous 6 months; hemodynamically significant valvular heart disease; chronic heart failure of NYHA functional class III–IV; severe pulmonary, renal, or hepatic failure; cancer; severe mental disorders; alcohol and substance abuse and other addiction; inability to complete questionnaires in Russian.

According to the study protocol, patients were randomized into three groups at the ratio of 1:1:1 – two

treatment groups and a control group (45 subjects per group).

Secondary prevention/rehabilitation programs I and II were implemented in Group 1 and Group 2, including an individual counseling at hospital followed by 3-month remote support. Individual counseling included informing the patient about the disease, methods of diagnosis, treatment, and prevention of complications, personalized counseling on the patient's risk factors for developing AF, cardiovascular diseases (CVDs) and their complications, such as, brain stroke. Patients were advised on the physical activity, optimal nutrition, weight/blood pressure/cholesterol control, quitting smoking and alcohol abuse. Remote support referred to preventive counseling by telephone (group 1) or email (group 2) once every 14 days for 3 months after enrollment (a total of 6 counseling sessions). Adherence to non-pharmacological and pharmacological recommendations, cases of recurrent AF attacks, seeking emergency medical service, and hospitalization were recorded at each contact. In the control group (group 3), patients received standard recommendations from the attending physician.

Patients were followed up for 12 months in this study; three follow-up visits (in 3, 6 and 12 months) were made in each group during this period. This article presents the results of the baseline and final visits and assesses changes in the indicators of interest within 12 months of follow-up. Patient's psychological status was assessed at baseline and on each visit. The Hospital Anxiety and Depression Scale (HADS) was used to identify anxiety and depression [15]. The questionnaire consists of 2 subscores: HADS-A (anxiety) and HADS-D (depression). Each subscore contains 7 questions, the answers to which are scored from 0 to 3. Results were interpreted according to the original HADS version separately for each subscore: 0–7=normal (no significant symptoms); 8–10=subclinical anxiety/depression; ≥11=symptomatic anxiety/depression. The presence and severity of depression symptoms were also assessed using the Patient Health Questionnaire-9 (PHQ-9) [16], which includes 9 questions concerning patient's emotional state in the past 2 weeks.

The severity of anxiety was determined using the State-Trait Anxiety Inventory (STAI) developed by Ch.D. Spielberger and adopted by Yu.L. Khanin [17]. The questionnaire consists of two scales containing 20 statements each, which separately evaluate state and trait anxiety. Trait anxiety is relatively stable and does not depend on the situation, as it is a personality trait. State anxiety on the contrary is caused by a specific situation. There are 4 answer options for each statement (from 1=complete disagreement with the situation to

4=perfect agreement with the situation). The indicators of state and trait anxiety were calculated using special formulas and interpreted as follows:  $\leq 30$  – mild anxiety; 31–44 – moderate anxiety;  $\geq 45$  – severe anxiety.

Visual analog scale (VAS) was used to assess the severity of stress, for which the patient was asked to mark the intensity of experienced stress on a 10 cm straight line. The beginning of the line (0) corresponded to the absence of stress and the end of the line (10) corresponded to severe stress.

All patients signed the voluntary informed consent to participate in the study. The study protocol was approved by the local ethics committee.

### Patient characteristics

The study included 135 patients (70 male, 65 female) with paroxysmal AF aged from 35 to 79 years (mean

age  $57 \pm 9$  years); 47% of the subjects were older than 60 years (Table 1).

According to Table 1, patients characteristics were comparable between the three groups. It should be noted that most patients in each group had AF symptoms corresponding to the modified EHRA score 3, which refers to the presence of severe symptoms that impair daily activity, and the median CHA2DS2 VASc score 2 is indicative of a high risk of stroke in at least 50% of patients. Thus, patients with paroxysmal AF with a history of interventions were randomized to three groups equal in numbers and comparable in basic characteristics.

Statistical data processing was conducted using SPSS 23.0 (SPSS Inc., USA). The type of distribution of quantitative variables was analyzed using the Kolmogorov–Smirnov test. In the case of parametric

**Table 1.** Social, demographic, anthropometric, and clinical characteristics of patients with paroxysmal AF with a history of interventional treatment (n=135)

| Parameter                                       | Group 1<br>(n=45) | Group 2<br>(n=45) | Control group<br>(n=45) | P <sub>1-3</sub> | P <sub>2-3</sub> |
|---|-------------------|-------------------|-------------------------|------------------|------------------|
| Age, years (M $\pm$ SD)                         | 57.0 $\pm$ 7.5    | 57.8 $\pm$ 9.7    | 57.0 $\pm$ 10.3         | N/s              | N/s              |
| Male, %   | 51.1              | 55.6              | 48.9                    | N/s              | N/s              |
| Higher education, %                             | 86.7              | 73.3              | 57.8                    | <0.005           | N/s              |
| <b>Social and labor status</b>                  |                   |                   |                         |                  |                  |
| • Any form of employment                        | 48.9              | 64.4              | 55.6                    | N/s              | N/s              |
| • Retired                                       | 48.9              | 35.6              | 33.3                    |                  |                  |
| • Unemployed                                    | 2.2               | 0                 | 11.1                    |                  |                  |
| <b>Level of income, %:</b>                      |                   |                   |                         |                  |                  |
| • Very low                                      | 4.4               | 0                 | 6.7                     | N/s              | N/s              |
| • Low   | 68.8              | 48.9              | 57.8                    |                  |                  |
| <b>Marital status, %:</b>                       |                   |                   |                         |                  |                  |
| Formally married                                | 80.0              | 80.0              | 75.6                    | N/s              | N/s              |
| Disability, %                                   | 8.9               | 11.1              | 13.3                    | N/s              | N/s              |
| Body mass index, kg/m <sup>2</sup> (M $\pm$ SD) | 29.9 $\pm$ 4.9    | 29.5 $\pm$ 3.6    | 29.9 $\pm$ 4.2          | N/s              | N/s              |
| Obesity, %                                      | 55.6              | 46.7              | 51.1                    | N/s              | N/s              |
| Arterial hypertension, %                        | 57.8              | 77.8              | 66.7                    | N/s              | N/s              |
| Coronary artery disease, %                      | 4.4               | 13.3              | 8.9                     | N/s              | N/s              |
| Diabetes mellitus type 2, %                     | 0                 | 2.2               | 8.9                     | N/s              | N/s              |
| Chronic heart failure, %                        | 35.6              | 57.8              | 44.4                    | N/s              | N/s              |
| <b>Total CHA2DS2 VASc score</b>                 |                   |                   |                         |                  |                  |
| • Me [25 %; 75 %]                               | 2 [0; 2.5]        | 2 [1; 3]          | 2 [1; 2]                | N/s              | N/s              |
| • M $\pm$ SD                                    | 1.6 $\pm$ 1.2     | 1.8 $\pm$ 1.2     | 1.7 $\pm$ 1.2           |                  |                  |
| <b>Symptom severity by modified EHRA</b>        |                   |                   |                         |                  |                  |
| • Me [25 %; 75 %]                               | 3 [3; 3]          | 3 [3; 3]          | 3 [3; 3]                | N/s              | N/s              |
| • M $\pm$ SD                                    | 2.9 $\pm$ 0.5     | 2.9 $\pm$ 0.3     | 3.1 $\pm$ 0.5           |                  |                  |
| <b>Symptom severity by modified EHRA score</b>  |                   |                   |                         |                  |                  |
| 1   | 0                 | 0                 | 0                       | N/s              | N/s              |
| 2   | 15.6              | 13.3              | 8.9                     |                  |                  |
| 3   | 77.8              | 84.4              | 75.6                    |                  |                  |
| 4   | 6.7               | 2.2               | 15.6                    |                  |                  |
| Systolic BP, mm Hg (M $\pm$ SD)                 | 129.3 $\pm$ 16.1  | 127.7 $\pm$ 15.7  | 126.6 $\pm$ 15.7        | N/s              | N/s              |
| Diastolic BP, mm Hg (M $\pm$ SD)                | 77.9 $\pm$ 9.2    | 77.6 $\pm$ 8.2    | 77.7 $\pm$ 7.0          | N/s              | N/s              |

M, mean; SD, standard deviation; n/s, nonsignificant.

**Table 2.** Changes in the severity of anxiety/depression symptoms by the HADS score over 12 months in patients with paroxysmal AF with a history of interventional treatment (n=135)

| Parameter  | Group 1 (n=45)       | Group 2 (n=45)       | Control group (n=45) | P <sub>1-3</sub> | P <sub>2-3</sub> |
|--|----------------------|----------------------|----------------------|------------------|------------------|
| <b>Total HADS-A (anxiety symptoms) subscore</b>                |                      |                      |                      |                  |                  |
| <b>Baseline</b>  |                      |                      |                      |                  |                  |
| • Me [25 %; 75 %]  | 8 [4; 10.5]          | 7 [4; 8]             | 7 [5.5; 10]          | N/s              | N/s              |
| • M±SD   | 7.8±4.2              | 6.3±3.5              | 7.6±3.5              |                  |                  |
| <b>In 12 months</b>  |                      |                      |                      |                  |                  |
| • Me [25 %; 75 %]  | 3 [1.5; 5]           | 4 [2; 5]             | 7 [5; 9.5]           | <0.001           | <0.001           |
| • M±SD   | 3.8±3.4              | 3.7±1.9              | 7.3±2.5              |                  |                  |
| Changes over 12 months, Δ% (Me [25 %; 75 %])                   | -50.0 [-77.8; -24.0] | -40.0 [-57.1; -20.0] | -9.1 [-17.8; 16.1]   | <0.001           | <0.001           |
| P <sub>base - M12</sub>  | <0.001               | <0.001               | N/s                  | —                | —                |
| <b>Any anxiety symptoms (HADS-A ≥ 8)</b>                       |                      |                      |                      |                  |                  |
| Baseline, %  | 51.1                 | 35.6                 | 48.9                 | N/s              | N/s              |
| In 12 months, %  | 13.3                 | 0                    | 48.9                 | <0.001           | <0.001           |
| P <sub>base - M12</sub>  | <0.001               | <0.001               | N/s                  | —                | —                |
| <b>Clinically pronounced anxiety symptoms (HADS-A ≥ 11)</b>    |                      |                      |                      |                  |                  |
| Baseline, %  | 24.4                 | 8.9                  | 22.2                 | N/s              | 0.081            |
| In 12 months, %  | 6.7                  | 0                    | 8.9                  | N/s              | N/s              |
| P <sub>base - M12</sub>  | 0.021                | N/s                  | 0.070                | —                | —                |
| <b>Total HADS-D (depression symptoms) subscore</b>             |                      |                      |                      |                  |                  |
| <b>Baseline</b>  |                      |                      |                      |                  |                  |
| • Me [25 %; 75 %]  | 5 [3.5; 7]           | 4 [2; 5]             | 6 [3.5; 8]           | N/s              | 0.007            |
| • M±SD   | 5.5±3.4              | 4.3±3.2              | 5.9±3.1              |                  |                  |
| <b>In 12 months</b>  |                      |                      |                      |                  |                  |
| • Me [25 %; 75 %]  | 3 [1; 4]             | 3 [2; 4]             | 5 [3; 8]             | <0.001           | <0.001           |
| • M±SD   | 3.1±2.5              | 3.2±2.3              | 5.3±2.9              |                  |                  |
| Changes over 12 months, Δ% (Me [25 %; 75 %])                   | -46.4 [-75.0; 0]     | -30.9 [-51.8; 0]     | -10.0 [-31.3; 0]     | <0.001           | 0.020            |
| P <sub>base - M12</sub>  | <0.001               | 0.001                | 0.014                | —                | —                |
| <b>Any symptoms of depression (HADS-D ≥ 8)</b>                 |                      |                      |                      |                  |                  |
| Baseline, %  | 22.2                 | 8.9                  | 35.3                 | N/s              | 0.002            |
| In 12 months, %  | 6.7                  | 6.7                  | 28.9                 | 0.006            | 0.006            |
| P <sub>base - M12</sub>  | 0.016                | N/s                  | N/s                  | —                | —                |
| <b>Clinically pronounced depressive symptoms (HADS-D ≥ 11)</b> |                      |                      |                      |                  |                  |
| Baseline, %  | 11.1                 | 4.4                  | 6.7                  | N/s              | N/s              |
| In 12 months, %  | 2.2                  | 0                    | 6.7                  | N/s              | N/s              |
| P <sub>base - M12</sub>  | N/s                  | N/s                  | N/s                  | —                | —                |

Me, median; M, mean; SD, standard deviation; P<sub>base - M12</sub>, significance of changes in 12 months; N/s, nonsignificant.

distribution, the means and standard deviations were calculated; the results are presented as M±SD. For non-parametrically distributed qualitative ordinal and quantitative variables, the medians (Me) and interquartile ranges (25th percentile; 75th percentile) were calculated; the results are presented as Me [25%; 75%]. In some cases, qualitative ordinal variables were represented simultaneously as Me [25%; 75%] and M±SD for more clarity. Two groups were compared using the Mann-Whitney U-test, Pearson's chi-squared test, or two-tailed Fisher's exact test. Intragroup changes in the indicators assessed using the Wilcoxon test and McNemar chi-squared test. Changes in the quantitative and qualitative

ordinal variables was also evaluated by delta%, which was calculated using the following formula:

$$\Delta\% = [(N1 - N0) / N0] \times 100\%;$$

where N0 is the initial value, N1 is the 12-month value. The differences were considered statistically significant with two-tailed p-value of less than 0.05.

## Results

At baseline, patients of both treatment groups did not differ from the control group in the prevalence and severity of anxiety symptoms (Table 2). During the 12-month follow-up, significant positive changes were observed in both treatment groups: the severity

**Table 3.** Changes in state anxiety assessed by the STAI inventory in patients with paroxysmal AF and a history of interventional treatment (n=135)

| Parameter                                    | Group 1 (n=45)       | Group 2 (n=45)     | Control group (n=45) | P <sub>1-3</sub> | P <sub>2-3</sub> |
|--|----------------------|--------------------|----------------------|------------------|------------------|
| <b>State anxiety, score</b>                  |                      |                    |                      |                  |                  |
| Baseline, M±SD                               | 31.6±10.0            | 32.1±11.6          | 31.1±12.5            | N/s              | N/s              |
| In 12 months, M±SD                           | 22.4±6.7             | 23.4±8.8           | 24.6±8.3             | N/s              | N/s              |
| Changes over 12 months, Δ% (Me [25 %; 75 %]) | -22.8 [-48.5; -11.3] | -17.2 [-42.9; 1.0] | -14.3 [-33.8; 3.2]   | N/s              | N/s              |
| P <sub>base-M12</sub>                        | <0.001               | <0.001             | <0.001               | —                | —                |
| <b>Degree of state anxiety, %</b>            |                      |                    |                      |                  |                  |
| <b>Baseline</b>                              |                      |                    |                      |                  |                  |
| • Mild                                       | 48.9                 | 48.9               | 51.1                 | N/s              | N/s              |
| • Moderate                                   | 42.2                 | 42.2               | 31.1                 | N/s              | N/s              |
| • Severe                                     | 8.9                  | 8.9                | 17.8                 | N/s              | N/s              |
| <b>In 12 months</b>                          |                      |                    |                      |                  |                  |
| • Mild                                       | 86.4                 | 84.4               | 80.0                 | N/s              | N/s              |
| • Moderate                                   | 13.6                 | 13.3               | 15.6                 | N/s              | N/s              |
| • Severe                                     | 0                    | 2.2                | 4.4                  | N/s              | N/s              |
| P <sub>base-M12</sub>                        |                      |                    |                      |                  |                  |
| • Mild                                       | <0.001               | <0.001             | <0.001               | —                | —                |
| • Moderate                                   | <0.001               | 0.002              | N/s                  | —                | —                |
| • Severe                                     | N/s                  | N/s                | 0.031                | —                | —                |

Me, median; M, mean; SD, standard deviation; N/s, nonsignificant; P<sub>base-M12</sub>, significance of changes in 12 months

**Table 4.** Changes in trait anxiety assessed by the STAI inventory in patients with paroxysmal AF and a history of interventional treatment (n=135)

| Parameter                                    | Group 1 (n=45)       | Group 2 (n=45)     | Control group (n=45) | P <sub>1-3</sub> | P <sub>2-3</sub> |
|--|----------------------|--------------------|----------------------|------------------|------------------|
| <b>Trait anxiety, score (M±SD)</b>           |                      |                    |                      |                  |                  |
| Baseline                                     | 48.0±9.6             | 45.5±8.6           | 47.6±9.5             | N/s              | N/s              |
| In 12 months                                 | 38.0±8.1             | 41.3±7.7           | 44.7±8.4             | <0.001           | 0.053            |
| Changes over 12 months, Δ% (Me [25 %; 75 %]) | -22.2 [-31.1; -10.2] | -5.4 [-11.8; -2.0] | -4.6 [-9.3; 0]       | <0.001           | N/s              |
| P <sub>base-M12</sub>                        | <0.001               | <0.001             | <0.001               | —                | —                |
| <b>Degree of trait anxiety, %</b>            |                      |                    |                      |                  |                  |
| <b>Baseline</b>                              |                      |                    |                      |                  |                  |
| • Mild                                       | 2.2                  | 4.4                | 4.4                  | N/s              | N/s              |
| • Moderate                                   | 33.3                 | 48.9               | 40.0                 | N/s              | N/s              |
| • Severe                                     | 64.4                 | 46.7               | 55.6                 | N/s              | N/s              |
| <b>In 12 months</b>                          |                      |                    |                      |                  |                  |
| • Mild                                       | 11.4                 | 4.4                | 2.2                  | N/s              | N/s              |
| • Moderate                                   | 70.5                 | 66.7               | 48.9                 | 0.038            | 0.088            |
| • Severe                                     | 18.1                 | 31.1               | 48.9                 | 0.002            | 0.085            |
| P <sub>base-M12</sub>                        |                      |                    |                      |                  |                  |
| • Mild                                       | N/s                  | N/s                | N/s                  | —                | —                |
| • Moderate                                   | 0.001                | 0.021              | N/s                  | —                | —                |
| • Severe                                     | <0.001               | 0.039              | N/s                  | —                | —                |

Me, median; M, mean; SD, standard deviation; N/s, nonsignificant; P<sub>base-M12</sub>, significance of changes in 12 months.

of anxiety symptoms decreased by the mean of 50% in treatment group 1 and 40% in treatment group 2, and the end of the follow-up period, the total HADS-A subscore was almost 2 times lower in both treatment groups than in the control group (p<0.001 for both comparisons).

The percentage of patients with anxiety symptoms significantly decreased in 12 months in both treatment groups (p<0.001 for each group) and was much lo-

wer than in the control group (p<0.001 for both comparisons). Moreover, a significant decrease in the percentage of patients with symptomatic anxiety was detected in treatment group 1. In the control group, there was only a trend a decrease in the percentage of patients with symptomatic anxiety with a constant yield of any anxiety symptoms, which remained relatively high after 12 months (49%).

**Table 5.** Changes in the severity of depression symptoms assessed by the PHQ-9 questionnaire in patients with paroxysmal AF and a history of interventional treatment (n=135)

| Parameter                                    | Group 1 (n=45)   | Group 2 (n=45)      | Control group (n=45) | P <sub>1-3</sub> | P <sub>2-3</sub> |
|--|------------------|---------------------|----------------------|------------------|------------------|
| <b>Total score</b>                           |                  |                     |                      |                  |                  |
| <b>Baseline</b>                              |                  |                     |                      |                  |                  |
| • Me [25 %; 75 %]                            | 6.7±4.8          | 6 [4; 9]            | 7 [2.5; 9.5]         |                  |                  |
| • M±SD                                       | 4 [3; 7]         | 5.5±4.7             | 7.3±5.7              | N/s              | 0.078            |
| <b>In 12 months</b>                          |                  |                     |                      |                  |                  |
| • Me [25 %; 75 %]                            | 2 [1.5; 4]       | 3 [2; 4]            | 3 [1.5; 5]           |                  |                  |
| • M±SD                                       | 3.2±3.3          | 3.8±3.1             | 4.1±3.7              | N/s              | N/s              |
| Changes over 12 months, Δ% (Me [25 %; 75 %]) | -56.3 [-83.3; 0] | -29.2 [-75.0; 57.6] | -47.2 [-84.3; 43.8]  | N/s              | N/s              |
| P <sub>base-M12</sub>                        | <0.001           | N/s                 | 0.005                | —                | —                |
| <b>Degree of depression symptoms, %</b>      |                  |                     |                      |                  |                  |
| <b>Baseline</b>                              |                  |                     |                      |                  |                  |
| • None/minimal                               | 37.8             | 53.3                | 35.6                 | N/s              | 0.072            |
| • Mild                                       | 42.2             | 35.6                | 37.8                 | N/s              | N/s              |
| • Moderate                                   | 13.3             | 2.2                 | 13.3                 | N/s              | N/s              |
| • Severe                                     | 2.2              | 4.4                 | 8.9                  | N/s              | N/s              |
| • Extremely severe                           | 4.4              | 2.2                 | 2.2                  | N/s              | N/s              |
| <b>In 12 months</b>                          |                  |                     |                      |                  |                  |
| • None/minimal                               | 82.2             | 71.1                | 57.8                 | N/s              | N/s              |
| • Mild                                       | 11.1             | 15.6                | 28.9                 | 0.035            | N/s              |
| • Moderate                                   | 6.7              | 6.7                 | 4.4                  | N/s              | N/s              |
| • Severe                                     | 0                | 0                   | 0                    | —                | —                |
| • Extremely severe                           | 0                | 0                   | 2.2                  | N/s              | N/s              |
| P <sub>base-M12</sub>                        |                  |                     |                      |                  |                  |
| • None/minimal                               | <0.001           | N/s                 | 0.078                |                  |                  |
| • Mild                                       | 0.003            | 0.078               | N/s                  |                  |                  |
| • Moderate                                   | N/s              | N/s                 | N/s                  | —                | —                |
| • Severe                                     | N/s              | N/s                 | N/s                  |                  |                  |
| • Extremely severe                           | N/s              | N/s                 | N/s                  |                  |                  |

Me, median; M, mean; SD, standard deviation; N/s, nonsignificant; P<sub>base-M12</sub>, significance of changes in 12 months.

During the 12-month follow-up, the severity of depressive symptoms significantly decreased in all three groups. However, the decrease was significantly greater in both treatment groups than in the control group ( $p<0.001$  for group 1 and  $p=0.020$  for group 2). The percentage of patients with any depressive symptoms decreased statistically significantly only in treatment group 1, and in 12 months, the percentage of patients with any depressive symptoms was much lower in both treatment groups than in the control group ( $p=0.006$  for both comparisons).

There were no differences at baseline and 12 months later in state anxiety between patients of the three groups, and its severity significantly decreased in all groups in 12 months, which increased in the percentage of patients with low state anxiety at the expense of individuals with moderate to severe anxiety (Table 3). Patients of the three groups did not differ in trait anxiety at baseline, and its severity was significantly lower 12 months later in treatment group 1 than in the control group, and there

was a trend to lower severity in treatment group 2 (Table 4). Over 12 months, a statistically significant decrease in the severity of trait anxiety was observed in all three groups, but the maximum decrease (the mean of 22%) was observed in treatment group 1, and the decrease was significantly more pronounced than in the control group ( $p<0.001$ ). Over 12 months, the percentage of individuals with severe trait anxiety decreased and, accordingly, the percentage of patients with moderate anxiety increased only in the treatment groups. No similar positive changes were observed in the control group.

The presence and severity of depressive symptoms were also assessed using the PHQ-9 questionnaire. At baseline and 12 months later, patients of the three groups did not differ in the severity of depressive symptoms (Table 5). Within 12 months, the severity of symptoms decreased in treatment group 1 and the control group, and there was no difference in the degree of decrease between these groups. Over 12 months, the percentage of

**Table 6.** Changes in the self-assessment of stress by VAS over 12 months in patients with paroxysmal AF with a history of interventional treatment (n=135)

| Parameter                                    | Group 1 (n=45)      | Group 2 (n=45)      | Control group (n=45) | P <sub>1-3</sub> | P <sub>2-3</sub> |
|--|---------------------|---------------------|----------------------|------------------|------------------|
| <b>Baseline</b>                              |                     |                     |                      |                  |                  |
| • Me [25 %; 75 %]                            | 5 [4; 7]            | 5 [2.5; 7]          | 6 [4; 8]             | N/s              | N/s              |
| • M±SD                                       | 5.3±2.3             | 5.1±2.9             | 5.6±2.6              |                  |                  |
| <b>In 12 months</b>                          |                     |                     |                      |                  |                  |
| • Me [25 %; 75 %]                            | 5 [3; 5]            | 3 [2; 4]            | 6 [5; 6]             | 0.003            | <0.001           |
| • M±SD                                       | 4.5±2.3             | 3.2±1.7             | 5.6±1.6              |                  |                  |
| Changes over 12 months, Δ% (Me [25 %; 75 %]) | -16.7 [-57.1; 25.0] | -50.0 [-60.0; -5.0] | -10.0 [-25.0; 50.0]  | 0.080            | <0.001           |
| P <sub>base-M12</sub>                        | 0.040               | <0.001              | N/s                  | —                | —                |

Me, median; M, mean; SD, standard deviation; VAS, visual analog scale; N/s, nonsignificant; P<sub>base-M12</sub>, significance of changes in 12 months.

patients without or with minimal depressive symptoms significantly increased only in treatment group 1.

At baseline, patients of all three groups had depression of similar severity according to VAS (Table 6). The severity of stress significantly decreased in both treatment groups 12 months later, and remained almost the same in the control group. The largest decrease (the mean of 50%) in the severity of stress was noted in treatment group 2.

## Discussion

The article presents the results of the study of changes in the severity of stress, anxiety/depression symptoms in patients with paroxysmal AF who have undergone interventional treatment, after conducting secondary prevention/rehabilitation with remote support in the 12 month follow-up period.

Stress, anxiety, depression are not only risk factors for developing various CVDs, including AF [18, 19], but are also associated with an increased risk of recurrent AF after catheter ablation, which is why the engagement of AF patients in the secondary prevention and rehabilitation programs after catheter ablation can contribute to solving their psychological problems and thus reduce the risk of recurrence. At the same time, patients with AF are in need of long-term rehabilitation with the greatest attention paid to continuous psychological assistance and support in order to overcome anxiety/depression symptoms because of the possible recurrence of arrhythmia. The efficacy of such programs in patients with AF with a history of catheter ablation has been studied in few trials. The impact of secondary prevention and cardiac rehabilitation programs on stress and anxiety/depression symptoms was mainly assessed in the patient population with coronary artery disease (CAD).

The randomized trial ENHANCED [20] including 151 patients with CAD showed that a 12 week training on stress management covering training, group support,

and cognitive behavioral therapy, in addition to the standard cardiac rehabilitation program, resulted in a more pronounced decrease in the levels of stress (assessed by the Perceived Stress Scale and the General Health Questionnaire;  $p=0.022$ ), anxiety (assessed by the STAI questionnaire;  $p=0.025$ ), and depression symptoms (assessed by the Beck Depression Inventory) as compared to the standard cardiac rehabilitation program. Prospective follow-up of these patients for up to 5.3 years (median 3.2 years) demonstrated a decrease in the incidence of cardiovascular complications in patients with a history of comprehensive rehabilitation (stress management training + standard cardiac rehabilitation) compared to the standard rehabilitation program (18% versus 33%, respectively; hazard ratio [HR] 0.49; 95% confidence interval [CI] 0.25–0.95;  $p=0.035$ ). Patients of the control group who did not participate in rehabilitation programs had higher incidence of cardiovascular complications (47%). The standard cardiac rehabilitation program (both in combination with and without stress management training) was associated with a 56% decrease in the risk of developing cardiovascular complications (HR 0.44; 95% CI 0.27–0.71;  $p<0.001$ ) as compared to the absence of rehabilitation measures. Thus, it has been shown that the inclusion of a 12 week stress management training in the standard cardiac rehabilitation program not only contributes to improving psychological status and reducing anxiety, depression and stress, but is also associated with a decrease in the risk of cardiovascular complications. Similar results were obtained in two large meta-analyses. The first meta-analysis [21] included 20 studies involving 4,450 patients with CAD and heart failure, the second once [22] included 35 studies involving 10,703 patients with CAD.

The need for secondary prevention and rehabilitation programs in patients with AF who underwent catheter ablation to improve their psychological status was demonstrated in a study based on the Danish National

Registry, which included 627 patients [23]. The incidence of anxiety (18%) and depression (13%) 6–12 months after catheter ablation was higher in these patients than in the general population (almost 5%), with female patients having lower scores for the psychological component of QoL (assessed by the SF-36 questionnaire) and higher prevalence of anxiety symptoms (assessed by the HADS-A subscore). Over 12 months of follow-up, 411 (59%) patients were repeatedly hospitalized, with a total of 1,167 hospitalizations. Repeat hospitalization, along with age >59 years, female sex, and the presence of co-morbidities, was associated with lower QoL, anxiety and poor perceived health. The investigators concluded that patients with AF require closer multidisciplinary observation and cardiac rehabilitation after catheter ablation.

The CopenHeartRFA trial [24–26] including 210 patients with paroxysmal or persistent AF and a history of catheter ablation showed that a 6 month comprehensive multidisciplinary cardiac rehabilitation program, compared to standard treatment, not only increased tolerance to physical activity, but also decreased the severity of anxiety symptoms. In this trial, patients were randomized into two groups: comprehensive cardiac rehabilitation, which included psychotherapeutic interventions (4 counseling sessions), physical training, and standard treatment. The purpose of the psychotherapeutic intervention was to provide emotional support, increase the awareness of AF patients about the disease, improve the disease control skills, and help to return to a full life. Counseling was performed by a specially trained nurse once every 5–7 weeks at the hospital or by telephone. The severity of anxiety symptoms by the HADS-A subscore decreased in the cardiac rehabilitation group from 33.7% to 13.1% 12 months later, and reached 12.8% ( $p=0.004$ ) in 24 months, and it did not undergo significant changes in the standard treatment group (from 28.6% to 23.8% in 24 months) [25].

In a Russian randomized trial including patients with paroxysmal AF who underwent catheter ablation showed that a personalized physical rehabilitation program not only increased physical performance and corrected risk factors, but also contributed a decrease in the severity of the symptoms of anxiety (by 46.7%;  $p<0.001$ ) and depression (by 43.8%;  $p<0.01$ ) as assessed by the HADS score [27, 28].

In contrast, the STAI and PHQ-9 inventories and VAS (stress severity) were used in this study to assess the psychological status of patients, as well as the HADS score, i.e., a comprehensive assessment of the psycho-emotional state of patients was performed. HADS-A

and STAI were used to assess anxiety, and HADS-D and PHQ-9 were used to assess depression.

Interesting results should be noted regarding state and trait anxiety. A significant decrease in the severity of state anxiety was revealed over 12 months of follow-up in all three groups, and there were no differences in the degree of its decrease between the control group and both treatment groups. Since state anxiety is usually caused by a specific stressful situation, in this case, probably hospitalization and interventional treatment, it is quite natural that it decreases significantly and equally over time. As for trait anxiety, although its level decreased in all three groups, the maximum changes were observed in treatment group 1, i.e., in patients who received remote telephone support, and the degree of anxiety reduction was significantly higher than in the control group ( $p<0.001$ ). Since trait anxiety is relatively stable and not related to a specific situation, the obtained data is indicative of the benefits of remote support of patients in the form of personal live communication with a physician over the phone, which beneficially influences the psychological state of patients. Patients from treatment group 2 who received remote support via e-mail, i.e., those who did not communicate personally with the physician, had the same degree of anxiety reduction as in the control group (median 5.4% versus 4.6%; nonsignificant differences).

Among the limitations to this study, we should mention the relatively small sample size, and the participation of mainly middle-aged patients with a sufficiently high educational background (more than 50% of subjects had higher education), which prevents the extrapolation of the findings to other patient categories.

## Conclusion

Thus, we established the efficacy of secondary prevention/rehabilitation programs, followed by 3 month remote support with regard to influencing the psychological status and severity of stress in patients with paroxysmal atrial fibrillation after interventional treatment. The results obtained can help optimizing approaches to the provision of medical care to patients with atrial fibrillation after interventional treatment, and offer new opportunities for controlling psychosocial risk factors and improving the general clinical condition in patients of this category.

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