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COMPARATIVE ANALYSIS OF LONG-TERM OUTCOMES OF THORACOSCOPIC AND ABLATION INDEX-GUIDED CATHETER ABLATION IN PATIENTS WITH NON-PAROXYSMAL ATRIAL FIBRILLATION

I.A.Taymasova, E.A.Artyukhina, A.Sh.Revishvili

A.V. Vishnevskiy National Medical Research Center of Surgery, Russia, Moscow, 27 Bolshaya Serpukhovskaya str.

Aim. To conduct a comparative assessment of the long-term results of thoracoscopic and catheter ablation using the ablation index in patients with non-paroxysmal atrial fibrillation (AF).

Methods. A comparative analysis of the long-term results of catheter ablation using the ablation index - group № 1 (36 patients) and thoracoscopic ablation with the left atrial appendage exclusion - group № 2 (42 patients) was performed.

Results. The effectiveness of catheter ablation was 57.14%, thoracoscopic ablation - 67.5% at 12-month follow-up (p=0,128). There were also no statistically significant differences in safety (p=0.55). Analyzing the structure of postprocedural atrial tachycardias in group №1 was demonstrated that AF recurrence was in 93.3%, in group №2 - in 50%. Atypical atrial flutter was documented in 6.6% of cases in group №1 and in 31.5% - in group №2. Typical atrial flutter was documented only in group №2 (18.75% (3)). However, AF recurrence was more common in the catheter ablation group after 6 months of follow-up (p=0.04).

Conclusion. Catheter and thoracoscopic ablation are comparable in terms of overall efficacy and safety, however, thoracoscopic ablation provides greater freedom from AF in a 6 month.

Key words: atrial fibrillation; thoracoscopic ablation; catheter ablation; ablation index

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Corresponding author: Irina Taymasova, E-mail: irina-tame@yandex.ru

I.A.Taymasova - ORCID ID 0000-0002-9280-9063, E.A.Artyukhina - ORCID ID 0000-0001-7065-0250, A.Sh.Revishvili - ORCID ID 0000-0003-1791-9163

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Atrial fibrillation (AF) is the most common arrhythmia in the population [1]. This type of heart rhythm disorder is associated with reduced quality of life, increased risk of heart failure, ischemic stroke, and death [2]. Developed by J.Cox in 1987, the Labyrinth operation and its modifications have become the mainstay of surgical treatment for AF, providing 95% relief from arrhythmia. However, the invasiveness of the intervention remained a limiting factor in the use of this intervention in patients with lone AF [3]. In this group of patients various variants of catheter isolation of pulmonary veins (PV) are widely used, their effectiveness reaches 80-83% in paroxysmal form of AF [4]. However, due to exacerbation of pathogenetic mechanisms, patients with persistent forms of AF require multiple catheter interventions to maintain stable sinus rhythm [5].

The method of minimally invasive epicardial thoracoscopic ablation of PV and the posterior wall of the left atrium (LA) has been introduced into clinical practice to improve the outcomes of interventional treatment of AF [6]. According to a number of systematic analyses, the efficacy of thoracoscopic ablation in patients with persistent form is 68-80% and in those with long-term persistent form is 25-72% at 12 months [7, 8]. The use of non-fluoroscopic electroanatomical mapping systems, improvement in methods for visualizing the anatomical and electrophysiological features of the atrial myocardium, the appearance of pressure-sensing ablation electrodes and the calculation of the ablation index (AI) allow the development of new, advanced protocols for catheter treatment of patients with non-paroxysmal forms of AF.

The aim of this study is a comparative evaluation of the long-term results of thoracoscopic and catheter ablation using AI in patients with nonparoxysmal forms of AF.

METHODS

The study included 78 patients with persistent and long-onset AF without valvular heart disease, coronary heart disease, or previous AF interventions.

Inclusion criteria:

- age over the 18 years old;
- nonparoxysmal AF (duration more than 7 days);
- symptomatic manifestation of AF (EHRA score > 2);
- left ventricular ejection fraction >40%;
- absence of contraindications to surgical treatment of AF;
- signed informed voluntary consent to participate in the study.

Exclusion criteria:

- congenital or acquired heart defects;
- contraindications to anticoagulant therapy;

- LA appendage thrombosis despite selected anticoagulant therapy;
- cerebrovascular events that occurred less than 6 months before study inclusion;
- previous open-heart surgeries, including those for AF;
- previous catheter interventions for AF;
- history of coronary heart disease;
- chronic diseases in the acute stage;
- the active phase of the infectious process.

Patients were on rate-control therapy with beta-blockers before the intervention. All patients were divided into two groups. Patients after catheter radiofrequency ablation (RFA) with AI were included in group 1, and patients after thoracoscopic ablation and amputation of the LA appendage were included in group 2. The mean age of patients in group 1 was 55.8±13.02 years, and in group 2, 57.36±7.64 years. The mean body mass index in group 1 was 30.36±4.44 kg/m^2, and 29.9±3.27 kg/m^2 in group 2. According to multislice computed tomography with contrast in group 1, the mean LA volume was 161.8±28.9 ml, in group 2, 170.6±39.8 ml, and the mean LA volume index in group 1 was 71.7±20.6 ml/m^2, in group 2, 76.9±17.8 ml/m^2 (Table 1). There are differences in the volume indices of LA but they are statistically insignificant.

All patients received rate-control and anticoagulant therapy prior to surgery. Preoperative preparation included the following studies: electrocardiography (ECG), daily ECG monitoring (daily ECG), coronary angiography, multislice computed tomography of LA and PV, echocardiography, esophagogastroduadenoscopy. Patients underwent transesophageal echocardiography to rule out LA appendage thrombosis.

Atrial fibrillation catheter RF technique

Before the intervention, the patient was connected to a CARTO 3 nephluoroscopic electroanatomic mapping system (Biosense Webster, USA). A ten-pole diagnostic electrode was placed through an access via the left subclavian vein into the coronary sinus. Through an access via the left femoral vein into the right ventricle, an electrode was placed for temporary bradycardia stimulation. After catheterization of the right femoral vein, a transseptal puncture was performed under fluoroscopic control, followed by administration of heparin at 100 U/kg, determination of activated clotting time and maintenance of this index at reference values for 300 seconds. Then, a multipolar circular diagnostic lasso electrode (Biosense Webster, USA) and a Thermocool Smarttouch irrigated ablation electrode (Biosense Webster, USA) with a pressure sensor were positioned in the LA cavity, followed by an anatomical reconstruction of the LA with construction of a bipolar voltaic map on the AF rhythm. The reference values for the bipolar voltage map were set at 0.1 and 0.3 mV. An esophageal temperature probe was positioned in the esophagus under fluoroscopic control (Astrocard-Esoseifti, Meditek) before the exposures were performed. RF interference was performed according to the point-by-point principle until the AI values were achieved: along the anterior wall 460, along the posterior wall 380, the distance between 2 ablation points did not exceed 6 mm. The following RF exposure parameters were set: maximum temperature 44ºC, maximum power 32W, irrigation rate during ablation 17-30 ml/min.

The first step was consecutive antral isolation of the right and left PVs. After performing antral isolation, a line was performed along the LA roof from the right upper PV to the left upper PV, then a line along the posterior LA wall

Table 1.

Clinical characteristics of patients, M±SD

Indicator	Group 1	Group 2	p
Number of patients, n	36	42	-
Age, years	55.8±13.02	57.36±7.64	0.63
Gender, male, % (n)	61% (22)	80.9% (34)	0.123
Persistent AF, %	44.4	38	0.2
Duration of anamnesis, months	7.1±2.4	7.1±3.1	0.24
Prolonged persistent AF, %	55.6	62	0.22
Duration of anamnesis, months	19.75±4.09	22.9±6.4	0.101
AP dimension of the LA, mm	54.68±7.34	53.02±8.98	0.38
LA volume, ml	161.8±28.9	170.6±39.8	0.09
LA volume index, ml/m^2	71.7±20.6	76.9±17.8	0.08
LV EF, %	61.14±7.17	60.64±6.65	0.74
EDV LV, ml	129.0±20.1	131.5±23.6	0.61
ESV LV, ml	54.8±10.7	56.21±12.2	0.59
EDD LV, mm	50.9±4.39	54.6±7.17	0.47
ESD LV, mm	32.92±4.71	36.83±6.44	0.33

Note: hereinafter referred to as AF- atrial fibrillation; AP - anteroposterior; LA - left atrium; EF - ejection fraction; LV - left ventricle; EDV - end-diastolic volume; ESV - end-systolic volume; EDD - end-diastolic dimension; ES - end-systolic dimension.

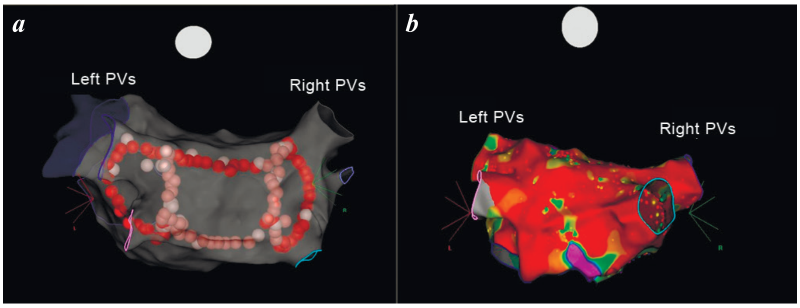

Fig. 1. Anatomical reconstruction of the left atrium (LA), posterior direct projection (a). The dots indicate radiofrequency (RF) applications: in red are RF applications with an ablation index of 460 and in pale pink are 360. Antral isolation of the right and left pulmonary veins (PV), a line along the LA roof, a line along the posterior wall of the LA were performed. Voltage map of the LA after RF ablation, posterior direct projection (b). Isolation of PV and posterior wall of LA is noted.

from the right lower PV to the left lower PV under temperature control on the channels of the temperature esophageal catheter (Fig. 1).

After RFA, a bipolar voltage map was repeated with the assessment of excitation breakthrough zones and additional point RF applications in these zones. The zone with the absence of electrical activity or with minimal amplitude of voltages (≤0.05 mV), not distinguishable from the noise pickup, was considered to be an isolation zone. After electric cardioversion on sinus rhythm, we checked the block of excitation entry and exit in the isolated veins and LA posterior wall. The mean duration of surgery was 203.8±61.3 minutes, the mean duration of fluoroscopy was 37.2±8.5 minutes, and the mean hospitalization period was 2.8±1.1 days.

Thoracoscopic atrial fibrillation ablation technique

Before thoracoscopic ablation, patients had a multipolar electrophysiological electrode positioned in the coronary sinus. Thoracoscopic ablation was performed in a cardiac surgical operating room. The surgical technique consisted in performing "box lesion" type interventions, which included antral isolation of the right and left PVs, a line along the LA roof - the upper "Box" line, a line along LA posterior wall - the lower "Box" line. The procedure ended with amputation of the LA appendage. The thoracoscopic ablation procedure was performed using bilateral access in the 3rd, 4th, and 5th intercostal spaces along the anterior and middle axillary lines. After installation of thoracoscopic ports on the right side, pericardiotomy above the diaphragmatic nerve was performed. Further, the oblique and transverse pericardial sinuses were distinguished. A conductor was placed behind the PV, along which a bipolar electrode (Synergy Ablation Clamp, AtriCure) was guided. Next, a series of RF applications (up to 28.5 W) were performed until tissue conductance decreased, displayed in real time on the AtriCure system panel, followed by exposure of the PV roof and posterior wall using a linear applicator (CoolRail Linear Pen, AtriCure) (up to 20 W). The left PV was similarly accessed by crossing the pericardium below the diaphragmatic nerve. Then, a series of RF-attacks were performed around the left PV until the tissue conductivity decreased, and the upper and lower "Box" lines were completed. The final step was amputation of the LA auricle using an endoscopic stapling device (EndoGia, Autosuture) (Fig. 2a). Next, signals from the isolation zones were read and evaluated using a reading electrode (Transpolar Pen, AtriCure). After electrical cardioversion on sinus rhythm, a check of the excitation input and output block in the isolated veins and posterior wall of the LA was performed: the Transpolar Pen (AtriCure) electrode was positioned in the isolation zones, followed by stimulation with 15 mA current and stimulation frequency of 600 ms with subsequent assessment of the presence of the stimulation conduction on the LA on ECG monitor and AtriCure system block. In the absence of a stimulus on the LA, the output block was considered verified. During stimulation with a temporary electrode in the coronary sinus, signals from the PV isolation zones and the posterior wall of the LA were read. If there is an isoline in the isolation zones, the input block was considered verified (Fig. 2b). The average duration of surgery was 268.69±80.02 minutes, and the average hospitalization period was 6.00±3.28 days.

After the interventions, patients were prescribed amiodarone for 3 months, followed by withdrawal. The intervention was considered effective if there were no atrial tachycardia recorded on ECG at 12 months follow-up. The safety of the intervention consisted in freedom from complications in the early and distant postoperative periods. Complications were considered as consequences of the intervention, requiring additional unplanned manipulations, increasing the duration of hospitalization by 48 hours or more, such as atrial wall perforation, cardiac tamponade, pericardial drainage, surgical conversion, pneumothorax, hemothorax, arterio-venous fistula, pulsatile hematoma in venous puncture.

Statistical processing of results

When quantitative values with a normal distribution were described, the mean values (M) and standard deviations (SD) were calculated. If the distribution differed from normal, the values were described using median (Me) and lower and upper quartiles (Q1-Q3). Nominal data were described with absolute values and percentages. When comparing the mean values in normally distributed populations

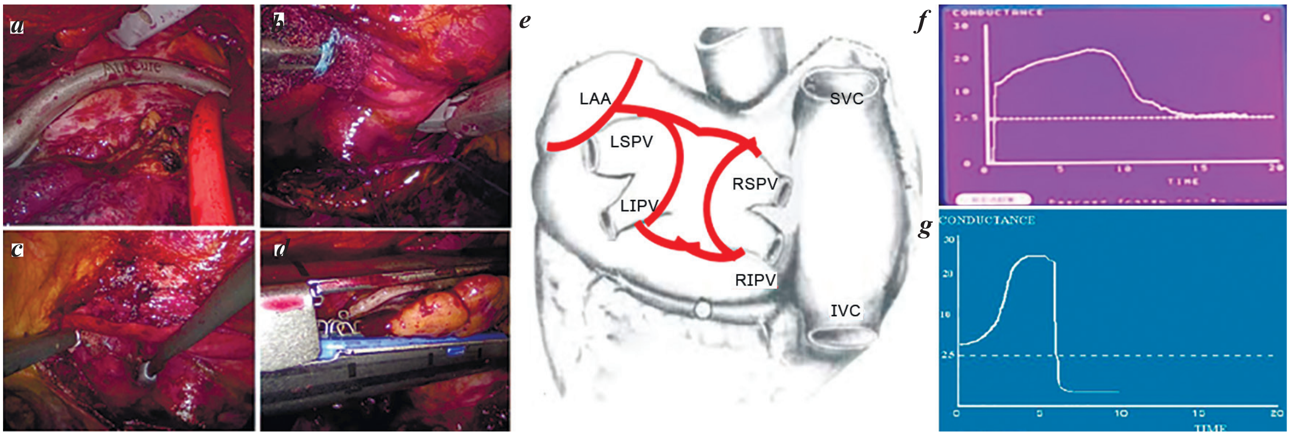

Fig. 2. Epicardial ablation of the left pulmonary veins (a), upper "box" line (b), lower "box" line (c), left atrial appendage (LAA) amputation with an endostapler (d). Schematic representation of the operation (e). Graphical representation of the tissue impedance drop during ablation (f). Schematic representation of tissue conductance reduction (g). Note: LSPV - left superior pulmonary vein, - RSPV - right superior pulmonary vein, SVC - superior vena cava, IVC - inferior vena cava, LIPV - left inferior pulmonary vein, - RIPV - right inferior pulmonary vein.

of quantitative data, Student's t-test was calculated. The Mann-Whitney test was used to compare quantitative data with a distribution other than normal. Differences were considered statistically significant at a significance level of $p<0.05$. Nominal data were compared using Pearson's χ^2 test or Fisher's exact test. The "survival" function of the patients was assessed using the Kaplan-Meier method. Comparative analysis of "survival" curves was performed using a number of tests: Log-Rank Test, Gehan's Wilcoxon Test, Cox's F-Test.

RESULTS

Long-term results of catheter ablation

At 12-month follow-up, according to daily ECG data, atrial tachycardia freedom was observed in 57.14% (n=20) of cases in group 1 (Fig. 3a). Atrial tachycardias were reported in 42.8% (n=15) of cases: 40% (n=14) had recurrent AF and 2.8% (n=1) had atypical left atrial flutter (AFl). The analysis of clinical characteristics of patients with stable sinus rhythm and with atrial tachycardia in group 1 revealed statistically significant differences in LA volume ($p<0.01$), LA volume index ($p=0.009$) (Table 2, Fig. 3b).

The overall complication rate of catheter ablation was 2.7% (n=1) of cases. The complication was intraoperative and was associated with the development of cardiac tamponade, which required pericardial puncture and drainage. The postoperative period lasted 4 days. There were no surgical complications in the distant postoperative period. This patient was excluded from the analysis of the technique results.

Long-term results of thoracoscopic ablation

At the follow-up period of 12 months according to the data of daily ECG in group 2, the efficacy of the procedure was 67.5% (n=27) of cases (Fig. 3c). Atrial tachy-

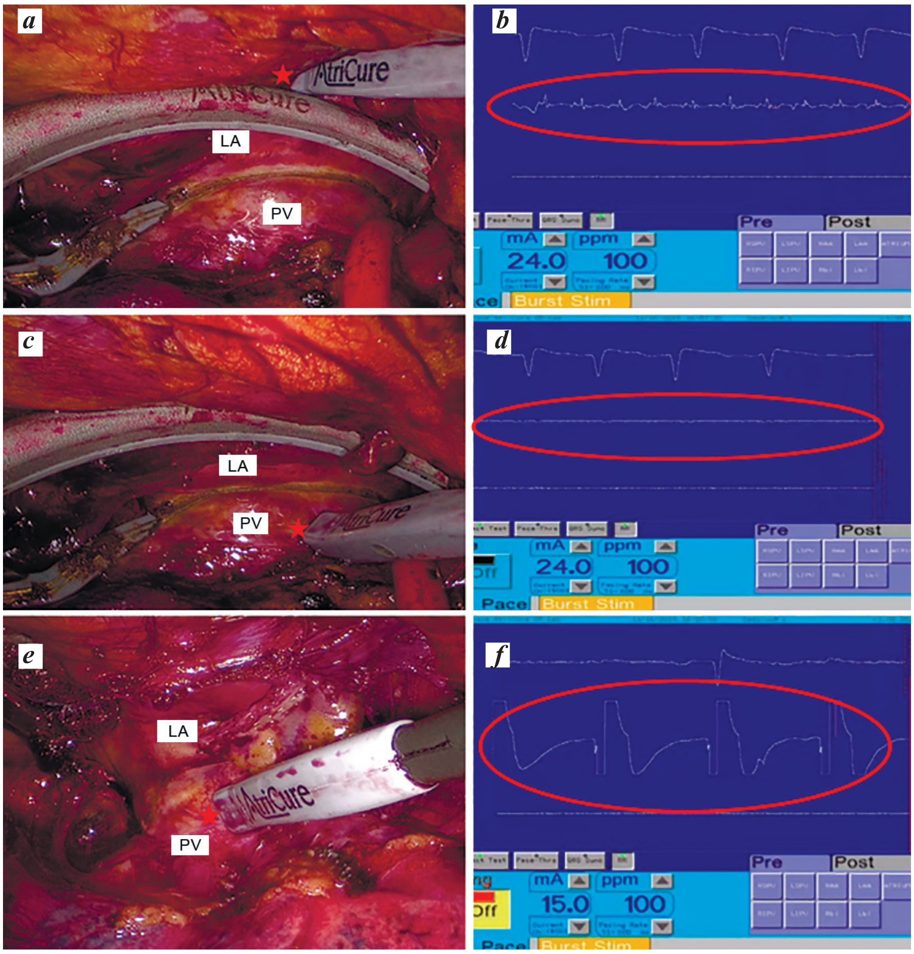

Fig. 3. Registration of signals from the left atrium (a): rhythm - atrial fibrillation (b). Registration of signals from the zone of isolated pulmonary veins (c): isoline - entry block (d). Stimulation of the isolated pulmonary vein zone after electrical cardioversion (e): exit block (f). Asterisks indicate activity registration zones; LA - left atrium, PV - pulmonary veins.

Table 2.

Comparative characteristics, Me (Q 25%-75%)

Indicator	Group 1			Group 2		
	SR	PAT	p	SR	PAT	p
Number of patients, n	24	16	-	20	15	-
Age, years	54 (50-63)	58 (51-64)	0.67	50 (38-64)	64 (54-68)	0.06
BMI, kg/m^2	29 (28-32)	31.2 (29-32)	0.18	30(27-34)	30 (29-33)	0.53
LA volume, ml	137.4 (118-141)	180 (171-195)	0.023	157(139-179)	187(180-221)	<0.01
LA volume index, ml/m^2	71.1(65-80)	89.7 (78.4-99.3)	0.036	60(45-70)	81(75-91)	0.009
LV EF, %	59 (55-66)	61.5 (59-64)	0.63	63(59-66)	59(58-63)	0.18
EDV LV, ml	133.4 (115-151)	131 (116-139)	0.49	120(100-144)	136(120-141)	0.72
ESV LV, ml	54.2 (48-65)	51 (48-59.5)	0.48	52(48-58)	52(48-63)	0.82
EDD LV, mm	56.7 (51-59)	53.5 (50-56)	0.16	50(45-54)	52(47-54)	0.78
КСР ЛЖ, мм	36.1 (32-42)	34 (31-38)	0.17	31(30-36)	33(30-35)	0.35

Note: hereinafter, SR - sinus rhythm; PAT - postoperative atrial tachyarrhythmia; BMI - body mass index.

cardias were reported in 40% (n=16) of cases: 20% (n=8) had recurrent AF, 12.5% (n=5) had atypical left-atrial AFl, and 7.5% (n=3) had typical AF. Cases of typical AFl were not included in the analysis of the effectiveness of the technique. The analysis of clinical characteristics of patients with stable sinus rhythm and with atrial tachycardia in group 2 revealed statistically significant differences in LA volume (p=0.023), LA volume index (p=0.036) (Table 2, Fig. 3g).

The total percentage of complications of thoracoscopic ablation was 4.7% (n=2) of cases. Complications developed due to perforation of the posterior wall of the LA with subsequent conversion to Labyrinth surgery. The causes of complications were damage of the LA roof during transverse pericardial sinus isolation in one case and damage of the posterior LA wall during an attempt to isolate the left PV in the second case. The average duration of the postoperative period was 11±1.4 days. There were no surgical complications in the distant postoperative period. These patients were excluded from the analysis of the technique results.

Comparative assessment of the long-term efficacy and safety of catheter ablation and thoracoscopic ablation

In a comparative evaluation of the results, no statistically significant advantage of thoracoscopic ablation was found (χ^2 =2.80, p=0.128). To compare the results at each follow-up time point, Kaplan-Meier curve analysis demonstrating freedom from postoperative atrial tachycardia at 12 months of follow-up in both groups was performed (Fig. 4a). Several tests were used to compare the two curves, the results of which showed no statistically significant differences between the curves (Log-Rank p=0.791, Gehan's Wilcoxon p=0.811, Cox's F p=0.323). Thus, the technique of catheter ablation using the IA index is comparable to thoracoscopic ablation in terms of overall effectiveness.

However, the assessment of the pattern of postoperative atrial tachycardias revealed that recurrent AF was recorded in most cases in group 1 (93.3%, n=14), whereas in group 2, recurrent AF was recorded in only 50% (n=8) of cases. Atypical AFl developed in 6.6% (n=1) of patients in group No.1 and in group No.2 in 31.5% (n=5) of patients (Table 3).

Kaplan-Meier curves were constructed for both groups to clearly assess the dynamics of freedom from AF in both groups. In order to assess the statistically significant difference in the degree of freedom from AF, a comparative analysis of the curves was performed (Fig. 4b). A number of tests were used to compare the two curves, the results of which showed no statistically significant differences between the curves (log-rank p=0.22412, Cox's F p=0.13784). It is possible that statistical differences were not detected because of the small sample size. Nevertheless, when comparing the long-term results according to the data of the visits, statistically significant differences between the groups were revealed. Thus, recurrence of AF was significantly more frequent in the catheter ablation group at 6 months of follow-up (p=0.04). Thus, a statistically significant tendency for recurrence of AF in group 1 at 6 months after the intervention compared to group 2 is determined (Fig. 4c).

Fisher's exact test was used to compare the safety of the interventions. Thus, it was found that the differences in the number of complications were not statistically significant (unilateral p=0.55, bilateral p=1.00). Thus, catheter and thoracoscopic methods are comparable in terms of safety. However, the duration of the early postoperative period was longer in group 2.

Table 3.

Structure of postoperative atrial tachyarrhythmias (PAT) in patient groups

Type of PAT	Group 1	Group 2
AF	93.3% (14)	50% (8)
Atypical AFl	6.6% (1)	31.5% (5)

Note: AFl - atrial flutter.

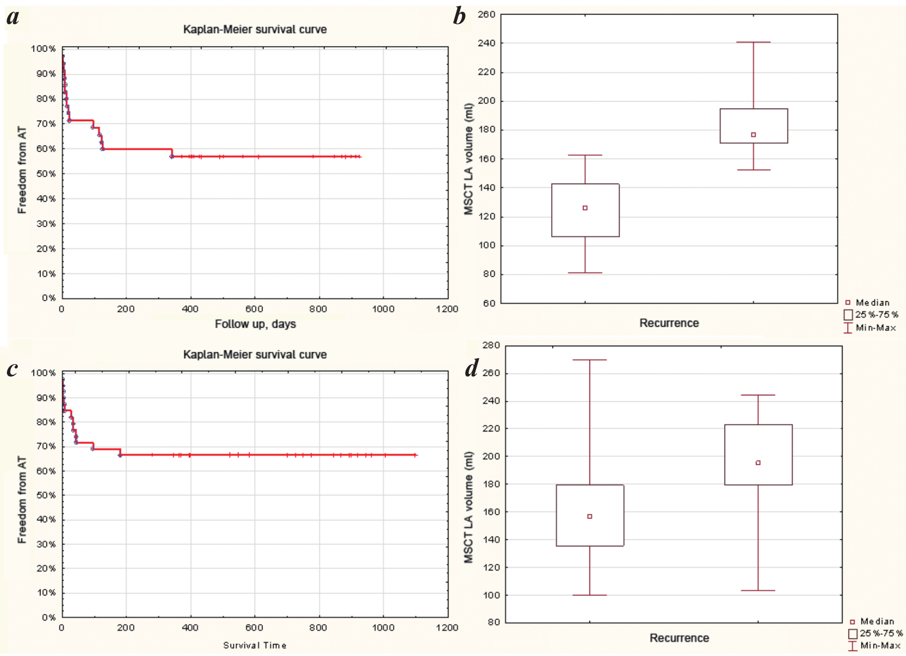

Fig. 4. Kaplan-Meier curves demonstrating freedom from atrial tachyarrhythmias at 12 months follow-up (a, c) and the distribution pattern (box plots) of left atrial volume values according to multislice computed tomography (b, d) after catheter and thoracoscopic ablation, respectively.

DISCUSSION

The technique of thoracoscopic ablation became widely known due to the first works of S.Krul, R.Wolf et al. (2005, 2011), devoted to the analysis of its efficiency, which demonstrated promising results [9, 10]. With the development of catheter technologies, there were published works on comparative analysis of two methods of surgical treatment of AF. One of the first studies comparing the results of thoracoscopic and catheter ablation of AF is the FAST study [11]. From 2007 to 2010, 124 patients were enrolled in the study and randomized into catheter and thoracoscopic ablation groups. Freedom from arrhythmias was significantly higher in the thoracoscopic ablation group compared with the catheter ablation group (65.6% vs. 36.5%, respectively, p=0.002). However, the rate of serious adverse events was higher in the thoracoscopic ablation group (34% versus 16%). Nevertheless, this study has a number of limitations. Most patients had a paroxysmal form of AF, and there was a history of previous catheter interventions for AF. The study of A.Adiyaman et al. (2018) presents the results of thoracoscopic and catheter ablation in patients with predominantly paroxysmal form of AF (74%) [12]. Catheter ablation was more effective than thoracoscopic ablation and provided freedom from AF in 56% of patients versus 29% of patients in the thoracoscopic ablation group (p=0.059).

A more in-depth analysis of the comparative characteristics of the two techniques has been conducted in several systematic and meta-analyses. According to a meta-analysis by W.R.Berger et al. (2018), thoracoscopic technique is associated with higher rates of freedom from AF in patients with persistent AF (69% vs. 51% in the catheter treatment group), but the risks of the procedure are also significantly higher [13]. Similar results are reflected in the systematic analysis of S. Yi et al. (2020) [14]. In patients with paroxysmal AF, thoracoscopic ablation has similar efficacy to catheter ablation, but in the group of patients with persistent AF it is associated with a greater percentage of freedom from AF, but also with a greater number of adverse events. According to a meta-analysis by A.Wang et al. (2020), catheter ablation provides less efficiency but greater safety compared to thoracoscopic ablation [15]. The authors recommend catheter ablation as the first-line treatment for patients refractory to antiarrhythmic therapy.

Despite similar results from meta-analyses, they also have several limitations. There was heterogeneity in the provision of data on patient history, which excludes the possibility of assessing potential predictors of effectiveness or ineffectiveness of interventions, heterogeneity in the designs of the analyzed studies, heterogeneity of forms of AF in patients included in the study, clinical characteristics, protocols for the procedures themselves.

In 2020, the results of the multicenter randomized CASA-AF study were published [16]. The study included 120 primary patients with long-term persistent AF, randomized into thoracoscopic and catheter ablation groups. However, catheter ablation was performed without AI index and esophageal temperature control compared to our study. According to the results of the study, freedom from AF without antiarrhythmic therapy was provided by 28% in the catheter ablation group, 26% in the thoracoscopic ablation group (p=0.83). Significant adverse events were reported in 15% of patients after thoracoscopic ablation versus 10% after catheter ablation within 30 days, and 40% after thoracoscopic versus 15% after catheter ablation within 12 months of intervention (p=0.003). Moreover, according to the data analyzed on the costs of one or another method, it turned out that catheter ablation is more cost-effective. The authors conclude that catheter ablation is associated with improvement of AF symptoms, quality of life and cost-effectiveness.

To achieve objective results, only patients without previous catheter interventions with nonparoxysmal forms of AF, without concomitant cardiac pathology were included in the study. Due to strict inclusion and exclusion criteria, the compared groups are comparable. All patients underwent interventions according to a unified strict protocol, which also contributes to a more objective analysis of the results. The peculiarity of this study is that catheter ablation was performed using the IA index. Thus, the present study has a number of advantages in comparison with the above-mentioned works, which allows an objective assessment of the results of catheter and thoracoscopic ablation. The long-term efficacy of catheter ablation with IA in the present study was slightly higher compared to the literature data and was 57.14% at 12-month follow-up. The efficiency of thoracoscopic ablation was 60%, which does not contradict the data of the world literature. It is worth noting that the duration of arrhythmological history and LA volume were slightly higher in the thoracoscopic ablation group compared to the catheter ablation group; however, the differences were not statistically significant.

Limitations of the study. The limitations of the study were the lack of randomization and the retrospective analysis of the data. To formulate clear recommendations on the choice of surgical treatment of AF, it is necessary to continue studying the problem in a larger sample of patients. Also, the use of multivariate analysis of clinical characteristics of a larger sample size would allow the identification of statistically significant predictors of intervention efficacy.

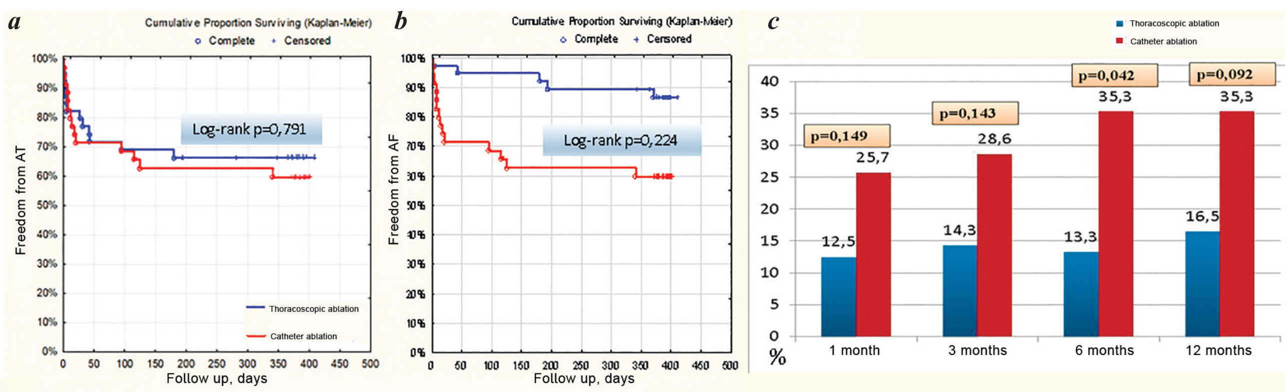

Fig. 5. Kaplan-Meier curves showing freedom from postoperative atrial tachycardia (a) and atrial fibrillation (b), dynamics of atrial fibrillation recurrence (c) in patient groups.

CONCLUSION

When comparing the results of long-term efficacy, it was found that catheter ablation of AF using the AI is comparable with thoracoscopic ablation in terms of overall efficacy and safety. Thoracoscopic ablation provides greater freedom from AF compared to catheter ablation in a time window of 6 months of follow-up. It was also revealed that in the group of patients with registered postoperative atrial tachycardia, the LA volume and the LA volume index were statistically significantly higher compared to patients with stable sinus rhythm.

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