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CHANGES IN THE PULMONARY VEINS OSTIA DEFORMATION AFTER RADIOFREQUENCY AND CRYOBALLOON ABLATION IN PATIENTS WITH PAROXYSMAL ATRIAL FIBRILLATION

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Aim. To study changes in pulmonary vein ostia strain after radiofrequency (RFA) and cryoballoon ablation (CBA) in patients with paroxysmal atrial fibrillation (AF) by intracardiac echocardiography.

Methods. Patients with paroxysmal AF (n=41) aged 60.1±7.1 years and duration of the disease 7.7±4.8 years were included in the study. Pulmonary vein (PV) isolation was performed with RFA (n=23) and CBA (n=18). All patients underwent transthoracic and intraoperative intracardiac echocardiography. Longitudinal strain of PV ostia was assessed before and after isolation.

Results. Groups were comparable in main clinical parameters. Regress of PV ostia strain after RFA and CBA was achieved in all of PV, which corresponded to complete PV isolation. Remarked trend toward a more pronounced regression of PV ostia longitudinal strain after CBA compared with RFA for left superior (10±0.7% and 6.1±0.8% respectively, p<0.001) and right inferior PV (9.3±0.7% vs 7.3±0.6%, p<0.001) requires continued observation and analysis of data in a larger group. There were no complications.

Conclusion. PV isolation is accompanied by a significant change in their longitudinal strain using intracardiac echocardiography both after CBA and after RFA.

Key words: atrial fibrillation; cryoballoon ablation; radiofrequency ablation; longitudinal strain; pulmonary vein isolation; intracardiac echocardiography.

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The use of interventional treatment today finds increasingly widespread application. The catheter ablation can be applied as a first-line treatment option for patients with paroxysmal atrial fibrillation (AF) as an alternative to antiarrhythmic therapy (recommendation class IIa, level of evidence B) according to the 2020 Clinical Guidelines for Atrial Fibrillation and Flutter of the Ministry of Health of the Russian Federation. Along with radiofrequency ablation (RFA), which has established itself as the "gold" standard for interventional treatment of AF, cryoballoon ablation (CBA) is strengthening its position every year, demonstrating clear advantages over antiarrhythmic therapy [1, 2].

Structural remodeling of atrial myocardium, pulmonary vein (PV) muscle, is considered one of the leading causes of AF due to development of atrial fibrosis and its electrical heterogeneity. The restoration of conduction in the PV is the cause of arrhythmia recurrence in 92.7% of cases. An earlier application of catheter AF treatment is a way to solve this problem and to reduce the structural remodeling of the left atrium (LA) and the frequency of arrhythmia recurrence [3]. Such a tactic allows reaching 80% of the effectiveness of AF treatment, considering repeated interventions. LA strain, as a manifestation of its remodeling, is currently considered one of the factors determining success in the strategy of maintaining sinus rhythm as well as predicting the risk of arrhythmia recurrence after catheter treatment [4]. Among the wide variety of instrumental methods, the most informative for studying of the atria are ultrasound and tomography [5]. The factors that might limit the tomography methods in a routine clinical practice are their high cost, the use of contrast, inability to use these methods in patients with implanted devices, time for image processing and obtaining results.

Speckle-tracking echocardiography (STE) allows for an accurate quantitative assessment of myocardial strain, systolic and diastolic function by analysis of the movement of gray scale spots obtained by two-dimensional sonography. The use of STE interventional treatment today finds increasingly widespread application. In 2018, a consensus of experts on imaging diagnostic methods in patients with AF was published (EACVI/EHRA Expert Consensus Document on the role of multi-modality imaging for the evaluation of patients with atrial fibrillation). This document specifies an approach to the use of STE for studying an atrial mechanical function. At the same time, the methodology for assessing the PV strain, as a structure directly involved in the electrophysiology of AF, is not mentioned in this agreement and has not yet been developed [6].

The dynamic intraoperative intracardiac echocardiography (ICE) using STE (before and after RFA) as a promising direction makes it possible to visualize all of PV ostia and assess the global longitudinal atrial strain, which is difficult with transesophageal way. The successful use of this technique made it possible to create a new method for assessing the damage transmurality in 2018. It's based on the changes in the PV ostia strain after its electrical catheter isolation. It has been shown that changes in the longitudinal PV ostia strain after the ablation on 6% and more correspondent to complete electrical PV isolation [7]. Based on the developed methodology the patent for invention of the Russian Federation No. 2645413 was obtained. In addition, the use of ICE allows to realize the intraoperative safety control to exclude possible complications of the intervention.

The treatment is aimed at disconnecting the bidirectional electrical conduction between the atria and PV ostia, achieved by damaging the muscle couplings. The expected effect is a change in the PV ostia longitudinal strain, realized by reducing of the muscle cells contractility, accessible to the study with ICE.

Another effect of the ablation is a change in the LA strain due to the lack of contractility of isolated PV ostia and their contribution to the realization of atrial contractility. However, due to the technical differences of RFA and CBA, a different severity of the damaging effects is assumed. This data are interesting in the perspective of studying the influence of PV ostia strain after RFA and CBA on the atria and ventricles mechanics. Now, this data is insufficient and is discussed only in individual articles. Based on this, the aim was to study the changes in the PV ostia strain intraoperatively after RFA and CBA of PVs in patients with paroxysmal AF using ICE.

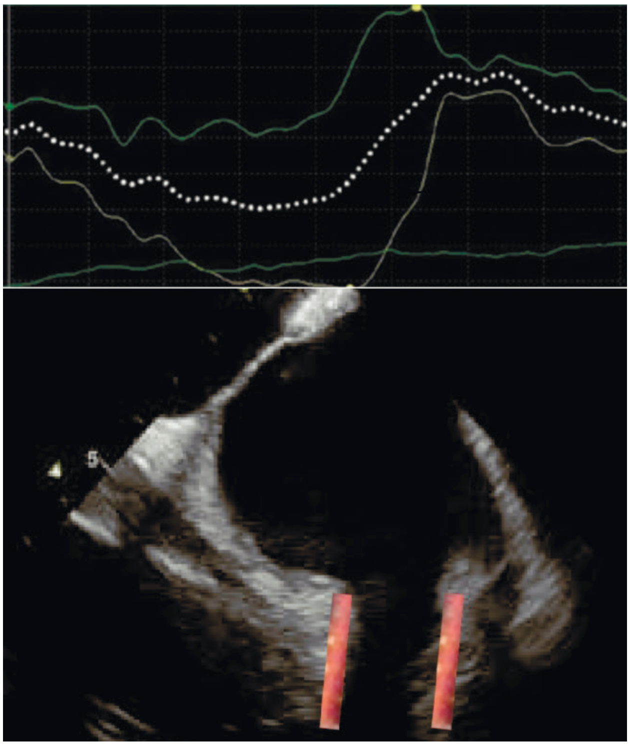

Fig. 1. Upper figure - the curve of longitudinal strain of the left superior pulmonary vein ostia; lower figure - installation of the control volume in the proposed area of the muscular coupling of the left superior pulmonary vein.

METHODS

The patients with paroxysmal AF aged 60.1±7.1 years were included in the study. AF had to be confirmed by 12-lead electrocardiogram or 24-hour electrocardiogram monitoring. All patients had been treated with anticoagulant and antiarrhythmic therapy in maximum tolerated therapeutic doses and had a duration of AF of 7.7±4.8 years. Among the included patients, 10 people were diagnosed with coronary artery disease, 35 with hypertension, 7 with type 2 diabetes mellitus, 4 - had anamnestic indications of a stroke.

The study was approved by the Ethics Committee of the Cardiology Research Institute, Tomsk National Research Medical Center, Russian Academy of Sciences and performed based on the Department of Surgical Arrhythmology and Cardiac Pacing (Tomsk).

Criteria for inclusion in the study:

• Patients of both sexes over 18 years of age
• Paroxysmal AF
• Written consent of the patient to participate in the study
• Availability of indications for interventional treatment

Exclusion Criteria:

• Persistent, long-term persistent and permanent forms of AF
• Thrombosis of heart chambers
• Any other medical condition precluding intervention in the study: acute myocardial infarction; stenosis or insufficiency of any valve requiring cardiac surgery; cardiomyopathy (hypertrophic or dilated cardiomyopathy): severe heart failure (IV functional class according to NYHA).

All patients underwent a standard preoperative clinical and instrumental examination, including transthoracic echocardiography using an expert class apparatus (Philips HD15) in accordance with the standard protocol.

The patients included in the study, in accordance with a simple non-stratified randomization sequence obtained using computer random number generation, were divided into 2 groups: group 1 - PV isolation was performed with RFA (n=23) and 2nd group - PV isolation was performed with CBA (n=18).

Interventional treatment

RFA of the PVs was performed in the X-ray operating room under medical sedation using the right femoral approach with the installation of 3 introducers: 8 Fr, 6 Fr and Fast-Cath 8.5 Fr. Catheter electrodes NaviStar ThermoCool 3.5 mm (Biosense Webster, USA) and 4-pole diagnostic Viking (Boston Scientific, USA) were inserted into the heart chambers through the first two introducers. Additionally, the left femoral vein was punctured, 10 Fr introducer was inserted and a catheter for ICE (SoundStar 3 D (Biosense Webster, USA)) was passed through it into the right atrium. Under the control of ICE, the atrial septum was punctured using a Fast-

Cath 8.5 Fr introducer and a BRK-1 needle (St. Jude Medical, USA). The Lasso circular electrode (Biosense Webster, USA) was passed through the introducer into the left atrium and an ablation electrode through the atrial septum with initiation of heparin infusion to the target range of activated clotting time of 300-350 sec. ICE was performed using STE, tissue PV strain was measured, expressed as a percentage, and the rate of PV strain, measured in 1/sec. Visualization of the left PVs was performed from the right atrium, for visualization of the right PVs an ultrasound catheter was passed through the post-operative opening of the atrial septum into the LA. An electrophysiological study was performed on the «Elkart» hardware-software complex (Electropulse, Russia). Anatomical reconstruction of the LA was performed using a three-dimensional non-fluoroscopic system CARTO 3 (Biosense Webster, USA) using FAM technology. The electrical PV isolation was performed using the ablation electrode and radiofrequency destructor RF100-TZ (Electropulse, Russia) with power control of 45 W, target temperature of 50ºC and exposure time of 10-15 seconds with the formation of radiofrequency damage lines at a distance of 0.5 -1 cm around the each PV ostia and subsequent control of the destruction efficiency. The disappearance of PV potentials on a Lasso circular electrode (Biosense Webster, USA) was the electrophysiological criterion of isolation. During the stimulation of PV and LA, a block of “input” and “output” was recorded. ICE was repeated after PV antral isolation to assess PV strain and the strain rate with STE. The results were analyzed on a GE Vivid q ultrasonic scanner (USA) using the Q-Analysis quantitative analysis software. The procedure was completed by removing the electrodes and introducers and applying pressure bandages to the puncture sites.

CBA of the PVs. After the puncture of the right femoral vein the puncture of the atrial septum was performed under the ICE control with following passing of FlexCath Advance (Medtronic, USA). The cryocatheter was alternately placed in all of PVs. Occlusion control was performed by injecting a contrast agent. Under the control of Achieve 20 mm electrode (Medtronic, USA), cryoisolation of PVs was performed using a second-generation Arctic Front Advance 28 mm catheter (Medtronic, USA), temperature up to -40-60 ºC and exposure time 180-240 seconds. Isolation of the right PVs was performed against the background of the phrenic nerve stimulation from the right subclavian vein. The ICE technique was the same.

Speckle-tracking echocardiography is a quantitative ultrasound technique for assessing myocardial function by analyzing the movement of “spots” (speckle) detected on conventional 2-dimensional echograms. When tracking the movement of “speckles” during the cardiac cycle, the strain and strain rate can be measured immediately after the study. Speckle nuclei are registered simultaneously in several zones within the image plane and provide information about local displacement with studying such parameters of myocardial function as speed, strain, and strain rate. Displacement is a parameter that determines the distance by which the “speckle” changes position in two consecutive frames and is measured in cm. Strain reflects the change in the length of the myocardial segment, is measured in percent and, at the same time, can have positive or negative values corresponding to shortening or lengthening of the segment.

STE analysis included 3 consecutive cardiac cycles to measure strain. STE provides data on myocardial strain in 3 spatial directions: longitudinal, radial and circular. In our study, we assessed only the longitudinal strain of the PV ostia. Based on the PVs structure, the PV ostia strain can be due to the inclusion of muscle cells in the wall, the thickness of which decreases towards the distal sections. The control volume for strain measurement was in the region of the PV ostia. At the same time, the longitudinal strain reflected changes in the length of the control volume directed from the PV ostia to their distal parts. The obtained data were processed using specific acoustic-tracking software (Fig. 1 and 2). This technique does not conflict

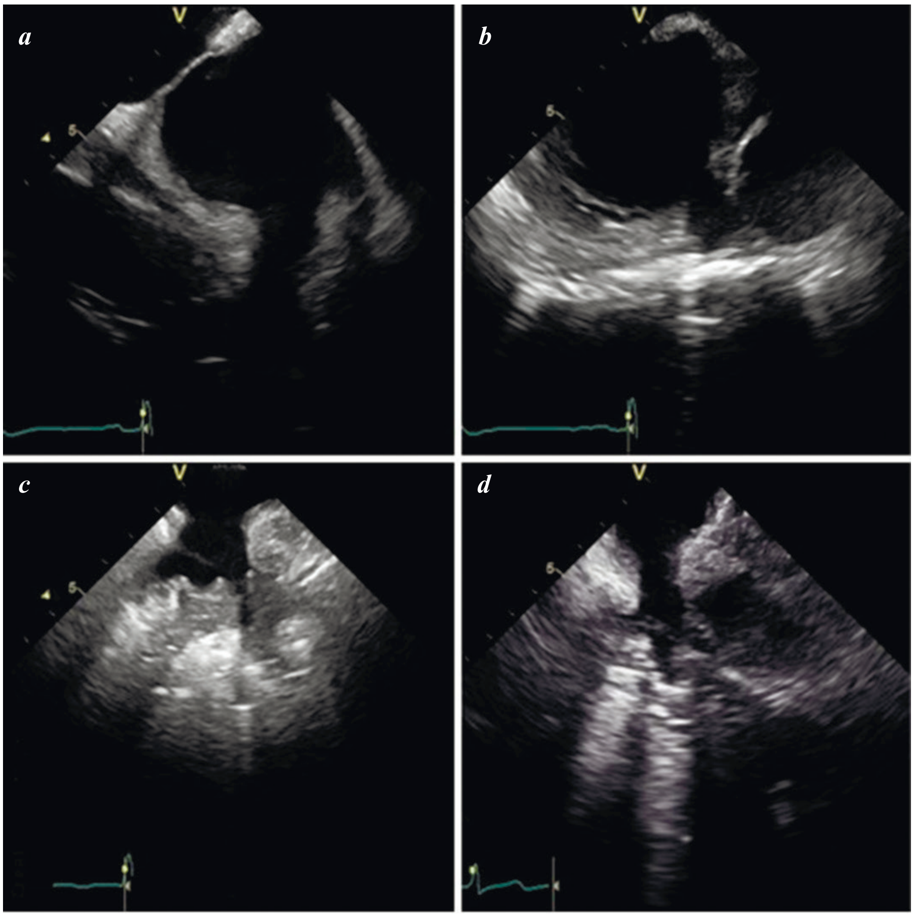

Fig. 2. Pulmonary vein ostia visualization using intracardiac echocardiography: a - left superior pulmonary vein, b - left inferior pulmonary vein, c - right superior pulmonary vein, d - right inferior pulmonary vein.

with the accepted consensus EACVI/EHRA Expert Consensus Document on the role of multi-modality imaging for the evaluation of patients with AF, because it does not affect the aspects of studying the mechanical properties of the LA.

Statistical analysis of the obtained data was performed using the STATISTICA ver. 10.0 application software package for Windows. The type of sample distribution was determined using the Shapiro-Wilkes criterion. The analysis was based on the use of the Student's t-test for two groups on a dependent and independent basis. To compare the percentages, the criterion of consent $\chi 2$ was applied. A p-value < 0.05 was considered as significant. The data is presented in the form of M±SD, M - the arithmetic mean, SD - the standard deviation,

Table 1.

Clinical characteristics of patient groups

	RFA	CBA
Number of patients, n	23	18
Age, years (M±SD)	58.1±7.0	62.1±7.3
Hypertension, n (%)	21 (91.3)	14 (77.7)
Diabetes mellitus, n (%)	3 (13.0)	4 (22.2)
CAD, n (%)	4 (17.3)	6 (33.3)
Stroke, n (%)	3 (13.0)	1 (5.5)
CHA_2DS_2-VASc (M±SD)	2.1±1.3	2.6±1.8
AF duration, years (M±SD)	9.1±4.7	6.3±3.0
Antiarrhythmic therapy, n (%)	23 (100)	18 (100)
Anticoagulant therapy, n (%)	23 (100)	18 (100)
LVEF (%)	65.7±4.5	66.2±4.5
LA diameter, mm (M±SD)	39.6±4.0	39.7±3.4

Note: RFA of PVs - radiofrequency ablation of pulmonary veins; CBA of PVs - cryoballoon ablation of pulmonary veins; CAD - coronary artery disease; LVEF - left ventricle ejection fraction.

Table 2.

The longitudinal strain of pulmonary veins ostia in patient groups after RFA and CBA, M±SD

	Longitudinal strain, %			p
	before	after	Δ	
RFA group				
LS PV	26±1.4	24.4±1.0	6.1±0.8	0.041
LI PV	26±1.4	22.6±0.8	13±0.8	0.023
RS PV	23.2±1.2	21.4±1.2	7.7±0.7	0.049
RI PV	24.5±1.1	22.7±1.3	7.3±0.6	0.038
CBA group				
LS PV	26±1.5	23.4±1.1	10±0.7	0.026
LI PV	24±0.9	21.6±0.9	11±0.8	0.019
RS PV	23.2±1.3	21.4±1.1	7.7±0.6	0.049
RI PV	24.5±1.1	22.2±1.1	9.3±0.7	0.042

Note: LS PV – left superior pulmonary vein; LI PV – left inferior pulmonary vein; RS PV – right superior pulmonary vein; RI PV – right inferior pulmonary vein.

RESULTS

The clinical characteristics of the patients' groups are presented in table 1.

The groups were comparable in terms of the main clinical and instrumental parameters. All patients had a normal PV anatomy according to the ICE data.

Both interventional treatments were performed in sinus rhythm with the possibility of pre- and post-operative ICE with STE analysis of 3 consecutive cardiac cycles for the strain measurement. The received data were processed using specific acoustic-tracking software.

The analyzed data of the RFA and CBA of PV ostia in patients' groups are presented in table 2.

According to analyzed data before and after isolation the longitudinal strain of PV ostia regressed in both groups. The value of regression corresponds to their complete electrical isolation according to previously obtained data [7].

The strain rate of PV ostia was excluded from the analysis due to the large variation in the values. It was associated with the difficulty of stabilizing the ultrasonic sensor in the longitudinal direction in the LA. The decision to exclude this indicator was also based on a small sample of patients and the high probability of distorting the results. Continuing the collection of data will minimize the measurement error and increase the reliability of the results.

A comparative analysis of the changes in the PV ostia longitudinal strain after the CBA and RFA has led to ambiguous results. A significantly better regression of longitudinal strain was shown after the CBA of PV ostia for the upper left (6.1±0.8% and 10.0±0.7%, p<0.001) and lower right PV (7.3±0.6% and 9.3±0.7%, p<0.001), with no significant differences for the upper right PV (7.7± 0.7% and 7.7± 0.6%, p= 0.844) compared with RFA. At the same time, a significantly better regression in the longitudinal strain of the left lower PV was shown after RFA (13,0±0,8% и 11,0±0,8%, p=0,018) (Fig. 3).

There were no periprocedural complications reported in the groups.

DISCUSSION

Intraoperative ICE with STE, used in our study as the main technique to assess the PV ostia strain, is not currently routine to evaluate the PV isolation. At the same time, the experience in the use of ICE in our center has proved the informative and practical value in the intraoperative assessment of the intervention efficacy, the possibility to determine the LA and PV anatomy along with the assessment of structural and functional changes, the exclusion of intracardiac thrombosis in patients with stable anticoagulation therapy in the previous 3 weeks and complications of intervention, and the information on the catheter position in the PV ostia. A search for other literature data on the use of ICE for assessment of PV ostia strain in the patients with AF reveals the absence of analogues and the uniqueness of the obtained data. Separate works studied the possibility of using ICE to study a PV anatomy; as a result, they defined the area of left upper PV cross-sectional opening as a prognostic criterion of RFA efficacy with the threshold value of 154 mm2/m2 (referred to the body surface area) [8]. The visualization capabilities for the detection of the ablation sites, local PV ostia changes and the surrounding tissue after PV isolation was investigated [9]. Despite the obvious possibilities and potential, the ICE method is obviously underestimated, so it is limiting its widespread introduction into surgical practice.

There are numerous studies devoted to the comparative analysis of two currently existing most effective methods for AF treatment, RFA and CBA of PVs, in the majority show comparable profiles of efficacy and safety. In separate studies CBA had superiority over RFA: lower risk of thrombosis in damaged sites, possibility of the LV isolation in one action that significantly reduces time of procedure, and the opportunity to be used in the centers with low experience of catheter treatment due to the simpler technical protocol. There were no significant changes between two methods in a safety profile [10].

Our study was performed on a group of patients who were divided into two groups: the 1st undergone CBA, the 2nd - RFA. Intraoperative analysis of PV ostia longitudinal strain with ICE allows us to conclude the significant regression of a longitudinal strain after the PV ostia isolation regardless of the energy type. Previously obtained in our center data used to form an alternative method of assessing the effectiveness of PV isolation. It indicates the successful isolation in a case of changes in PV ostia longitudinal strain by the 6% and more in a comparison with data of the control electrophysiological study [11]. In our study, these benchmarks were achieved in all patients regardless of the type of interventional treatment used. Two of the four PVs showed a multidirectional response with a trend of greater regression of the longitudinal strain immediately after the CBA. Revealed differences are most likely due to technical features of CBA. While the common goal of the two techniques, leading to complete electrical PV isolation, its achievement is realized by different lesion area and depth. The use of cryoballoon has several technical features: a wider damage area, a uniformly circular depth of the muscle couplings necrosis in opposition to the damage severity fading at the periphery during pointwise RFA. Search of studies does not allow us to find analogues of this study and the results are contradictory.

For example, in the works of Mamchur I.N. et al. (2019) the parameters of LA and PV mechanical function before and after catheter ablation were deeply studied. Out of 104 included patients who were subjected to the study of LA function, invasive manometric study of PV mechanics was performed in only a small group of patients (n=17). All of them were treated with RFA. There is no data on invasive study of PV function among patients who underwent CBA. Nevertheless, study of LA mechanical function in dynamics of observation in the patients group allowed to document a regression of reservoir and pump function after PV ostia isolation both after RFA and CBA with more significant changes immediately after RFA procedure. Authors explained this fact by the judgment of deeper and more heterogeneous damage during RFA in contrast to more homogeneous one during CBA [12]. Earlier the same group of scientists proposed a method of ICE assessment of muscle couplings contractility by measuring the lumen diameter of PV ostia before and immediately after isolation [13]. In 2021 Gottlieb L. et al. studied changes of PV and LA volume according to magnetic resonance imaging after RFA procedure for patients with AF and healthy sheep. They showed that reduction of PV diameter after its isolation was associated with scar length, and reduction of contractility was observed only in places of ablation. So the authors have supposed that atria size reduction after ablation is a consequence of energy type and scar formation in contrast to the data on an opposite development of structural remodeling [14]. Analogous conclusions were received in research of 100 patients with AF, where the area of PV cross section at 0.5 cm from the ostium after RFA decreased both in a group of responders and group of non responders, that excluded predictive ability of this data in maintenance of sinus rhythm [15]. Perhaps, the specificity of the damaging effect of cryoballoon leads to the formation of an extended homogeneous scar tissue and can explain a greater change in PV strain after CBA compared with RFA. Obviously, we should consider the fact that our study is small and requires refinement of the obtained results on a larger sample of patients. Therefore, the revealed tendency of greater changes in the longitudinal strain of two out of four PVs cannot be clearly assessed at present and gives grounds at this stage only to

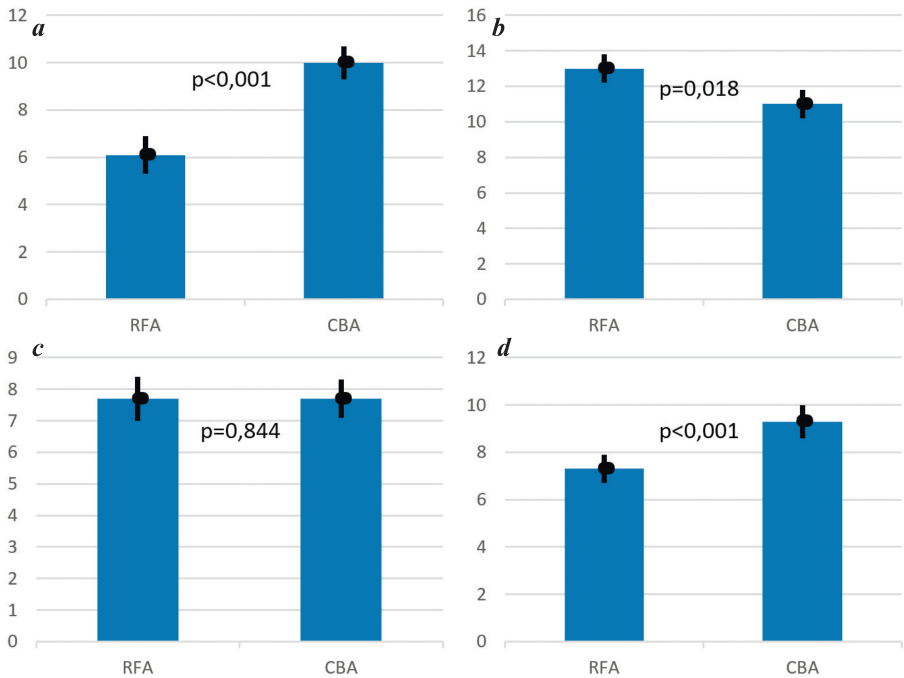

Fig. 3. Comparative analysis of changes in the longitudinal strain of pulmonary veins ostia after radiofrequency and cryoballoon ablation: a) left superior pulmonary vein, b) left inferior pulmonary vein, c) right superior pulmonary vein, d) right inferior pulmonary vein.

state the fact of significant changes in the PV ostia strain after both types of ablations.

An absence of contact force sensors on the ablation electrodes used was a limitation of the work performed, which did not allow taking this data into analysis of the results obtained. However, implementation of radiofrequency exposure in a persistent mode, allowed achieving continuity of the ablation line around the PVs. The data of the delayed ICE with the study of PV ostia strain could provide additional information in the aspect of comparative analysis of two techniques, but the study was not performed in the dynamics due to the difficulties in obtaining such data in patients without recurrent arrhythmias.

CONCLUSION

Both CBA and RFA significantly reduce PV longitudinal strain immediately after isolation according to ICE data. Further monitoring of arrhythmia recurrence rates and dynamics of cardiac structural and functional changes in the patients' groups will help to evaluate the predictive ability of the revealed changes in treatment efficacy and influence on atrial and ventricular mechanics. Also, it will help to consider the method of ICE with STE as an alternative to intraoperative electrophysiological study for control of PV isolation and its widespread introduction into practice.

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