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Original Research Article

Mechanical function of left atrium and pulmonary vein sleeves before and after their antrum isolation

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ABSTRACT

Background and objective: Pulmonary vein (PV) sleeves are established as the main substrate taking part in the mechanisms of atrial fibrillation (AF) initiation. However, we have extremely few data concerning their physiological role in the heart contractility. The aim of the study was to estimate the mechanical function of the left atrium (LA) and PV sleeves before and early after their isolation.

Materials and methods: A total of 17 patients with a mean age of 57.4 ± 8.3 years who underwent PVs isolation due to AF were enrolled in the study. A day before the procedure a computed tomography (CT) of the LA and PVs and dopplerography of transmitral flow were performed. During the procedure the mechanical function of the LA and PV sleeves were estimated by transesophageal echocardiography and manometry in the left heart chambers.

Results: During the invasive study the patterns of the heart chambers and PV sleeves pressure were identified. These patterns confirmed the active role of the PV sleeves in LA filling and active LA relaxation during left ventricular systole. After PV isolation an alteration of transmitral blood flow and increase of LA pressure were registered. However, diastolic dysfunction was ruled out by LV manometry, thereby testifying LA mechanical function disturbance. The change in PV hemodynamics also occurred as a result of the decrease in PV sleeves contractility, revealed by manometry and paired CT scans.

Conclusions: The PVs take an active part in left atrial filling by contraction of their sleeves. Antrum isolation of the PVs leads to the deterioration of their contractility and LA reservoir function.

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1. Introduction

Traditionally, left atrial mechanical function implies three different mechanisms: the left atrium (LA) actively empties immediately before the onset of left ventricle (LV) systole, the LA is a reservoir that stores pulmonary venous return during LV contraction and isovolumic relaxation, the LA passively empties into the LV down the pressure gradient during LV diastasis [1]. Up to this day, LA mechanical function has been evaluated only in the context of its stunning, which is the development of LA appendage mechanical dysfunction usually accompanied by spontaneous echocardiographic contrast [2]. Mechanisms of stunning are well known, but the overwhelming majority of data concerning these mechanisms were obtained in experimental studies on isolated heart specimens [3]. The analysis of LA mechanical function in humans in so far published studies included peak A presence and amplitude in transmitral blood flow [4–6], measured by the LA dimensions and volume [7] or LA appendage outflow velocity [8,9]. The majority of studies suggested only the fact of contractility decrease or the presence of spontaneous echo contrast after the restoration of the sinus rhythm [10]; in a few studies, there were control groups with sinus rhythm at baseline [2]. As to the LA and pulmonary vein (PV) sleeves mechanical function after their antrum isolation in sinus rhythm patients, in none of the studies the evaluation of any pathogenetic component alteration has been undertaken.

PV sleeves are established as the main arrhythmogenic substrate taking part in the mechanisms of atrial fibrillation (AF) initiation and maintenance [11–14]. However, we have extremely few data concerning their physiological role, namely their direct or mediated participation in contractile function of the heart. Recently, the role of the PV sleeves receptor complex in inotropic responses was established [15], and contradictory data concerning their muscle fibers active contraction was obtained [16–18]. Some authors linked physiological means of this contraction with an obturative function of PV sleeves preventing blood regurgitation during atrial systole [11]. These data were also obtained mainly in experimental studies in animals. There are unpublished reports indicating the ability of the PVs to change the diameter of their ostia during the cardiac cycle. The question is whether these diameter changes depend on active muscle contraction or on passive stretching by the blood pressure.

The objective of the study is to estimate the mechanical function of the LA and PV sleeves before and early after their antrum isolation.

2. Materials and methods

A total of 17 consecutive patients (12 men and 5 women) with a mean age of 57.4 ± 8.3 years were enrolled in the noncontrolled study. The duration of symptoms was 25.2 ± 8.1 months. In 12 patients, arrhythmia was considered idiopathic; 5 of them had postmyocardial infarction syndrome 17.2 ± 6.1 months ago and underwent percutaneous coronary revascularization. All of the patients suffered from paroxysmal atrial fibrillation due to which they underwent antrum PV isolation. All patients had sinus rhythm before, during and immediately after ablation. No one had echocardiographic signs of LA "stunning."

The day before the procedure the ECG-gated contrast multislice computed tomography (MSCT) of the LA and PVs in 4-D mode and simultaneous transmitral blood flow dopplerography were performed. For MSCT a 64-sliced Somatom Sensation 64 (Siemens, Germany) computed tomographic scanner was used. For LA opacification, 100-mL bolus of 350-mg/mL contrast agent was injected in the cubital vein with an automated injection device at a pump rate of 5 mL/s. The section thickness of axial scans was 1 mm with a 0.9-mm interval. Multiplanar and 4-D images were analyzed on a Leonardo workstation (Siemens, Germany) using cardiology preset. ECG gating allowed obtaining images in all the phases of the cardiac cycle. For transthoracic dopplerography Aloka SSSD-5500 Prosound (Aloka, Japan) scanner with sector 3 MHz phased-array transducer was used. After simultaneous registration of both data, the cardiac cycle was divided into 10 equal intervals with an increment of 10%. At the beginning of each interval the diameters of each PV at the sleeve level were measured (Fig. 1), then these measurements were compared with transmitral blood flow pattern (Fig. 2).

During the PV isolation procedure the mechanical function of the left atrium and PV sleeves was estimated by simultaneous

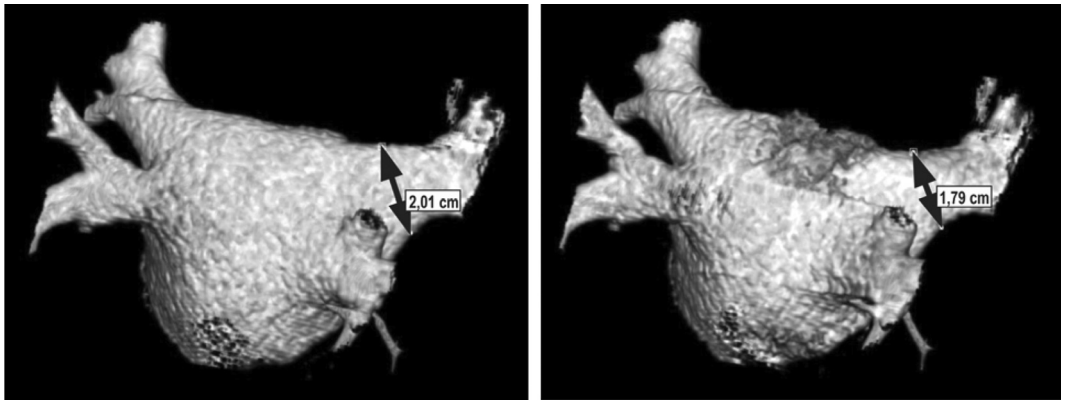

Fig. 1 – Variability of the right superior PV sleeve diameter (1.79–2.01 cm) in the same patient during the cardiac cycle by 4-D multislice computed tomography.

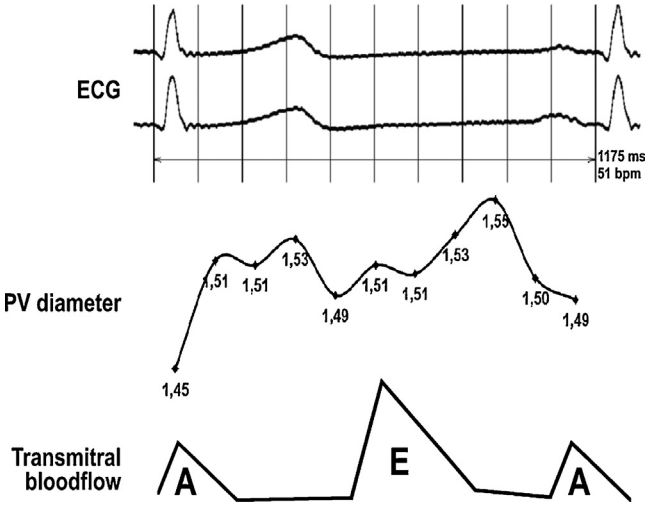

Fig. 2 – Comparison of ECG-gated data of the four PV sleeves diameter and the transmitral blood flow curve in one patient. Cyclic narrowing of the PV sleeves coincides with E and A transmitral blood flow peaks.

transesophageal echocardiography and invasive manometry in the left heart chambers including the balloon inflated PV sleeves (Fig. 3A and B).

The elastic balloon was inflated by contrast until total occlusion of the PV lumen but not overdistenting the PV sleeves. This was verified by the absence of contrast interflow from the PVs to LA chamber (Fig. 3C). These measurements were performed before and after PV antrum isolation. The total pressure in the balloon consists of three components: LA pressure, pulmonary capillary wedge pressure and the assumed pressure of PV sleeves contraction. As far as the pulmonary capillary wedge pressure is relatively equal to the LA pressure, their sum is constant, and pressure fluctuations in the balloon are almost entirely due to the compressive strength of the PV sleeves (Fig. 3D).

For echocardiography, an Aloka SSSD-5500 Prosound (Aloka, Japan) scanner with a transesophageal 5 MHz biplane transducer was used.

PV isolation was performed under general anesthesia. The electrophysiological study with left atrial anatomical mapping was carried out in all the cases using CARTO3 (Biosense Webster, USA-Israel) navigation mapping system and Biotok-1000

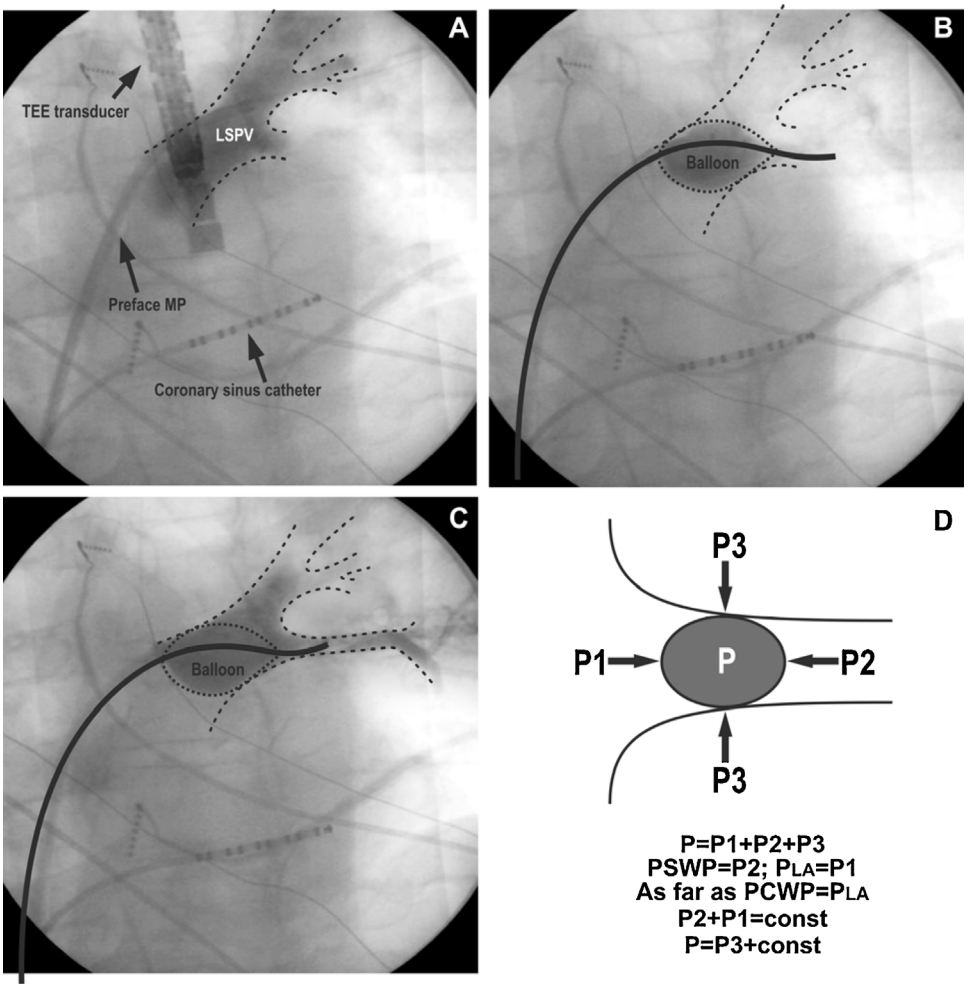

Fig. 3 – Direct (invasive) measurement of PV sleeves contraction pressure. (A) Left superior PV angiography; (B) balloon positioning and inflation at the level of the PV sleeves; (C) angiographic verification of PV balloon occlusion; (D) physical explanation of the balloon pressure and PV sleeves contraction pressure identity.

(Biotok, Russia) electrophysiology recording system. The left atrium was accessed through a transseptal puncture under transesophageal echocardiographic control. Radiofrequency lesions were made in an irrigated mode of 17 mL/min with the power of 30–40 W and the temperature of 40 °C–45 °C using Navistar Thermocool and EZ Steer Thermocool NAV (Biosense Webster, USA) catheters. PV isolation was verified electrophysiologically in all the cases. The mean duration of the procedure was 132 ± 34 min and fluoroscopic time was 48 ± 18 min.

The variables were presented as means and standard deviations. All the statistical calculations were done with the Statistica 6.0 software package (Statsoft, USA) using paired Student's *t* test.

3. Results

In the majority of patients, there were changes of transmitral blood flow pattern typical of LV diastolic dysfunction. A baseline pattern of normal LV filling transformed into pseudonormal in 2 of 12 cases (17%), and restrictive in 10 cases (83%). In all the five cases of initially hypertrophic diastolic dysfunction, the restrictive type of LV filling was observed after the procedure (Fig. 4). Meanwhile, invasively measured end diastolic LV pressure after PV isolation remained constant: 8.2 ± 2.3 and 8.3 ± 2.2 mmHg, respectively; therefore, indicating the association of the changes with the mechanical dysfunction of the LA itself, but not with LV diastolic dysfunction. While assessing the blood flow in the pulmonary veins the decrease in both antegrade and retrograde peak velocities was observed (Table). The duration of the retrograde phase of the PV flow also showed LA mechanical, namely reservoir, function disorder. Invasive manometry revealed the significant increase in maximal, mean and minimal left atrial pressures. At the same time, no statistically significant changes in LA volume and LA appendage outflow velocity were observed, so PV isolation does not change the contractility of the appendage, which is the main contracting structure in the LA. Active LA ejection fraction was either not affected but its passive ejection fraction was significantly decreased.

The mechanical function of 8PV sleeves was investigated in the same patients.

In humans in in vivo the cyclic changes in the PV sleeves were found, their maximal narrowing coinciding with transmitral blood flow E and A peaks (Fig. 2). PV sleeves narrowing during ''passive'' LV filling may be associated both with the blood flow by the pressure gradient between the PVs and LA and with active PV sleeves contraction. During LA systole, the blood flow in the PVs is retrograde, so the PVs should widen, but, on the contrary, they shrink. This fact gives evidence of active LA filling by PV sleeves contraction. Another hypothesis

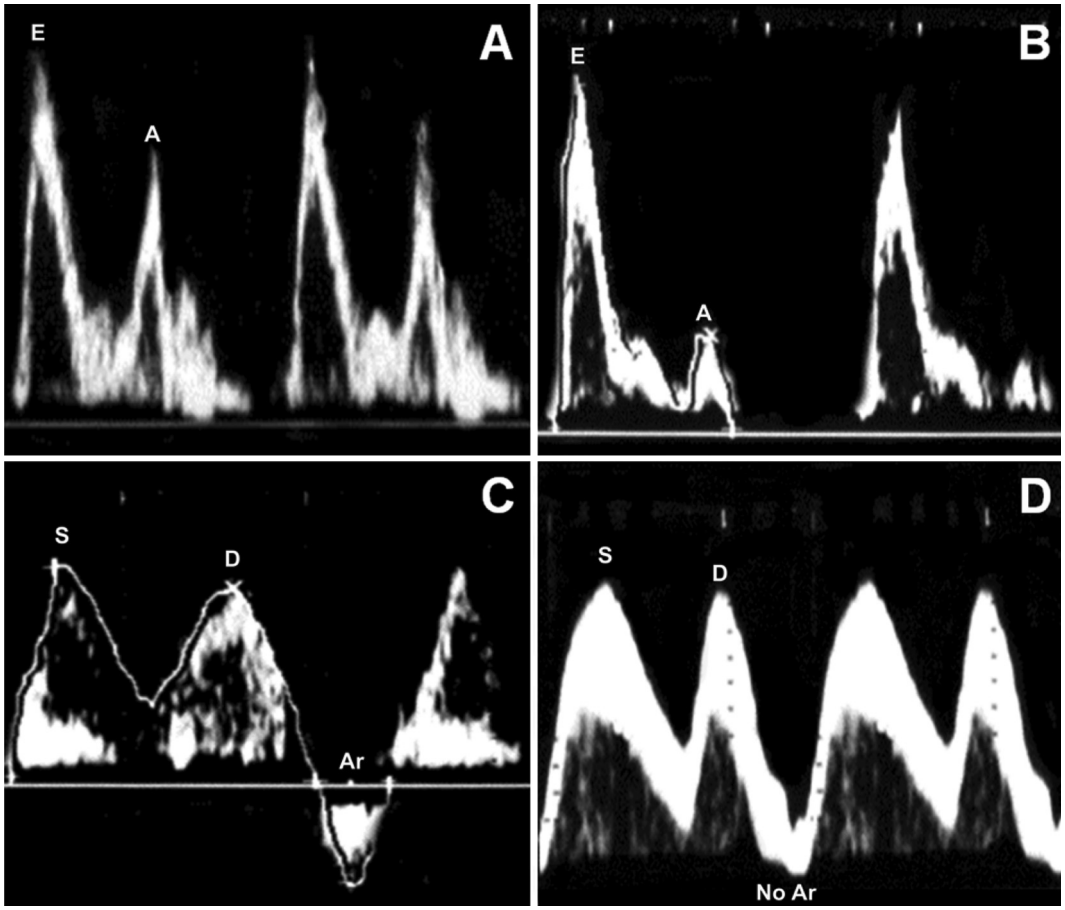

Fig. 4 – Typical transmitral (A and B) and pulmonary vein (C and D) blood flow patterns in the same patient before (A and C) and immediately after (B and D) PV isolation.

Table – Echocardiographic dynamics before and immediately after antrum PV isolation.

Indicator	Before PV isolation	After PV isolation	P
Peak E, cm/s	77.2 ± 12.1	106.3 ± 14.1	0.038
Peak A, cm/s	61.4 ± 10.6	38.5 ± 8.8	0.048
Peak S, cm/s	55.3 ± 17.4	37.4 ± 14.5	0.048
Peak D, cm/s	78.5 ± 13.9	49.1 ± 11.9	0.050
Peak Ar, cm/s	13.3 ± 6.6	7.5 ± 2.1	0.048
Ar duration, ms	70.2 ± 11.5	121.1 ± 35.2	0.010
LA volume, ml	88.1 ± 5.8	87.4 ± 7.0	0.621
Passive LA EF, %	18.3 ± 4.1	15.7 ± 2.1	0.012
Active LA EF, %	16.8 ± 4.5	16.9 ± 5.1	0.013
LA appendage ejection velocity, cm/s	64.7 ± 13.9	57.6 ± 12.2	0.244
Maximal LA pressure, mmHg	11.2 ± 2.9	18.2 ± 3.0	0.033
Minimal LA pressure, mmHg	4.5 ± 1.1	8.5 ± 1.9	0.050
Mean LA pressure, mmHg	7.7 ± 1.2	11.6 ± 2.3	0.048
Left superior PV diameter, mm	11.0 ± 1.9	10.8 ± 1.9	0.873

Values are mean ± standard deviation.

that could explain this finding is hemodynamic "underthrust" of pulmonary vessels tone, which is known as a mechanism of transmitral blood flow changes in the presence of LV diastolic dysfunction. However, this mechanism was also ruled out because in this case the PVs should also widen, not shrink.

Dealing with the obtained data, it was impossible to eliminate completely the third unknown mechanism that affects the cyclical changes in the LV diameter. Therefore, mechanical function of PV sleeves was examined by simultaneous transesophageal echocardiography and invasive manometry in the LV, LA and balloon inflated PV sleeves (Fig. 3A and B).

When analyzing the data obtained, it was possible to find several stereotypical changes in hemodynamics and mechanical properties of the LA and PVs:

1. Peaks of the balloon pressure do not fully coincide with transmitral blood flow E and A peaks. The first pressure increase in the balloon precedes peak E and the beginning of diastole and coincides with the beginning of the isovolumic relaxation period (Fig. 5).
2. The pressure in the PVs during transmitral blood flow peak E should decrease because at this moment, LA passively empties, but, on the contrary, it increases. Therefore, during passive LV inflow the PV sleeves contract.
3. There is high pressure in the LA and the balloon also at the time of active atrial systole; therefore, at this moment the PV sleeves also contract. The end of peak A, as we recall the results of MSCT data analysis, coincides with a minimum diameter of the LV. In addition, the balloon pressure is falling more slowly than in the LA, reaching a minimum before LV systole, which occurs at the end of isovolumic contraction. Consequently, during peak A the PV sleeves contract.
4. At the beginning of LV systole the pressure in the occluded PVs and LA decreases. However, as we know from physiology, at this moment the blood flow in the non-occluded PVs is anterograde. This contradicts active LA relaxation during LV systole.
5. After electrophysiologically verified PV isolation damping of the pressure curve in the balloon occurs, which evidences the disappearance of active mechanical function in the PV sleeves (Fig. 6A). MSCT imaging also shows a marked decrease in PV diameter variation (Fig. 6B).

4. Discussion

AF itself makes a significant influence on the LA contractile function after the restoration of sinus rhythm. This manifests in such a well-described phenomenon as a left atrial stunning. In order to exclude this mechanism, in the present study only patients with paroxysmal AF having the sinus rhythm before the ablation and no initial LA and PV sleeves mechanical

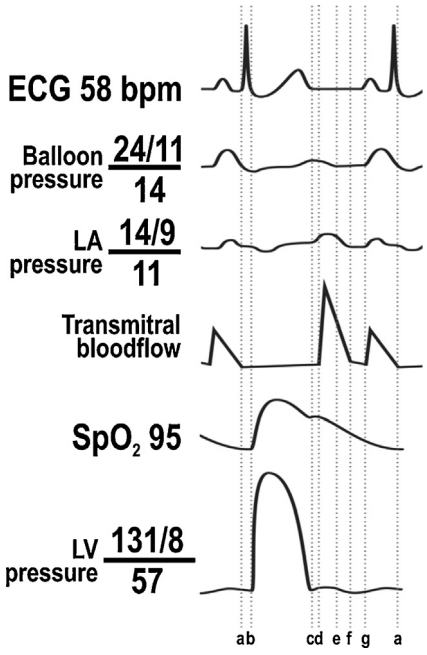

Fig. 5 – Comparison of transmitral blood flow dopplerography, direct manometry in the LA and LV cavities and in the balloon. a, LV isovolumic contraction onset; b, LV isometric contraction onset; c, LV isovolumic relaxation onset; d, "passive" LA ejection (peak E) onset; e, end of the first PV sleeves contraction; f, end of the 'passive' LA ejection (peak E); g, LA systole (peak A) onset.

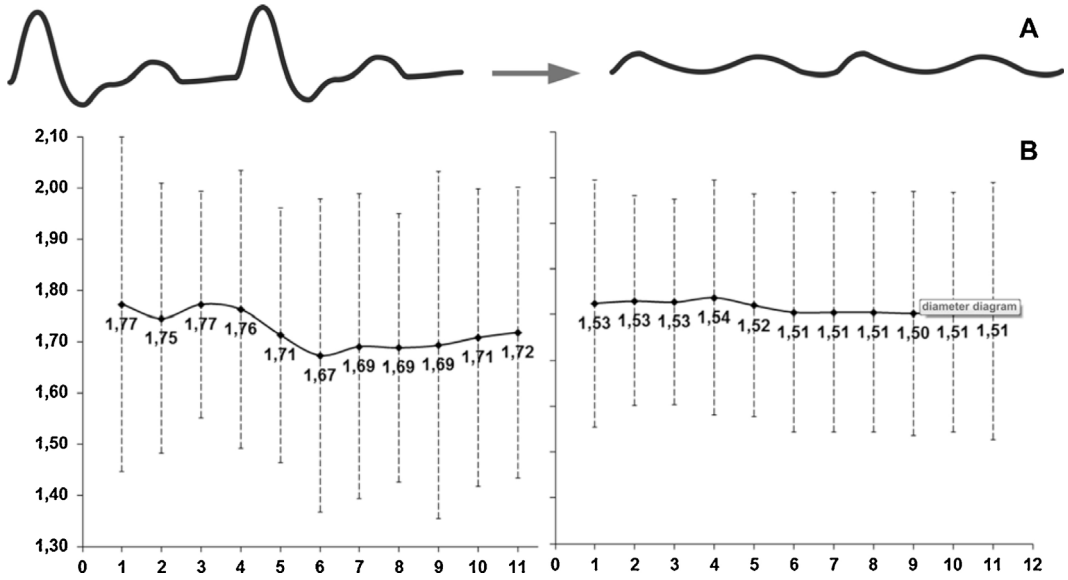

Fig. 6 – Mechanical function deterioration of the four PV sleeves in the same patient after antrum isolation. (A) Damping of the pressure curve in the balloon placed at the level of the PV sleeves; (B) decrease in PV diameter variations by MSCT imaging on the fifth day after PV isolation.

disorders were included. The data obtained in this study implies that antrum PV isolation itself strongly deteriorates the LA reservoir function. It does not change the contractility of the LA appendage, although the appendage is known to be the main contracting structure in the LA. This is logical because, according to the design of LA isolation, it has not been impacted. As indicated in previous works [19,20], pathogenesis of LA compliance deterioration has been well studied in the model of LV diastolic dysfunction. The main manifestation of this condition is a dramatic increase in LA end-systolic pressure and the emergence of a restrictive pattern of transmitral flow and flow in the PVs. It is characterized by a very rapid increase in the velocity of early diastolic filling (peak E) and a simultaneous decrease in the rate of the peak A (atrial systole). The present study was carried out with simultaneous invasive measurement of LV pressure; therefore, LV diastolic dysfunction was completely ruled out. This gave us a reason to state that the main cause of the revealed changes is namely the deterioration of the mechanical function of the LA and LP sleeves. The ''stiff left atrial'' syndrome, associated, of course, with massive radiofrequency exposure, plays an important role in the ''pseudorestriction'' of the transmitral blood flow [13]. It should be mentioned that ''pseudorestriction'' is a common finding in patients who had undergone sinus rhythm restoration, not only by radiofrequency ablation [21,22]. Obviously, one of the main contributing mechanisms is the changes in the PV hemodynamics due to their violations of their sleeves contraction. This was confirmed by methods that involved a direct measurement, which could allow excluding the ambiguity in the interpretation. The most important and open questions are whether the recovery of LA and PVs mechanical function occurs late after the procedure or these changes are irreversible, what their clinical significance is, if they have a significant effect on central and intracardiac hemodynamics as well as the risk of thrombosis.

5. Conclusions

The PVs take an active part in LA filling by contraction of their muscular sleeves. Antrum PV isolation leads to the deterioration of LA reservoir function and LV contractile function.

Conflict of interest

The authors state no conflict of interest.

REFERENCES

[1] Pagel PS, Kehl F, Gare M, Hettrick DA, Kersten JR, Warltier DC. Mechanical function of the left atrium: new insights based on analysis of pressure–volume relations and Doppler echocardiography. Anesthesiology 2003;98(4):975–94.

[2] Sparks PB, Jayaprakash S, Vohra JK, Mond HG, Yapanis AG, Grigg LE, et al. Left atrial ''stunning'' following radiofrequency catheter ablation of chronic atrial flutter. J Am Coll Cardiol 1998;32(2):468–75.

[3] Sun H, Gaspo R, Leblanc N, Nattel S. Cellular mechanisms of atrial contractile dysfunction caused by sustained atrial tachycardia. Circulation 1998;98(7):719–27.

[4] Dogan A, Gedikli O, Ozaydin M, Acar G, Avsar A, Altinbas A. Mitral annular velocity by Doppler tissue imaging for the evaluation of atrial stunning after cardioversion of atrial fibrillation. Int J Cardiovasc Imaging 2009;25(2):113–20.

[5] Eren M, Oz D. Akut atriyal fibrilasyonda sinıs ritmi elde edildikten sonra mitral ge3 diyastolik akım akselerasyon eğimi: Atriyal fonksiyonla ilişkisi ve zamanla değişimi The mitral late diastolic flow acceleration slope after the restoration of sinus rhythm in acute atrial fibrillation:

relationship to atrial function and change over time Anadolu Kardiyol Derg 2010;10(6):488–94 [Turkish].
[6] Zapolski T, Wysokiński A. Ogłuszenie lewego przedsionka po farmakologicznym umiarowieniu migotania przedsionków Stunning of the left atrium after pharmacological cardioversion of atrial fibrillation Kardiol Pol 2005;63(3):254–62 [Polish].
[7] Perea RJ, Tamborero D, Mont L, De Caralt TM, Ortiz JT, Berruezo A, et al. Left atrial contractility is preserved after successful circumferential pulmonary vein ablation in patients with atrial fibrillation. J Cardiovasc Electrophysiol 2008;19(4):374–9.
[8] Antonielli E, Pizzuti A, Bassignana A, Tanga M, Baralis G, Rovere ME, et al. Transesophageal echocardiographic evidence of more pronounced left atrial stunning after chemical (propafenone) rather than electrical attempts at cardioversion from atrial fibrillation. Am J Cardiol 1999;84 (9):1092–6.
[9] Falcone RA, Morady F, Armstrong WF. Transesophageal echocardiographic evaluation of left atrial appendage function and spontaneous contrast formation after chemical or electrical cardioversion of atrial fibrillation. Am J Cardiol 1996;78(4):435–9.
[10] Dabek J, Gasior Z, Monastyrska-Cup B, Jakubowski D. Kardiowersja a ogłuszenie przedsionków Cardioversion and atrial stunning Pol Merkur Lek 2007;22(129):224–8 [Polish].
[11] Imnadze GG, Serov RA, Revishvili AS. Морфология легочных вен и их мышечных муфт, роль в возникновении фибрилляции предсердий Morphology of pulmonary veins and their muscular sleeves, their role in atrial fibrillation onset Vestn Arytmologii 2003;34:32–7 [Russian].
[12] Chen PS, Chou CC, Tan AY, Zhou S, Fishbein MC, Hwang C. The mechanisms of atrial fibrillation. J Cardiovasc Electrophysiol 2006;17(3):S2–7.
[13] Gibson DN, Di Biase L, Mohanty P, Patel JD, Bai R, Sanchez J, et al. Stiff left atrial syndrome after catheter ablation for atrial fibrillation: clinical characterization, prevalence, and predictors. Heart Rhythm 2011;8(9):1364–71.
[14] Morel E, Meyronet D, Thivolet-Bejuy F, Chevalier P. Identification and distribution of interstitial Cajal cells in human pulmonary veins. Heart Rhythm 2008;5(7):1063–7.
[15] Kurz MA, Wead WB, Roberts AM. Reflex inotropic responses to distension of left atrium or pulmonary veins. Am J Physiol 1990;258(1 Pt. 2):H121–6.
[16] Guerra PG, Thibault B, Dubuc M, Talajic M, Roy D, Crépeau J. Identification of atrial tissue in pulmonary veins using intravascular ultrasound. J Am Soc Echocardiogr 2003;16 (9):982–7.
[17] Jia B, Li ZC, Zhang LL, Dong MQ, Wang YM, Zhou SS. 心房钠尿肽对内毒素血症大鼠肺动脉和主动脉舒缩的影响 Pulmonary artery in endotoxemia rat. Effects of atrial natriuretic peptide on relaxation and constriction of aorta and pulmonary artery in endotoxemia rat Zhongguo Ying Yong Sheng Li Xue Za Zhi 2004;20(2):136–40 [Chinese].
[18] Sweeney CM, Jones JF, Bund SJ. Adrenoceptor and cholinoceptor modulation of rat pulmonary vein cardiac muscle contractility. Vascul Pharmacol 2007;46(3):166–70.
[19] (a) Mehta S, Charbonneau F, Fitchett DH, Marpole DG, Patton R, Sniderman AD. The clinical consequences of a stiff left atrium. Am Heart J 1991;122:1184–91;Ć(b) Plehn JF, Southworth J, Cornwell III GG. Brief report: atrial systolic failure in primary amyloidosis. N Engl J Med 1992;327: 1570–3.
[20] Dardas PS, Fillippatos GS, Tsikaderis DD, Michalis LK, Goudevenos IA, Sideris DA, et al. Noninvasive indexes of left atrial diastolic function in hypertrophic cardiomyopathy. J Am Soc Echocardiogr 2000;13:809–17.
[21] Kelley GP, Dalati GA, Helmcke FR, Jain N, Al-Bataineh M, Glancy DL, et al. Atrial stunning masquerading as restrictive Doppler flow pattern: a case of mitral inflow "pseudorestriction". Echocardiography 2006;23(2):172–5.
[22] Yamada H, Donal E, Kim YJ, Agler DA, Zhang Y, Greenberg NL, et al. The pseudorestrictive pattern of transmitral Doppler flow pattern after conversion of atrial fibrillation to sinus rhythm: is atrial or ventricular dysfunction to blame? J Am Soc Echocardiogr 2004;17(8):813–8.