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Синтопия устьев лёгочных вен в левом предсердии сердца человека

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АННОТАЦИЯ

Введение. Синтопия структур левого предсердия (ЛП) относится к наименее изученным аспектам нормальной анатомии сердца. Морфометрические данные о положении устьев лёгочных вен в стенках ЛП по отношению к близлежащим структурам сердца и присердечных сосудов важны как референсные величины в кардиоморфологии, а также востребованы при эндоваскулярном лечении фибрилляций предсердий.

Цель. Методом морфометрии анатомических препаратов условно-нормального сердца взрослого человека установить общие закономерности и топоспецифические особенности локализации устьев лёгочных вен по отношению к овальной ямке и устьям полых вен.

Материалы и методы. Исследовали 54 влажных анатомических препарата сердца без макроскопических признаков гемодинамически значимой сердечной патологии. Препараты были получены от пациентов 35–89 лет, умерших от заболеваний, не связанных с болезнями сердца. Диастолу ЛП моделировали путём заполнения его полости силиконом, после затвердевания которого штангенциркулем измеряли расстояния от овальной ямки и устьев полых вен до устьев лёгочных вен.

Результаты. В статье представлены показатели вариации, медианы и крайние значения расстояний от овальной ямки и устьев полых вен до устьев лёгочных вен в месте их впадения в ЛП. Оценена значимость различий морфометрических параметров топографии, выполнен их корреляционный и однофакторный регрессионный анализ. Установлено, что наиболее сильная регрессионная зависимость характерна для значений ширины ЛП (X) и расстояния от устья верхней полой до устья левой нижней лёгочной вены (Y) ($r^2 = 0,45$; $X = 19,94 + 0,545Y$). Размеры сердца и длина ЛП не являлись значимыми предикторами для изучаемых параметров.

Заключение. Правые лёгочные вены по сравнению с левыми закономерно находились ближе к устьям полых вен, а также к овальной ямке. Самым узким было пространство между впадениями верхней полой и правой верхней лёгочной вены. Наиболее далеко от устьев обеих полых вен находилось устье левой нижней лёгочной вены. Наиболее сильные корреляционные взаимосвязи характерны для расстояний от устьев обеих полых вен до устьев гомолатеральных лёгочных вен, что предлагаем считать одним из критериев гармоничности строения предсердного комплекса.

Ключевые слова: *анатомия сердца человека; морфометрия сердца; сердце; левое предсердие; лёгочные вены; овальная ямка*

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Syntopy of Pulmonary Vein Orifices in the Left Atrium of the Human Heart

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ABSTRACT

INTRODUCTION: The syntopy of the left atrial (LA) structures is the least studied aspect of the normal heart anatomy. The morphometric data on the position of orifices of the pulmonary veins in the LA walls relative to the adjacent heart structures and heart vessels are important as reference parameters of heart morphology and are needed in the endovascular treatment of atrial fibrillations.

AIM: To establish the general patterns and topospecific peculiarities of the location of the pulmonary vein orifices relative to the oval fossa and orifices of the venae cavae using morphometric methods of anatomical preparations of conventionally normal adult human heart.

MATERIALS AND METHODS: Fifty–four wet anatomical preparations of the heart without macroscopic signs of hemodynamically significant cardiac pathology were studied. The preparations were obtained from patients aged 35–89 years who died from diseases not related to heart pathology. LA diastole was modeled by filling its cavity with silicone; after it hardened, the distances from the oval fossa and orifices of the venae cavae to the orifices of the pulmonary veins were measured using sliding calipers.

RESULTS: The article presents variation, medians, and extreme values of distances from the oval fossa and orifices of the venae cavae to the orifices of the pulmonary veins at the site of their opening to LA. The significance of differences of morphometric parameters of the topography was evaluated, and their correlation and one–way regression analyses were implemented. The strongest regression dependence was found for LA width and distance from the orifice of the superior vena cava to the orifice of the left inferior pulmonary vein (Y) $r^2 = 0.45$; $X = 19.94 + 0.545Y$). The heart dimensions and LA length were not significant predictors for the studied parameters.

CONCLUSION: The right pulmonary veins were located expectedly closer to the orifices of the venae cavae and the oval fossa than the left pulmonary veins. The narrowest was the space between the orifices of the superior vena cava and the right superior pulmonary vein. The farthest from the orifices of both venae cavae was the orifice of the left inferior pulmonary artery. The strongest correlation relationships were characteristic of the distances from the orifices of both venae cavae to the orifices of the homolateral pulmonary veins, which we propose to consider as one of the criteria of the harmoniousness of the structure of the atrial complex.

Keywords: *human heart anatomy; heart morphometry; heart; left atrium; pulmonary veins; oval fossa*

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ECO•VECTOR

LIST OF ABBREVIATIONS

SVC — superior vena cava
PV — pulmonary vein
LSPV — left superior pulmonary vein
LIPV — left inferior pulmonary vein
LA — left atrium
IVC — inferior vena cava
RSPV — right superior pulmonary vein
RIPV — right inferior pulmonary vein

INTRODUCTION

The structure and topography of the left atrium (LA) are considered as the least studied aspects of the normal heart anatomy. In the fundamental guidelines on cardiomorphology, the normal anatomy of the LA is rarely described [1, 2]. Although some publications have described the elements of the extracardiac LA topography, such as the relationship of the LA with mediastinal vessels, esophagus, left vagus, and phrenic nerves [3–6], the local (intracardiac) topography is examined insufficiently.

After atypical cardiac myocytes have been described to act as a morphological substrate of supraventricular arrhythmias in the myocardial "sleeves" of the pulmonary veins (PV) under certain conditions, the interest of researchers in the anatomy of LA increased. However, studies have gone in two directions: the study of the microstructural organization of the left atrial wall and the study of the LA using radiation diagnostics methods performed for clinical indications in patients with heart diseases. However, publications reporting the macroscopic anatomy of the LA obtained on cadaveric materials of patients without a burdened "cardiac" history are rare [4, 6]. According to the results of information search and analysis of original articles indexed in Scopus, PubMed, and Web of Science Core Collection for 50 years (1970–2020), the local topography of the LA was the subject of 10 anatomical studies, and the normal anatomy of the orifices of the PVs was presented in 14 publications.

The review article by Whiteman et al., which described the orifices of the PVs, emphasized their number and the presence of myocardial "sleeves" in the PV walls [6]. Ho et al. highlighted the myoarchitecture of the LA and the structural–topographic relations of this heart chamber with the neighboring structures [5, 7]; however, the local syntopy of the LA is characterized descriptively without the use of morphometry. No quantitative data on the distances between the orifices of venae cavae and PVs and the distances from the oval fossa to the orifices of the PVs in the normal anatomy have been found. Thus, it is unknown which dimension of the heart or the LA can be used to predict the above distances with the greatest reliability. Meanwhile, precise morphometric data on the distances between the oval fossa, orifices of the venae cavae, and PVs and knowledge of the relationship between these distances and dimensions of the heart and LA are necessary for planning and performing interventions, particularly transatrial electrocryodestruction and radiofrequency ablation of ectopic pacemakers [3, 4]. These morphometric data may help improve the mathematical models of the LA to "educate" neuronal networks in the differential assessment of the normal and pathological patterns of the LA [8]. As for the relevance of such studies for fundamental biomedical science, information about the existence and type of correlation and regression relationships between parameters will help understand the patterns of heart structures, particularly of the LA. Morphometric data and their correlations can be used as the basis for the development of the anatomical standards of the left atrial structure, which corresponds to the tasks in the field of human anatomy.

This study **aimed** to establish general patterns and topospecific peculiarities of the location of the orifices of the PVs relative to the oval fossa and to the orifices of the venae cavae by morphometry of the anatomical preparations of a conventional normal heart of an adult human.

MATERIALS AND METHODS

Heart preparations (n = 54) were obtained from human cadavers that were not demanded for burial; there was no possibility of obtaining informed consent. The work with section material was performed by taking into account the requirements of Article 5 of Federal Law No. 8 "Concerning Burial and Funeral Business" of January 12, 1996 (as amended, in the current version). The study protocol was approved by the Local Ethics Committee of Ural State Medical University (Protocol No. 8 of November 20, 2020).

Inclusion criteria: (1) death from diseases other than heart diseases, (2) aged 35–89 years, (3) typical left-sided position of the heart, (4) externally normally formed heart, (5) concordant relations of the heart chambers and heart vessels, and (6) heart mass 250 g–400 g.

Non-inclusion criteria: (1) macroscopic signs of complications of coronary heart diseases, cardiomyopathy, diseases of the atrioventricular valves, and heart surgeries identified at autopsy of the heart ventricles; (2) damage or deformation of the upper wall of the LA; and 3) atypical number of the PV orifices in the left atrial wall.

Morphometry was performed on wet preparations, on which the diastole phase of the LA was modeled by filling the LA with liquid silicone. For this, after evisceration, the preparations were thoroughly washed from clots, placed in 1% formalin solution for several hours to 5 days, and then completely washed from formalin. Thereafter, the left ventricle and right atrium were packed with cotton tampons, and the LA was filled with liquid silicone with a hardener, through the orifice of the right superior PV (RSPV). During the hardening period of the silicone, preparations were suspended so that the diaphragmatic surface of the heart was elevated over the horizontal surface by 10°–15° — the orientation was close to the natural orientation of the heart in a human in the orthograde position. After hardening of the silicone, left atrial walls were prepared for better visualization of the orifices of the PVs. The number of orifices of the PVs was determined in places of opening into the LA, and the length, width, and anteroposterior dimensions of the heart and LA, the shortest distance from each PV orifice to the oval fossa and to the orifices of the superior and inferior venae cavae (SVC and IVC, respectively) were measured. Morphometry was performed using ShCC-1-125 0.01 caliper (CHIZ, Chelyabinsk, Russian Federation) with accuracy of 0.03 mm.

The distribution of values was evaluated in Statistica 10.0 program (Stat Soft Inc., USA) using the Shapiro–Wilk W-test. If the distribution deviated from the normal, the results were presented as medians, 25th and 75th percentiles (p25 and p75, respectively), and extreme values. For the analysis of variance, the Kruskal–Wallis H–test was used. In the pairwise comparison, which was performed in the "post hoc" tab, two tests with different sensitivities were used: Fisher's least significant difference test (LSD test) and the Bonferroni test. The differences were considered significant if α did not exceed 0.05 for both tests. For the correlation analysis, the Spearman test (Rs) was used. To assess the influence of the heart and left atrial dimensions on the values of the morphometric parameters of the PV orifices, regression analysis was performed, the determination coefficient r2 was found, and the influence of the predictor variable on the response variable was considered significant at $p < 0.01$.

RESULTS

Significant differences were found in the multiple comparisons of the eight parameters of distances from the orifices of the venae cavae to the orifices of the PVs ($H = 309.8$; $p = 0.0$) (Table 1). In the pairwise comparison using statistical tests with different levels of sensitivity, the distances from the orifice of the SVC to the orifices of the PVs were different ($p < 0.0003$).

Table 1. Distances between the orifices of the venae cavae and pulmonary veins

Distance		Statistical Parameters					
From the orifice of	To the orifice of	M, mm	Me, mm	p25–p75, mm	min–max, mm	VC	W; p
Superior vena cava	RSPV	6.8	6.3	4.0–9.4	1.75–16.0	51	0.956; 0.077
	RIPV	25.6	25.0	21.0–28.3	9.0–46.3	27	0.968; 0.244
	LSPV	42.0	41.8	36.5–48.0	19.8–63.0	21	0.995; 0.999
	LIPV	51.6	50.4	45.2–59.2	29.0–73.9	18	0.986; 0.860
Inferior vena cava	RSPV	26.9	26.0	22.2–32.8	13.0–42.5	28	0.979; 0.562
	RIPV	19.3	18.9	16.2–22.3	8.0–31.7	28	0.975; 0.421
	LSPV	56.4	54.5	50.5–62.3	26.9–78.0	18	0.976; 0.496
	LIPV	51.5	51.0	45.3–56.4	35.6–71.7	15	0.986; 0.849

Note: RSPV, right superior pulmonary vein; RIPV, right inferior pulmonary vein; LSPV, left superior pulmonary vein; LIPV, left inferior pulmonary vein; M, mean; Me, median; p25–p75, percentiles; min–max, extreme values; VC, variation coefficient; p, probability for acceptance of the hypothesis of the correspondence of the values to the normal distribution based on the Shapiro–Wilk (W) test

The RSPV was closest to the orifice of the SVC (Figure 1). The values of this distance were characterized by the greatest variation, and their distribution shifted toward smaller values; thus, the distribution deviated from the normal one. The orifice of the left inferior PV (LIPV) was the farthest from the SVC. This parameter was 1.2 times the distance from the SVC to the left superior PV (LSPV) and 1.7 times the distance from the SVC to the orifice of the right inferior PV (RIPV). No differences were found between the distances from the SVC to the RIPV and from the IVC to the RSPV ($p = 0.42$, LSD test). The orifice of the LSPV was the farthest from the orifice of the IVC. This distance was 2.1 times the distance from the IVC to the RSPV and three times the distance from the IVC to the RIPV ($p < 0.0008$). The medians of the distances from the IVC to the left PVs differed only by 5%; in the assessment of the significance of these differences, the probability for type 1 error varied from 0.002 by the LSD test to 0.052 by the Bonferroni test. Of the four PVs, the orifice of the LIPV was the only one that was located at the same distance from the orifices of both venae cavae ($p = 0.94$, LSD test).

The correlation analysis revealed strong relationships between parameters, such as the distance from the orifice of the IVC to the orifices of the right PVs (Rs = 0.75), from the orifice of the IVC to the orifices of the left PVs (Rs = 0.79), and from the orifice of the SVC to the orifices of the left PVs (Rs = 0.73). Only two pairs of distances from the SVC to the orifices of the right PVs had moderate correlations (Rs = 0.41). In relation to the oval fossa, the orifices of the left PVs were located farther than the orifices of the right PVs (p < 0.0008, Table 2). The values of the distances from the oval fossa to the orifices of the right PVs closely correlated with each other (Rs = 0.77), and their differences were on the border of significance (p = 0.069, Bonferroni test). The distances from the oval fossa to the LSPV and to the LIPV were similar (p = 0.125, Bonferroni test), and their values also formed a correlation pair (Rs = 0.66). The correlation relationships between other distances from the oval fossa to the orifices of the PVs were less strong (Rs < 0.52).

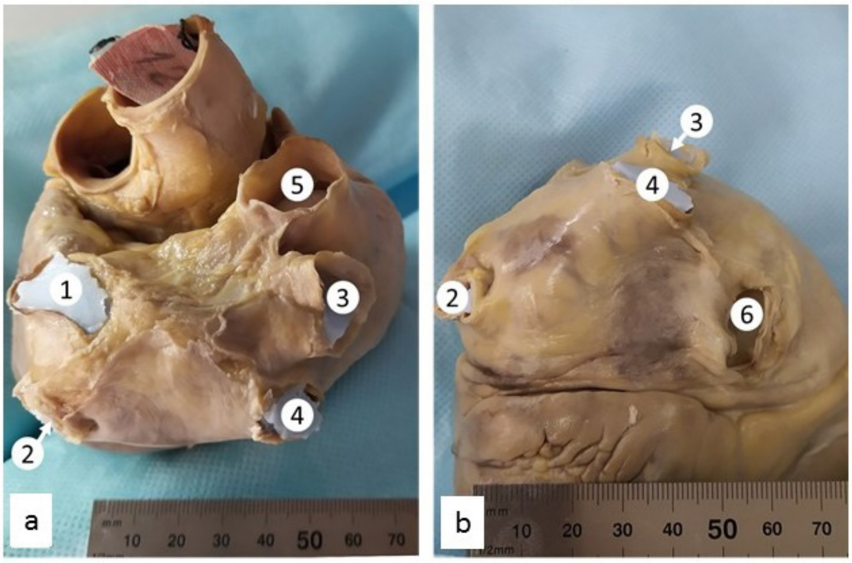

Fig. 1. Upper (a) and posterior (b) walls of the left atrium of the human heart with a typical number of orifices of the pulmonary veins. Orifices of the left superior (1), left inferior (2), right superior (3), and right inferior (4) pulmonary veins. Orifices of the superior (5) and inferior (6) venae cavae. Preparation No. 129.

Table 2. Distances from the oval fossa to the orifices of the pulmonary veins

Distance from the oval fossa to the	Statistical parameters					
	M, mm	Me, mm	p25–p75, mm	min–max, mm	VC	W; p
RSPV	19.6	19.2	15.0–22.5	10.0–30.8	27	0.974; 0.396
RIPV	14.8	14.0	11.8–18.2	8.6–30.4	32	0.910; 0.002
LSPV	48.2	45.8	43.0–50.0	28.8–62.5	15	0.968; 0.232
LIPV	44.0	43.8	41.1–47.3	26.0–57.7	14	0.961; 0.122

Note: RSPV, right superior pulmonary vein; RIPV, right inferior pulmonary vein; LSPV, left superior pulmonary vein; LIPV, left inferior pulmonary vein; M, mean; Me, median; p25–p75, percentiles; min–max, extreme values; VC, variation coefficient; p, probability for acceptance of the hypothesis of the correspondence of the values to the normal distribution based on the Shapiro–Wilk (W) test

According to the results of the one-factor linear regression analysis, the *length of the LA and overall dimensions of the heart did not have any significant effect on the parameters of the morphometric topography of the PV orifices*. The parameter that can be predicted with the highest reliability by the overall dimensions of the LA was the distance between the *orifices of SVC and LIPV*. This distance (Y) depended on the width of the LA (r^2 = 0.45; X1 = 19.94 + 0.545Y, where X1 is the width of the LA) and to a lesser extent on the sagittal dimension of the LA [(X2) at r^2 = 0.36, X_2 = 20.65 + 0.44Y]. The left atrial width demonstrated weak influence on the distance from the orifice of the SVC to the RIPV (r^2 = 0.22) and LSPV (r^2 = 0.19) and from the orifice of the IVC to the RSPV (r^2 = 0.19), LSPV (r^2 = 0.29), and LIPV (r^2 = 0.18). The contribution of the sagittal dimension of the LA to the values of the distances from the orifice of the SVC to the RIPV and to the LSPV and from the orifice of the IVC to the RSPV did not exceed 19% (r^2 = 0.19). For the remaining distances from the venae cavae to the PVs, the width and sagittal dimension of the LA were not significant predictors..

All three LA dimensions made a certain contribution to the change in the distances from the oval fossa to the superior PVs; however, no significant dependence was found between the LA length, its sagittal dimension, and distances from the oval fossa to the inferior PVs (Table 3).

Table 3. Determination coefficient and slope of the regression line characterizing the influence of the dimensions of the left atrium on the distance from the oval fossa to the orifices of the pulmonary veins

Dimension of the left atrium (predictor variable)	Distance from the oval fossa (response variable) to the			
	RSPV	LIPV	LSPV	LIPV
Length	***0.19 (0.66)***	0.03 (0.27)	**0.26 (0.54)**	0.09 (0.38)
Width	***0.35 (0.91)***	***0.19 (0.68)***	***0.34 (0.64)***	***0.24 (0.63)***
Sagittal dimension	***0.27 (0.69)***	0.09 (0.41)	**0.16 (0.38)**	0.06 (0.28)

Note: LA, left atrium. RSPV, right superior pulmonary vein; RIPV, right inferior pulmonary vein; LSPV, left superior pulmonary vein; LIPV, left inferior pulmonary vein. The slope of the regression line is indicated in brackets. In bold italics, the values are given at which at α = 0.01 the hypothesis of the existence of linear dependence between the respective predictor variable, and the response variable can be accepted

For distances from the oval fossa to the PVs, the most significant predictor was the width of the LA. As shown in the comparison of the correlations of the determination coefficients, the influence of the left atrial width on the change in distances from this fossa to the superior PVs is 1.4–1.8 times greater than the contribution of this parameter to the change in distances to the inferior PVs. For the regression line, the largest regression slope (0.91) was noted in the pair of variables *"LA width—distance from the oval fossa to the orifice of the RSPV"*. This shows that with an increase in the left atrial width by 1 cm, the distance from the oval fossa to the RSPV will increase by approximately 9 mm, whereas that to the other PV orifices by 6.3mm–6.8 mm ($p < 0.01$).

DISCUSSION

This study found that in most cases there were four orifices of the PVs in the left atrial wall. This number of PV orifices was found in 70.8% (92 of 130) [9] and 73.2% (41 of 56) of the cases [10]. Gupta et al. (2019) found this variant in 87% (26 of 30) of cases [11], which is consistent with our results. The RSPV naturally passed behind the SVC, between it and the right atrium. The right inferior PV passed behind the "intercaval region" [6]. The orifices of both right PVs were always located near the interatrial septum and the posterior interatrial sulcus (Watterson sulcus). The local topography of this sulcus, which is a fold between the right PVs and venous sinus of the right atrium, is important for access to the LA [1]. In this study, the proximity of the PV orifices to the Watterson sulcus revealed enables consideration of the areas of the sulcus directly adjacent to the PVs as places of the greatest operational risk in accessing the LA. This risk is enhanced by two factors: the probability of passage here of the sinoatrial node artery arising from the left circumflex coronary artery [1] and the presence of thin, sometimes muscle-free, zones in the medial walls of the right PVs.

In four preparations that were initially included into the total sample, but later were excluded because of the atypical quantity of the orifices of the PVs, the left PVs entered the LA through a common opening, whereas the right PVs always entered separately. Ikiz et al. found the common opening of the PVs in 14.3% of cases on the left and 3.6% of cases on the right [10]. Meanwhile, variations of the opening are more inherent to the right PVs than to the left ones [12, 13]. Thus, Prasanna et al. observed the common orifice of the right PVs in 28% and of the left only in 6% of the cases [12]. These contradictions may reflect ethnic, ecological, and individual variabilities; however, they may be determined by methodology, for example, by differences in stud design and criteria of formation of selective totalities.

In the literature, there are indications that with a typical number of orifices, the left PVs enter the LA on a higher level than the right [7]. These morphometric differences are reflected in the degree of remoteness of the orifices of the PVs from the left atrioventricular opening, particularly on the length of the "mitral isthmus" [14] and on the width of the "left lateral (left atrial) ridge"— a muscle embankment within this isthmus [15]. The length of the "mitral isthmus" did not depend on the variants of the opening of the left PVs [14]. Muscle bundles are described, which, passing from the anterior atrial (Bachman) bundle through this ridge to the adjacent left atrial walls and the myocardial "sleeve" of the coronary sinus, can become an anatomical substrate for the conduction of impulse by re-entry mechanisms [5, 7]. Conditional lines from the orifices of the left PVs to the attachment of the posterior (mural) cusp of the mitral valve can be considered potential ablation lines [16]. Considering the methods of access to these orifices, it is important to know their remoteness not only from the mitral valve but also from the orifices of the venae cavae and the oval fossa, which is the focus of this study.

Sánchez-Quintana et al. revealed the proximity of the esophagus to the orifices of the left PVs, and the posterior wall of the LA is thinning in the upward direction [17]. Gupta et al. investigated the projection of the esophagus onto potential ablation lines connecting the orifices of superior and inferior PVs. According to the authors, the esophagus crossed the upper line near the orifice of the LSPV and the lower one approximately on the border of the middle and left third between the orifices. The same authors presented data on the distances between the orifices of the PVs, but no morphometric data were found with which the results obtained could be compared [11]. This study showed that the orifice of the LIPV is the farthest from the orifices of both venae cavae. The distance between the orifices of the SVC and LIPV can be predicted by the width and sagittal dimension of the LA. Taking into account the fact that the myocardial "sleeves" are better developed in the terminal sections of the left PVs than that of the right PVs, and the left PVs have a greater tendency to the generation of ectopic impulses [6]. These conclusions acquire clinical significance in planning atrial interventions.

CONCLUSION

On the preparations of the heart with the typical (four-orifice) variant of the opening of the PVs into the left atrium, the orifices of the PVs were at different distances from the orifices of the venae cavae: the right PVs were naturally located closer to the orifices of the venae cavae and to the oval fossa than the left veins. The narrowest space was between the orifices of the SVC and RSPV (in the upper Watterson sulcus. The orifice of the LIPV was the farthest from the orifices of both venae cavae. The strongest correlation was characteristic of the distances from the orifices of both venae cavae to the orifices of the homolateral PVs, which can be considered one of the criteria of the harmoniousness of the structure of the atrial complex.

ADDITIONAL INFORMATION

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Финансирование. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.
Конфликт интересов. Авторы заявляют об отсутствии конфликта интересов.
Вклад авторов: *Гапонов А. А.* — разработка концепции и дизайна исследования, изготовление препаратов, выполнение измерений, анализ данных, написание текста статьи; *Носкова М. Е.* — изготовление препаратов, выполнение измерений, редактирование текста статьи; *Якимов А. А.* — руководство работой, разработка концепции и дизайна исследования, анализ данных, написание и редактирование текста статьи. Все авторы подтверждают соответствие своего авторства международным критериям ICMJE (все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией).

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