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Statistical modeling to determine severity of respiratory sarcoidosis and parameters associated with cardiac sarcoidosis: as a way to stratify the risk of developing pulmonary hypertension

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ABSTRACT

Aim. Using statistical modeling techniques, we aim to develop a model that optimizes the prediction of severity of sarcoidosis that affects the respiratory system (SRS) based on the identification and determination of signs (anamnestic, clinical, laboratory, instrumental examination data, etc.) associated with disease severity and subsequent stratification of the long-term risk for pulmonary hypertension (PH) development.

Materials and methods. The 12-year observational cohort comparative study included 298 participants, both male and female, who had SRS. More than 200 different patient examination parameters were analyzed. The models were built using logistic regression and linear discriminant analysis. The quality of the models was assessed by constructing a classification matrix, calculating sensitivity and specificity as well as calculating the area under ROC curve.

Results. As a result of the study, optimal classification models were developed for predicting SRS severity, constructed using various methods of statistical modeling. The models demonstrated that several characteristics, including parameters of echocardiography examination of patients (including indicators that allow for indirect diagnosis of PH), are associated with disease severity. A set of characteristics associated with particular sarcoidosis severity will allow for its prediction upon confirmation of diagnosis (individual prognosis), as well as patient management (observation or requiring the prescription of pathogen-specific immunosuppressive therapy).

Conclusion. Such a complex model for predicting disease severity in patients with non-cardiac diseases (SRS) is of great importance for risk stratification in terms of PH development in patients with severe sarcoidosis. Further analysis of the features identified during model construction can help clinicians to contribute to more accurate predictions of SRS severity in real-world clinical practice.

Keywords: pulmonary hypertension, respiratory sarcoidosis, transthoracic echocardiography, prognosis of pulmonary hypertension

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Статистическое моделирование для определения типа течения саркоидоза органов дыхания и параметров, ассоциированных с поражением сердца, как способ стратификации риска развития легочной гипертензии

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РЕЗЮМЕ

Цель. С помощью методов статистического моделирования разработать оптимальную модель прогнозирования типа течения саркоидоза органов дыхания (СОД), основанную на выявлении и определении признаков (анамнестических, клинико-лабораторных, данных инструментального обследования и других), ассоциированных с тяжестью течения заболевания и последующей стратификацией долгосрочного риска развития легочной гипертензии (ЛГ).

Материалы и методы. В 12-летнее наблюдательное когортное сравнительное исследование включено 298 больных СОД обоего пола. Проанализировано более 200 различных параметров обследования пациентов. Модели построены методами логистической регрессии и линейного дискриминантного анализа. Качество моделей оценивалось с помощью построения матрицы классификации и расчета чувствительности и специфичности, а также построения и расчета площади под ROC-кривой.

Результаты. Разработаны оптимальные классификационные модели прогнозирования типа течения СОД, построенные с применением разных методов статистического моделирования. Модели продемонстрировали, что ряд характеристик, включая параметры эхокардиографического обследования пациентов (в том числе показатели, позволяющие косвенно диагностировать ЛГ), имеют связь с типом течения заболевания. Совокупность характеристик, ассоциированных с типом течения саркоидоза, позволит прогнозировать тип течения СОД уже при подтверждении диагноза (индивидуальный прогноз), а также тактику ведения пациентов с данной патологией (наблюдательная или требующая назначения патогенетической иммуносупрессивной терапии).

Заключение. Подобная комплексная модель прогнозирования типа течения заболевания у больных некардиологического профиля (СОД) имеет важное значение в отношении стратификации риска развития ЛГ для пациентов с неблагоприятным типом течения саркоидоза. Дальнейший анализ выделенных при построении моделей признаков может помочь клиницистам в реальной клинической практике способствовать более точному прогнозированию типа течения СОД.

Ключевые слова: легочная гипертензия, саркоидоз органов дыхания, трансторакальная эхокардиография, прогнозирование легочной гипертензии

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INTRODUCTION

Pulmonary hypertension (PH) is a hemodynamic and pathophysiological condition that complicates the course of various respiratory and cardiovascular disorders [1]. The issue of predicting PH course in various nosological subtypes at different stages is a significant challenge, which is particularly true when employing clinical, laboratory, and instrumental examination techniques available to clinicians [2–4].

Pulmonary hypertension in sarcoidosis of the respiratory system (SRS) belongs to clinical group V according to the clinical classification of pulmonary hypertension (2020), which includes unclear and/or multifactorial mechanisms of the disease as well as pulmonary hypertension developed in patients with systemic and metabolic disorders. At the same time, sarcoidosis can be caused not only by damage to the lung parenchyma but also by heart damage (pathology of left chambers) and granulomatous arteriopathy [2].

Right heart catheterization (RHC) is necessary to determine the pressure in the pulmonary artery (PA) and is the basis for the diagnosis of pulmonary hypertension. The diagnosis of PH is set when the mean pressure in the pulmonary artery (mPAP) is more than 25 mm Hg at rest and more than 30 mm Hg during exercise [2, 5]. The assessment of hemodynamic parameters, as well as the diagnosis of PH, is most often one of the main indications for RHC. Despite the fact that the RHC is a minimally invasive procedure that requires careful medical monitoring to ensure patient safety, its use is limited in clinical routine.

The limitations include the availability of specialized equipment and units in a hospital, as well as the mandatory hospitalization of the patient 4–6 hours prior to heart catheterization; limited research due to a lack of staff qualified in interventional cardiology with specific research skills; invasive risks and potential development of a number of complications (including risk of infection at catheter insertion sites, bleeding, etc.); patient's refusal to undergo the procedure, etc. Literature does not present a unanimous opinion on the use of the RHC in the monitoring of patients with PH over time [2, 4–6].

In this regard, a worthy alternative to the RHC is transthoracic echocardiography (echo), whose doppler techniques make the most significant contribution to the assessment of PH. According to the 2020 clinical guidelines on PH of the Ministry of Healthcare of the Russian Federation, echocardiography is the only widely available non-invasive method which makes it possible to assess blood pressure in patients with suspected PH [2]. All patients at risk of developing PH should undergo thorough examination using echocardiography, which makes it possible to non-invasively assess intracardiac hemodynamics and calculate blood pressure in the chambers of the heart and in the PA in real time [4–7]. Echocardiography helps not only assess the systolic blood pressure in the PA, but also obtain important information on the cause and complications of PH. This diagnostic method helps exclude the heart valve damage, myocardial diseases, and congenital heart disorders with left-to-right cardiac shunts leading to the development of PH [4, 8].

It is still difficult to predict the life expectancy of a patient with PH since the disease may progress very quickly, leading to sudden deterioration and death, or slowly over several years. It can only be noted that usually the patient's life expectancy depends on the type and causes of PH [9–11].

Sarcoidosis is a systemic inflammatory disease of unknown etiology with a wide range of clinical manifestations involving immune system activity. Given the absence of specific clinical manifestations of this pathology, its diagnosis is rather complicated [12]. A characteristic feature of sarcoidosis is the formation of non-caseating granulomas, affecting almost all organs, causing their dysfunction and altering the tissue structure [11–13].

The number of patients with severe sarcoidosis and complications is increasing every year. A specific treatment strategy is chosen based on SRS severity. When sarcoidosis is mild, drug treatment is not required, while the prescription of systemic glucocorticoids (SGCS) and cytostatics is necessary for patients with severe sarcoidosis. The degree of activity of this pathology can be different and depends on both the severity of the general inflammatory symptoms and on the number of organs involved in the pathological process and the degree of structural and functional disorders [14–16].

It is highly important to predict the severity of the pathological process, which implies that a promising approach is to analyze the obtained data on clinical and laboratory tests and instrumental examinations and identify signs that directly affect sarcoidosis severity [16]. As a rule, PH in sarcoidosis is associated with severe disease. Despite the fact that it is most common in patients with later stages of sarcoidosis, it can sometimes develop without lung parenchyma damage. Among patients with end-stage sarcoidosis awaiting lung transplantation, PH occurs in approximately 75% of cases, which indicates a high mortality rate. PH may be an early manifestation of sarcoidosis in patients without indications for transplantation. This is the reason for significant interest in the interdisciplinary problem of PH formation associated with mortality in SRS [17, 18].

The aim was to develop optimal classification models for predicting SRS severity based on the identification and determination of signs (anamnestic, clinical, laboratory, instrumental examination data, etc.) associated with the severity of sarcoidosis and subsequent risk stratification of PH development.

MATERIALS AND METHODS

The study was carried out in 2007–2019 in Tomsk Regional Clinical Hospital. We analyzed 298 sarcoidosis cases in patients aged 19 to 74 years (107 (35.9%) men and 191 (64.1%) women) at the pulmonary hospital and in the outpatient sarcoidosis room of the consultative and diagnostic polyclinic. At the time of diagnosis, 145 patients underwent echocardiography.

The average age of the SRS onset was 42 (34; 52) years. The average duration of sarcoidosis at the time of inclusion in the study was 5.6 ± 0.2 years, with the longest history of the disease in the patient aged 30 years. The diagnosis of sarcoidosis was established based on the criteria set by the statement of the World Association for Sarcoidosis and Other Granulomatous Disorders (1999), confirmed morphologically and/or in the presence of a typical clinical presentation and radiological data, provided that other diseases with similar manifestations are excluded [19].

According to the results of the assessment of the features of chronic sarcoidosis, two groups of patients were formed: group 1 included 163 patients with mild sarcoidosis; group 2 – 135 patients with severe sarcoidosis. Mild sarcoidosis was determined in the presence of spontaneous regression of the disease, including spontaneous, without SGCS or during short-term administration of small doses of SGCS, in the absence of relapses of the disease, weight loss, and generalized sarcoidosis. Patients with progression and recurrence of sarcoidosis or its generalized forms have severe sarcoidosis [4, 7, 8]. When describing the nature of the disease severity, we used concepts such as the active phase (progression), the regression phase (spontaneous or after treatment), and the stabilization phase (inpatient), which are mentioned in the Federal Clinical Guidelines for the Diagnosis and Management of Sarcoidosis 2022 [4].

The work analyzes more than 200 different parameters and characteristics obtained during examination of patients. Thus, the following data were collected and analyzed from all patients with SRS: complaints, medical history, assessment of laboratory parameters over time (complete blood count and blood biochemistry, general urinalysis, Diaskintest), data from functional and instrumental examination (spirometry, radiography, and high-resolution computed tomography (CT scan) of the chest and lungs, abdominal and kidney ultrasound examination, ECG, transthoracic echocardiography), and the presence of granulomas in internal organs. Histologic examination of biopsy samples from the affected lesions in the lungs and/or intrathoracic lymph nodes was used to confirm the diagnosis of sarcoidosis.

Statistical data analysis was performed using the RStudio v. 4.3.1 software package and the Statistica 13.3 software package. Descriptive statistics of quantitative parameters that do not fit a normal distribution are presented as the median and the upper and lower quartiles of *Me* (Q_1; Q_3). The comparison of differences between the groups was performed using the nonparametric Mann – Whitney test. The results were considered statistically significant at $p < 0.05$. The mathematical forecasting model was developed using the logistic regression with stepwise selection. The quality of the models was assessed by constructing a classification matrix, calculating sensitivity and specificity as well as calculating the area under ROC curve [9].

RESULTS AND DISCUSSION

Among all types of sarcoidosis severity, the combination of changes in the lungs with cardiac involvement is a difficult issue in managing this patient group due to severe SRS and difficulties encountered at the stage of diagnosis of the disease [13, 14]. Currently, diagnosing sarcoidosis is rather difficult, as the etiology, pathogenesis, and risk factors for the development of the disease itself are not fully understood [15, 16]. Literature contains different opinions about the dependence of the frequency of PH detection on the stage of sarcoidosis and the activity of the pathological process [8, 15]. The intravital diagnosis of cardiac sarcoidosis is quite difficult due to the low specificity of clinical signs and the low (20–30%) sensitivity of endomyocardial biopsy results [18].

According to the results of of Doppler echocardiography, changes in the morphometric parameters of the left and right sides of the heart were noted in patients with SRS. Thus, dilation of the left atrium (LA) was noted in 10.3% of patients and the left ventricle (LV) in 3.4% of cases. To diagnose dilation of the right ventricular outflow tract, trunk, and branches of the LA, measurements were performed from a parasternal approach along a short axis at the level of the aortic root [5, 6]. LV dilation was detected in 17.9% of patients, of which the majority (65.3%) belonged to the group with severe sarcoidosis. The analysis did not reveal any statistically significant differences between the groups in terms of parameters reflecting the functions of the right heart, as well as when comparing them with those in the control group, with the exception of mPAP.

According to the standard echocardiography protocol, the generally accepted diagnostic criterion, which makes it possible to diagnose PH, is the predicted value of the mean pulmonary artery pressure (pmPAP) > 35 mm Hg [1, 6–8]. As a result of the study, a predicted value of mPAP > 35 mm Hg was detected in 11 (7.6%) patients with SRS, which was 2.7% of SRS cases with mild sarcoidosis and 12.7% (more than 4 times more often) in the group with severe disease ($\chi^2 = 409.5$; $p = 0.01$). On average, patients were diagnosed with PH after 2.6 years of SRS. To assess the pressure in the LA during Doppler echocardiography, the tricuspid regurgitation rate (TR) was assessed. The breakpoint in this case is > 2.8 m/s. [1, 5, 6, 8]. The TR value in group 1 (2.4 m/s) did not differ from that in group 2 (2.6 m/s), $p = 0.18$.

Given the absence of specific PH symptoms in patients without cardiac involvement, its diagnosis requires strict adherence to a diagnostic algorithm with a gradual transition from the most common causes of PH to the rarer ones in order to consistently eliminate them. In this regard, the main purpose of a comprehensive examination of a patient with suspected PH is to diagnose it at an early stage, as well as to assess the functional and hemodynamic status [14, 16].

We compared patients with mild and severe sarcoidosis to develop models for predicting its severity. Next, a model was developed based on the parameters of transthoracic echocardiography, which indirectly reflect the damage to the heart in sarcoidosis, which is difficult to verify in clinical practice [1, 5, 6, 8].

The following predictors were used in the model: gender, age at the onset of the disease, the presence of extrapulmonary localizations of sarcoidosis, computed tomography (CT) data: quantitative assessment of the lung parenchyma lesion, areas of pronounced pulmonary fibrosis, new elements of the disseminated sarcoidosis, interstitial component, lymphopenia, predominant lesion area, and skin manifestations.

The model was obtained by binary logistic regression using stepwise elimination of predictors. The final model included: the presence of extrapulmonary localizations in the patient (odds ratio (OR) 2.99, 95% confidence interval (CI) (1.32; 7.03)), skin manifestations (OR 3.19, 95% CI (1.12; 9.46)), severe pulmonary fibrosis (OR 4.50, 95% CI (1.38; 16.24)), new elements of the disseminated sarcoidosis (OR 8.84, 95% CI (3.32; 26.72)), interstitial component (OR 3.76, 95% CI

(1.20; 12.55)), lymphopenia (OR 1.88, 95% CI (0.87; 4.15)), as well as quantitative assessment of changes in the lungs (OR 1.65, 95% CI (1.21; 2.31)), gender (OR 2.51, 95% CI (1.06; 6.32)).

The sensitivity of the model was 84%, the specificity was 86%, and the percentage of correct solutions was 85%. The area under ROC curve was 0.9, which indicates the high quality of the model.

The equation of the model was the following:

$$p = \frac{1}{1+e^{-(-4.916 + 1.097 * \text{EP} + 1.159 * SM + 1.504 * SPF + 2.180 * \text{NEDS} + 1.329 * IC + 0.633 * L + 0.500 * QACL + 0.919 * \text{Gender})}}$$

If the value of the function for the variable p is greater than 0.5, then severe sarcoidosis is predicted, if less – mild sarcoidosis.

Then, a model was developed based on the parameters of transthoracic echocardiography, radiographic findings, and CT scan. We chose the binary logistic regression method to develop the model. The model included: hypokinetic zones detected during echocardiography, the LV posterior wall thickness (LV PWT, mm), stage of sarcoidosis based on the pattern of chest radiographic findings, and the presence of few lesions in the lungs based on the high-resolution CT scan (Table).

Table

Predictors of sarcoidosis severity

Parameter	Ratio	OR	CI		*p*
			2.5%	97.5%	
Intercept term	–3.9				<0.025
LV PWT, mm	0.1	1.16	0.84	1.62	0.383
Few lesions in the lungs	–0.8	0.43	0.16	0.91	0.049
Hypokinetic zones based on echocardiography	1.3	3.51	0.52	69.28	0.265
Stage of sarcoidosis based on the pattern of chest radiographic findings	1.4	4.15	1.79	10.94	0.002

The logistic regression equation is as follows:

$$p = \frac{1}{1+e^{-(-3.886 + 1.255 * HZ + 0.145 * \text{LVPWT} + 1.423 * RS - 0.839 * FLL)}}, \quad (1)$$

where HZ is hypokinetic zones identified based on the echocardiography data (yes / no); LV PWT is the LV posterior wall thickness (mm); RS is the stage of sarcoidosis based on the pattern of chest radiographic findings (stage 0, 1, 2, 3); FLL is the presence of few lesions in the lungs (yes / no).

The standard value of 0.5 is used as the cut-off point. The decision rule (1) is as follows: if the probability p, calculated by formula (1), is greater than 0.5, then the disease is classified as severe, if less than 0.5, then mild.

Example of applying model 1. Patient M. had verified stage 3 SRS based on the patterns of radiological findings, absence of hypokinetic zones based on echocardiography, no lesions in the lungs; LV PWT was 11 mm. The calculated p value was 0.99, which is more than 0.5. Therefore, sarcoidosis is classified as severe. The predicted value is the same as the actual value set after 13 months of follow-up.

The quality of the model was assessed using a test sample. The sensitivity was 80%, the specificity was 73%, and the percentage of correct solutions was 77%. The area under ROC curve was 0.81.

Most of the parameters assessed in patients in clinical practice relate to signs that are determined by physicians. Therefore, models developed using quantitative features can be assumed to have a greater diagnostic value. Linear discriminant analysis is the method of statistical modeling, in which quantitative features are predictors.

Using this method, a model was developed that included the following predictors: age at the time of the onset of the disease, blood calcium levels, the Tiffeneau – Pinelli index (prebronchodilatory), as well as some echocardiographic parameters.: LV PWT (mm), interventricular septal thickness (IST, mm), volume of the right ventricle, LV ejection fraction (LVEF) (%), and AST level (U/l).

All the listed predictors of the model are very diverse and non-specific. The size of the right ventricle may indicate the development of a chronic pulmonary heart. In addition, the detection of structural changes in the heart, primarily in its right side (enlarged right atrium and ventricle), is important in the echocardiographic diagnosis of PH [5, 6]. The presence of hypokinetic zones, LVEF of less than 50%, and LV IST (≤ 4 mm at a distance of 10 mm from the aortic fibrous ring or its hypertrophy in the basal parts) may also indicate the onset of early signs of PH [4, 16].

These data also allow us to imply heart damage in sarcoidosis, which is very difficult to prove in clinical practice, given that the intravital diagnosis of SRS in the heart is quite difficult due to the non-specific clinical signs [19]. The AST level can also indicate damage to the heart muscle or myositis (clinically rarely diagnosed), as well as liver damage in sarcoidosis.

The resulting model is statistically significant (Wilks' lambda is 0.83; F (8.143) = 3.7; $p < 0.001$).

The equation was as follows:

$$y = 0.380*Ca^{2+}+0.096*RV-0.941*TPI+ \\ +0.349*LV\ PWT - 0.173*IST-0.098*LVEF+ \\ +0.407*AST+0.063*A, \quad (2)$$

where Ca^{2+} is the calcium level in the blood (mmol/l); RV is the volume of the right ventricle (ml); TPI is the the Tiffeneau – Pinelli index (%); LV PWT is the LV posterior wall thickness (mm); IST is the interventricular septal thickness (mm); LVEF is the LV ejection fraction (%), AST (U/l); A is the age of the onset of the disease (years).

The decision rule (2) is the following: if the y value calculated by formula (2) is less than 0.01, then the disease is classified as severe, if it is greater than 0.01, then mild.

Example of applying model 2. Patient K. was diagnosed with SRS and was 50 years old (0.56) when the diagnosis was verified, had the following indicators: blood calcium level of 2.54 mmol/l (0.36), the Tiffeneau – Pinelli index (prebronchodilatory) of 100% (–3.21), LV PWT – 10 mm (–0.40), IST – 9 mm (–0.21), the RV volume was 22 ml (1.06), LVEF was 69% (–0.20), and the AST level was 36 U/l (–0.71). The calculated value of y = 2.93, which is greater than –0.01, therefore, the disease is classified as mild. The predicted value is the same as the actual value set after 10 months of follow-up.

The quality of the model was assessed using a test sample. The sensitivity was 86%, the specificity was 87%, and the percentage of correct solutions was 85%.

CONCLUSION

To date, it is very difficult to identify the phenotype in SRS, as well as to assess disease severity. According to various literature data, it may take at least 1 to 10 years to establish the duration and assess severity of sarcoidosis in patients due to completely different reasons, including anything from the lack of a universal marker of sarcoidosis activity to a tendency to chronic intermittent course [20, 21].

As a result of the study, models were developed using various statistical modeling methods to predict sarcoidosis severity.

1. Patients with severe SRS developed PH more than 4 times more often than those with mild one ($\chi^2 = 409.5$; $p = 0.01$).

2. The first model, based on the signs used in clinical practice, has a high quality of prediction and includes predictors such as gender, age of the onset, the presence of extrapulmonary localization of sarcoidosis, CT data, lymphopenia, predominant lung lesion area, and skin manifestations. Model 1 is characterized by 84% sensitivity and 86% specificity.

4. The second model, based on the parameters of transthoracic echocardiography, including indicators that indirectly assess the development of PH and heart damage in sarcoidosis, depending on its severity, has a sensitivity of 80% and a specificity of 73%.

Both models include different groups of features that allow us to assess the relationship of various factors with SRS severity from different points of view. The application of the proposed models in clinical practice will make it possible to predict SRS severity already upon confirmation of the diagnosis, which may be useful for deciding on the patient management strategy (observation or requiring the prescription of pathogenetic immunosuppressive therapy). In addition, the set of characteristics associated with sarcoidosis severity includes some echocardiographic indicators (LV PWT, IST, RV volume, LVEF), taking into account the higher risk of developing PH in patients with severe sarcoidosis.

Thus, complex prediction models combining a variety of parameters associated with sarcoidosis severity are crucial for making prognosis regarding disease severity, including taking into account the higher risk of developing PH.

REFERENCES

1. Chazova I.E., Martynyuk T.V., Shmalts A.A., Gramovich V.V., Danilov N.M., Veselova T.N. et al. Eurasian Guidelines for the Diagnosis and Treatment of Pulmonary Hypertension (2023). *Eurasian Heart Journal.* 2024;(1):6–85 (in Russ.). DOI: 10.20538/1682-0363-2018-4-229–237.
2. Pulmonary hypertension, including chronic thromboembolic pulmonary hypertension. Clinical guidelines. Russian Society of Cardiology. "Approved at the meeting of the Scientific and Practical Council of the Ministry of Healthcare of the Russian Federation (meeting of 16.10.2020)." (in Russ.) URL: https://cr.minzdrav.gov.ru/recomend/159_1
3. Rudenko B.A., Feshchenko D.A., Shanoyan A.S. Endovascular methods of pulmonary artery denervation in the treatment

of patients with pulmonary hypertension: guidelines edited by O.M. Drapkina / S.O. Bukin. Moscow: Federal State Budgetary Institution NMRI TPM of the Ministry of Healthcare of Russia, 2020:60 (in Russ.).
4. Interregional public organization "Russian Respiratory Society". All-Russian public organization "Russian Scientific Medical Society of Therapists". All-Russian public organization "Pediatric Respiratory Society". Clinical guidelines. Sarcoidosis. 2022. (in Russ.) URL: https://cr.minzdrav.gov.ru/recomend/736_1
5. Neklyudova G.V., Naumenko Zh.K. Echocardiography in the diagnosis of pulmonary hypertension. *Practical Pulmonology.* 2015;17(4):48–56. (In Russ.).
6. Glazun L.O. Modern echocardiographic assessment of pulmonary hypertension and right ventricular function. *Healthcare in the Far East.* 2020;4:112–120. (In Russ.). DOI: 10.33454/1728-1261-2020-3-112-120.
7. Avdeev S.N. Pulmonary hypertension in sarcoidosis. *Pulmonologiya*. 2016;26(6):725–735. (In Russ.). DOI: 10.18093/0869-0189-2016-26-6-725-735.
8. Zhang R.F., Zhou L., Ma G.F., Shao F.C., Wu X.H., Ying K.J. Diagnostic value of transthoracic Doppler echocardiography in pulmonary hypertension: a meta-analysis. *American Journal of Hypertension.* 2010;23:1261–1264. DOI: 10.1038/ajh.2010.188.
9. Shanygin S.I., Kovalev V.V. Correlation and regression analysis: textbook for universities. Moscow: Yurait, 2024:70. (In Russ.). (Higher education). ISBN 978-5-534-18393-1.
10. Voronkova O.O., Tsvetkova O.A., Avdeev S.N., Rogova E.F., Abdullayeva G.B. Sarcoidosis with cardiac involvement and monoclonal gammopathy. *Kardiologiia*. 2020;60(4):151–156. (In Russ.). DOI: 10.18087/cardio.2020.4.n712.
11. Vizel A.A., Avdeev S.N., Vizel I.Yu., Shakirova G.R., Vlasenko A.E. Sarcoidosis severity in patients treated with systemic corticosteroids. *Pulmonologiya*. 2023;3(5):634–644. (In Russ.). DOI: 10.18093/0869-0189-2023-33-5-634-644.
12. Berg E.E., Kudryavtsev I.V., Kudlay D.A., Starshinova A.A. Features of the course and diagnosis of chronic sarcoidosis. *Translational Medicine*. 2024;11(1):6–18. (In Russ.). DOI: 10.18705/2311-4495-2024-11-1-6-18.
13. Lebedeva E.V. Functional state of the myocardium and features of hemodynamics of the pulmonary circulation in patients with pulmonary sarcoidosis based on echocardiography. St. Petersburg Research Institute of Pulmonology: Pavlov First Saint Petersburg State Medical University, 2004:23. (In Russ.).
14. Shariya A.M., Martynyuk T.V. Data of modern registries on clinical course and prognosis of patients with idiopathic pulmonary arterial hypertension. *Russian Cardiology Bulletin.* 2021;16(3):23–27. (In Russ.). DOI: 10.17116/Cardiobulletin20211603123.
15. Trisvetova E.L., Yudina O.A., Smolensky A.Z., Cherstvyi E.D. Diagnosis of isolated cardiac sarcoidosis. *Russian Journal of Archive of Pathology*. 2019;81(1):57–64. (In Russ.). DOI: 10.17116/patol20198101157.
17. Zhang R., Dai L.Z., Xie W.P., Yu Z.X., Wu B.X., Pan L. et al. Survival of Chinese patients with pulmonary arterial hypertension in the modern treatment era. *Chest.* 2011;140(2):301–309. DOI: 10.1378/chest.10-2327.
16. Mairina S.V., Ryzhkova D.V., Mitrofanova L.B., Ryzhkov A.V., Murtazalieva P.M., Moiseeva O.M. Modern approaches to the diagnosis and treatment of cardiac sarcoidosis: results of a cohort study. *Russian Journal of Cardiology*. 2023;28(5):5301. (In Russ.). DOI: 10.15829/1560-4071-2023-5301.
18. Poponina Yu.S., Poponina T.M., Mochula O.V., Chernyavskaya G.M., Ryabov V.V. Cardiac sarcoidosis: Difficulties and possibilities of differential diagnosis for acute coronary syndrome without ST segment elevation in real clinical practice. *Siberian Journal of Clinical and Experimental Medicine*. 2022;37(1):142–148. (In Russ.). DOI: 10.29001/2073-8552-2022-37-1-142-148.
19. Bickett A.N., Lower E.E., Baughman R.P. Sarcoidosis diagnostic score: a systematic evaluation to enhance the diagnosis of sarcoidosis. *Chest.* 2018;154(5):1052–1060. DOI: 10.1016/j.chest.2018.05.003.
20. Avdeev S.N., Barbarash O.L., Bautin A.E., Volkov A.V., Veselova T.N., Galyavich A.S., et al. Pulmonary hypertension, including chronic thromboembolic pulmonary hypertension. Clinical guidelines 2020. *Russian Journal of Cardiology*. 2021;26(12):4683. (In Russ.). DOI: 10.15829/1560-4071-2021-4683.
21. Terpigorev S.A., El Zein B.A., Vereshchagina V.M., Paleev N.R. Sarcoidosis: problems in classification. *Bulletin of the Russian Academy of Medical Sciences.* 2012;(5):30–37. (In Russ.). DOI: 10.15690/vramn.v67i5.271.

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