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ЭХОГРАФИЧЕСКАЯ ВЕРИФИКАЦИЯ И КЛИНИЧЕСКОЕ ЗНАЧЕНИЕ ПАТОЛОГИИ ОКОЛОСУСТАВНЫХ СТРУКТУР ПРИ ОСТЕОАРТРИТЕ КОЛЕННОГО СУСТАВА

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Sonographic Verification and Clinical Significance of the Features of Surrounding Structures in Knee Osteoarthritis

Резюме

Актуальность. Остеоартрит (ОА) коленного сустава — одно из самых распространенных заболеваний, наиболее значимым клиническим проявлением которого является хронический болевой синдром. Известно о низкой корреляции между рентгенологической стадией ОА и интенсивностью болей. Прежде всего, это объясняется разнообразием источников болевого синдрома, среди которых важное значение имеет патология многочисленных околосуставных структур (ОС). На сегодняшний день вклад этого вида патологии в клиническую картину ОА изучен недостаточно, в первую очередь в связи с тем, что перечень и частота этих поражений до сих пор не описаны. **Цель** — описание патологии основных околосуставных структур у пациентов с различными рентгенологическими стадиями первичного ОА коленного сустава по данным клинического и ультразвукового исследования. **Материалы и методы**. В наблюдательное поперечное исследование в настоящий момент включено 88 пациентов, обратившихся на амбулаторный прием ревматолога по поводу остеоартрита коленного сустава в период с 2021-2023 гг. В ходе исследования оценено 110 коленных суставов с использованием клинического и ультразвукового методов. **Результаты:** наиболее частыми околосуставными УЗ-изменениями независимо от рентгенологической стадии были тендопатия сухожилий «гусиной лапки» (57,3 %), киста Бейкера (45,5 %), фиброз жирового тела Гоффа (40 %) и лигаментопатия медиальной коллатеральной связки (36.4 %). Выявлена значимая корреляция между количеством изменений по данным УЗИ и рентгенологической стадией (ρ=0,45 [95 % ДИ: 0,28; 0,59], p <0,001), а также между ВАШ и количеством выявленных УЗ-изменений (ρ=0,29 [95 % ДИ: 0,11; 0,46], p=0,002). Кроме того, продемонстрировано, что поздние стадии ОА ассоциированы с бóльшим количеством изменений (p <0,001). **Заключение**. Изменения околосуставных структур имеются у большинства пациентов с остеоартритом коленного сустава; их количество коррелирует с величиной ВАШ, рентгенологической стадией ОА. Детализация этих изменений, их клиническая значимость и патогенетический вклад в прогрессирование ОА КС требуют дальнейшего изучения.

Ключевые слова: *остеоартрит, коленный сустав, околосуставная патология*

Конфликт интересов

Авторы заявляют, что данная работа, её тема, предмет и содержание не затрагивают конкурирующих интересов

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Abstract
Background: Osteoarthritis (OA) of the knee joint is one of the most dangerous diseases, the most significant manifestation of which is chronic pain syndrome. There is a low correlation between the radiographic stage of OA and pain progression. First of all, this is a variety of pain syndromes, among which is the pathology of periarticular structures (AS). To date, the contribution of this type to the clinical picture of OA has been sufficiently studied, primarily due to the fact that the list and frequency of these lesions have not yet been described. **Aim:** to describe the basis of the main periarticular structures in patients with different radiographic stages of knee OA according to ultrasound data. **Materials and methods:** The observational study has currently included 88 patients who had an outpatient appointment with a rheumatologist for knee osteoarthritis between 2021 and 2023. The study assessed 110 knee joints using clinical and ultrasound techniques. **Results:** The most common periarticular ultrasound changes, regardless of radiographic stage, were pes anserine tendinopathy (57.3 %), Baker's cyst (45.5 %), fibrosis of the severe Hoffa body (40 %) and ligamentopathy of the medial collateral ligament (36). ,4). %). A significant correlation was found between the number of changes according to ultrasound and the radiological stage (ρ=0.45 [95 % CI: 0.28, 0.59], p <0.001), as well as between the VAS and the definition of identified ultrasound changes (ρ= 0.29 [95 % CI: 0.11, p=0.002); In addition, it was shown that late stages of OA are associated with a greater content of changes (p <0.001). **Conclusion:** Changes in periarticular structures are present in most patients with knee osteoarthritis; their number correlates with the VAS value and radiographic stage of OA. Details of these changes, their clinical significance and pathogenetic contribution to the progression of knee OA require further study.

Key words: *osteoarthritis, knee joint, knee pain*

Conflict of interests
The authors declare no conflict of interests

Sources of funding
The authors declare no funding for this study

Conformity with the principles of ethics
The study was approved by the LEC of the N.I. Pirogov Russian National Research Medical University (protocol No. 213 dated December 13, 2021). Patients were included in the study after signing written informed voluntary consent.

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OA — osteoarthritis, KJ — knee joint, PAS — periarticular structures, CR — clinical recommendations

Introduction

According to the WHO, at least 1.71 billion people all over the world have musculoskeletal diseases, which are a significant cause of disability.[1] The most common joint condition is osteoarthritis (OA). In 2017 in Russia, the incidence of OA exceeded 4.3 mln people,[2] and the primary disease incidence grows annually. [34] About 73 % of patients with osteoarthritis are aged over 55 years old.[5] The most common location is the knee joint (KJ).[5]

It is currently believed that KJ OA is associated not only with progressive degeneration of the articular cartilage and subchondral bone, but also with significant changes in other structures, including components of the periarticular soft skeleton.[6] Therefore, KJ OA involves the joint as a whole and not its individual tissues.

Periarticular structures in the KJ are numerous and versatile. Given no clear anatomic boundaries and a strict listing of periarticular structures in the KJ, they include at least 5 ligaments, 9 tendons, 1 fascia structure and a variable amount of bursa (8 to 13), as well as fatty pads.[7, 8] Thus, there are a number of organs near the KJ, which are expected to be a part of the pathological processes in OA and can be a source of pain. Obviously, verification of a pain source in a specific patient is a necessary condition for efficient therapy.

However, involvement of periarticular structures (PAS) in KJ OA is still understudied. Recent studies have been focusing mainly on the study of processes in intraarticular tissues. At the same time, there are a very few studies of periarticular pathologies, which are based on small samples and take into account changes

in individual PAS.[9–12] The currently available data do not allow getting an idea of which PAS, how and how often are damaged in patients with KJ OA.

OA diagnostics is based on clinical parameters or their combinations with X-ray observations.[13] The existing criteria allow making a diagnosis, but they do not provide for a possibility to find out the source of pain in a specific patient, i.e. they do not create conditions for patient-specific therapy. In particular, the role of PAS pathology in the clinical presentation of OA is not discussed in any version of the current CRs. At the same time, being the main diagnostic method, X-ray examinations do not visualise PAS.

By contrast, ultrasound is a highly informative method of PAS evaluation.[14–16] Besides, ultrasound is popular due to its swiftness, accessibility, no radiation exposure, possibility to performed targeted examination in the place of pain, and stress tests. The examination can be repeated, also for the evaluation of therapy efficiency.

Therefore, the **objective** of this study is to describe PAS pathology in patients with primary KJ OA depending on the X-rate stage, using clinical and ultrasound methods.

Materials and Methods

The study enrolled patients over 50 years old, diagnosed with primary KJ OA in accordance with the classification criteria of the American College of Rheumatology.[17] OA was staged using the Kellgren — Lawrence X-ray classification.[18] Pain syndrome intensity was evaluated using VAS. To study PAS pathology, knee ultrasound was performed using Alpinion Ecube 8 with multifrequent linear 3–12 MHz sensors. Evaluation included all RASs which could be visualised, in the anterior, medial, lateral, and posterior knee joint areas: patellar tendon, kneecap ligament, Hoffa's fat pad in the anterior section of the joint; medial collateral ligament, pes anserinus tendons — in the medial section; lateral collateral ligament, biceps femoris tendon, distal iliotibial tract, popliteal muscle tendons — in the lateral section; semimembranosus muscle tendons — in the posterior section of KJ. Also, all sections of the joint were assessed for cysts and bursitis.

Identification of key ultrasound changes

Ultrasound results demonstrated that patients had signs of tendon pathology, ligament pathology, bursitis, as well as changes in Hoffa's fat pad. Changes were evaluated on a grey scale, with axial and transverse scanning, and were compared to a reference area. All ultrasound examinations were performed using same equipment, same method by same experienced specialist.

Following an ultrasound examination, a tendon pathology is diagnosed on the basis of the following changes:[16, 19] homogeneously or focally hypoechogenic signal in tendon, tendon thickening, loss of the normal fibrillar drawing pattern, signs of peritendinitis (swelling, oedema and hyperaemia of soft tissue surrounding the tendon). Also, possible presence of vascularisation, hyperechoic inclusions, and signs of partial rupture was taken into account.

A ligament pathology was a change in the ligament: thickening, hypoechogenic signal, loss of normal pattern, presence of inclusions and vascularisation, signs of partial rupture.[16 19]

Baker's cyst is an anechogenic, non-vascular lump with liquid contents, clear contour, variable size, located between the inner head of the calf muscle and semimembranosus muscle.[20]

Bursitis is an abnormal anechogenic or hypoechogenic extraarticular mass between tissue layers. On ultrasound, the mass can be squeezed, depending on location [21]. Knee bursas are observed in all sections and located between various structures (between bone and tendon, between tendon and ligament, etc.) [22]

Hoffa's fat pad is located below the kneecap, posteriorly to the kneecap ligament and anteriorly to femoral condyles. This is an intracapsular, but extrasynovial structure.[23] The most common conditions in patients were Hoffa's fat pad fibrosis, which manifested as changes in the normal structure of the fatty tissue and appearance of diffuse areas with increased echogenicity.

Statistical Analysis

Statistical analysis and visualisation of the obtained data were performed in R 4.3.2 (R Foundation for Statistical Computing, Vienna, Austria).

Descriptive statistics for categorial variables is presented as an absolute and relative frequencies; while for quantitative variables — as a mean (± standard deviation) and median (1st–3rd quartiles) values.

Associations of quantitative variables were analysed with the help of Spearman rank correlation (ρ) with a respective 95 % confidence interval (95 % CI). Correlation was statistically significant at $p < 0.05$.

Results

The study included 88 patients: 71 (80.7%) women and 17 (19.3%) men aged 50 to 83 years old (mean age was 66.9 (±7.7) years). 110 knee joints were examined, of which 22 (20%) cases of X-ray stage 1, 41 (37.3%) — stage 2, 45 (40.9%) — stage 3, and 2 (1.8%) cases of stage 4.

Table 1 shows that the most common periarticular ultrasound changes (irrespective of X-ray stage) were pathologies of pes anserinus structures (tendon pathology, enthesopathy, pes anserinus bursitis) — 59.1%, Baker's cyst (45.5%), Hoffa's fat pad fibrosis (40%) and ligament pathology in the medial collateral ligament (36.4%), while the most uncommon changes were observed in infrapatellar bursa, biceps tendon and kneecap ligament (Fig. 1). Besides, changes in some PAS were not observed at all. For instance, there were no cases of prepatellar bursitis and tendon pathology of semimembranosus muscle tendon.

Thus, the most common changes were observed in anterior, medial and posterior section of the joint, irrespective of OA stage. Changes were reported in all PAS types: in tendons, ligaments, bursa, as well as in Hoffa's fat pad. Quite common was a combination of several changes in one knee joint (up to 6 changes). The overall number of changes grew statistically with a higher OA stage ($p < 0.001$). Currently, the small sample size prevents from identifying the correlation between OA stage and individual changes in PAS. Available data show that the list of involved structures remains constant irrespective of the stage, and there were no stage-specific changes.

Statistical data processing showed a significant correlation between the number of changes on ultrasound and X-ray stage ($\rho = 0.45$ [95% CI: 0.28; 0.59], $p < 0.001$), between VAS score and the number of identified ultrasound changes ($\rho = 0.29$ [95% CI: 0.11; 0.46], $p = 0.002$). Also, comparative analysis revealed that stage 3–4 OA is associated with a larger number of changes ($p < 0.001$, Fig. 2,3).

Table 1. *General characteristics of the list, frequency and number of ultrasound changes depending on the radiological stage (n=110).*

Characteristics	All joints n=110	1-2 grade n=63	3-4 grade n=47	p
Number of changes in one knee joint according to ultrasound*	2 (1-3) 2 (0-6)	2 (1-3) 2 (0-5)	3 (2-4) 3 (0-6)	**<0,001**
0 (n, %)	9 (8,2%)	6 (9,5%)	3 (6,4%)	
1	29 (26,4%)	25 (39,7%)	4 (8,5%)	
2	26 (23,6%)	15 (23,8%)	11 (23,4%)	
3	31 (28,2%)	14 (22,2%)	17 (36,2%)	
4	8 (7,3%)	2 (3,2%)	6 (12,8%)	
5	5 (4,5%)	1 (1,6%)	4 (8,5%)	
6	2 (1,8%)	0 (0%)	2 (4,3%)	
Pes anserine tendons tendopathy/enthesopathy	55 (50%)	28 (44,4%)	27 (57,4%)	0,189
Pes anserine bursitis	10 (9,1%)	4 (6,3%)	6 (12,8%)	0, 286
Baker's cyst	50 (45,5%)	26 (41,3%)	24 (51,1%)	0, 325
Hoffa's fat pad fibrosis	44 (40%)	18 (28,6%)	26 (55,3%)	0, 005
Hoffa's fat pad inflammation	2 (1,8%)	0 (0%)	2 (4,3%)	<0,001
Medial collateral ligament ligamentopathy	40 (36,4%)	15 (23,8%)	25 (53,2%)	0,002
Lateral collateral ligament ligamentopathy	3 (2,7%)	2 (3,2%)	1 (2,1%)	0,741
Popliteus tendinopathy	20 (18,2%)	9 (14,3%)	11 (23,4%)	0,288
Iliotibial band changes	7 (6,4%)	3 (4,8%)	4 (8,5%)	0,421
Quadriceps tendinopathy	7 (6,4%)	2 (3,2%)	5 (10,6%)	0,157
Patellar ligament ligamentopathy	3 (2,7%)	2 (3,2%)	1 (2,1%)	0,573
Biceps femoris tendinopathy	2 (1,8%)	0 (0%)	2 (4,3%)	0,18
Infrapatellar bursitis	1 (0,9%)	1 (1,6%)	0 (0%)	0,7

***Comments:** the number of changes in one knee joint is presented as median (Q1-Q3), median (minimum-maximum), respectively.

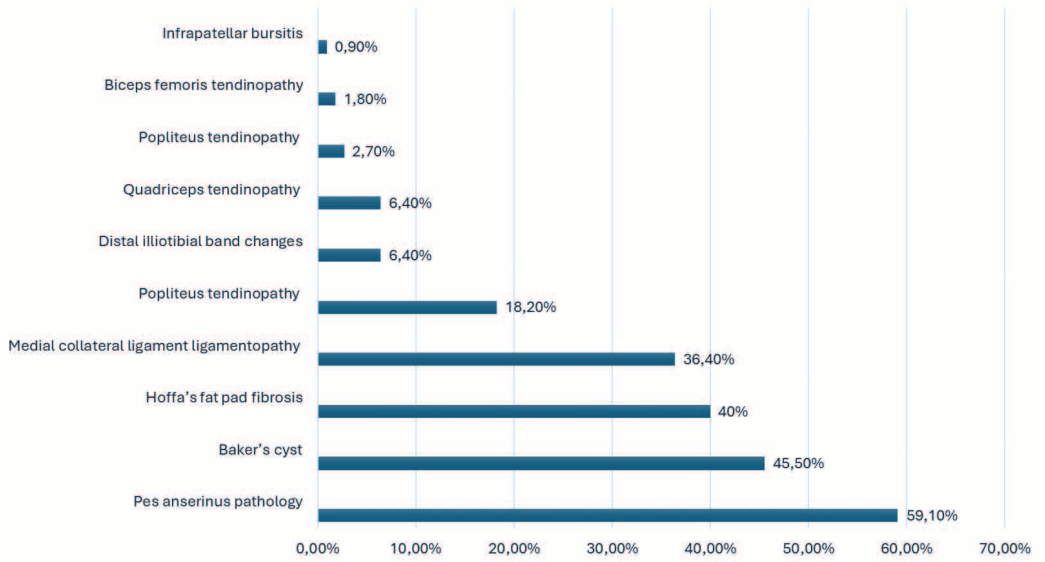

Figure 1.
Frequency of ultrasound changes regardless of the osteoarthritis grade

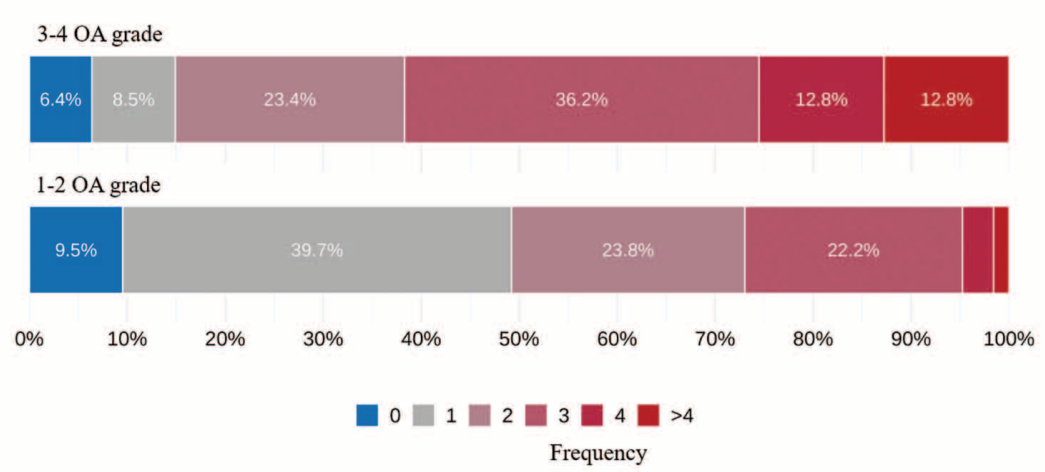

Figure 2.
Number of ultrasound changes depending on the radiographic stage.
Comments: No changes — more often at 1-2 grades, one change — much more often at 1-2 grades, 3 or more changes were present more often at 3-4 grades

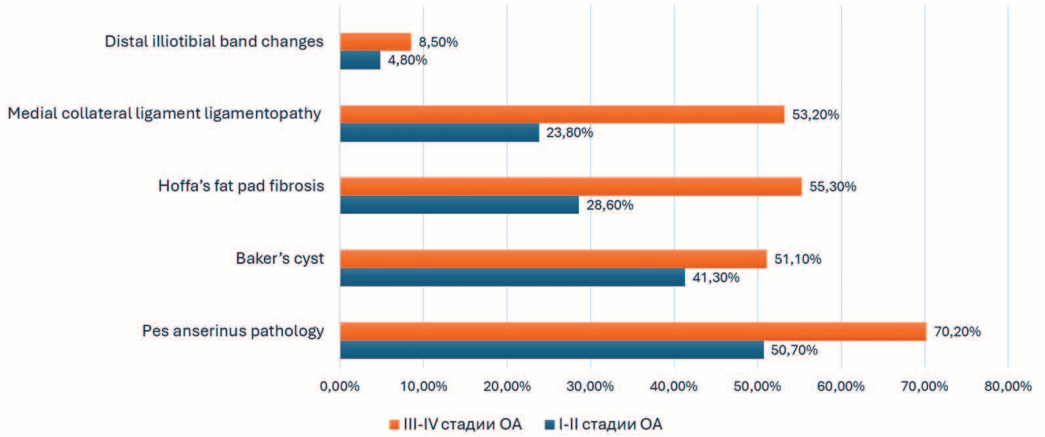

Figure 3.
Frequency of main ultrosound changes depending on the radiographic stage.
Comments: all changes were significantly more often detected at more progressive OA stages

Discussion

It is well known that changes in various PAS are often found in patients with KJ OA, and recently it had been confirmed, also due to the wide-spread use of musculoskeletal ultrasound. Nevertheless, the problem of periarticular involvement in KJ OA is undermined both in routine clinical practice and scientific research. Inadequate state of exploration of the problem of periarticular involvement is seen in clinical recommendations for OA: none of the versions describe this pathology; it means it is beyond the list of diagnostic and therapeutic objectives.

The current articles on the ultrasound verification of PAS pathology discuss just selected changes, which, according to the authors, are the most important: usually, these are pes anserinus bursitis, Baker's cyst and certain tendon pathologies.[9–12] In this article, we examined all PASs, which are suitable for ultrasound imaging; in other words, we have conducted the most comprehensive examination. The absolute majority of our patients had a pathology of this or that PAS, where all PASs were involved; and the list of such problems is quite typical.

The most common problems identified were pes anserinus conditions. According to our data, pes anserinus bursitis is quite a rare condition (9.1 % of cases), unlike other articles, where the incidence of this condition is significantly higher (20–46 %).[24, 25] However, we noted that pes anserinus tendon pathology and enthesopathy were more common than bursitis (50 % of cases); and they did not always coincide with bursitis. It is interesting to note that, despite the abundance of sources dedicated to ultrasound verification of bursitis, pes anserinus tendon pathology and enthesopathy are outside the research interest. Nonetheless, our data show that pes anserinus tendon pathologies and enthesopathies are the most commonly identified PAS changes, and this fact requires additional studies and interpretation.

Another common abnormality in our patients was changes in Hoffa's fat pad — fibrosis (40 %) — and, less common, signs of inflammation (2 %). Currently, Hoffa's fat pad is being actively studied, because it has been shown that this organ greatly influences KJ OA progression. On the other hand, Hoffa's fat pad undergoes pathological changes as well: patients with KJ OA are known to have inflammation and fibrosis of Hoffa's fat pad tissue.[26, 27] These changes can be visualised on ultrasound;[28] however, we could not find any studies where sonographic changes in Hoffa's fat pad of patients with KJ OA were taken into account. Nevertheless, in our patients, these changes were very common, indicating the need for evaluating their clinical significance.

According to the modern idea, KJ OA is thought to primarily affect the medial part of the joint,[29] where major morphological and clinical events indeed take place. In this context, it was surprising to see a relatively considerable involvement of the structure lying in the lateral and posterior sections: in the examined patients, tendopathy of popliteal muscle tendon was diagnosed in 18.2 %, taking the fifth place in the frequency of PAS changes.

A tendon pathology is usually a result of a long-term tendon overload[30] and, in addition to its clinical significance, it indicates persistent dysfunction of the respective muscle. Muscle dysfunctions in patients with KJ OA have been actively discussed; however, in a majority of cases, they related to femoral muscles,[31–33] while the shank muscle conditions (more specifically, popliteal muscle) are mentioned just in a few studies.[34, 35] The interest to the state of tendons in patients with KJ OA has been recently stimulated by the growing amount of sonographic examination data; however, the subject of research in this case is usually tendons of the musculus quadriceps femoris,[36] while popliteal muscle tendons are left unstudied. In this context, the results of our research imply that changes in popliteal muscle and its tendons in patients with KJ OA require through evaluation.

The study has limitations. The absence of a control group could have limited our conclusions.

Conclusions

PAS damages are the least studied area of pathological changes in KJ OA. At the same time, PAS is a potential source of pain and an area of therapeutic intervention in OA. Our study demonstrates the high incidence and versatility of PAS changes and confirms that they contribute greatly to the clinical presentation of OA, being an important source of pain. The correlation between the pain syndrome intensity, OA stage and the number of periarticular changes indicates that this pathology is a significant component of the clinical presentation and pathologic response in OA and should be treated as a sign and not as a set of concomitant conditions. Detailed examination of these changes, their clinical significance and pathogenic contribution to KJ OA progression are a perspective area of further studies.

Вклад авторов:

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Скрипниченко Э.А.: концепция и дизайн статьи, обзор публикаций по теме, написание первого варианта статьи, научное редактирование и переработка, утверждение финального варианта

Лялина В.В.: концепция и дизайн статьи, обзор публикаций по теме, научное редактирование и переработка, утверждение финального варианта статьи

Приписнова С.Г.: научная консультация, выполнение УЗИ, интерпретация УЗ-изменений, редактирование и переработка статьи, утверждение финального варианта

Голубев В.Г.: научное редактирование и переработка, утверждение финального варианта статьи

Author contribution:

All the authors contributed significantly to the study and the article, read and approved the final version of the article before publication

Skripnichenko E.A.: concept and design of the article, scientific editing and revision, review of literature, writing the first draft of the article, approval of the final version of the article

Lyalina V.V.: concept and design of the article, scientific editing and revision, review of literature, approval of the final version of the article

Pripisnova S.G.: scientific consultation, ultrasound examination, interpretation of ultrasound changes, editing and revision of the article, approval of the final version

Valery G. Golubev: scientific editing and revision, approval of the final version of the article

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