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Osteonecrosis of the Femoral Head: Another Legacy of COVID-19?

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Abstract

Background. Recovery from COVID-19 does not always proceed without complications, especially in patients who have suffered severe forms of the disease. Most researchers confirm a significant increase in the incidence of osteonecrosis of the femoral head (ONFH) after COVID-19. However, there is no clear opinion on the individual aspects of the development and course of the disease. This is an extremely important issue that allows us to identify the main risk groups for the development of post-COVID-19 osteonecrosis and, consequently, to perform the earliest possible screening of this complication.

***Aims of the study*:** 1) To evaluate the impact of the past COVID-19 on epidemiologic parameters and clinical course of osteonecrosis of the femoral head in patients; 2) to study the causes of its development.

Methods. We have analyzed the data of medical histories of 674 patients diagnosed with osteonecrosis of the femoral head who sought medical care in 2018 and in 2022. Patients were divided into 4 groups according to the presumed causes of development of the disease. The first group enrolled 183 patients who underwent COVID-19 and received steroid therapy (ST). The second group included 78 patients who underwent COVID-19 without ST therapy. The third group consisted of 103 patients with ONFH that manifested in 2022 without COVID-19 in the previous medical history. The comparison group was made up of 310 patients who developed ONFH in 2018 before the appearance of the SARS-CoV-2 virus.

Results. The sample of patients with COVID-19-associated osteonecrosis differed significantly from patients without COVID-19, in terms of gender, age, time of disease onset, extent of the femoral head damage, and disease progression rate ($p<0.001$). The level of early ONFH diagnosis was extremely low, not differing from that in the pre-pandemic period.

Conclusions. The COVID-19 pandemic has increased the incidence of ONFH, significantly modifying both its epidemiology and clinical picture. Nevertheless, the vigilance of practitioners remains extremely low, which affects the timely diagnosis of the disease.

Keywords: COVID-19, osteonecrosis of the femoral head, avascular necrosis, diagnosis of osteonecrosis, steroids.

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Остеонекроз головки бедренной кости — еще одно наследие COVID-19?

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Реферат

Актуальность. Выздоровление после COVID-19 не всегда проходит без осложнений, особенно у пациентов, перенесших тяжелые формы заболевания. Большинство исследователей подтверждают значительный рост частоты развития остеонекроза головки бедренной кости (ОГБК) вследствие перенесенного COVID-19. При этом нет четкого мнения относительно индивидуальных аспектов развития и течения заболевания. Это является крайне важными моментом, позволяющим выделить основные группы риска развития остеонекроза после перенесенного COVID-19 и, как следствие, осуществить максимально ранний скрининг данного осложнения.

***Цели исследования*:** 1) оценить влияние перенесенного COVID-19 на эпидемиологические показатели и клиническое течение остеонекроза головки бедренной кости у пациентов; 2) изучить причины его развития.

Материал и методы. Проанализированы данные медицинской документации 674 пациентов с диагнозом «остеонекроз головки бедренной кости», обратившихся за медицинской помощью в 2018 и в 2022 гг. Пациенты были разделены на 4 группы по предполагаемым причинам развития заболевания: первая группа — 183 пациента, перенесших COVID-19 и получавших лечение глюкокортикостероидами (ГКС); вторая группа — 78 пациентов, перенесших COVID-19 без терапии ГКС; третья группа — 103 пациента с ОГБК, дебютировавшем в 2022 г. и без COVID-19 в анамнезе. Четвертую группу (сравнения) составили 310 пациентов, у которых ОГБК развился в 2018 г., до появления вируса SARS-CoV-2.

Результаты. Пациенты с остеонекрозом, ассоциированным с COVID-19, значительно отличались от пациентов, не болевших COVID-19, по полу, возрасту, срокам дебюта заболевания, объему поражения головки бедренной кости и скорости течения патологического процесса (p<0,001). Уровень ранней диагностики ОГБК был крайне низким, не отличаясь от такового в допандемийный период.

Заключение. Пандемия COVID-19 привела к увеличению частоты ОГБК, серьезно изменив как его эпидемиологию, так и клиническую картину. Тем не менее настороженность практикующих врачей остается крайне низкой, что сказывается на своевременной диагностике заболевания.

Ключевые слова: COVID-19, остеонекроз головки бедренной кости, аваскулярный некроз, кортикостероиды.

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BACKGROUND

Osteonecrosis of the femoral head (ONFH) is a severe, rapidly progressing disease affecting mainly young people of working age. Attempts to solve the problem by performing hip arthroplasty in this case seem questionable due to their high physical activity and, as a consequence, premature failure of the artificial joint. Before the COVID-19 pandemic, the share of the discussed pathology in the structure of requests for orthopedic care, according to various sources, amounted to 5-15% of cases [1, 2]. We have identified the main risk groups for the development of ONFH, as well as the criteria for its early diagnosis, allowing the most effective use of techniques aimed at preventing or delaying hip arthroplasty [3, 4, 5]. Unfortunately, the new coronavirus infection has changed this situation, as evidenced by the constant increase in the number of publications devoted to this topic [6, 7]. When analyzing them, we have found a number of interesting features that make it difficult to systematize the information obtained.

Some authors suggest a diametrically opposite approach when highlighting the key points of the studies. Thus, a number of authors underline the importance of the isolated problem of the increased incidence of COVID-19-associated ONFH [7, 8]. Others focus not on the increase in incidence, but on the aggressive course of ONFH in the category of patients being considered [9, 10]. At the same time, the main mechanism of vascular thrombosis in the femoral head remains unclear. Undoubtedly, uncontrolled use of steroids may be one of the reasons for ONFH development [11, 12, 13, 14]. The widespread use of steroids in the treatment of patients with SARS in 2003 to reduce the inflammatory infiltration of the lungs and improve oxygenation led to the subsequent development of ONFH in almost a quarter of patients [15, 16]. However, we cannot exclude the possibility of direct damage to the vascular wall by the virus by analogy with the described thrombosis of various organs in meningococcemia, HIV, hepatitis, rubella, and varicella [17, 18, 19, 20]. It is also worth noting that a significant part of the studies we have found are based on limited series of observations.

Aims of the study: 1) to evaluate the impact of the past COVID-19 on epidemiologic parameters and clinical course of osteonecrosis of the femoral head in patients; 2) to study the causes of its development.

METHODS

A single-center retrospective cross-sectional study was based on the medical histories of 674 patients with confirmed non-traumatic osteonecrosis of the femoral head who had sought medical care at the Vreden National Medical Research Center for Traumatology and Orthopedics in 2018 and 2022.

According to the study design, the patients were divided into 4 groups. Group 1 consisted of 183 patients with ONFH due to severe form of COVID-19 that had required steroid therapy during inpatient treatment. Group 2 consisted of 78 patients with milder forms of COVID-19 treated in hospital or at home without steroids. Group 3 included 103 patients with ONFH that had developed in 2022 with no prior COVID-19 infection. Group 4 (comparison group) was made up of 310 patients who had suffered from ONFH in 2018 before the appearance of the SARS-CoV-2 virus.

Exclusion criterion for the Groups 1 and 2 was the detection of ONFH prior to COVID-19 disease. Cases of post-traumatic ONFH were exclusion criteria for all study groups.

To assess the validity of the results obtained, the first stage was to analyze the ratio of patients excluded from the study in 2022 and 2018. In parallel, the total number of ONFH cases was compared according to the year of referral.

At the second stage, an intergroup analysis was performed according to the following parameters.

1. Distribution of patients by age and gender.
2. Extent of the femoral head defect. Calculation was based on the results of computed tomography. The average damage radius was calculated according to the formula:

$$(R1+R2+R3) : N,$$

where R1 is minimum, R2 — mean, R3 — maximum damage radius, respectively, N — number of measurements.

Then the size of necrosis focus was determined according to the formula:

$$4/3\ \pi R^3,$$

where R is previously calculated average damage radius.

The final calculation of the ratio of the osteonecrosis focus size to the healthy bone tissue was performed according to the formula:

(focus size / head volume) × 100%.

The foci were divided by size in accordance with the classification of M.E. Steinberg: up to 15% of the femoral head volume – small, 15-30% - medium, more than 30% — large [21].

3. The rate of pathologic process progression was assessed by the duration of the "lucid interval" from the appearance of primary pain syndrome caused by bone marrow edema to the development of secondary pain syndrome, which is a marker of impression fracture of the loaded pole of the femoral head.

4. Period from COVID-19 (from the onset of coronavirus infection according to medical records) to the onset of primary hip pain for Groups 1 and 2. This indicator was not monitored for patients in Groups 3 and 4.

At the third stage of the study, the criteria influencing early diagnosis were evaluated:

– awareness of COVID-19 patients about the risks of developing ONFH;

– frequency of patients' referral at the onset of the first symptoms of disease;

– frequency of diagnosing the disease at the first visit;

– time and reasons for delayed diagnosis, provided that the patient was referred timely.

Statistical analysis

Calculations were performed in Excel for Windows (Microsoft, USA) and SPSS v. 26.0 software. Descriptive statistics methods were used to summarize the primary results obtained from individual patient registration cards: mathematical expectation, standard deviation, median, quartiles, minimum/maximum. The Pearson's chi-square test, paired and unpaired Student's t-test were used for comparison of qualitative parameters. For parameters with non-normal distribution, non-parametric tests were used, in particular, the Mann-Whitney test and the Wilcoxon's test. Differences were considered statistically significant at $p<0.05$.

RESULTS

The number of patients excluded from the study according to the above-mentioned criteria relative to the total number of cases between 2022 and 2018 showed no statistically significant difference. However, a statistically significant increase in the overall incidence of ONFH was found in 2022. Also in 2022, there was a decrease in the incidence of osteonecrosis of non-traumatic genesis due to an increase in COVID-19-related ONFH cases (Table 1).

Subsequent intergroup analysis showed a quantitative predominance of patients receiving steroid therapy for COVID-19 (Group 1) over all other forms of ONFH in 2022 (Groups 2 and 3). Also, patients in Group 1 differed statistically significantly by age and gender from all other studied groups. However, there were no statistically significant differences in all the previously mentioned criteria between patients with COVID-19 without steroid therapy (Group 2), with other forms of osteonecrosis in 2022 (Group 3), and patients with ONFH in 2018 (Group 4) (Table 2).

When studying the extent of the femoral head demage, it was found that patients who had received steroids in COVID-19 treatment had exclusively large and medium-sized foci, which significantly distinguished Group 1 from all other groups, in which no statistically significant

Table 1

Comparative characteristics of patients with ONFH

Parameter	2022	2018	p 2022 vs 2018
Total number of referrals, n	592	509	<0.001
Patients excluded from the study, n / %	228 / 38.5	198 / 38.9	0.503
Patients included in the study, n	364	310	<0.001
Increase in cases of non-traumatic ONFH in 2022, %	14.8	–	–
Etiology of ONFH			
COVID-19 / other causes, n	261 /103	310	<0.001
% ratio	71.7 / 28.3	100	–

Table 2

Comparison of patients in the four groups by number of ONFH cases, gender, and age

Parameter	2022			2018	p 1 vs 2 1 vs 3 1 vs 4	p 2 vs 3	p 2 vs 4	p 3 vs 4
	Group 1 (1)	Group 2 (2)	Group 3 (3)	Group 4 (4)				
Number of cases, n	183	78	103	310		<0.001	<0.001	<0.001
Age, years	56/18	43/11	41.5/11.6	42.4/12.3		0.873	0.236	0.353
Me / interquartile range (min-max)	(21–79)	(25–58)	(27–60)	(25–57)	<0.001 in all comparisons	–	–	–
Age >50 years, n/%	134 / 73.2	9 / 11.5	12 / 11.6	35 / 11.3		0.960	0.502	0.601
Male / female								
n	102 / 81	57 / 21	75 / 28	226 / 84		0.786	0.202	0.516
% ratio	55.7 / 44.3	73.1 / 26.9	72.8 / 27.2	72.9 / 27.1		–	–	–

difference in the extent of the femoral head damage was recorded. There was also a persistent tendency for the prevalence of medium-sized foci over small foci and small foci over large foci. In at least 80% of cases in Groups 2, 3, and 4, the development of large foci was associated with initial steroid therapy for comorbid pathology. In Group 1 no such tendency was noted. In turn, larger foci in patients receiving steroids for therapy of severe forms of COVID-19 led to more rapid development of impression fracture of the femoral head, whereas no statistically significant difference in this parameter was observed between Groups 2, 3, and 4 (Table 3).

When comparing Groups 1 and 2 in terms of the time elapsed from COVID-19 to the development of primary pain syndrome in the hip joint, a statistically significant relationship between the time of disease manifestation and steroid therapy was established. Thus, in patients of Group 1, the time from the moment of reconvalescence to the period of the first pain in the joint was shorter and varied less in contrast to Group 2. It should also be noted that several patients in Group 1 complained of primary pain syndrome occurring during COVID-19 steroid therapy, while in Group 2 such cases were absent (Table 4).

Table 3

Comparison of patients by extent of the femoral head damage, steroids intake, comorbidities, and rate of development of the femoral head impression fracture

Parameter	2022			2018	p 1 vs 2 1 vs 3 1 vs 4	p 2 vs 3	p 2 vs 4	p 3 vs 4
	Group 1 (1)	Group 2 (2)	Group 3 (3)	Group 4 (4)				
Extent of the femoral head damage	–	24 / 30.8	31 / 30.1	93 / 30		0.541	0.338	0.526
under 15%, n / %	103 / 56.3	43 / 55.1	57 / 55.3	171 / 55.2		0.790	0.432	0.801
15–30%, n / %	80 / 43.7	11 / 14.1	15 / 14.6	46 / 14.8		0.756	0.371	0.534
over 30%, n / %								
Initial steroid therapy* in case of foci >30%, n / %	6 / 7.5	8 / 81.8	12 / 80	37 / 80.4	<0.001 in all comparisons	<0.001	<0.001	0.603
Time to an impression fracture development, months								
Me / interquartile range (min-max)	6/4.6 (3–12)	8/4.1 (3–17)	8.2/4 (3–16)	8/3.9 (3–16)		0.514 –	0.385 –	0.472 –

* For diseases prior to SARS-CoV-2 infection.

As the survey showed, none of the patients who underwent COVID-19 were warned about the possibility of this complication. The vast majority of patients, regardless of the etiology of osteonecrosis, sought outpatient care at the first manifestations of the disease. Timely diagnosis of COVID-19-associated and non-COVID-19-associated ONFH was 10.6% and 10.7% of cases, respectively. The rest of the patients were observed by neurologists with suspicion of lumbar spine pathology. In this case, the diagnosis was made only when a bright clinical picture due to the femoral head collapse developed at 4.2 and 6.0 months for COVID-19-associated and non-COVID-19-associated osteonecrosis, respectively (Table 5).

Table 4

Time to development of primary hip pain syndrome depending on steroids intake

Parameter	Group 1 (1)	Group 2 (2)	p 1vs2
Time to primary manifestations of ONFH, months Me / interquartile range (min-max)	3/5 (0–18)	8/7 (0–17)	<0.001 in all comparisons
Occurrence of hip pain during steroid therapy for COVID-19, n / %	11 / 6	0	

Table 5

Physicians' vigilance and timely diagnosis in patients with COVID-19-associated and non-COVID-19-associated osteonecrosis

Parameter	Cases of osteonecrosis with COVID-19 in medical history n = 261	Cases of non-COVID-19-associated osteonecrosis, n = 413	p
Warned about the risk of ONFH, n	0	0	–
Contacted the outpatient clinic at the first symptoms of ONFH, n / %	235 / 90	365 / 88.4	0.268
Timely diagnosis of ONFH, n / %	25 / 10.6	39 / 10.7	0.704
Observed by neurologists without suspected ONFH, n / %	210 / 89.4	326 / 89.3	0.621
Timing of diagnosis from ONFH onset, months Me / interquartile range (min-max)	4.2/1.3 (2–17)	6/2.1 (1–18)	<0.001 –

DISCUSSION

Recovery from COVID-19 is not always without complications, especially in patients who have had severe forms of the disease. In addition to general manifestations, such as weakness, dyspnea, anxiety, and depression, there are more and more frequent reports of osteonecrosis of the femoral head associated with COVID-19 [22, 23]. According to a number of authors, this is extremely alarming, as ONFH is characterized by a rapidly progressing course [24, 25]. It can easily be assumed that the increase in the number of such patients will become a heavy burden for the health care system [26, 27]. Therefore, timely diagnosis is crucial for the treatment of early stages of osteonecrosis, allowing the preservation of the affected joint. This necessity is dictated by the indication of ischemia foci significantly exceeding 30% of the femoral head volume [13, 28]. These changes reduce the possibilities of organ-preserving treatment methods to the use of decompression only at the stage of bone marrow edema [29, 30, 31]. In turn, early screening of ONFH is almost impossible without

understanding the conditions of development and features of the clinical course of ONFH [32, 33, 34].

The COVID-19 pandemic has not only caused an increase in the overall incidence of ONFH in the patient population, but has also largely crowded out other forms of non-traumatic osteonecrosis compared to 2018. A similar trend was noted by J.O. Okewunmi et al. When analyzing over one million hip arthroplasties, they indicated a significant increase in ONFH in 2021 compared to the pre-pandemic 2016. [32]. We have found that the increased incidence of COVID-19-associated ONFH (more than 70%) occurred in patients receiving steroid therapy for severe coronavirus infection, which fully confirms the results of the study by J.O. Okewunmi et al.

A more detailed analysis revealed significant heterogeneity of COVID-19-treated patients according to the criterion of steroid intake in the acute phase of the disease. Thus, the mean age and gender of patients in the Group 2 (COVID-19 treatment without steroids) was comparable to the group of patients without coronavirus infection. Patients in Group 1 (COVID-19 + steroids) were on average significantly older. This feature was predominantly associated with atypical age of osteonecrosis development. The maximum recorded age was 79 years, whereas in other groups this parameter did not exceed 60 years. A similar trend can be observed in the study by A.V. Glukhov et al. According to their data, the frequency of ONFH after coronavirus infection in patients older than 50 years approached 30% [35]. We have revealed a tendency of ONFH development in patients over 60 years of age who had mild forms of COVID-19 but received steroids for concomitant pathology.

The extent of the femoral head damage also showed a significant difference between the first and other study groups. The patients in this group had only medium and large damage foci with no small foci, while medium and small foci were predominant in other groups. At the same time, large foci in these groups were clearly associated with steroid therapy, whereas in Group 1 (COVID-19 + steroids) no such correlation was found. It should also be noted that the patients in Group 1 developed the fracture of the loaded pole of the femoral head significantly earlier compared to other study groups.

The study of the time of development of the primary pain syndrome from the moment of reconvalescence from new coronavirus infection also showed a significant difference. Patients in the first group began to feel pain syndrome much earlier than patients in other groups in which hormone therapy was not used. In addition, in the first group there were precedents of primary pain syndrome at the stage of steroid therapy, while in the second group there were no such cases.

We have been unable to find a clear association of SARS-CoV-2 virus with the development of ONFH. Nevertheless, the early onset of pain syndrome, more rapid and extensive damage to the femoral head indirectly testify to the combined effect of the virus and hormonal therapy. Again, it should be noted that steroids were used in severe forms of COVID-19, which means that the viral load and the probability of microthrombosis were higher. On this basis, patients who underwent COVID-19, especially those who required steroid therapy, should necessarily be aware of the risk of osteonecrosis and symptoms indicating the development of this disease. In this case, the earlier development of the fracture of the loaded pole of the femoral head in the first group of COVID-19 patients was probably also due to the extensive foci and, therefore, more aggressive course of the disease compared with other cases of ONFH development.

We have revealed extremely low alertness of physicians regarding the risk of this complication. Thus, despite numerous publications, the diagnosis of ONFH at the early stages in this category of patients did not exceed 11% of cases. In all other cases, the clinical picture was mistaken for lumbar spine pathology, for which patients received conservative treatment up to the development of the femoral head collapse. Therefore, it is worth highlighting that all physicians, regardless of their specialty, should be warned about the high risks and possible negative consequences of late diagnostics of ONFH. This will most likely allow early diagnosis (before the osteonecrosis focus is delimited) and treatment, enabling in some cases to count on the preservation of the damaged joint.

Limitation of the study

Our study, like most similar studies, has a significant limitation in terms of the size of the study groups, but the factors we have identified should be considered by specialists working with patients who have suffered COVID-19.

CONCLUSIONS

With the development of the COVID-19 pandemic, the structure of osteonecrosis of the femoral head has undergone significant epidemiologic, pathomorphologic, and, accordingly, clinical changes. We have managed to record a significant increase in this pathology and an increase in the average age of patients compared to the pre-pandemic values. Also in the first group, an atypical gender distribution of patients was observed. In addition, a more aggressive course of the disease was recorded due to the initially larger extent of the femoral head damage, especially in patients treated with steroids for the coronavirus infection. Nevertheless, the vigilance of practitioners remains extremely low. This approach is likely to increase the need for primary and, consequently, revision hip arthroplasty in future, significantly burdening the health care system as a whole.

DISCLAIMERS

Author contribution

Myasoedov A.A. — study concept, data analysis and interpretation, statistical analysis of results, writing the article.

Shubnyakov I.I. — data analysis and interpretation, statistical analysis of results, writing the article.

Sereda A.P. — data collection and processing, drafting the article.

Karelkin V.V. — data collection and processing.

*Yunkina E.*A. — data collection and processing.

Berezin G.V. — data collection and processing.

All authors have read and approved the final version of the manuscript of the article. All authors agree to bear responsibility for all aspects of the study to ensure proper consideration and resolution of all possible issues related to the correctness and reliability of any part of the work.

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REFERENCES

1. Guidelines on hip surgery. Ed. by R. Tikhilov, I. Shubnyakov. St. Petersburg; 2014. Vol. 1. p. 155-173. (In Russian).
2. Mont M.A., Cherian J.J., Sierra R.J., Jones L.C., Lieberman J.R. Nontraumatic Osteonecrosis of the Femoral Head: Where Do We Stand Today? A Ten-Year Update. *J Bone Joint Surg Am.* 2015;97(19):1604-1627. doi: 10.2106/JBJS.O.00071.
3. Hines J.T., Jo W.L., Cui Q., Mont M.A., Koo K.H., Cheng E.Y. et al. Osteonecrosis of the Femoral Head: an Updated Review of ARCO on Pathogenesis, Staging and Treatment. *J Korean Med Sci*. 2021;36(24):e177. doi: 10.3346/jkms.2021.36.e177.
4. Mont M.A., Salem H.S., Piuzzi N.S., Goodman S.B., Jones L.C. Nontraumatic Osteonecrosis of the Femoral Head: Where Do We Stand Today?: A 5-Year Update. *J Bone Joint Surg Am.* 2020;102(12):1084-1099. doi: 10.2106/JBJS.19.01271.
5. Korytkin A.A., Zykin A.A., Zakharova D.V., Novikova Y.S. Bone grafting enhanced by platelet-rich plasma in treatment of avascular necrosis of femoral head. *Traumatology and Orthopedics of Russia.* 2018;24(1):115-122. (In Russian). doi: 10.21823/2311-2905-2018-24-1-115-122.
6. Sinha P.R., Mallick N., Sahu R.L. Avascular Necrosis of the Hip after the COVID-19 Pandemic. *J Pharm Bioallied Sci.* 2023;15(Suppl 1):S661-S664. doi: 10.4103/jpbs.jpbs_87_23.
7. Hassan A.A.A., Khalifa A.A. Femoral head avascular necrosis in COVID-19 survivors: a systematic review. *Rheumatol Int.* 2023;43(9):1583-1595. doi: 10.1007/s00296-023-05373-8. Epub ahead of print.
8. Shetty G.M. Double Trouble-COVID-19 and the Widespread Use of Corticosteroids: Are We Staring at an Osteonecrosis Epidemic? *Indian J Orthop*. 2021;56(2):226-236. doi: 10.1007/s43465-021-00546-8.
9. Dhanasekararaja P., Soundarrajan D., Kumar K.S., Pushpa B.T., Rajkumar N., Rajasekaran S. Aggressive Presentation and Rapid Progression of Osteonecrosis of the Femoral Head After COVID-19. *Indian J Orthop.* 2022;56(7):1259-1267. doi: 10.1007/s43465-022-00635-2.
10. Agarwala S., Vijayvargiya M., Sawant T., Kulkarni S. Bisphosphonates for Post-COVID Osteonecrosis of the Femoral Head: Medical Management of a Surgical Condition. *JBJS Open Access.* 2022;7(4):e22.00060. doi: 10.2106/JBJS.OA.22.00060.

11. Leung T., Chan A., Chan E., Chan V., Chui C., Cowling B. et al. Short-and potential long-term adverse health outcomes of COVID-19: a rapid review. *Emerg Microbes Infect.* 2020;9(1):2190-2199. doi: 10.1080/22221751.2020.1825914.
12. Mahase E. Covid-19: What do we know about «long covid»? *BMJ.* 2020;370:m2815. doi: 10.1136/bmj.m2815.
13. Ardakani M.V., Parviz S., Ghadimi E., Zamani Z., Salehi M., Firoozabadi M.A. et al. Concomitant septic arthritis of the hip joint and femoral head avascular necrosis in patients with recent COVID-19 infection: a cautionary report. *J Orthop Surg Res.* 2022;17(1):302. doi: 10.1186/s13018-022-03192-4.
14. Powell C., Chang C., Naguwa S.M., Cheema G., Gershwin M.E. Steroid induced osteonecrosis: An analysis of steroid dosing risk. *Autoimmun Rev.* 2010;9(11):721-743. doi: 10.1016/j.autrev.2010.06.007.
15. Zhang S., Wang C., Shi L., Xue Q. Beware of steroid-induced avascular necrosis of the femoral head in the treatment of COVID-19-Experience and lessons from the SARS epidemic. *Drug Des Devel Ther.* 2021;15:983-995. doi: 10.2147/DDDT.S298691.
16. Guo K.J., Zhao F.C., Guo Y., Li F.L., Zhu L., Zheng W. The influence of age, gender and treatment with steroids on the incidence of osteonecrosis of the femoral head during the management of severe acute respiratory syndrome: A retrospective study. *Bone Joint J.* 2014; 96-B(2):259-262. doi: 10.1302/0301-620X.96B2.31935.
17. Edler C., Schröder A.S., Aepfelbacher M., Fitzek A., Heinemann A., Heinrich F. et al. Dying with SARS-CoV-2 infection-an autopsy study of the first consecutive 80 cases in Hamburg, Germany. *Int J Legal Med.* 2020;134(4):1275-1284. doi: 10.1007/s00414-020-02317-w.
18. Fahmy O.H., Daas F.M., Salunkhe V., Petrey J.L., Cosar E.F., Ramirez J. et al. Is microthrombosis the main pathology in coronavirus disease 2019 severity? A systematic review of the postmortem pathologic findings. *Critical Care Explor.* 2021;3(5):e0427. doi: 10.1097/CCE.0000000000000427.
19. Chacko A., Babu M., Thomas D.K. Osteonecrosis of bilateral femoral head in a post COVID-19 patient: Case report. *Int J Res Orthop.* 2021;7(3):674-678. doi: 10.18203/issn.2455-45.
20. Wichmann D., Sperhake J.-P., Lütgehetmann M., Steurer S., Edler C., Heinemann A. et al. Autopsy findings and venous thromboembolism in patients with COVID-19: a prospective cohort study. *Ann Intern Med.* 2020;173(4):268-277. doi: 10.7326/M20-2003.
21. Steinberg M.E., Hayken G.D., Steinberg D.R. A quantitative system for staging avascular necrosis. *J Bone Joint Surg Br.* 1995;77:34-41.
22. Muthu S., Jeyaraman M., Selvaraj P., Jeyaraman N., Potty A.G., Gupta A. Dose-Response Meta-Analysis of Corticosteroid Effects in SARS Outbreak: A Model for Risk Stratification and Screening Strategy for Osteonecrosis of Femoral Head Post-Corticosteroid Therapy for COVID-19. *Life (Basel).* 2023;13(4):907. doi: 10.3390/life13040907.
23. Disser N.P., De Micheli A.J., Schonk M.M., Konnaris M.A., Piacentini A.N., Edon D.L. et al. Musculoskeletal Consequences of COVID-19. *J Bone Joint Surg Am.* 2020;102(14):1197-1204. doi: 10.2106/JBJS.20.00847.
24. Takashima K., Iwasa M., Ando W., Uemura K., Hamada H., Mae H. et al. MRI screening for osteonecrosis of the femoral head after COVID-19. Mod Rheumatol. 2023:road095. doi: 10.1093/mr/road095.
25. Zhang S., Wang C., Shi L., Xue Q. Beware of Steroid-Induced Avascular Necrosis of the Femoral Head in the Treatment of COVID-19-Experience and Lessons from the SARS Epidemic. *Drug Des Devel Ther.* 2021;15: 983-995. doi: 10.2147/DDDT.S298691.
26. Sereda A.P., Shubnyakov I.I., Dzhavadov A.A., Mametov M.V., Tikhilov R.M. Economics of Total Hip Arthroplasty: Review. *Traumatology and Orthopedics of Russia.* 2022;28(4):175-182. (In Russian). doi: 10.17816/2311-2905-1778.
27. Musil D., Šnorek M., Gallo J., Jahoda D., Stehlík J. Economic Analysis of the Costs of Hospital Stay of Patients with Infection as a Complication of Total Replacements - Part 2: Total Hip Arthroplasty. *Acta Chir Orthop Traumatol Cech.* 2019;86(4):241-248. (In Czech).
28. Snowden G.T., Clement N.D., Zhang S., Xue Q., Simpson A.H.R.W. Orthopaedic long COVID - the unknown unknowns: are we facing a pandemic of avascular necrosis following COVID-19? *Bone Joint Res.* 2022;11(1): 10-11. doi: 10.1302/2046-3758.111.BJR-2021-0505.
29. Tikhilov R.M., Shubnyakov I.I., Myasoedov A.A., Irzhansky A.A. Comparison of different core decompression techniques for treatment of early stages of osteonecrosis of the femoral head. *Traumatology and Orthopedics of Russia.* 2016;22(3):7-21. (In Russian). doi: 10.21823/2311-2905-2016-22-3-7-21.
30. Zhao D., Zhang F., Wang B., Liu B., Li L., Kim S.Y. et al. Guidelines for clinical diagnosis and treatment of osteonecrosis of the femoral head in adults (2019 version). *J Orthop Translat.* 2020;21:100-110. doi: 10.1016/j.jot.2019.12.004.
31. Hoogervorst P., Campbell J.C., Scholz N., Cheng E.Y. Core Decompression and Bone Marrow Aspiration Concentrate Grafting for Osteonecrosis of the Femoral Head. *J Bone Joint Surg Am.* 2022;104(Suppl 2):54-60. doi: 10.2106/JBJS.20.00527.
32. Okewunmi J.O., Duey A.H., Zubizarreta N., Kodali H., Poeran J., Hayden B.L. et al. Did the COVID-19 Pandemic Coincide With an Increase in Osteonecrosis as Indication for Total Hip Arthroplasty in Older Patients? *J Arthroplasty.* 2023:S0883-5403(23)00643-5. doi: 10.1016/j.arth.2023.06.007.
33. Chen F., Hao L., Zhu S., Yang X., Shi W., Zheng K. et al. Potential Adverse Effects of Dexamethasone Therapy on COVID-19 Patients: Review and Recommendations. *Infect Dis Ther.* 2021;10(4):1907-1931. doi: 10.1007/s40121-021-00500-z.
34. Tsed A.N., Mushtin N.E., Dulaev A.K., Shmelev A.V. Pathological changes in the osteoarticular system during COVID-19 drug therapy (review of literature). *Grekov's Bulletin of Surgery.* 2022;181(2):85-91. (In Russian). doi: 10.24884/0042-4625-2022-181-2-85-91.
35. Glukhov A.V., Lapukhin A.O., GusevS.S. Early diagnosis and treatment of aseptic bone necrosis amid COVID-19 consequences. *Medico-Biological and Socio-Psychological Problems of Safety in Emergency Situations.* 2023;(3):29-37. (In Russian). doi: 10.25016/2541-7487-2023-0-3-29-37.

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