

Results of Densitometric Studies in Patients with Aseptic Bone Necrosis of Large Joints After Covid-19

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Annotation: The aim of the study is to evaluate the results of densitometric studies in patients with post-COVID aseptic necrosis of large joint bones. The results of examinations of 136 patients who applied to the clinic of the Republican Scientific and Practical Medical Center for Traumatology and Orthopedics in 2020-2024 were studied. All patients underwent the following studies: clinical (survey), digital radiographic, MRI, dual-energy X-ray densitometric (DXA). The data obtained were summarized.

Keywords: aseptic necrosis, COVID-19, SARS-CoV-2, large joint, MRI, X-ray densitometry, dual-energy absorptiometry (DXA), osteoporosis, osteopenia.

Aseptic osteonecrosis is a serious polyetiological disease in which bone cells die in certain areas of bone tissue, blood flow is disrupted, and secondary arthritis quickly develops in adjacent joints. The most common site of damage is the femoral head, then the femoral condyles, tibial condyles, less often the humeral head, talus, etc. According to literary sources [1,2], osteonecrosis occurs in 5-58% of patients with severe COVID-19 [3,4], while 39% of patients with SARS-CoV-2 developed osteonecrosis of the femoral head within a few months after the onset of SARS [5]. Without timely treatment, 80% of patients develop femoral head collapse within three to four years and require intra-articular surgery, arthroplasty. At the same time, aseptic necrosis of the femoral head is a risk factor for early implant instability.

A number of scientific studies around the world are focused on improving the early diagnosis and surgical treatment of post-COVID aseptic necrosis: the possible involvement of the SARS-CoV-2 virus in the pathogenesis of aseptic necrosis in COVID-19 is discussed; it was found that viral infiltration causes expression of the TRIM 55 gene in biquitin ligase E3 in vascular smooth muscle cells, which leads to inflammation of the vessel wall and aggregation of leukemia cells, a cytokine storm [6]. These disorders, combined with increased blood clotting, can lead to microthrombosis and osteonecrosis. It was found that the administration of glucocorticoids has a great impact on the risk of developing aseptic necrosis in COVID-19, since after recovery from COVID-19, a negative response of the body to glucocorticoids is observed [7]. Therefore, observations of patients with atypical pneumonia revealed a possible decrease in bone mineral density (BMD) after recovery. The extent of bone loss has been found to be highly dependent on the dose and duration of corticosteroids [8,9] – the mainstay of treatment aimed at reducing inflammation during the initial infection and in the early stages of subsequent rehabilitation and recovery.

Objective of the study: To study the state of bone mineral density in patients with aseptic necrosis of large joint bones after COVID-19.

Materials and methods: The results of radiation studies of aseptic necrosis of large joint bones were studied in 136 patients who applied to the clinic of the Republican Scientific and Practical Medical Center for Traumatology and Orthopedics in 2020-2024.

All patients underwent clinical (WOMAC survey), radiological (Sonialvision G4; Flexavision HB (Japan)) and magnetic resonance imaging (Multiva Philips 1.5 Tesla (Netherlands)) studies to clarify the presence and severity of aseptic necrosis of bones. We also performed dual-energy X-ray absorptiometry – osteodensitometry (Lunar Prodigy (GE, USA)). The studies were conducted

according to the standard program at the levels of the lumbar spine (Spine L1-4), proximal right and left femurs (RHip, LHip).

During the survey of patients, the degree of pain syndrome and its duration were identified, records were made of the intake and duration of corticosteroid use, the history of COVID-19 and vaccination, the degree of lung damage, etc. Patients who received treatment for COVID-19 were classified according to the following criteria:

- ✓ SARS-CoV-2 PCR result "+";
- ✓ taking corticosteroids during treatment for COVID-19;
- ✓ no pain in large joints before COVID-19 infection.

The patients undergoing the studies (main group) were selected according to the following criteria:

- ✓ SARS-CoV-2 patients with a PCR result "+" or vaccinated against COVID-19;
- ✓ taking corticosteroids during treatment for COVID-19;
- ✓ no pain in large joints before COVID-19 infection.

The control group included patients with aseptic bone lesions who had not experienced the clinical picture of SARS-CoV-2 infection and were not vaccinated against COVID-19.

Results and discussion: During the conversation with the patients, such points as the duration of the pain syndrome, the time of the onset of pain syndrome after SARS-CoV-2 infection or after vaccination, the duration of corticosteroid intake during treatment were clarified. The presence or absence of pain in large joints before COVID-19 infection was also determined.

Radiological studies revealed the presence or absence of structural changes in the epimetaphyseal zones of the bones of the joints, the presence or absence of degenerative-dystrophic lesions, while degenerative changes are classified according to J.H. Kellgren & J.S. Lawrence (1955) (Table 1).

Table 1. Classification of OA of the KS according to J.H. Kellgren & J.S. Lawrence

Stage	Grade	Changes to the Constitutional Court
0	There is no arthrosis	No special features
I	Doubtful	Questionable narrowing of the joint space and possible sharpening of the edges
II	Minor	Single osteophytes and slight narrowing of the joint space
III	Moderate	moderate multiple osteophytes, moderate joint space narrowing and subchondral sclerosis and severe bone end deformity
IV	Heavy	large osteophytes, pronounced narrowing of the joint space, pronounced sclerosis and obvious deformation of the edges of the bones

Magnetic resonance imaging (MRI) changes are divided according to the ARCO classification. The following changes were identified: synovitis, arthritis, reconversion and bone marrow edema, the "geographical map" symptom, a combination of hyper- and hypointensity of MRI signals in the acute stage of the disease, possible spread of necrosis foci towards the diaphysis, the presence of a polyostotic nature and other changes characteristic of aseptic necrosis. Dual-energy absorptiometry (DXA) determined the degree of bone density using parameters such as T-score or Z-score depending on age, gender, menopause and postmenopause, etc. The diagnosis of "osteoporosis (OP)" or "osteopenia (OA)" was used, which was established according to the criteria of the World Health Organization (WHO), (2008), (Table 2).

Таблица 2. Diagnosis of OP based on a decrease in BMD according to WHO criteria [WHO Collaborating Centre, University of Sheffield, UK, 2008]

Classification	IPC	T-score
Norm	Within 1 SD of the mean in young healthy populations	-1,0 and above
ОЯ	1.0 to 2.5 SD below the mean compared to young healthy population members	from -1,0 to -2,5
ОП	2.5 SD or below the mean in young healthy populations	-2,5 and below
Heavy ОП	2.5 SD or below the mean in young healthy populations	-2.5 and below with one or more fractures

Among the 136 patients who participated in the study, women accounted for 40.4% (55 out of 136) and men – 59.6% (81 out of 136) (Fig. 1).

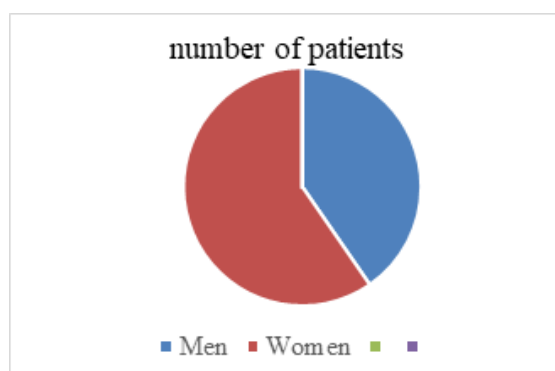


Fig. 1. Ratio of gender data in the subjects

The average age of women was 51.1 ± 1.7 years (20 to 74 years), the average age of men was 45.9 ± 1.3 years (31 to 79 years). As can be seen from the presented data, women were significantly older than men ($P < 0.01$), but had an earlier age of seeking medical attention.

Unilateral joint damage was 2.2 times more often observed in men than in women (19.8% versus 9.2%, respectively, $P < 0.05$).

Localization of aseptic necrosis was more often observed in the area of the femoral head and epimetaphyseal bones of the knee joints (Fig. 1).

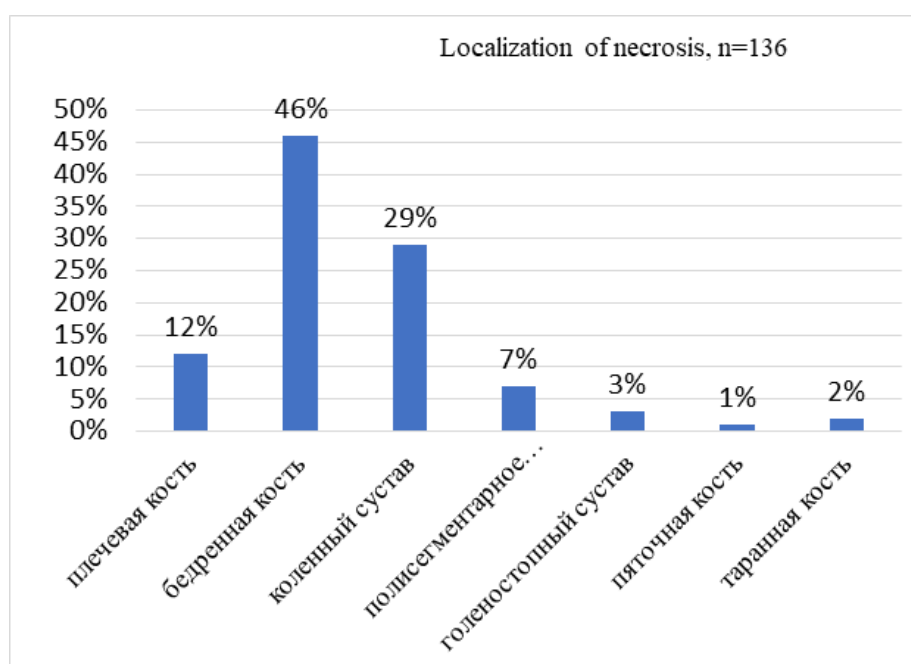


Fig. 2. Localization of aseptic necrosis

When analyzing the data, the time of patients' appeal from the moment of COVID-19 disease was taken into account, which ranged from 3 to 21 months (an average of 11.5 months), most often they applied after 6-8 months, with an aggravation of the course of necrotic lesions.

Quantitative osteodensitometric indicators T-score and Z-score, as well as BMD indicators were established depending on gender and the area of study as follows (Table 2, 3):

Table 3. General densitometry indicators of the lumbar spine in all patients with post-COVID aseptic bone necrosis depending on gender

T-/Z-score	Men (n=83)		Women (n=53)		Data reliability
	abs.	%	abs..	%	
Average meanings BMD backs (L1-L4)	1,01±0,02 (0,6-1,9)		0,958±0,03 (0,6-1,6)		P>0,05
T-/Z-score to -1,0 and above (norm)	30	36,1±5,3	20	37,7±6,6	t=0,187; P>0,05
T-/Z-score from -1,0-2,5 (osteoporosis)	43	51,8±5,5	23	43,4±6,8	t=0,962; P>0,05
T-/Z-score -2,5 and below (osteoporosis)	10	12,0±3,6	10	18,9±5,4	t=1,056; P>0,05

Densitometric studies conducted in the lumbar spine showed a general decrease in BMD regardless of gender, that is, in women the norm was 37.7%, damage 62.3%; in men, respectively, the norm was 36.1% to 63.9% damage. At the same time, if we consider the ratio of pathological indicators in these groups, the percentage of people suffering from osteopenia is higher in men (51.8%), while in women the proportion of people suffering from osteoporosis is higher (18.9%).

Table 4. General densitometry indicators of the right and left femurs in patients with post-COVID aseptic bone necrosis depending on gender

T/Zscore	Men (n=83)		Women (n=53)		Data reliability
	abs.	%	abs.	%	
Average back BMD values (L1-L4)	0,763±0,02 (0,55-1,25)		0,717±0,02 (0,35-1,1)		P<0,05
T-/Z-score to -1,0 and above (normal)	44	53,5±6,5	19	36,8±6,8	t=1,738; P>0,05
T-/Z-score от -1,0-2,5 (osteopenia)	35	42,0±6,5	28	54,7±6,8	t=1,043; P>0,05
T-/Z-score -2,5 and below (osteoporosis)	4	4,5±2,5	6	8,5±3,8	t=1,256; P>0,05

The conducted densitometric studies in the lumbar spine showed a general decrease in BMD regardless of gender, that is, in women the norm was 36.8%, damage 63.2%; in men, respectively, the norm was 53.5% to 46.5% of lesions. At the same time, if we consider the ratio of pathological indicators in these groups, the percentage of people suffering from osteopenia is higher in women (54.7%), while in women the proportion of people suffering from osteoporosis is higher (8.5%).

Conclusion: Sequential analysis of quantitative osteodensitometric data T-score and Z-score showed the following relationship with gender data: a general decrease in mineral density regardless of gender, that is, in women the norm on average was 37.2%, damage on average 62.7%; in men, respectively, the norm on average was 44.8% to 55.2% of lesions. Moreover, if we consider the ratio of pathological indicators in these groups, the percentage of those suffering from osteopenia is higher in men (on average 53.2%), while in women the proportion of those suffering from osteoporosis is higher (on average 13.7%).

The presence of a general loss of BMD of varying severity in a third of patients with aseptic necrosis of the condyles of the femur and tibia once again confirms the underestimation of osteoporosis in the development and course of the disease, and requires a more extensive examination, followed by long-term osteotropic therapy.

Использованная литература:

1. Муштин Н.Е., Цед А.Н., Дулаев А.К., Ильющенко К.Г., Шмелев А.В. Влияние новой коронавирусной инфекции COVID-19 на развитие остеонекроза. // В кн.: Медицинская помощь при травмах, новое в организации и технологиях, роль национальной общественной профессиональной организации травматологов в системе здравоохранения РФ. Санкт-Петербург. - 2021. - С. 98-99.
2. Насонов Е.Л., Бекетова Т.В., Решетняк Т.М., Лиля А.М., Ананьева Л.П., Лисицина Т.А. и др. Коронавирусная болезнь 2019 (COVID-19) и иммуновоспалительные ревматические заболевания: на перекрестке проблем тромбовоспаления и аутоиммунитета. // Научно-практическая ревматология. – 2020. - №58(4). – С. 353-367.
3. Панин М.А. Остеонекроз головки бедренной кости после COVID-19: серия клинических наблюдений. // Травматология и ортопедия России. – 2022. - №28(1). – С. 110-117.
4. Awosanya O.D., Dalloul C.E., Blosser R.J., Dadwal U.C., Carozza M. Boschen K, et al. Osteoclast-mediated bone loss observed in a COVID-19 mouse model. // Bone. – 2022. – 154. – P. 116227.
5. Beketova T., Kulikov A., Babak V., Suprun M., Beketova M. Longterm consequences of COVID-19 among patients with rheumatic diseases. // Chest. – 2021. - 160(4). – P. 583.
6. Billett H.H., Reyes-Gil M., Szymanski J., Ikemura K., Stahl L.R., Lo Y. et al. Anticoagulation in COVID-19: Effect of Enoxaparin, Heparin, and Apixaban on Mortality. // Thromb Haemost. – 2020. - 120(12). – P. 1691-1699.
7. Han J., Gao F., Li Y., Ma J., Sun W., Shi L., Wu X., Li T. The Use of Platelet-Rich Plasma for the Treatment of Osteonecrosis of the Femoral Head: A Systematic Review. // Biomed Res Int. – 2020. - 7.
8. Harapan H., Itoh N., Yufika A. et al. Coronavirus disease 2019 (COVID-19): a literature review. // J Infect Public Health. – 2020. - 13(5). – P. 667-673.
9. Zheng Y., xiong C., Liu Y., qian x., Tang Y., Liu L. et al. Epidemiological and clinical characteristics analysis of COVID-19 in the surrounding areas of Wuhan, Hubei Province in 2020. // Pharmacol Res. – 2020. – 157.