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# MULTIFOCAL OSTEONECROSIS OF LARGE JOINTS AFTER COVID-19: CLINICAL AND IMAGING FEATURES

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#### **Abstract**

**Background**: Osteonecrosis (ON) is a serious musculoskeletal complication that may occur after COVID-19 infection. It is associated both with vascular endothelial dysfunction and with corticosteroid therapy used for severe cases. There is limited knowledge regarding the characteristics of multifocal osteonecrosis (MFON) in post-COVID patients.

**Objective**: To analyze clinical, radiographic, and magnetic resonance imaging (MRI) features of osteonecrosis in patients with a history of COVID-19. **Methods**: We studied 161 patients (96 men, 65 women; mean age of men 45.9±1.3 years, women 51.1±1.7 years) who presented to the Republican Scientific and Practical Medical Center of Traumatology and Orthopedics between 2020–2024. All underwent WOMAC clinical assessment, radiography (Sonialvision G4, Flexavision HB, Japan), MRI (Philips Multiva 1.5T, Netherlands), and dual-energy X-ray absorptiometry (DXA; Lunar Prodigy, GE, USA). Data were collected on corticosteroid therapy, vaccination, COVID-19 severity, and lung involvement. Results: Female patients were significantly older than male patients (p<0.01). Unilateral ON was 2.2 times more frequent in men than in women (19.8% vs. 9.2%, p<0.05). The most common sites were femoral heads and epimetaphyseal regions of the knees. The interval from COVID-19 to ON manifestation ranged from 3 to 21 months (mean 11.5 months), with a peak at 6–8 months. MRI was more sensitive than radiography for early detection.



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DXA demonstrated decreased bone mineral density in a subset of patients. Conclusion: Post-COVID osteonecrosis is characterized by aggressive progression, frequent multifocal involvement, and predominance in femoral and knee joints. Early MRI screening is essential for timely diagnosis and management of high-risk patients.

**Keywords:** Osteonecrosis; Multifocal osteonecrosis; COVID-19; MRI; Femoral head; Corticosteroids

#### Introduction

Since the outbreak of the COVID-19 pandemic, musculoskeletal complications have emerged as significant long-term sequelae. Among them, osteonecrosis (ON) has attracted growing attention. The pathogenesis of ON is multifactorial, involving ischemia, microvascular thrombosis, and impaired bone remodeling. Corticosteroid therapy, widely used for severe COVID-19 pneumonia, is a well-established risk factor for ON. Endothelial dysfunction and hypercoagulability caused by SARS-CoV-2 infection may further increase the risk. Multifocal osteonecrosis (MFON), defined as ON affecting three or more anatomical sites, is rarely described in the literature. Recent reports indicate a potential rise in ON incidence in the post-COVID population, but systematic studies remain limited. This study aimed to evaluate the clinical and imaging characteristics of ON in a large cohort of patients with prior COVID-19.

#### Materials and Methods

This retrospective study included 161 patients (96 men, 65 women) who presented with joint pain and functional impairment between 2020 and 2024 at the Republican Scientific and Practical Medical Center of Traumatology and Orthopedics. The mean age was  $45.9\pm1.3$  years for men (range: 31-79 years) and  $51.1\pm1.7$  years for women (range: 20-74 years). Women were significantly older than men (p<0.01).

All patients underwent clinical evaluation using the WOMAC index, radiography (Sonialvision G4, Flexavision HB, Japan), MRI (Philips Multiva 1.5T, Netherlands), and DXA (Lunar Prodigy, GE, USA). DXA scans were performed



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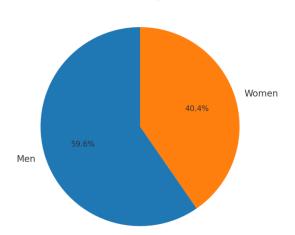
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at the lumbar spine (L1–L4) and proximal femora (RHip, LHip). Data were also collected regarding corticosteroid use, vaccination, severity of COVID-19 pneumonia, and degree of lung involvement.

The time interval between COVID-19 infection and onset of ON symptoms was recorded. Patients were stratified by localization, laterality (unilateral vs bilateral), and number of affected joints.

#### Results

Gender distribution: Of 161 patients, 96 (59.6%) were men and 65 (40.4%) were women (fig.1.). Women were significantly older than men (p<0.01).



Gender distribution of patients (n=161)

Figures 1.

Figure 1. Gender distribution of patients.

Laterality: Unilateral ON was observed in 19.8% of men compared with 9.2% of women (p<0.05).

Localization: The most frequent sites of ON were the femoral heads and the epimetaphyseal regions of the knees (fig.2.). Figures 2.



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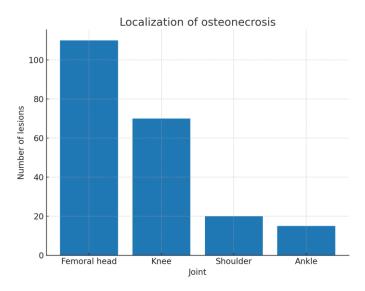


Figure 2. Localization of osteonecrosis in large joints.

COVID-19 timeline: The interval between COVID-19 infection and ON manifestation ranged from 3 to 21 months (mean 11.5 months). Most cases occurred at 6–8 months after infection (fig.3.). Figures 3.

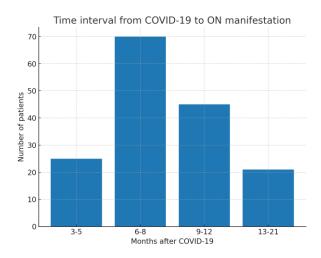


Figure 3. Time interval from COVID-19 to ON manifestation.



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Figure 4.

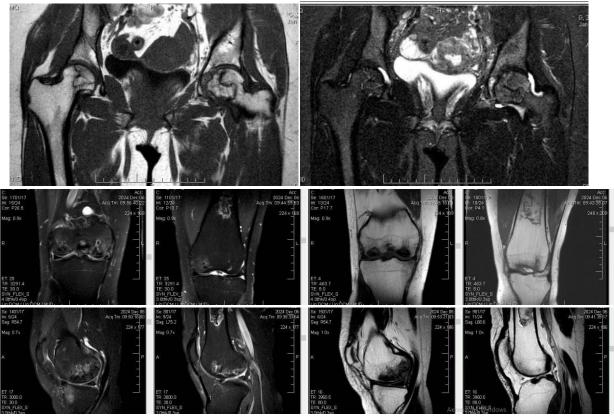


Fig. 4. A 33-year-old female patient with multifocal osteonecrosis. The heads of both femurs and the distal epimetadiaphyses of both femurs are affected.

Imaging: Radiography detected late-stage ON but was less sensitive in early disease. MRI identified subchondral changes, bone marrow edema, and necrotic lesions at earlier stages. DXA results indicated osteopenia or osteoporosis in a proportion of patients, suggesting compromised bone quality. Overall, post-COVID ON demonstrated rapid progression and multifocal involvement.

Discussion. This study represents one of the largest series investigating osteonecrosis in post-COVID patients. Our findings confirm that ON may develop within months after infection, with an average onset of 11.5 months and a peak incidence at 6–8 months. This aligns with earlier reports suggesting that corticosteroid therapy and viral-induced coagulopathy are important contributors to ON development.



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Compared to the classical steroid-induced ON described before the pandemic, post-COVID ON appears to have more aggressive progression, with higher rates of multifocal involvement. The predominance of femoral and knee lesions is consistent with mechanical load distribution, but the multifocality suggests a systemic vascular etiology. Our data indicate that men more often presented with unilateral lesions, whereas women, though older, tended to seek medical attention earlier.

MRI remains the gold standard for early ON diagnosis, allowing detection before radiographic changes. Early identification is crucial for joint-preserving treatment and for preventing rapid progression to osteoarthritis or the need for arthroplasty.

Limitations of this study include its retrospective nature and the lack of long-term follow-up beyond 24 months. Nevertheless, the large sample size provides valuable insights into the post-COVID musculoskeletal burden.

Conclusion.Post-COVID osteonecrosis of large joints is characterized by aggressive progression, frequent multifocal involvement, and predominant localization in femoral and knee regions. Women presented at an older age but tended to seek care earlier, while men more frequently exhibited unilateral disease. The average time from COVID-19 to ON onset was 11.5 months, with a peak at 6–8 months. MRI should be considered the primary diagnostic tool for early detection in at-risk patients. Early recognition and monitoring are vital to optimize treatment outcomes.

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