



## Conservative Therapy Outcomes In Early Covid-19–Related Femoral Head Necrosis

Zakirhodjaev Sherzod Yahyaevich<sup>1</sup>, Talibdjanova Malika Xusanovna<sup>2</sup>, Alikulov Ikhtiyor Tilovqobilovich<sup>3</sup>, Salikhov Mirilkham Usmanovich<sup>4</sup>, Ulugbek S.Abdullaev<sup>5</sup>, Khudaybergenova Dilafruz Khamzayevna<sup>6</sup>, Nizametdinova Ulugoy Jamin qizi<sup>7</sup>, Botirova Nigina Akram qizi<sup>8</sup>

- <sup>1</sup> Professor of the department of Propedeutics of Internal disease. Tashkent State Medical University. Uzbekistan, Tashkent, sherzod\_medline@mail.ru, <https://orcid.org/0000-0001-7708-2698>
- <sup>2</sup> Tashkent State Medical University Associate professor of the department of Propedeutics of Internal disease. Uzbekistan, Tashkent, malikapattahova@gmail.com, <https://orcid.org/0000-0001-6030-6229>
- <sup>3</sup> Tashkent State Medical University Associate professor of the department of Propedeutics of Internal disease. Uzbekistan, Tashkent, alikulov\_83@mail.ru, <https://orcid.org/0000-0002-8767-2242>
- <sup>4</sup> Tashkent state medical university Senior lecturer of the department of Propedeutics of Internal disease. Uzbekistan, Tashkent, mirilhomsalikhov@gmail.com
- <sup>5</sup> Assistant of Department of Propaedeutics of Internal Diseases №1, PhD. Uzbekistan, Tashkent, abdullaevulugbek11.04.1987@gmail.com, <https://orcid.org/0000-0001-5074-2107>
- <sup>6</sup> PhD. Assistant. Uzbekistan, Tashkent, Tashkent state medical university, hidoyatova93@gmail.com, <https://orcid.org/0009-0002-7261-7889>
- <sup>7</sup> Assistant of Department of Propaedeutics of Internal Diseases №1 Uzbekistan, Tashkent, ulugoy.nizametdinova@gmail.com, <https://orcid.org/0009-0003-1117-4583>
- <sup>8</sup> Tashkent State Medical University, Tashkent, Uzbekistan; PhD, Scientific Researcher. Uzbekistan, Tashkent botirovanigina@mail.ru, <https://orcid.org/0009-0005-0555-7822>

### Abstract

This study presents an analysis of the functional outcomes in patients with avascular necrosis (AVN) of the femoral head associated with COVID-19 infection. The clinical manifestations of COVID-19–related AVN varied widely, ranging from asymptomatic cases incidentally identified through imaging to severe hip pain accompanied by functional impairment. Diagnosis was established based on a comprehensive clinical evaluation supported by magnetic resonance imaging (MRI) and relevant laboratory investigations. In summary, avascular necrosis of the femoral head linked to COVID-19 represents a multifactorial and challenging clinical condition that requires timely recognition and individualized management to optimize therapeutic outcomes.

**Keywords:** avascular necrosis, femoral head, COVID-19, hip joint, MRI

### Introduction

The emergence of avascular necrosis of the femoral head (ANFH)—a progressive pathological condition characterized by the deterioration of bone tissue resulting from compromised blood supply—has become a subject of growing concern amid the COVID-19 pandemic. Early-stage ANFH presents substantial diagnostic and therapeutic challenges for clinicians, as timely recognition and appropriate intervention are essential to preserve hip joint function and prevent disease progression that may ultimately necessitate total hip arthroplasty.

In recent years, the potential association between COVID-19 infection and the onset of ANFH has gained increasing attention within the orthopedic community. Although the precise pathophysiological mechanisms remain unclear, they are believed to reflect a multifactorial process involving viral-induced systemic inflammation, endothelial dysfunction, hypercoagulability, and vascular injury. The cytokine storm and endothelial impairment observed in COVID-19 may contribute to microvascular thrombosis and ischemic damage to the femoral head, thereby accelerating the necrotic process.

Early detection and prompt management are crucial for achieving favorable outcomes in patients with COVID-19–related ANFH. However, identifying the disease at an early stage often requires a high level of clinical suspicion and the application of advanced imaging modalities such as radiography, computed tomography (CT), and especially magnetic resonance imaging (MRI) to accurately evaluate bone viability. Timely diagnosis facilitates the initiation of conservative therapeutic approaches aimed at preserving hip function and delaying or preventing further progression of necrosis.

**The objective of this study** was to assess the functional outcomes of conservative management in patients diagnosed with early-stage avascular necrosis of the femoral head associated with COVID-19 infection.

### Materials and Methods

#### Study Design

A retrospective cohort study was conducted to evaluate the functional outcomes of patients with early-stage avascular necrosis of the femoral head (ANFH) associated with COVID-19 following a combination of pharmacological and physical therapy interventions.

## Participants

The study included 200 patients diagnosed with COVID-19–related ANFH, who were selected based on clinical and imaging records from the Multidisciplinary Clinic of the Tashkent Medical Academy. Data were collected retrospectively from February 2021 to January 2022. All participants had a confirmed history of COVID-19 infection and met the eligibility criteria described below.

## Inclusion Criteria

1. Radiologically confirmed diagnosis of ANFH based on pelvic X-ray (bilateral hips) and magnetic resonance imaging (MRI).
2. Laboratory-confirmed COVID-19 infection verified by polymerase chain reaction (PCR) or serological assays for SARS-CoV-2 IgG and IgM antibodies.
3. Age 18 years or older.
4. Early stages of ANFH (stages I and II according to the Ficat–Arlet classification, 1985).

## Exclusion Criteria

1. Advanced stages of ANFH (stages III and IV according to the Ficat–Arlet classification).
2. History of prior hip surgery or traumatic hip injury.
3. Presence of concomitant musculoskeletal disorders that could affect gait or hip joint mobility.
4. Incomplete medical documentation or absence of follow-up data.

## Treatment Protocol (Rephrased Version)

All patients underwent a standardized management protocol combining pharmacotherapy and physical therapy interventions.

## Pharmacotherapy

Pharmacological management included the intravenous administration of zoledronic acid (Aclasta) to inhibit osteoclast-mediated bone resorption and promote bone remodeling [1]. Anticoagulant therapy with low-molecular-weight heparin or rivaroxaban was prescribed to reduce the risk of thromboembolic complications associated with COVID-19 infection [14]. Nonsteroidal anti-inflammatory drugs (NSAIDs) were administered for pain control [3], while agents enhancing microcirculation, such as pentoxifylline, were used to improve blood flow and oxygen delivery to the necrotic femoral head region [17].

## Physical Therapy

Each patient participated in an individualized physiotherapy program designed to improve hip joint mobility, muscle strength, and overall functional recovery. The rehabilitation regimen included passive and active range-of-motion exercises, muscle-strengthening routines, and gait training tailored to the patient's stage of recovery and physical capacity [4, 16].

## Data Collection

Comprehensive demographic, clinical, radiological, and laboratory data were obtained from medical records and patient files. Baseline parameters included age, sex, comorbidities, severity and duration of COVID-19 symptoms, and the stage of avascular necrosis based on the Ficat–Arlet classification.

Functional outcomes were assessed using validated tools: the Modified Harris Hip Score (HHS, 2000) [9] to evaluate hip function and the Visual Analog Scale (VAS) to assess pain intensity.

## Statistical Analysis

Descriptive statistical methods were applied to summarize baseline and post-treatment variables. Continuous data were expressed as mean  $\pm$  standard deviation (SD) or as median and interquartile range (IQR), depending on distribution. Categorical variables were presented as frequencies and percentages.

Pre- and post-treatment functional indicators were compared using paired t-tests or Wilcoxon signed-rank tests when appropriate. A p-value  $< 0.05$  was considered statistically significant.

The study adhered to the ethical principles of the Declaration of Helsinki and received approval from the Institutional Ethics Committee of the Tashkent Medical Academy. Written informed consent was obtained from all participants or their legal representatives prior to enrollment. Data confidentiality and patient anonymity were strictly maintained throughout the study period.

## Results and Discussion

### Baseline Characteristics

Baseline demographic and clinical characteristics of the study population are presented in Table 1. The cohort included 200 patients with a mean age of  $38.7 \pm 8.3$  years, the majority of whom were male (80%). Comorbid conditions were prevalent, most frequently hypertension (34%) and diabetes mellitus (12%).

The median duration of COVID-19 symptoms was 10 days (IQR: 7–14). According to the Ficat–Arlet classification, 33% of patients were diagnosed with stage I and 67% with stage II avascular necrosis of the femoral head.

**Table 1. Baseline characteristics of the study group**

Characteristic	Value
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Age (years), mean $\pm$ SD	38.7 $\pm$ 8.3
Sex, n (%)	Men: 160 (80%) Women: 40 (20%)
Comorbidities, n (%)	Hypertension: 68 (34%) Diabetes mellitus: 24 (12%) Others: 30 (15%)
Duration of COVID-19 symptoms (days), median (IQR)	10 (7–14)
Ficat–Arlet stage, n (%)	Stage I: 66 (33%) Stage II: 134 (67%)

**Note:** SD – standard deviation, IQR – interquartile range

The demographic profile of the study participants reflects the typical population of patients affected by COVID-19-associated ANFH. The mean age of 38.7 years suggests that ANFH may affect young and middle-aged individuals, which is inconsistent with previous literature indicating a higher prevalence of ANFH in the middle-aged and older population. The male predominance observed in this cohort is also consistent with existing epidemiological data on ANFH [15], which often show a higher incidence in men compared to women. Comorbidities such as hypertension and diabetes mellitus are common risk factors for the development of ANFH [12, 19], as they can impair vascular perfusion of the femoral head, predisposing individuals to ischemic injury and subsequent necrosis. The median duration of COVID-19 symptoms, 19 days, indicates the acute phase of the viral illness, during which ANFH may develop as a complication.

#### Functional Outcomes:

Following treatment with pharmacotherapy and physical therapy, patients demonstrated significant improvement in functional outcomes compared to baseline. The mean Harris Hip Scale (modified HHS) score increased from 62.4 (SD  $\pm$  8.9) before treatment to 83.7 (SD  $\pm$  6.7) after treatment, indicating a significant improvement in hip function. Similarly, the visual analog scale (VAS) for pain assessment significantly decreased from a mean of 7.2 (SD  $\pm$  1.5) to 2.9 (SD  $\pm$  1.2), reflecting a marked reduction in pain severity (Table 2).

**Table 2. Functional Outcomes Before and After Treatment**

Outcome measure	Before treatment (Mean $\pm$ SD)	After treatment (Mean $\pm$ SD)	p-value
Modified Harris Hip Score	62.4 $\pm$ 8.9	83.7 $\pm$ 6.7	<0.05
VAS (Visual Analog Scale)	7.2 $\pm$ 1.5	2.9 $\pm$ 1.2	<0.05

**Note:** SD – standard deviation, IQR – interquartile range, VAS – visual analog scale, p – significance level less than 0.05

The improved functional outcomes observed in this study highlight the effectiveness of a combined treatment approach, including pharmacotherapy and physical therapy, in the early stages of COVID-19-associated ANFH [4]. A significant increase in modified HHS scores after treatment indicates a significant improvement in hip function, which is critical for maintaining mobility and quality of life for patients. A decrease in VAS scores indicates a significant reduction in pain severity after treatment, which is important for improving patient comfort and overall well-being. These results indicate that the proposed treatment regimen effectively addresses both functional impairment and pain associated with ANFH, leading to significant improvements in patient outcomes [16].

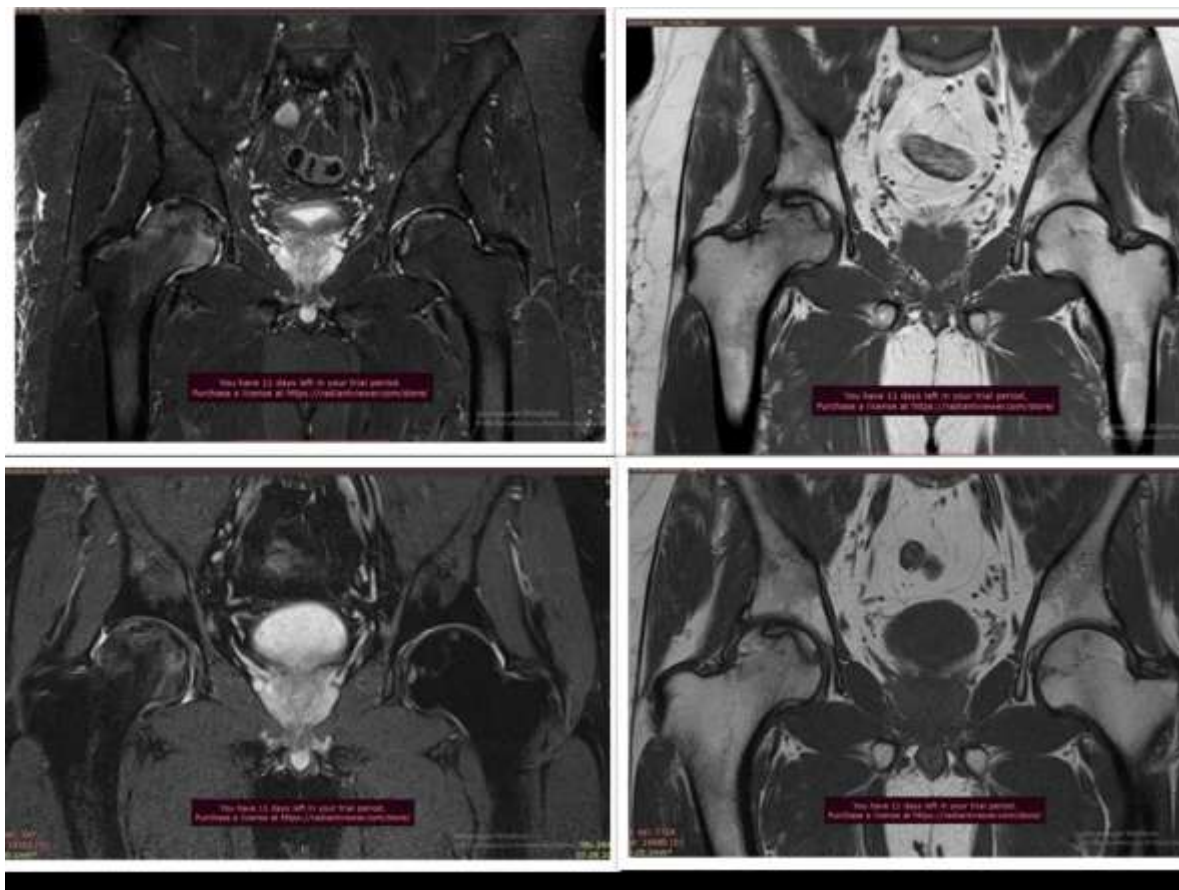
#### Complications and Adverse Events:

The incidence of complications and adverse events related to the treatment regimen was low. A small proportion of patients (8%) reported transient gastrointestinal symptoms, such as nausea and dyspepsia, after taking NSAIDs. No cases of osteonecrosis progression to late stages were observed during the six-month study period; however, over the 12-month follow-up period, 12% (24 patients) had clear radiographic evidence of ANFH progression. No treatment-related or COVID-19-related thromboembolic complications were observed.

The low incidence of complications and adverse events observed in this study indicates a relatively high safety profile for the proposed treatment protocol for COVID-19-associated ANFH. Transient gastrointestinal symptoms reported by a group of patients after taking NSAIDs are consistent with the known adverse effects of these medications and are generally mild and self-limited [20]. Importantly, 24 cases of disease progression were identified, suggesting that the therapeutic benefits of conservative intervention outweigh the associated risks. These results support the feasibility and safety of implementing the proposed treatment approach in clinical practice for the management of ANFH in patients with COVID-19.

#### Radiological assessment:

Radiological assessment of the hip joints revealed favorable outcomes in terms of bone remodeling and preservation of joint architecture. Follow-up MRI scans demonstrated regression of avascular necrosis foci in 21% of patients, absence of osteonecrosis progression at the identified stage in 47% of patients, resolution of bone edema, and restoration of trabecular bone structure, indicating healing.



**Figure 1. Patient M., 38 years old. STIR and T1-weighted MRI images showing a significant reduction in bone edema and cessation of progression of avascular necrosis of the femoral head.**

Radiographic findings provide objective evidence of disease regression and bone healing after treatment of COVID-19-associated ANFH. The resolution of foci of avascular necrosis on MRI images (Fig. 1) suggests that combined drug therapy and physical therapy effectively promote bone regeneration, leading to the restoration of normal bone architecture. The absence of bone edema and restoration of trabecular bone structure also indicate reversal of ischemic injury and the establishment of adequate blood supply to the affected femoral head [13]. These radiographic improvements confirm the functional outcomes observed in this study and highlight the effectiveness of the treatment protocol in promoting disease resolution and joint preservation in patients with COVID-19-associated ANFH.

Subgroup analysis based on Ficat-Arlet ANFH stages revealed similar improvements in functional outcomes in both the ANFH stage I and II groups. Furthermore, no significant differences in HHS or VAS scores were found between the two groups after treatment ( $p > 0.05$ ). (Table 3.)

**Table 3. Analysis of subgroups of functional outcomes by stages of ANFH**

Outcome measure	Stage I (n = 66)	Stage II (n = 134)	p-value
Harris Hip Score	84.1 ± 6.5	82.3 ± 7.2	0.182
VAS (Visual Analog Scale)	2.8 ± 1.3	3.1 ± 1.1	0.317

**Note:** VAS – visual analog scale for pain; p – significance level less than 0.05.

Subgroup analysis provides valuable information on the effectiveness of the treatment approach for early-stage COVID-19-associated ANFH. Comparable improvements in functional outcomes observed in both the ANFH stage I and II groups suggest that the proposed intervention is equally beneficial regardless of disease severity at presentation. These results highlight the importance of early detection and intervention in ANFH, as prompt treatment can lead to favorable outcomes even in cases with more advanced disease. Furthermore, the lack of significant differences in functional outcomes between the two stages of osteonecrosis highlights the potential for successful disease management and functional recovery with the proposed treatment protocol, regardless of disease severity.

The results of this study demonstrate that combination treatment with pharmacotherapy and physical therapy leads to favorable functional outcomes in patients with early-stage COVID-19-associated ANFH. Following treatment, significant improvement in hip function and pain relief were observed with a low incidence of adverse effects. These results highlight the importance of early intervention and multidisciplinary management to optimize outcomes in patients with COVID-19-associated ANFH. The positive results observed in this study support the efficacy of the proposed treatment protocol and provide valuable information for the management of this patient population. Further research is needed to confirm these results and explore additional therapeutic modalities to improve outcomes in this patient population. Additionally, long-term follow-up studies are needed to assess the durability of treatment effects and potential disease recurrence in patients with COVID-19-associated ANFH. Overall, this study contributes to the

growing literature on the treatment of musculoskeletal manifestations of COVID-19 and highlights the importance of a comprehensive approach to patient care when managing the various clinical consequences of the disease.

## Conclusion

Conservative treatment of COVID-19-associated avascular necrosis of the femoral head is a complex clinical challenge requiring a multidisciplinary approach to optimize patient outcomes. This study examined functional outcomes after treatment of early-stage ANFH, emphasizing the importance of conservative treatments to promote bone healing and functional recovery.

In conclusion, early recognition and intervention, combined with a comprehensive treatment approach including pharmacotherapy and physical therapy, are essential for achieving favorable functional outcomes in patients with COVID-19-associated ANFH. Further studies with a control group are needed to confirm these findings and explore additional therapeutic modalities to improve outcomes in this patient population.

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