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Modern Treatment Methods of Hip Osteoarthritis in Patients After COVID-19 and Their Long-Term Outcomes

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Abstract The study is devoted to comparing the clinical, laboratory, and instrumental features of hip osteoarthritis (HOA) in patients who have recovered from COVID-19 infection with those of idiopathic osteoarthritis (IOA). During 2023–2024, 119 patients were examined at medical institutions in Samarkand: 62 with idiopathic OA and 57 with post-COVID OA. Patients in the second group received standard therapy combined with an anticoagulant (rivaroxaban 20 mg/day). Non-pharmacological measures included physical activity, body weight control, and physiotherapy, while pharmacological treatment consisted of chondroprotectors, nonsteroidal anti-inflammatory drugs (NSAIDs), steroids, calcium, and vitamin D. In the group receiving anticoagulant therapy, reduction in pain (7.1%), crepitus (7.1%, pI-IIB=0.043), limping (3.5%, p=0.041), and muscle spasms (p=0.041) was observed. Laboratory analysis showed decreased levels of inflammatory markers (ESR, C-reactive protein, IL-6, TNF-α) and a reduction in D-dimer concentration to 0.131 mg/L ($p<0.001$), indicating a lower risk of thrombosis and improved microcirculation under the influence of anticoagulant therapy. Thus, anticoagulant therapy in post-COVID osteoarthritis represents an important component of comprehensive treatment, effectively reducing inflammation and thrombosis, improving microcirculation, and restoring musculoskeletal function. These findings provide a scientific basis for incorporating anticoagulants into individualized rehabilitation and pharmacotherapy strategies for patients with post-COVID osteoarthritis.

Keywords Hip osteoarthritis, COVID-19, Anticoagulant therapy, Rivaroxaban, Inflammatory markers, Microcirculation, Rehabilitation

1. Introduction

Hip osteoarthritis (HOA) is one of the most prevalent chronic degenerative diseases of the musculoskeletal system and represents a major cause of pain, disability, and reduced quality of life worldwide. According to the Global Burden of Disease study, osteoarthritis affects more than 500 million people globally, with hip involvement accounting for a significant proportion of cases and contributing substantially to years lived with disability. The prevalence of hip osteoarthritis increases with age and is expected to rise further due to population aging, increasing obesity rates, and decreased physical activity levels [1,2,3].

In recent years, the COVID-19 pandemic has introduced new challenges in understanding the pathogenesis and clinical course of musculoskeletal diseases. Numerous international studies have demonstrated that SARS-CoV-2 infection is associated with systemic inflammation, endothelial dysfunction, and hypercoagulability, which may significantly affect joint tissues and periarticular microcirculation. Persistent post-COVID syndrome has been linked to chronic inflammatory responses and microvascular damage, potentially accelerating degenerative processes in articular cartilage and subchondral bone [4,5].

Several studies from Europe, the United States, and China have reported that patients recovering from COVID-19 frequently experience musculoskeletal complications, including arthralgia, myalgia, and exacerbation of pre-existing osteoarthritis. Elevated levels of inflammatory cytokines such as IL-6 and TNF-α, as well as increased D-dimer levels, have been associated with impaired microcirculation and increased thrombotic risk, which may worsen joint perfusion and contribute to disease progression. These findings highlight the potential role of anticoagulant therapy not only in preventing thrombotic events but also in improving tissue perfusion and reducing inflammation in patients with post-COVID osteoarthritis [6,7,8].

In Uzbekistan, osteoarthritis remains a significant public health concern, particularly among the aging population. Epidemiological observations indicate a steady increase in the incidence of degenerative joint diseases, including hip osteoarthritis, over the past decade. In addition, the high

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burden of COVID-19 infection in the region has led to a growing number of patients presenting with post-COVID complications, including musculoskeletal disorders. Clinical observations in Samarkand and other regions of Uzbekistan suggest that patients with a history of COVID-19 often demonstrate a more severe clinical course of osteoarthritis, characterized by increased pain, functional limitations, and laboratory signs of systemic inflammation [9,10,11].

Given the growing number of patients with post-COVID osteoarthritis and the potential role of microcirculatory disturbances and hypercoagulability in its pathogenesis, the search for effective therapeutic strategies is of great clinical importance [12,13]. In particular, the use of anticoagulant therapy as part of complex treatment may represent a promising approach to improving clinical outcomes in this patient population.

The aim of this study was to compare the clinical, laboratory, and instrumental parameters of patients with hip osteoarthritis after COVID-19 infection with those of idiopathic osteoarthritis, as well as to evaluate the effectiveness of treatment using an anticoagulant (rivaroxaban).

2. Materials and Methods

The scientific study was conducted in 2023–2024 on the basis of the Samarkand City Medical Association and the Samarkand Branch of the Republican Specialized Scientific-Practical Medical Center of Traumatology and Orthopedics. The study included 119 patients, in particular, 62 (52.1%) of them - 21 men (33.9%) and 41 women (66.1%) - were diagnosed with idiopathic osteoarthritis (main group) and were with aged from 20 to 66 years (48.01±1.4). 57 (47.9%) patients aged from 19 to 55 years (42.17±1.28) with hip joint osteoarthritis after COVID-19 infection (comparative group) - 24 (42.1%) men and 33 (57.9%) women - were included in the study within the framework of prospective analysis from the Samarkand City Medical Association and the Samarkand Branch of the Republican Specialized Scientific-Practical Medical Center of Traumatology and Orthopedics. Both groups of patients received traditional treatment methods. The control group consisted of 78 practically healthy individuals. Additionally, the patients of the second study group were divided into two subgroups due to the addition of supplementary drugs to the traditional treatment regimen: subgroup IIA consisted of 28 patients who received only standard treatment methods; subgroup IIB patients (n=29) received, in addition to standard therapy, oral anticoagulant medication Rivaroxaban 20 mg, 1 tablet once daily for a long period (at least 6 months) under control of blood coagulation parameters. In the subgroups, studies were conducted based on the analysis of clinical and laboratory results during one year. When patients in the study were treated with non-drug and drug therapy, the long-expected outcomes were as follows.

Non-drug therapy: The treatment method was chosen based on mutual decision between the patient and the specialist. Weight reduction: normalization of body weight is recommended for patients with knee and hip joint osteoarthritis suffering from overweight or obesity. For patients with excessive body weight (BMI >25 kg/m^2), it is recommended to lose at least 5% of their weight within 6 months or at least 10% within 1 year. The following exercises are recommended: aerobic, strength or resistance, flexibility and stretching exercises, preferably performed in water. Orthopedic recommendations included choosing shoes that are comfortable, with good cushioning, large enough to ensure the comfortable position of the toes, and without high heels. Physiotherapeutic treatment methods was represented by balneotherapy (sulfur and radon baths).

Drug therapy: Basic chondroprotectors: Chondroitin sulfate 500 mg twice a day, Glucosamine sulfate 750 or 1500 mg twice a day, Combined preparations (Chondroitin and Glucosamine) from 250 to 500 mg 1 to 3 times a day, Diacerein 50 mg twice a day - these medicines were used for a long time (at least 6 months) according to the indicated dosages. Anti-inflammatory steroid drugs - according to indications (in case of synovitis or severe pain): Betamethasone dipropionate/sodium phosphate 7 mg/ml intramuscularly or intra-articularly according to the scheme; Triamcinolone acetonide 40 mg/ml intramuscularly or intra-articularly according to the scheme. Non-steroidal anti-inflammatory drugs: in cases where joint inflammation signs were pronounced and pain was severe, treatment began with injectable forms of drugs: Diclofenac 3 ml amp. 25 mg/ml intramuscularly once a day, Ketoprofen 2 ml 50 mg intramuscularly once a day, Tenoxicam 20 mg lyophilized powder and solvent vial intramuscularly or intravenously once a day, Lornoxicam 8 mg vial intravenously or intramuscularly, Meloxicam 15 mg/1.5 ml ampule intramuscularly once a day - in chronic course with constant pain, NSAIDs were prescribed in outpatient conditions. Calcium-containing drugs: Calcemin, calcium gluconate, and combined forms with vitamin D3 (Calcium D3) were used. Aqua D3 10,000 IU once daily for 1 month, Vitamin D3 10,000 IU tablet once daily for 1 month were used in the same dosage.

Statistical analysis was performed with IBM SPSS 27 by using nonparametrical criterias and exact Fisher’s/Pearson's chi-squared test.

3. Obtained Results

In the study, clinical signs in Group I and Group II, as well as long-term treatment results between patients treated with standard and additional anticoagulant therapy, were compared. Based on the results, pain syndrome - in Group I was observed in 17.7% of patients. In Group IIA (standard treatment), pain was noted in 17.5% of patients; in Group IIB (standard + oral anticoagulants), pain was observed in 6.9% of patients. No statistical difference was observed, however the lower incidence of pain in Group IIB, where anticoagulants were prescribed, might be associated with the improvement of microcirculation in bone and joint tissues and the reduction of inflammation by these drugs.

Crepitus (crackling) - in Group I: 18 (29%), in Group IIA: (25%), in Group IIB: 6.9%. The decrease in crepitus in Group IIB ($p_{I\text{-}IIB}$=0.043), where anticoagulants were used, indicates a possible reduction in degenerative processes in the joints and the restoration of joint lubrication (synovial fluid) volume.

Limping was observed in 21 (33.9%) patients of Ist, 10 (35.7%) - IIA and 1 (3.4%) - IIB groups. In Group IIB, the incidence of limping decreased almost tenfold ($p_{I\text{-}IIB}$=0.022, $p_{IIA\text{-}IIB}$=0.021). This indicates that anticoagulants improve microcirculation, accelerate recovery of muscles and ligaments, and enhance motor functions.

The frequency of muscle spasms was as follows: in Group I - 9 (14.5%) patients, in Group IIA - 3 (10.7%), and in Group IIB - 1 (3.4%). Despite the apparent reduction in the frequency of spasms in Group IIB, no statistically significant differences were found between the groups. Nevertheless, the observed trend is consistent with the hypothesis that anticoagulants, by improving peripheral circulation in the musculoskeletal system, may promote muscle relaxation.

The reduction of thigh circumference (indicating muscle atrophy) was observed in 19 (30.6%) patients in Group I, 7 (25%) in Group IIA, and 3 (10.3%) in Group IIB. Although the incidence in Group IIB was approximately twofold lower, no statistically significant differences were found between the groups. Nonetheless, this numerical trend aligns with the possibility that anticoagulant therapy may contribute to positive changes in the musculoskeletal system.

The incidence of such symptoms as difficulty in movement, which was reported in 17 (27.4%) of subjects in Group I, 7 (25%) - in Group IIA, and 6,9% - in Group IIB; and cramping in one or both legs, which occurred in 11.3% (Group I), 13.8% (Group IIA), and 3.57% (Group IIB); psycho-social disorders were present in 12.9% (Group I), 10.3% (Group IIA), and 3.57% (Group IIB) outlined the fact that Group IIB demonstrated a notably lower frequency across all measured parameters, statistical analysis did not reveal significant differences between the groups. The consistent numerical trends, however, suggest a potential positive correlation between anticoagulant therapy and the alleviation of these symptoms (Figure 1).

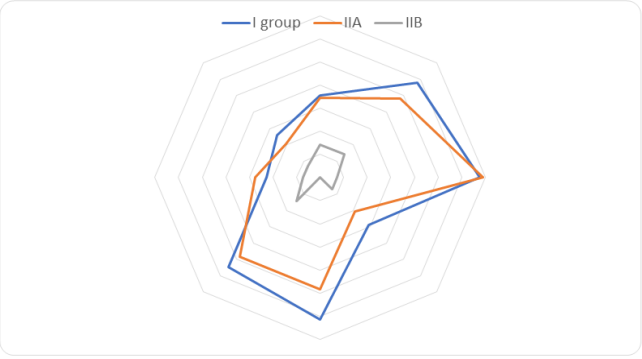

Figure 1. Results of the influence of long-term treatment on the clinical symptoms of patients with hip joint osteoarthritis

In group IIB, psycho-social disorders significantly decreased. This may be associated with a decrease in pain, improvement of movement capabilities, and an increase in overall quality of life. In group IIB, where anticoagulants were added, improvement of all clinical symptoms was observed, including a significant decrease in pain, crepitus, limping, muscle spasms, and movement difficulties. The use of anticoagulants together with orthopedic and rehabilitation treatments improves mobility and helps prevent muscle atrophy. Anticoagulants can accelerate the process of recovery of bones and joints by improving blood circulation, which is of great importance in reducing pain and improving movement. Improvement of psycho-social condition confirms the positive effect of treatment on increasing the quality of patients' life. These results show that anticoagulants in osteoarthritis treatment should be studied more and widely used in clinical practice in the future. Based on these results, it can be recognized that treatment with anticoagulants can be recommended in complicated cases of osteoarthritis. To evaluate long-term results, large-scale studies are required. When anticoagulants are used together with special rehabilitation programs, the results can be even more effective. These results will serve as a basis for developing new therapeutic approaches for patients with osteoarthritis.

Evaluation of long-term treatment effects in laboratory examinations According to our study results, laboratory indicators in group I (idiopathic osteoarthritis) and group II (post-COVID-19 osteoarthritis) were analyzed. Subanalysis included studying of differences between patients in group II who received standard treatment (IIA) and standard + oral anticoagulants (IIB).

The analysis of systemic inflammatory markers revealed distinct patterns across the study cohorts (Table 1). The Erythrocyte Sedimentation Rate (ESR) was measured at 13.7 ± 0.03 mm/h in Group I (idiopathic osteoarthritis). In the post-COVID-19 osteoarthritis groups, ESR values were 12.4 ±0.04 mm/h in Group IIA (standard treatment) and 10.1 ± 0.06 mm/h in Group IIB (standard treatment plus oral anticoagulants). This indicates a reduction in this acute-phase marker among anticoagulant recipients compared to their post-COVID counterparts receiving standard care alone. Levels of C-reactive protein (CRP) showed a more pronounced trend. While Group I demonstrated a mean CRP of 7.4 ±0.08 mg/L, Group IIA exhibited an elevated level of 9.4 ± 0.09 mg/L, consistent with a heightened inflammatory state in post-COVID-19 osteoarthritis. In contrast, Group IIB presented with a mean CRP of 7.0 ±0.02 mg/L, a value comparable to, or slightly lower than, that observed in the idiopathic osteoarthritis group.

Bone metabolism and vitamins and Calcium (Ca) Group I 2.11±0.02; IIA group 2.21±0.07; IIB group 2.22±0.03. Calcium levels were within normal range in all groups, and slightly, but statistically insignificant, higher in group II. Vitamin D Group I: 39.87±0.01 IIA group: 49.87±0.01 IIB group: 54.87±0.01 In post-COVID-19 osteoarthritis patients (group II), the vitamin D level was statistically significant higher, especially in group IIB who received anticoagulants ($p_{I\text{-}IIB}$=0,029). This shows the effectiveness of vitamin D therapy in improving calcium-phosphorus metabolism in COVID-19 infection and osteoarthritis.

Table 1. Results of the effect of long-term treatment on laboratory parameters in the study groups

Laboratory indicators	reference	I group (n=58)	II group (n=57)		p
			IIA (standard therapy) n=29	IIB (standard + oral anticoagulants) n=28	
ESR	5-15	13,7±0,03	12,4±0,04	10,1±0,06	
CRP	6-10 mg/l	7,4±0,08	9,4±0,09	7,0±0,02	
Ca	2,02 – 2,6 mmol/l	2,11±0,02	2,21±0,07	2,22±0,03	
Vitamin D	50nm/l (30ng/ml)	39,87±0,05	49,87±0,09	54,87±0,02	$p_{I\text{-}IIB}$=0,029
IL 6	0-7 pg/ml	5,41±0,03	7,27±0,04	3,16±0,04	$p_{IIA\text{-}IIB}$=0,036
TNF-a	<8,1pg/ml	4,12±0,01	7,96±0,05	5,96±0,02	
D dimer	<0,5mg/l	0,211±0,066	0,411±0,097	0,131±0,083	$p_{IIA\text{-}IIB}$<0,001

Table 2. Results of the effect of long-term treatment on instrumental examination indicators in the study groups

		I group (n=40)	**II group**		
			IIA (standard therapy) n=19	**IIB** (standard + oral anticoagulants) n=20	
X-ray	According to K–L III	14 (35%)	8 (42,1%)	4 (20%)	
	According to K–L IV	3 (7,5%)	2 (10,5%)	1 (5%)	
MRI	Synovial membrane thickening	12 (30%)	6 (31,5%)	3 (15%)	
	Subchondral osteosclerosis	14 (35%)	7 (36,8%)	4 (20%)	
	Asymmetric narrowing of the joint space	4 (10%)	1 (5,26%)	1 (5%)	
MSCT	Osteosclerosis	15 (37,5%)	6 (31,5%)	3 (15%)	
	Small tears in the menisci	4 (10%)	3 (15,8%)	1 (5%)	
	Synovitis	3 (7,5%)	2 (10,5%)	1 (5%)	
	Femoral head necrosis (FHN)	6 (15%)	3 (15,8%)	2(10%)	
ECG	Metabolic disorder and ischemia	8 (20%)	11 (57,9%)	3 (15%)	$p_{IIA\text{-}IIB}$=0,017

Interleukin-6 (IL-6) levels were 5.41±0.03 pg/mL in Group I (idiopathic OA). A significantly elevated level was observed in Group IIA (post-COVID OA) at 7.27 ± 0.04 pg/mL. In contrast, Group IIB (post-COVID OA with anticoagulant therapy) demonstrated a marked reduction to 3.16±0.04 pg/mL, with the difference between Groups IIA and IIB being statistically significant ($p_{IIA\text{-}IIB}$=0,036). A similar pattern was observed. TNF-α concentration was 4.12 ± 0.01 pg/mL in Group I. It was substantially higher in Group IIA (7.96±0.05 pg/mL), indicating an active inflammatory state. Following anticoagulant therapy, Group IIB showed a decrease to 5.96±0.02 pg/mL, suggesting a moderating effect on this key inflammatory pathway. This shows their effect in reducing the inflammatory process and enhancing the efficiency of anti-inflammatory drugs.

Baseline of D-dimer levels were 0.211 ± 0.066 μg/mL in Group I. Group IIA exhibited a pronounced elevation to 0.411 ± 0.097 μg/mL, reflecting a heightened pro-thrombotic state associated with post-COVID sequelae. Anticoagulant treatment in Group IIB was associated with a significant reduction in D-dimer to 0.131±0.083 μg/mL ($p_{IIA\text{-}IIB}$<0,001), indicating effective amelioration of hypercoagulability and improved microcirculatory parameters (Table 1).

Inflammatory markers (IL-6, TNF-α, CRP, ESR) were higher in group IIA and significantly decreased in group IIB. This indicates that anticoagulants enhance the effect of anti-inflammatory drugs. D-dimer was high in group IIA and decreased in group IIB, showing that anticoagulants reduce the risk of thrombosis. In patients with a history of COVID-19, treatment with anticoagulants was effective in improving microcirculation and preventing thrombosis risk. Calcium and vitamin D levels were higher in group IIB patients who received anticoagulants. This indicates that the combined use of vitamin D with anticoagulants may be effective in improving calcium metabolism in osteoarthritis.

Evaluation of long-term treatment effects in instrumental examinations, according to the study results, radiological, MRI, MSCT, and ECG examinations of patients in group I (idiopathic osteoarthritis, n=40) and group II (post-COVID-19 osteoarthritis, n=39) were analyzed. In group II, subgroup IIA (standard treatment, n=19) and subgroup IIB (standard + oral anticoagulants, n=20) were evaluated separately (Table 2).

X-ray Findings (Kellgren-Lawrence Classification): The distribution of advanced radiographic stages differed between groups. Grade III osteoarthritis was observed in 14 patients (35%) in Group I, 8 (42.1%) in Group IIA, and 4 (20%) in Group IIB. Grade IV osteoarthritis was present in 3 (7.5%), 2 (10.5%), and 1 (5%) of patients in Groups I, IIA,

and IIB, respectively. The lower prevalence of advanced grades in Group IIB suggests a potential disease-modifying effect of the combined therapeutic regimen.

Magnetic Resonance Imaging (MRI) Metrics included synovial membrane thickening (Group I: 30% (n=12); Group IIA: 31.5% (n=6); Group IIB: 15% (n=3)), subchondral osteosclerosis (Group I: 35% (n=14); Group IIA: 36.8% (n=7); Group IIB: 20% (n=4)), asymmetric joint space narrowing (Group I: 10% (n=4); Group IIA: 5.26% (n=1); Group IIB: 5% (n=1)). The consistent reduction in these pathological features in Group IIB supports the hypothesis that anticoagulant therapy may attenuate progressive joint damage, potentially by mitigating post-infectious microvascular pathology that differs from idiopathic disease mechanisms.

Multislice Computed Tomography (MSCT) findings corroborated the trends seen on MRI. The incidence of osteosclerosis was 37.5% in Group I, 31.5% in Group IIA, and 15% in Group IIB, indicating that anticoagulation may slow pathological bone remodeling. Other findings included meniscal tears (Group I: 10% (n=4); Group IIA: 15.8% (n=3); Group IIB: 5% (n=1)), synovitis (Group I: 7.5% (n=3); Group IIA: 10.5% (n=2); Group IIB: 5% (n=1)), femoral head necrosis (FHN) (Group I: 15% (n=6); Group IIA: 15.8% (n=3); Group IIB: 10% (n=2)).

While FHN was slightly more prevalent in the post-COVID cohorts, comprehensive conservative management appeared to moderate its severity. A marked difference was observed in the composite indicator of metabolic disorders and ischemia, which was present in 20% of Group I, 57.9% of Group IIA, and 15% of Group IIB. The high prevalence in Group IIA underscores the significant impact of COVID-19 on the vascular system, while the pronounced reduction in Group IIB highlights the potential efficacy of anticoagulants in correcting post-infectious ischemia.

4. Conclusions

Patients with a history of COVID-19 were observed to experience a more accelerated progression of hip osteoarthritis compared to those with the idiopathic form of the disease, characterized by a higher prevalence of pain, movement restriction, and inflammatory signs. The adjunctive use of anticoagulant therapy (rivaroxaban 20 mg/day) to standard treatment was associated with a significant reduction in pain syndrome, muscle spasms, and movement limitation. This clinical improvement corresponded with the normalization of key laboratory parameters-including IL-6, TNF-α, D-dimer, CRP, and ESR-indicative of diminished systemic inflammation and thrombotic risk. Instrumental assessments (X-ray, MRI, MSCT) further proved these findings, revealing reductions in subchondral osteosclerosis, synovitis, and ischemic alterations. These collective outcomes support the hypothesis that anticoagulants exert a positive effect on microcirculation and subsequent tissue regeneration. Integrating anticoagulation with established non-pharmacological interventions, such as physiotherapy, guided physical activity, and weight control, enhanced the overall efficacy of the comprehensive management strategy. In conclusion, anticoagulant therapy in the context of post-COVID-19 osteoarthritis appears to alleviate pain, improve mobility, mitigate inflammation, and promote structural recovery. This approach can be recommended as a pathogenetically grounded component in the management protocol for this condition.

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