

Diagnosis and Structural Modification Treatment of Osteoarthritis of the Knee

1. **Khamidov Obid Abdurakhmanovich**
2. **Ametova Alie Servetovna**
3. **Yakubov Doniyor Javlanovich**
4. **Nurmurzaev Zafar Narbay ugli**

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Abstract: The paper considers basic current methods for the diagnosis of knee osteoarthritis. It gives for the first time data on the impact of long-term theraflex therapy (a 3-year follow-up) on the progression of knee joint structural changes (X-ray joint space narrowing, osteophytosis) in patients with gonarthrosis.

Key words: osteoarthritis, gonarthrosis, arthrosonography, theraflex.

^{1,2,3,4} Samarkand State Medical University,
Department of Medical Radiology,
Republic of Uzbekistan, Samarkand

Osteoarthritis (OA) is the most common form of joint disease. Arthrosis accounts for up to 70% of rheumatic diseases. Osteoarthritis is an extremely serious condition that significantly affects the quality of life, affecting the articular cartilage and subchondral bone by the age of 40-50 years and even earlier, with a tendency to become chronic and progressive, often with the patient's disability. The current issues of prognosis, prevention, early detection and therapy of arthrosis are not only of a medical, economic, but also of a social nature.

Until the mid-1980s, there was no standard definition of osteoarthritis. It has been widely interpreted as a disease of unknown etiology, in which mainly the cartilage is affected (in contrast to rheumatoid arthritis, in which the synovial membrane is mainly involved in the pathological process), indicating the degenerative nature of the changes. The definition of osteoarthritis proposed at the "New Horizons in Osteoarthritis" seminar organized by the American Academy of Orthopedic Surgeons (USA, 1995) emphasizes that osteoarthritis encompasses several nosologies: osteoarthritis is a group of diseases that overlap and have different etiologies, but require identical biological, morphological and clinical findings. The pathological process extends not only to the articular cartilage, but to the entire joint, including the subchondral bone, intra- and periarticular soft tissues, ligaments, capsule, synovial membrane and articular muscles. Ultimately, there is degeneration of the articular cartilage with its atrial fibrillation, fissure formation, ulcerations and its complete loss.

Although osteoarthritis is considered to be a systemic pathology of the cartilaginous structures of the synovial joints, particular attention is paid to individual, primarily load-bearing joints. These are primarily the knee (KS) and hip joints, the severe damage to which leads to disability in the patient. It

is not surprising that special attention is paid to the prevention and prognosis of this pathology, its early detection, the characteristics of risk factors and treatment.

Arthrosis of the knee joint, gonarthrosis (GA), is characterized by a high prevalence, an insidious course with early disability of the patient, as well as a constant pain syndrome, which significantly impairs motor activity and contributes to the development of depression, which undoubtedly worsens quality of life of the patients.

The CS consists of three components: the patellofemoral (PFD), lateral, and medial tibiofemoral (TPD) sections. Each of these areas can be affected individually by osteoarthritis, or different combinations of lesions are possible. The most common is an isolated lesion of the medial TFO and a combined lesion of the PFO and medial TFO. On average, medial TFO is achieved in 75% of cases, lateral TFO in 26%, and PFO in 48% of cases.

Articular cartilage loss is generally more pronounced in PFD and on the articular surface of the tibia in TFO in the area less covered by the menisci. According to magnetic resonance imaging (MRI), AG affects not only the articular cartilage but also the menisci. The osteophytosis is more pronounced in the lateral TFO, while maximum articular cartilage destruction can be found in the medial TFO.

The diagnosis of AG is based on the analysis of risk factors for the disease, clinical symptoms, results of instrumental and laboratory studies.

GA results from the interaction of many genetic and environmental factors. Some studies have shown that knee OA is more common in black women than white women. The risk factors for HA in the PFO joint have been shown to differ from those in the medial TFO. The former are more associated with family history and the latter with obesity.

Among the many etiological factors in the development of HA, general constitutional factors (age, gender, body weight, heredity, reproductive characteristics) and unfavorable local mechanical factors (occupation, lifestyle, etc.) are of the greatest importance.

The most common early clinical manifestation of HA is diffuse intermittent knee pain, which usually occurs immediately or after exercise. The pain in overt GA is not as pronounced as in other, more localized arthritis, but as the disease progresses it becomes persistent. The mechanism of pain associated with osteoarthritis has not yet been fully elucidated.

Possible Causes of Pain in GA:

- 1) it is known that in osteoarthritis, the intraosseous pressure in the subchondral bone increases due to obstruction of venous outflow. It is believed that this mechanism is responsible for the pronounced pain syndrome - prolonged, occurring at rest, at night;
- 2) Violation of biomechanics in the affected joint contributes to the development of secondary periarticular syndromes - bursitis, tenosynovitis. The involvement of periarticular tissue in the disease process is a common cause of pain in the early stages of HA;
- 3) synovitis of varying severity often accompanies GA, contributes to increased pain.

Pain mechanisms associated with inflammation are actively studied. Synovitis in GA can be subclinical, mild, moderate, significant; by prevalence - limited, diffuse; have not only diagnostic but also pathogenetic value. The discovery of inflammatory mediators in the synovial fluid of patients with knee OA, even at an early stage, led to a revision of the previously existing concept of the pathogenesis of the disease as "an inevitable consequence of the aging process of the joints". There is a lot of data that inflammation may play an initiating role in the development of osteoarthritis.

Among the modern imaging methods, such as magnetic resonance imaging (MRI), computer tomography (CT), arthroscopy, ultrasound, radiography takes first place in diagnostics and effectiveness control for the treatment of osteoarthritis, especially knee arthrosis. This is due to its availability, simplicity, economy and informative content.

The radiographic diagnosis of HA is based on the demonstration of radiographic joint space narrowing (RSJ) as the major sign of osteoarthritis, osteophytes (OF), subchondral sclerosis (SS).

The narrowing of the RSC indicates a decrease in the volume of the articular cartilage, while the SS and OF at the edges of the articular surfaces, according to most researchers, indicate the response of the bone tissue to an increase in the mechanical load on the joint, which in turn is the result of degenerative changes and a decrease in articular cartilage volume. These signs are important not only for diagnosis but also for assessing treatment efficacy and disease progression.

X-ray examination of CS allows you to determine the stage of AG. Traditionally, to determine the stage of HA, the classification of J. Kellgren and J. Lawrence is used, based on an assessment of the severity of the narrowing of the RSC, the presence of OP and SS. Among the early radiological signs of HA (Kellgren-Lawrence Stage 0-II) include:

- stretching and sharpening the edges of the intercondylar eminence of the tibia (at the site of attachment of the cruciate ligament);
- slight narrowing of the RSC, more commonly in the medial part of the joint;
- sharpening the edges of the articular surfaces of the condyles of the femur and tibia, more often in the medial part of the joint.

For an early diagnosis of HA it is necessary to examine all parts of the joint: the medial and lateral TFO and the medial and lateral PFO.

The use of ultrasound and ultrasound in rheumatology is a relatively new and promising avenue. In the last 10 years, ultrasound has established itself in the examination, control and treatment of rheumatic diseases of the joints. Typically, arthrosonography (ASH) is used to assess soft tissue pathology and identify fluid, but it can also depict cartilaginous and bony surfaces. A number of undeniable advantages - non-invasive (unlike arthroscopy), accessibility, simplicity, cost-effectiveness (compared to CT and MRI) have given priority to common ultrasound, among other methods of instrumental visualization of the musculoskeletal system. Ultrasound is very revealing about the small details of the bone surface, the ligament tendon apparatus and helps to detect and control inflammatory changes in the tissue.

Table 1. Characteristics of patients of the main group

Index	Patients of the main group, n=104
Age, years	47,4±11,6
Gender:	
f.	83 (79,7)
m.	21 (20,3)
Disease duration, months	11,5±6,7
X-ray stage:	
0	22 (20,8)
I	51 (49,4)
II	31 (29,8)
Bilateral GA	71 (68,5)
Synovitis (+)	31 (29,4)

Note. Here and in Table. 2: in brackets - percentage indicators.

X-ray, in most cases, allows you to determine the damage to the elements of the bone of the knee joint. These changes are often already irreversible and the treatment of these patients is difficult. The advantage of ASG of the knee joint is the ability to detect early signs of damage to all structures of the joint, which are practically not detected radiologically. The technique of ASG KS allows to determine the main features of joint pathology - traumatic injuries, degenerative-dystrophic and inflammatory processes. Depending on the position of the sensor, the tendons of the quadriceps femoris muscle, the contours of the upper pole of the patella, the suprapatellar bursa (superior volvulus), the study of which is especially important for the diagnosis of degenerative-dystrophic and inflammatory lesions.

With normal HA, the synovial membrane is not visualized, with synovitis, increased suprapatellar bursa, straightening of folds, excess fluid and thickening of the synovia are noted. Ultrasound makes it possible to visualize the PFO of the joint, in particular the hyaline cartilage and the presence of excess fluid on it, as well as to assess the degree of degradation of the articular cartilage of the lateral and medial femoral condyles in the early stages of AG, when the radiographic examination does not yet provide information about the narrowing of the joint space. Detection of changes in the shape of the articular surfaces of the femur, marginal (even the smallest) of ACH in ACH helps to identify the first manifestations of HA in the preradiological period of the process. Ultrasonography of the popliteal fossa may reveal Baker's cysts.

Despite the high informative content of MRI in the diagnosis of early stages of knee OA, this study has not yet found widespread application, mainly due to high costs.

Laboratory research methods do not allow to diagnose osteoarthritis. Most patients with osteoarthritis show no changes in blood and urine tests, except in cases of severe synovitis, when increased ESR, hypergammaglobulinemia, and increased acute phase proteins can be detected. Examination of synovial fluid shows no significant difference from the norm.

In recent years, potential biological markers (BM) of inflammation, degradation and repair of joint tissues (mainly cartilage and bone) have been actively sought. BM should reflect these dynamic changes, serve as predictors of OA prognosis and markers of pathogenetic treatment efficacy. The discovery of new, more in-depth studies of known DMs will allow a better understanding of the pathogenesis of OA.

The treatment of osteoarthritis and in particular of knee OA remains a challenge. It can cover different areas: patient education programs, physical exercises; analgesics and nonsteroidal anti-inflammatory drugs (NSAIDs); orthopedic surgery. Revisiting the role of NSAIDs in the treatment of osteoarthritis has contributed to the development of drugs that directly affect disease progression.

The American College of Rheumatology and EULAR guidelines define all drugs used to treat OA as either symptom-modifying or pattern-modifying, based on their ability to modify disease progression. When using structure-modifying drugs, prospective evaluation of radiological changes is recommended.

The effectiveness of drugs such as chondroitin sulfate (CS) and glucosamine (GAm) in osteoarthritis has been demonstrated in numerous randomized clinical trials, mainly conducted from 1984 to 2003.

The proven effectiveness of GAm and CS as monotherapy served as a prerequisite for the development of combined preparations. Using a combination of cholesterol and GAm seems more promising. Thus, an experimental model showed that the combination of cholesterol and GAm increased the production of glycosaminoglycans by chondrocytes by 96.9%, compared to 32% when only cholesterol or only GAm was prescribed. Recent studies aim to investigate the effectiveness of the combination of cholesterol and GAm in the treatment of osteoarthritis.

The Osteoarthritis Treatment Society (OARSI) recommendations conclude the following on the use of cholesterol and GAM in the treatment of knee OA: Treatment with GAM and/or cholesterol may have a symptomatic effect in patients with osteoarthritis of the knee. If there is no response within 6 months, these drugs should be stopped (level of evidence: Ia). In patients with osteoarthritis of the knee joint, accompanied by clinical manifestations, GAM and cholesterol may have a structuring effect (level of evidence — Ib).

Of the combination drugs, Teraflex (Bayer Health Care) has found the most widespread use in the treatment of osteoarthritis. In previous studies, the drug showed great effectiveness in treating the symptoms of osteoarthritis, mainly AG. As mentioned above, long-term observation and radiological monitoring of structural changes in the joint are necessary to assess the disease-modifying effect of the drug.

Purpose of the study — to assess the effect of long-term treatment with Teraflex (3-year follow-up) on the rate of radiographic progression of knee OA.

Patients and methods. We studied 244 outpatients with a reliable diagnosis of knee OA who gave written informed consent to participate in the study. The disease was diagnosed according to the GA criteria of the American College of Rheumatology. In the absence of radiological criteria, the diagnosis was made based on the association of clinical symptoms (mechanical pain, joint stiffness < 30 min, functional impairment) and an irregularity in the contour of the articular surfaces of the bones forming the articulation, revealed in ASH. The radiological stage of AG was determined according to the classification of J. Kellgren - J. Laurentius.

Patients with knee OA were divided into main and control groups. The primary group included 104 patients with knee OA who started treatment with Teraflex upon enrollment in the study: 83 (79.7%) women and 21 (20.3%) men (mean age 47.4 ± 11.6 years; average duration of GA — 11.5 ± 6.7 months). According to the classification of J. Kellgren - J. Lawrence stage 0 HA was present in 22 (20.8%) patients, I - in 51 (49.4%), II - in 31 (29.8%). The characteristics of the patients of the main group are presented in the table. 1. Teraflex was prescribed 1 capsule 3 times a day for 1 month, then 1 capsule 2 times a day for 5 months. Repeated courses of Teraflex at a dose of 2 capsules per day for 2 months were repeated at 1 month intervals. The total duration of the drug at the end of the study was 3 years. With increased pain in the joints, diclofenac was allowed in a dose of 100 mg / day.

The control group consisted of 140 patients with knee OA: 107 (76.4%) women and 33 (23.6%) men (mean age - 46.7 ± 10.4 years; mean duration of knee OA - 11.7 ± 5.9 months). According to the classification of J. Kellgren - J. Lawrence, stage 0 HA was detected in 29 (20.7%) patients, I - in 67 (47.9%), II - in 44 (31.4 %). The characteristics of patients in the control group are presented in the table. 2. Upon inclusion in the study, patients in the control group were recommended to take diclofenac 100 mg/day in combination with various types of physiotherapy. When a positive effect was achieved, patients took diclofenac at a dose of 100 mg / day only with increased pain in the joints.

At the time of study entry, the main and control groups were comparable with respect to joint syndrome parameters.

To assess the effect of treatment on radiological parameters (degree of CRS narrowing and presence of OF), all patients underwent knee joint radiographs at study entry and during follow-up. Control observation periods in the forward, lateral and axial projections in the position of maximum knee extension for better visualization of the anterior RSC, examining the lateral and medial divisions of the TFO.

1. RSC was measured in the most constricted area of the medial TFO using a loupe with a division value of 0.1 mm. The degree of RSC narrowing was determined by a semi-quantitative method in points: 0, no narrowing;
1 point - RSC 4.5-5 mm; 2 points - RSC 4-4.5 mm; 3 points - RSC <4 mm.
2. The severity of osteophytosis was assessed by a semi-quantitative method in points: 0 - OP absent;
1 point - sharpening of the articular surfaces; 2 points - no more than 2 small OF; 3 points - 3 or more minor OFs.

Radiographs were evaluated by one radiologist. All of the listed radiographic parameters were studied at the time of inclusion in the study and during the control periods of observation: after 1; 2; 3 years of therapy with Teraflex.

Statistical data processing was carried out using the statistical package STATISTICA.

Table 2. Характеристика больных контрольной группы

Index	Patients in the control group, n=140
Age, years	46,7±10,4
Gender:	
f.	107 (76,4)
m.	33 (23,6)
Disease duration, months	11,7±5,9
X-ray stage:	
0	29 (20,7)
I	67 (47,9)
II	44 (31,4)
Bilateral GA	89 (63,6)
Synovitis (+)	36 (25,7)

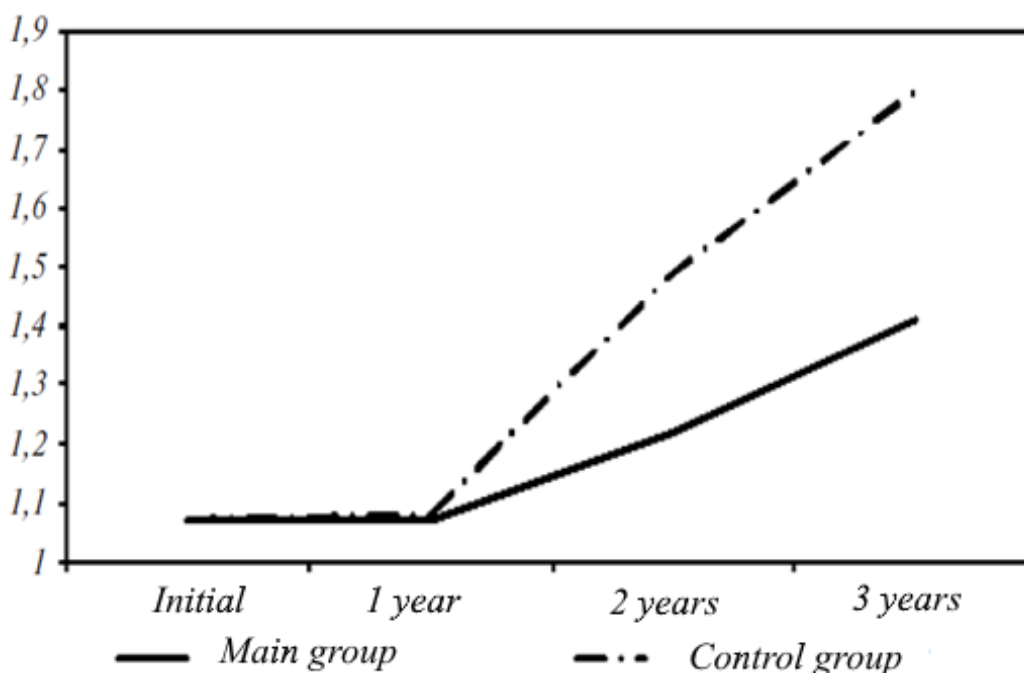


Fig. 1. Dynamics of RSC in the medial part of the TFO in the main group (treatment with Teraflex) and in the control groups ($p < 0.05$ after 3 years of follow-up)

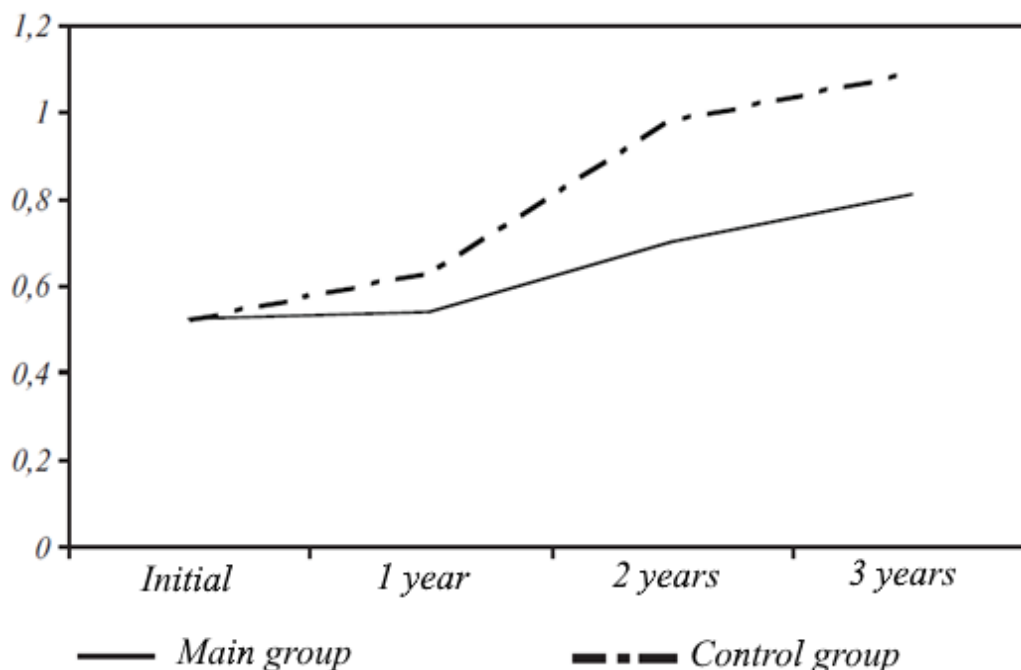


Рис. 2. Динамика остеофитоза в основной (лечение терафлексом) и контрольной группах ($p < 0,05$ через 3 года наблюдения)

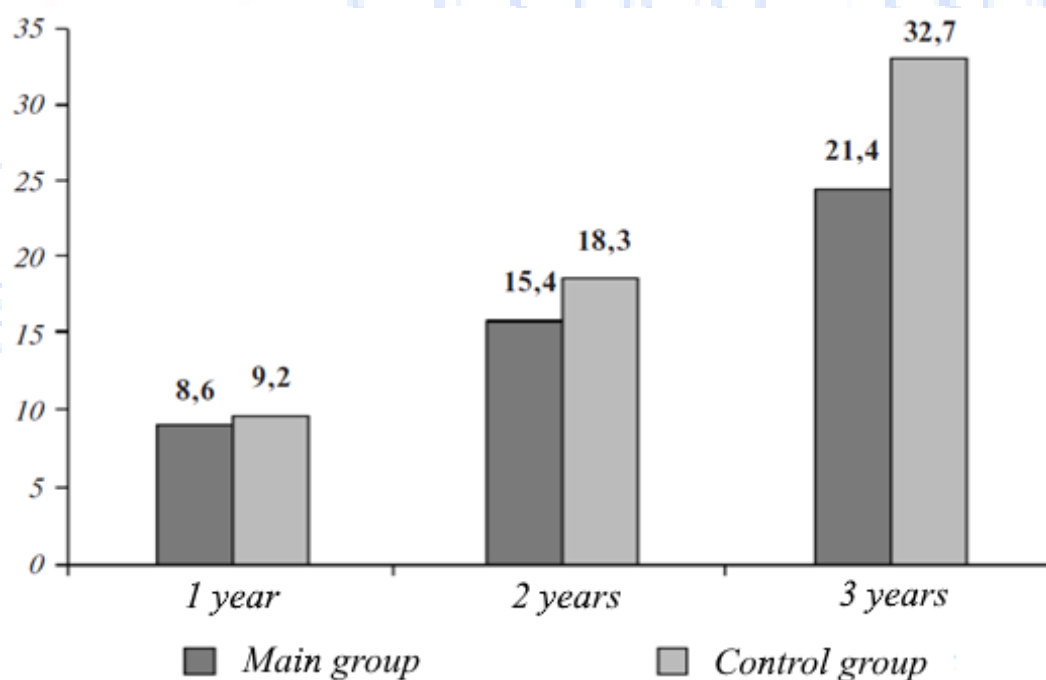


Fig. 3. Percentage of patients with radiological progression of GA in the main (Teraflex treatment) and control groups ($p < 0.05$ after 3 years of follow-up)

Research results. After 1 year of treatment with Teraflex, there was practically no negative dynamics of RSC height; after 2 and 3 years, differences in RSC height with baseline values did not reach statistical significance (Fig. 1).

OP (increase in number and size) is one of the important indicators of the progression of structural changes in the knee joint in AG. According to some authors, it is more the FO than the RSC level that

reflects the negative radiological dynamics in osteoarthritis, and it is the FO that would be more responsible for the aggravation of the symptoms of knee OA.

During treatment with Teraflex, a slight progression of osteophytosis was observed after 1 year of observation. After 2 and 3 years, there were no statistically significant differences from baseline in the group of patients taking Teraflex for a long time (Fig. 2).

Radiographic progression according to J. Kellgren - J. Lawrence with > 1 radiological stage in the context of long-term treatment with Teraflex was observed in 9 (8.6%) patients after 1 year, in 15 (15.4 %) after 2 years and in 25 (24.1%) diagnosed after 3 years of observations (Fig. 3).

In the control group, after one year of treatment, there was also no negative RSC height dynamics in the medial part of the TFR. After two years of follow-up, differences in RSP scores did not reach statistical significance compared to baseline. However, a statistically significant negative dynamics of the RSC level was already evident after three years ($p < 0.05$). The negative dynamics of osteophytosis was observed after 1 and 2 years of follow-up. After 3 years of treatment, statistically significant differences ($p < 0.05$) were observed between this indicator and baseline. In the control group, worsening of the radiographic stage of HA was observed in 13 (9.2%) at 1-year follow-up, 26 (18.3%) at 2-year follow-up, and 46 (32.7%) at 3-year follow-up ($p < 0.05$).

Thus, in this study, long-term Teraflex treatment had an inhibitory effect on the rate of progression of structural changes in CS, suggesting a potential disease-modifying effect of the drug. However, more studies are needed on the effect of Teraflex on the progression of OA.

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