



# Diagnosis and Management of Osteoarthritis with Hyaluronic Acid

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## Abstract

**Edited by:** Sinisa Stojanoski  
**Citation:** Kola S, Kola I, Frroku E, Abazaj E. Diagnosis and Management of Osteoarthritis with Hyaluronic Acid. OpenAccessMacedJMedSci.2022Jun22;10(B):1801-1805. https://doi.org/10.3889/oamjms.2022.9640  
**Keywords:** Hyaluronic acid; Osteoarthritis; Radiography; Rehabilitation  
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**Received:** 04-Apr-2022  
**Revised:** 23-May-2022  
**Accepted:** 14-Jun-2022  
**Copyright:** © 2022 Sandër Kola, Irena Kola, Erinda Frroku, Erjona Abazaj  
**Funding:** This research did not receive any financial support  
**Competing Interests:** The authors have declared that no competing interests exist  
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**BACKGROUND:** Osteoarthritis (OA) of the genu joint is a degenerative disease of the genu joint, which due to functional limitations leads to deterioration of the quality of life of these patients. In many cases, surgical therapy prosthesis of articular surfaces represents the gold standard of treatment for these patients.

**AIM:** In this study, it is proposed to evaluate the effectiveness of hyaluronic acid (HA) injected under the direction of Echo (ultrasound) in the genu articulation accompanied by a rehabilitation program.

**MATERIALS AND METHODS:** Fifteen patients with knee OA were studied. According to the Kellgren-Lawrence radiological classification, Grade II-III arthrosis does not qualify for surgical treatment. Patients underwent intra-articular injection with HA, under ultrasound guidance, and after 6 days continued with rehabilitative treatment aimed at combating the patient's analgesic posture, recovery of muscle traction participating in genu joint movement, decompression maneuvers, and decompaction in monopodial load. Patients were evaluated at the beginning and after 3 months.

**RESULTS:** In the evaluation of patients at the beginning and after 3 months, a reduction in > 60% of the pain was found, and the Western Ontario and McMaster University Osteoarthritis test in 40% of patients after the first intra-articular injection. No significant side effects were observed during infiltrative procedures.

**CONCLUSIONS:** This study confirms the effectiveness of the combined treatment of the rehabilitation program and intra-articular therapy under the guidance of Echos, in patients suffering from knee OA, significantly reducing pain and recovery of functional capacity.

## Introduction

The prevalence of patients with osteoarthritis (OA) is growing rapidly worldwide due to population demographics shifting [1]. Knee OA is a common progressive multifactorial joint disease and is characterized by chronic pain and functional disability [2]. The origin of OA injury starts in the cartilage but also affects other articular structures such as bones, ankle capsules, menisci, ligaments, bursae, and periarticular muscles [3]. It is approximated that 250 million people worldwide suffer from OA, with an increasing trend in prevalence during the last decades, which continues to rise [2]. About one in four people over the age of 55 have persistent knee pain and one in ten of these people have painful disabling knee OA [4], [5]. The most predominant risk factors are aging, obesity, female gender, previous trauma, and repetitive use [1]. The disease increases with increasing longevity and obesity [6], [7]. The increase in obesity has translated into not only increasing knee OA incidence but also the onset at a younger age [8], [9]. The majority of patients have to live with the disease for the rest of their lives, with few being able to receive total joint replacement due to cost and other issues. Obesity is another risk that also increases OA even at a young age, where cases are in advanced stage [4], and need surgery.

Optional and traditional treatments for OA include analgesics, AINS, AIS, and lifestyle improvements such as physical therapy, exercise, weight loss, and partial or total arthroplasty for advanced cases. Recent therapies include intra-articular therapy with intra-articular viscous supplementation which involves local injections of hyaluronic acid (HA) that serves as a joint lubricant [10]. There are different recommendations related to the use of HA for OA of the knee. Hence, one study conducted by the American College of Rheumatology in 2012, a recommendation that local HA injections use in patients who had an inadequate response to initial therapy [11], but, on the other hand, a study by the American Academy of Orthopaedic Surgeons in 2013, authors of this study were against the use of HA for the treatment of symptomatic patients [12]. Systematic reviews for OA play an important role in establishing and adapting the study-based clinical guidelines. Studies have shown the improvement of methods for medical treatments of OA by creating standardized treatment degrees [13].

## Aim of study

The research purpose of this study is to evaluate the effectiveness of HA injected (HA) under the direction of Echo (ultrasound) in the genu articulation

accompanied by a rehabilitation program.

This purpose will be achieved through the two following objectives:

- To evaluate the effect of intra-articular injection of HA using the Western Ontario and McMaster University Osteoarthritis (WOMAC) scale (subjective evaluation from the patient) on the progression or relief of pain before and after intervention in patients with knee OA
- To evaluate the radiological changes to check the objective condition of knee OA before and after the intervention of intra-articular injection of HA.

## Materials and Methods

### Study population

This is a prospective study conducted at the Rheumatology Clinic at Tertiary University Hospital Centre "Mother Theresa" in Tirana, and Eigan medical clinic Albania from November 2017 until March 2019. About seventy patients 65+ diagnosed with knee OA by Kellgren and Lawrence test in Grades II and III and treated with HA were included in this study. Gonarthrosis patients were divided into two groups. The first group included forty-five patients that underwent intra-articular injection with HA. In 45 HA-treated groups that fulfilled the inclusion criteria [30 women (66.7%) and 15 men (33.3%)], the hylan G-F20 (group A-Synvisc) was performed in 28 patients, and in 17 was performed sodium hyaluronate (group B-Suplasyn). In the second group is included 25 patients (18 women [72%] and 7 men [28%]) undergoing only drug therapy with AINS.

### Inclusion criteria

The following criteria were included in the study:

1. All patients diagnosed with OA disease by conventional radiography (the "gold" standard for assessing structural changes of OA) during the study period are included
2. Patients who have not used AINS in the past 3 weeks
3. Patients who do not have joint trauma.

### Exclusion criteria

The following criteria were excluded from the study:

1. Patients under 65 years
2. Patients who have used AINS in the past 3 weeks
3. Patients with acute knee trauma or

inflammation.

### Methods

The stages of OA are assessed by the Kellgren-Lawrence Scale [14]. Radiological changes are present in the second or higher stage. Description of the Kellgren-Lawrence scale is as follows:

- Stage 0: No radiographic changes of OA;
- Stage 1: Slight narrowing of the joint space and formation of osteophytes;
- Stage 2: Presence of osteophytes with marked narrowing of the articular space;
- Stage 3: Multiple osteophytes, narrowing of the articular space, sclerosis, and possible bone deformity;
- Stage 4: Large osteophytes, narrowing to the disappearance of articular space, severe sclerosis, and certain bone deformity.

Another assessment except for the radiographic examination and examination of OA stages was done on all patients. Hence, for all patients, the evaluation of knee joint pain and function was done before and after 3 months of treatment with intra-articular injections with the WOMAC scale [15].

Intra-articular injection of HA was performed according to protocols. Each patient was given three infusions of HA, one injection in a week. Three months after injection to all patients a reassessment was scheduled. Both, the evaluation and reassessment of two groups of patients consisted of a knee radiograph and a WOMAC questionnaire, for joint pain and function before and 3 months after injection.

### Statistical analysis

The software SPSS, version 20.0 was performed for data analyses. Statistical t-tests were performed to compare the means of two quantitative independent variables of each group while  $\chi^2$  for the qualitative variables. For some of the variables, the mean  $\pm$  standard deviation was employed. Results were considered statistically significant with  $p < 0.05$ .

## Results

Overall, among seventy patients included in this study, 68.6% (48/70) were women while 31.4% (22/70) were men. The mean age was  $66.65 \pm 8.24$ , while the minimum and maximum age was 65 and 82 years old, respectively. Related to the living area 61.4% (43/70) of patients lived in the urban area and 38.6% (27/70) lived in rural areas. The body mass index (BMI) mean in all patients was  $27.9 \pm 10.4$  (Table 1).

**Table 1: Characteristic demographic data for all patients**

Demographic variables of all patients		
Groups	Hyaluronic acid-treated group	AINS drug therapy -treated group
Age	67.8 ± 9.87	65.5 ± 6.68
Gender (%)		
Women (48)	30 (62.)	18 (37.5)
Men (22)	15 (68.2%)	7 (31.8)
Living area (%)		
Rural area (27)	17 (63)	10 (37)
Urban area (43)	28 (65.1)	15 (34.9)
BMI (kg/m <sup>2</sup> ) (mean=27.9 ± 10.4)	28.02 ± 11.45	27.75 ± 9.32

BMI: Body mass index, AINS: Anti-inflammatory nonsteroidal.

Related to the demographic characteristics of patients treated with HA; the mean age resulted in 66.5 years for Synvisc and 65.35 for Suplayn. Women in Synvisc were 63.3% while in Suplayn 36.7%. Men were 60% in Synvisc and 40% in Suplayn. In the urban living area lived 66.7% of patients and 33.3% in the rural area. Furthermore, patients that lived in rural areas appeared difference between Synvisc and Suplayn in 66.7% and 36.7%, respectively, while from the urban area in Synvisc living 60% of patients and in Suplayn 40%. Most of the patients (77.8%) were over 25 kg/m<sup>2</sup> and classified as overweight and/or obese. The BMI mean resulted in 28.35 ± 10.42 in Synvisc and 27.05 ± 8.56 in Suplayn. There is found a significant association related to the HA and living area  $\chi^2 = 23.8$   $p = 0.02$ , but for other demographic characteristics, there was no found association  $p > 0.05$  (Table 2).

**Table 2: Characteristic demographic data for patients of the first group treated with hyaluronic acid**

Demographic variables			
Variables	Synvisc	Suplayn	p
Age	66.5	65.35	
Gender (%)			
Women (30)	19 (63.3)	11 (36.7)	0.8
Men (15)	9 (60)	6 (40)	
Living area			
Rural area (15)	10	5	0.02
Urban area (30)	18	12	
BMI (kg/m <sup>2</sup> ) (mean)	28.35 ± 10.42	27.05 ± 8.56	>0.05

BMI: Body mass index.

Based on the stages of OA, all patients included in this study resulted in Grades II and III. In Grade II, Synvisc resulted in 12 (26.6%) and Suplayn resulted in 6 (13.3%) cases. In Grade III, Synvisc resulted in 16 (35.6%) and Suplayn resulted in 11 (24.4%). There is no found significant association between the grade and HA (Synvisc and Suplayn)  $p = 0.6$  (Figure 1).

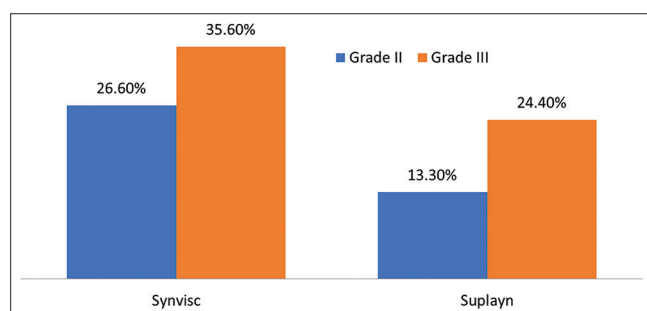


Figure 1: Distribution of knee OA grade in the first group according to the Synvisc and Suplayn

Table 3 showed the degree of pain based on WOMAC index scale and articular function based on radiological findings before and after injection of acid hialorunik. As it appears the degree of pain in men was 17 before injection and decreased to 5 after 3 months of treatment with HA. A decrease is seen also in the articular function before and after in men from 67 is evaluated at 18.

**Table 3: Evaluation of pain and articular function before and after 3 months of treatment with hyaluronic acid**

Gender	Number of patients	Degree of pain before treatment with HA	Degree of pain after 3 months of treatment with HA	Articular function before injection of HA	Articular function after 3 months of injection of HA
Men	15	17	5	67	18
Women	30	18	6	66	20
Total	45	17.5	5.75	66.5	19

HA: Hyaluronic acid.

The same situation is also for women. From 18-degree pain before treatment or injection of HA, after 3 months is evaluated to 6, and for articular function from 66 before treatment is evaluated 20 after 3 months (Table 3).

Based on what we presented in table three, in 45 patients of the first group that underwent intra-articular injection with HA, the result was; that 84.4% (38/45) patients have shown radiographic improvements of OA after being treated with HA injection, of which 78.9% (30/38) were women and patients 21.1% (8/38) were men while for 15.6% (7/45) of patients no radiographic improvements had been shown (Table 4).

**Table 4: Radiological findings after 3 months of treatment with hyaluronic acid**

Radiological findings	Patients, n (%)	Female, n (%)	Male, n (%)
Radiological improvements	38/45 (84.4)	30/38 (78.9)	8/38 (21.1)
No radiological improvements	7/45 (15.6)	0	7/45 (15.6)

Regarding the evaluation of knee joint pain and function by the WOMAC scale, all patients 45 (100%) show an apparent improvement in pain 3 months after the third injection. In addition, 88.8% (40/45) patients show better ankle function after the injection of HA, while five patients had not shown significant improvement in knee function according to the WOMAC scale. Furthermore, there were no complications for patients after HA injection (Table 5).

**Table 5: Evaluation of knee joint pain and function by the Western Ontario and McMaster University Osteoarthritis scale**

WOMAC scale evaluation	Improvement of knee function (%)	No improvement in knee function (%)
45 (100)	40 (88.8)	5 (11.2)

WOMAC: Western Ontario and McMaster University Osteoarthritis

Meantime, for the second group (25 patients in total treated with AINS), after 3 months the results were as below: There was no found improvement in radiographic changes regarding the OA in patients in the second group, but 25 patients appeared to have a slight improvement in pain exactly 3 months after treatment, while 20 patients show better knee joint functionality. We did not have significant improvement in function

according to the WOMAC scale in five patients in the second group (Table 6).

**Table 6: Evaluation of pain and articular function before and after 3 months of treatment with AINS**

Gender	Number of patients	Degree of pain before treatment with AINS	Degree of pain after 3 months of treatment with AINS	Articular function before AINS	Articular function after 3 months of AINS
Men	7	18	10	70	35
Women	18	19	12	67	30
Total	25	18.5	11	68.5	32.5

AINS: Anti-inflammatory nonsteroidal.

According to this summary comparative table, it is clear from the evaluation of pain and joint function of both groups of patients treated with AINS and HA, that the superiority of treatment with HA. Based on our findings, the treatment of OA with HA injections resulted much better compared to alternative treatment AINS (Table 7).

**Table 7: Comparative evaluation for the two types of treatment (AINS-hyaluronic acid)**

Study groups	Degree of pain before treatment	Degree of pain after 3 months of treatment	Articular function before treatment	Articular function after 3 months of treatments
HA (45 patients)	17.5	5.75	66.5	19
AINS (25 patients)	18.5	11	68.5	32.5

HA: Hyaluronic acid, AINS: Anti-inflammatory nonsteroidal.

## Discussion

HA's powerful anti-inflammatory and analgesic potential have proven effective in several disease states including knee OA. For that reason, HA has been used for more than four decades in the treatment of OA in humans. In clinical practice, different types of HA are not equivalent, and their characteristics depend on the origin, dose, and molecular weight [16]. Studies show that there is no significant difference between the two types of HA used to treat patients to improve knee function based on the WOMAC rating scale, reduce pain, and improve radiological changes of the knee OA [17], [18], [19].

In this study, we used two different types of HA (Synvisc and Suplayn) which have different molecular weights. The evaluation of the effect of HA applied was done at the beginning and after three months. Most of the cases taken in the study belong to the female sex and also many of them were in the obese category. The finding results of this study are agreed with some other studies [2], [20], [21].

Also based on the findings of this study, in terms of treatment with both types of HA, it is noted that patients have improved in terms of pain, stiffness, and functional limitation according to the degree of WOMAC assessment before and after HA infiltration. Hence, the results of our study agree with the literature. In this study, we observed that overweight and obese patients who underwent intra-articular hybrid HA injection experienced a significant reduction in pain severity.

*Bannuru et al.*, in their study, conclude that HA therapy for the management of pain in knee OA is effective at 4 weeks, reaches its maximum effectiveness at 8 weeks, and exercises a distinct residue at week 24. Likewise, HI treatment is greater than the published effects of nonsteroidal analgesics and anti-inflammatory drugs [22].

A weakness of this study is the follow-up time short (only 3 months after injection). There are various studies with follow-up for a long time from 6 to 12 months of treatment of patients with OA, in which functional improvement is observed in a percentage of 30%–40% measured by the WOMAC scale [23]. Another study by *Bruyère et al.* found that OA management consisted of the need for a combined pharmacological and non-pharmacological treatment with an OA rehabilitation protocol, including access/education to information, weight loss if overweight, and an appropriate exercise program [24]. Based on the findings of this study, it is recommended to include pharmacological and non-pharmacological treatments in future studies of patients suffering from OA of the knee.

## Conclusions

This study showed good short-term results in radiographic progression, pain, and function of the knee joint after injection of HA into gonarthrosis. We can say that Group I of patients treated with two intra-articular injections with HA, regardless of the type of HA used, have a significant improvement in function according to the WOMAC scale, pain, and radiological changes of the knee OA, compared to patients treated with AINS. This treatment may be a good choice for patients with gonarthrosis who are not fit or do not want to undergo knee surgery, which can improve their symptoms and quality of life and slow its progression.

### Limitation

Finally, limitations of the study include the small number of patients and the lack of long-term follow-up due to the short observation period of the study. Further studies are, therefore, warranted to assess the superiority of such a treatment in the knee OA population.

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