Radiologically Guided Versus Blinded Intra-articular Injection in Patients With Hip Osteoarthritis: A Retrospective Comparative Study

Clinical Medicine Insights: Arthritis and Musculoskeletal Disorders
Volume 15: 1–11

DOI: 10.1177/11795441221118920
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ABSTRACT

OBJECTIVES: The aim of this study was to present the clinical results of patients with Kellgren-Lawrence (KL) stage 2-4 hip osteoarthritis who were administered intra-articular corticosteroid (CS) or hyaluronic acid (HA), with or without fluoroscopy.

METHODS: This retrospective comparative study was conducted in the clinics where the authors worked between 2010 and 2018. Patients with stage 2-4 hip osteoarthritis according to KL criteria were included in the study. Age, body mass index, American Society of Anesthesiologists stages, and Western Ontario and McMaster Universities Arthritis Index (WOMAC) scores (3rd, 6th, and 12th months) were recorded. Two groups were created as patients who underwent injection with or without fluoroscopy guidance. In group 1, CS (triamnisolone) was administered, and in group 2, sodium hyaluronate 88 mg/4 mL was administered. Obtained parameters were compared.

RESULTS: The WOMAC scores at 3 months of both the CS and HA groups were statistically significantly better than before the application, with the improvement in the CS group found to be significantly better than in the HA group ($P = .047$). At 6 months, the mean WOMAC scores of the CS and HA groups were better than prior to the application, and there was a statistically significant difference ($P < .001$). No significant difference was found in either the CS or HA group in the comparison of 12-month WOMAC scores with the baseline scores ($P = .744$ and $P = .054$).

CONCLUSION: In symptomatic hip OA patients, intra-articular administration of CS and HA was seen to be effective at 3 and 6 months after administration. However, the effectiveness was determined to have disappeared within 1 year. Furthermore, in hip OA intra-articular drug applications, it was determined that the blinded technique without radiological guidance performed in the outpatient clinic is as effective and safe as the radiologically guided technique administered in the operating room.

KEYWORDS: Hip osteoarthritis, hyaluronic acid, corticosteroids, intra-articular injection, fluoroscopy

RECEIVED: March 20, 2022. **ACCEPTED:** July 21, 2022.

TYPE: Original Research Article

FUNDING: The author(s) received no financial support for the research, authorship, and/or publication of this article.

COMPETING INTERESTS: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Introduction

Osteoarthritis (OA) is the most common, serious joint disease that affects 1 in 3 individuals aged >65 years, more men than women, causing pain, physical restrictions, and permanent morbidity, and it ultimately diminishes quality of life.[1] The hip is the second most common large joint affected by OA, and the prevalence of hip OA ranges between 3% and 11% in Western populations aged >35 years.[2] Osteoarthritis is not just a simple "wear and tear" disease, but is a complex and destructive process involving all the structures of the joint mediated by inflammatory and metabolic factors.[3,4]

Chronic overloading on the joint, abnormal joint tissue metabolism, and impaired biomechanical surroundings lead to inflammation and destruction of the joint cartilage.[3,4] With the damage to cartilage, impairments occurring in other structures with rich innervation of the joint with subchondral bone and pain receptors mediate the formation of pain by sensitizing primary afferent nerves.[4,5] Within this process, structural problems involving the whole joint cause stiffness, swelling, and loss of movement.[3,5] Pain is the most evident symptom of OA, and it is probable that structural pathologies and individual perception of pain play a role in this. Symptoms associated with pain and other structural impairments start to affect daily activities by decreasing the functionality of the joint over time.[3,5]

Both pharmacological and non-operative treatment strategies such as intra-articular injection have traditionally aimed to reduce pain, stiffness, and physical disability.[6-8] In the literature, the intra-articular injections applied for hip OA have been reported to be usually corticosteroid (CS) and hyaluronic acid (HA).[7-9] In addition, there are new therapeutic agents such as platelet-rich plasma (PRP) and mesenchymal stem cells (MSC) which are promising as intra-articular injection treatment for hip OA. It has been reported that the combined use of PRP and HA could be clinically effective and safe in patients with OA.[10] In current guidelines, there is a strong recommendation for

intra-articular corticosteroid injection for patients with hip OA.[11] Although there is low evidence related to intra-articular HA treatment,[11] the chance of HA success can be increased in early radiological stages with the use of a single-injection regimen with a good application technique under imaging guidance.[12] Platelet-rich plasma and MSC injections are not yet recommended as the existing evidence is of low quality and formulations have not yet been standardized.[11,13]

Clinical experience has shown that CS is effective in the treatment of OA exacerbations, but does not alter the underlying process and may have some side effects.[6-9] By returning the elasticity and viscosity of synovial fluid to normal, an intra-articular HA injection can contribute to tissue regeneration by increasing protection, lubrication, and the shock-absorbing effect.[3-5,7-9] However, although intra-articular CS injections have been found to be useful in the short term in the treatment of hip OA, the effectiveness of HA compared with CS is controversial.[3-9]

Unlike the knee joint, access to the hip joint is quite difficult as a result of the anatomical features of the joint and the proximity of important structures, such as the surrounding neurovascular tissues.[6,14,15] Therefore, it has been recommended that injections are performed under fluoroscopy or ultrasound.,[6,8,14-18] Although most studies have shown a preference for fluoroscopy or ultrasonography-guided (USG) methods for hip joint injection, it has also been reported that it can be performed using anatomical landmarks and without any imaging.[19-21] However, there is no consensus on the hip injection technique (imaging-guided or anatomical reference) in relevant studies.[21,22] To the best of our knowledge, there is no study in the literature that has presented the clinical results of blind/anatomically referenced intra-articular hip injection in patients with hip OA and the clinical results of the application performed by fluoroscopic verification of needle localization.

For the above-stated reasons, the research questions of this study are as follows: (1) Is a blind/anatomically referenced intra-articular hip injection as effective and safe as the application performed with fluoroscopic verification of needle localization, in patients with hip OA? (2) Is intra-articular CS and HA application effective in symptomatic hip OA patients, and are the effects of CS and HA similar? Therefore, the primary aim of this study was to compare the clinical results of intra-articular CS and HA injections for hip OA treatment, and a secondary objective was to compare the results of intra-articular injection of the hip, with and without radiological guidance.

Patients and Methods

This retrospective comparative study was conducted in the clinics where the authors worked between 2010 and 2018. All patients were informed, their approval to use their medical data for scientific purposes was obtained, and Ethics Committee approval was received.

From patients who presented with hip pain, those who were diagnosed with hip OA according to the criteria of the American College of Rheumatology (ACR)[23] after physical, laboratory, and radiological examinations and who met the inclusion criteria were included in the study.

The study inclusion criteria were defined as the absence of benefit despite at least 3 months of conservative treatment, patients with weightbearing anteroposterior/lateral radiographs of the hip at stages 2-4 according to the Kellgren-Lawrence (KL) criteria,[24] and who had been followed up for at least 2 years.

Exclusion criteria: During systemic interrogation and physical examination, patients with a history of allergy who had used oral or intramuscular CS in the last 3 months, or those who had had an infectious, inflammatory, metabolic, or severe systemic disease, were excluded from the study.

The patient sample size for both groups in this study was calculated using G*Power software (Universities of Kiel, Dusseldorf and Mannheim). In the 2-way analysis at the level of at least 80% (1–β) power and type 1 error $\alpha = 0.05$, the number of patients per group was calculated to reach a statistically significant change at a moderate or high effect value in the Western Ontario and McMaster Universities Arthritis Index (WOMAC) score.[25] From a review of previous studies in literature related to effect size estimation, benefit was taken from the findings which would be consistent with comparative studies conducted with methodology close to or similar to that of the current study, and the effect size was calculated as 0.6 and 0.8, respectively.[26,27] To compensate for loss of power due to missing observations and/or patients lost to follow-up, the number of patients to be included was increased by 10%.[8,28] Finally, it was calculated that it was necessary to analyze the results of a minimum of 29 (26 + 10%) and a maximum of 50 (45 + 10%) patients per group.

The patients were retrospectively divided into 2 groups according to their hip treatment: A single dose of intra-articular CS triamnisolone was given to patients in group 1, and the patients in group 2 were administered 88 mg/4 mL moderately cross-linked, high-molecular-weight HA, sodium hyaluronate.

Post-injection immobilization was not required, but the patients were advised to avoid strenuous activities and mechanical stress on the hip joint. Various motion exercises were performed to the hip joint twice a day. The use of analgesic drugs was discontinued prior to the injection and the patients were not permitted to use drugs other than paracetamol during the follow-up period. Side effects and complications were recorded during intra-articular injections and follow-ups.

Age, body mass index (BMI), American Society of Anesthesiologists (ASA) stages, and WOMAC scores (3rd, 6th, and 12th months) were recorded.

Pain, stiffness, and functional evaluation of the patients were performed at the 3rd, 6th, and 12th months using the Turkish version of the WOMAC scores.[29] The WOMAC is a valid and reliable criterion specific to OA and includes 24 questions under 3 subheadings: pain, stiffness, and physical function. Each section score is calculated within itself, and the total score ranges between 0 and 100, with higher scores indicating an increase in pain and stiffness and a deterioration in physical function.[29,30] The Turkish version of the WOMAC

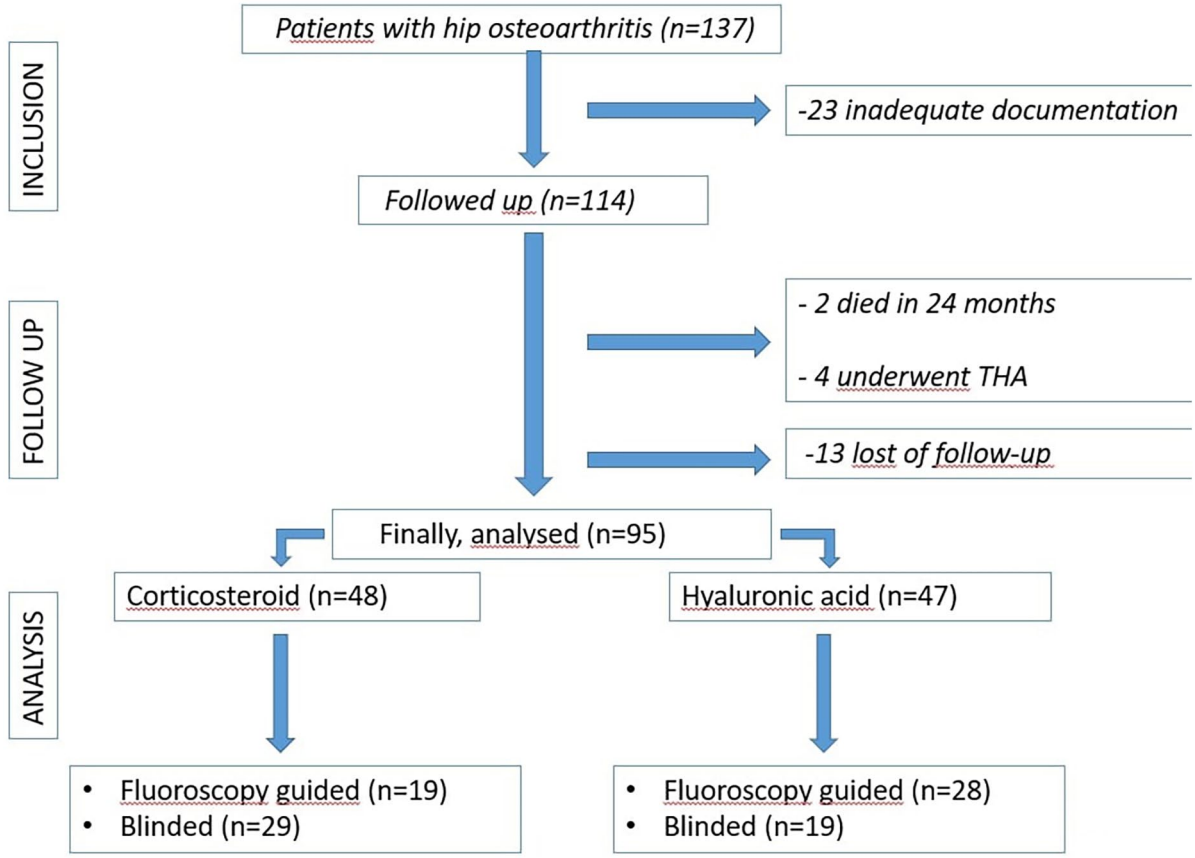

Figure 1. Flowchart of patients.

score is routinely used in our daily practice as it evaluates both pain and function, and therefore the researchers are familiar with this classification system.

Evaluation was made of the results of 48 cases with healthy data and regular follow-ups treated with cortisone and 47 cases treated with HA (flowchart, Figure1). To investigate the progression of hip OA, the radiographic stages of patients with at least 2 years of follow-up were compared in respect of the final visit radiographic grading and the initial radiographic grading pre-injection according to the KL criteria.[24] The KL criteria are routinely used in patients with OA because it is the most widely used classification for OA and has been reported to have higher validity, reliability, and interobserver consistency than other classifications.[31]

Hip intra-articular injection technique

Fluoroscopy-guided injection technique in the operating room. The patients were positioned supine on the operating table. The greater trochanter (GT) was palpated and marked 1 cm proximal to the midline. The skin was disinfected with an antiseptic solution and sterile draped (Figure 2). Local anesthesia was provided with 2% prilocaine, and the joint was imaged under fluoroscopy with a number 22 spinal needle from the marked point, targeting the femoral head-neck point, until the bone was felt. Once the bone was felt, the inner needle (chuck) was removed and pulled back enough to allow free flow by injecting saline (SF), confirming joint presence with the reflux technique (Figure 3) and/or by injection of 1 mL of contrast material. A successful attempt was demonstrated by visualizing the outline of the capsule on fluoroscopy (Figure 4). Finally, a single dose of 4 mL of HA was injected.

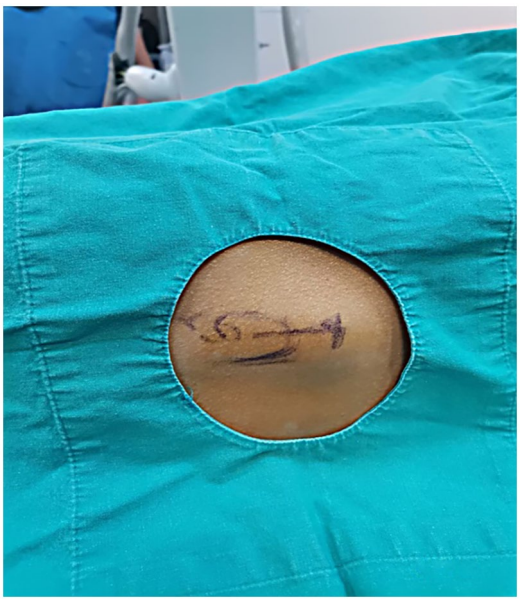

Figure 2. The patient was covered with a sterile drape and 1 cm proximal to the greater trochanter (GT) was marked.

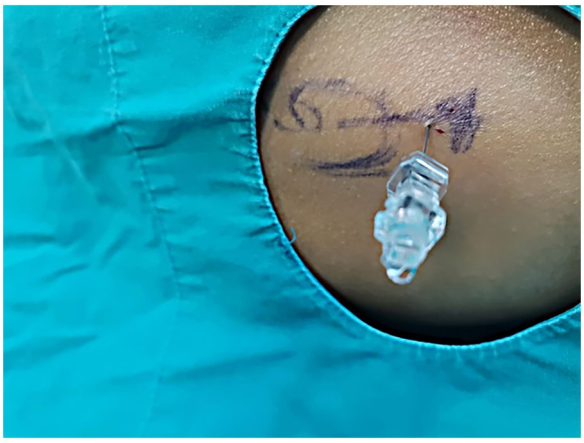

Figure 3. Observation of backflow.

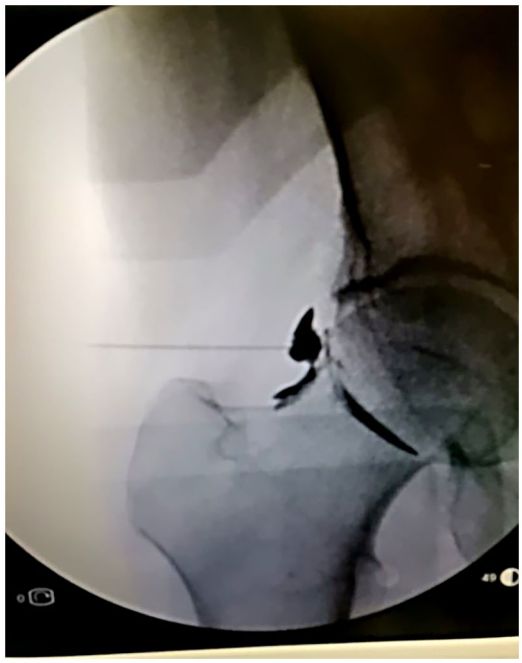

Figure 4. Confirmation of needle position in the joint with contrast agent injection.

Outpatient blinded non-radiological-guided injection technique. The patients were placed on a polyclinic examination table in a supine position. The intersection point was marked by the vertical line drawn from the medial to the distal (superior to inferior) of the spina iliaca anterior superior (SIAS), and the horizontal lines were drawn 1 cm distal of the GT (from lateral to medial) (Figure 5). After sterile draping of the patient, local anesthetic was infused into the entry point and subcutaneous tissues, where a no. 22 spinal needle was placed from anterior to posterior. When bone resistance was felt, the inner needle was removed and 1-2 mL of SF was injected. If there was considerable resistance at the beginning of the injection, SF reflux was observed by retracting a few millimeters (Figure 6). Subsequently, 40 mg of triamcinolone was injected into the hip joint.

The procedures followed were in accordance with the ethical standards of the committee responsible for human

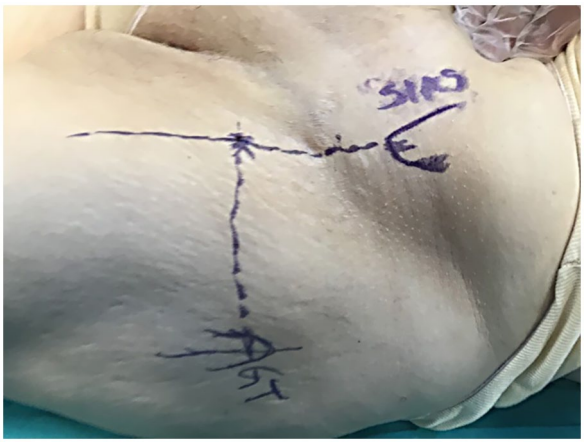

Figure 5. The junction of the vertical lines from spina iliaca anterior superior and the horizontal lines from greater trochanter are marked anteriorly.

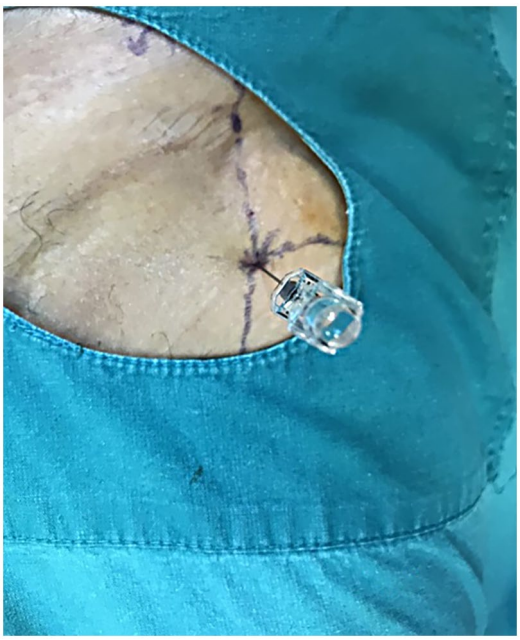

Figure 6. After the spinal needle was inserted from front to back and bone resistance was felt, the inner needle was removed, and backflow was observed by injecting 1 to 2 ml of saline (SF).
All figures submitted have been created by the authors, who confirm that the images are original with no duplication and have not been previously published in whole or in part.

experimentation and with the Helsinki Declaration of 1975, revised in 2000. This study was approved by the Local Ethical Research Institutional Review Board (Alanya Alaaddin Keykubat University Faculty of Medicine Clinical Research Ethics Committee, document date and number: 28.04.2021/08-02).

Statistical analysis

Statistical analysis of the data obtained was performed using the Statistical Package for Social Sciences software (SPSS). Continuous variables were expressed as mean ± standard deviation, and categorical variables as number (n) and percentage (%). The Kolmogorov-Smirnov test was used to test for normal

Table 1. Comparisons of the demographic data of the groups.

	GROUP-1 (N=48) (GLUCOCORTICOID) MEAN ± SD	GROUP-2 (N=47) (HYALURONIC ACID) MEAN ± SD	*P* VALUE
Age, y	64.54 ± 9.70	62.53 ± 13.43	.732*
BMI, kg/m²	26.93 ± 3.08	25.72 ± 2.44	.056*
ASA (stage)	2.17 ± 0.78	1.92 ± 1.04	.076*
Follow-up, mo	31.21 ± 4.42	29.62 ± 4.15	.087*
Gender	No. (%)	No. (%)	.292**
Female	21 (43.8)	15 (31.9)	
Male	27 (56.3)	32 (68.1)	
Side	No. (%)	No. (%)	.390**
Right	34 (70.8)	29 (61.7)	
Left	14 (29.2)	18 (38.3)	
Fluoroscopy-guided	No. (%)	No. (%)	.066**
+	19 (39.6)	28 (59.6)	
–	29 (60.4)	19 (40.4)	

ASA, American Society of Anesthesiologists; BMI, body mass index.
*Mann-Whitney *U* test.
**Pearson chi-square.

distribution. Data were compared between groups using the Mann-Whitney *U* test and the change between pre- and post-injection using the paired *t* test. A *P* value of <.05 was considered statistically significant.

Results

The mean age of the 95 patients whose results were evaluated was 63.55 ± 11.68 years and the mean follow-up period was 30.42 ± 4.34 months. The demographic data of the patients according to the groups are presented in Table 1. In the CS group (group 1), 19 of the 48 patients were administered intra-articular injection under fluoroscopy and 29 without fluoroscopy, and of the 47 patients in the HA group (group 2), the injection was performed in 28 with fluoroscopy and in 19 without fluoroscopy. The third-month WOMAC scores of both the CS and HA groups were statistically significantly better than before the application ($P<.001$ and $P<.001$, respectively; Table 2). The improvement in the third-month mean WOMAC scores was significantly greater in the CS group than in the HA group ($P=.047$; Table 3). The sixth-month WOMAC scores of the CS and HA groups were statistically significantly better than before the application ($P<.001$ and $P<.001$, respectively; Table 2). The mean sixth-month WOMAC scores were found to be significantly better in the HA group than in the CS group ($P=.042$; Table 3). No significant difference was found regarding the 12th-month WOMAC scores in either the CS or HA group compared with pre-application ($P=.744$ and $P=.054$, respectively; Table 2). There was no difference between the 2 groups regarding the 12th-month WOMAC scores ($P=.122$; Table 3).

Table 2. Comparisons of WOMAC results of the groups.

	MEAN ± SD	MEAN ± SD	*P* VALUE***
	First WOMAC	3rd-month WOMAC	
Group 1	67.94 ± 9.01	58.73 ± 7.95	.000
Group 2	71.64 ± 9.05	61.32 ± 5.75	.000
	First WOMAC	6th-month WOMAC	
Group 1	67.94 ± 9.01	60.92 ± 6.68	.000
Group 2	71.64 ± 9.05	63.55 ± 8.03	.000
	First WOMAC	12th-month WOMAC	
Group 1	67.94 ± 9.01	67.75 ± 8.96	.744
Group 2	71.64 ± 9.05	70.54 ± 7.28	.054
	First radiogram	Last radiogram	
Group 1	2.77 ± 0.69	2.94 ± 0.67	.019
Group 2	2.55 ± 0.58	2.72 ± 0.68	.010

WOMAC, Western Ontario and McMaster Universities Arthritis Index.
***Paired *t* test.

Considering that it might be more objective, the amount of improvement (difference in improvement obtained according

Table 3. Comparisons of the mean results of the groups.

	GROUP-1 (N = 48) (GLUCOCORTICOID) MEAN ± SD	GROUP-2 (N = 47) (HYALURONIC ACID) MEAN ± SD	*P* VALUE**
First WOMAC	67.94 ± 9.01	71.64 ± 9.05	.057
3rd-month WOMAC	58.73 ± 7.95	61.32 ± 5.75	.047
6th-month WOMAC	60.92 ± 6.68	63.55 ± 8.04	.042
12th-month WOMAC	67.75 ± 8.96	70.53 ± 7.28	.122
Improvement in WOMAC at 3 mo	9.21 ± 6.92	10.32 ± 6.49	.701
Improvement in WOMAC at 6 mo	7.03 ± 9.04	8.09 ± 9.72	.361
Improvement in WOMAC in 1 y	0.19 ± 3.95	1.11 ± 3.83	.160
First radiographic stage	2.77 ± 0.69	2.55 ± 0.58	.131
Last radiographic stage	2.94 ± 0.67	2.72 ± 0.68	.115

WOMAC, Western Ontario and McMaster Universities Arthritis Index.
Improvement in WOMAC: Mean difference between the pre-injection score and the score at 3, 6, and 12 months.
**Mann-Whitney *U* test.

to the pre-application WOMAC scores) at 3, 6, and 12 months was also compared, and no statistically significant difference was found between the groups ($P = .701$, $P = .361$, and $P = .160$, respectively; Table 2).

In the radiological follow-up for at least 2 years (mean: 30.42 ± 4.34 months), the OA stage at the final follow-up examination was determined to have increased significantly in both treatment groups compared with the initial state ($P = .019$ and $P = .010$, respectively; Table 2).

When the demographic and clinical results were compared according to whether the injection was performed under fluoroscopy or not, age, BMI, ASA, and follow-up time were found to be higher in those with injection under fluoroscopy, but not at a statistically significant level (Table 4). It should be stated that, prior to the injection applied without fluoroscopy in the outpatient clinic, this application had been performed on at least 10 patients under operating room conditions. No serious side effects and/or complications developed in any of the patients.

Discussion

The main results of this study demonstrated that patients benefit from both treatments, although the effect of cortisone was seen to be more pronounced in the third month and the effect of HA in the sixth month. It was also determined that the efficacy of both drugs disappeared over a period of 1 year. However, no significant difference was found between the results of the patients who were treated with or without fluoroscopy in the hip OA intra-articular drug applications. Finally, the secondary result of this study showed that the radiological stage of hip OA progressed significantly over an average follow-up period of 30 months.

Previous studies on CS and HA, which are generally accepted for intra-articular injection in hip OA, have indicated that CSs are useful in the short term in the intra-articular treatment of hip OA, but that the effectiveness of HA remains controversial.[3-9,16] In a recent systematic review and meta-analysis,[32] it was reported that intra-articular steroid therapy (IAST) was more effective in 3 months (12 weeks) of follow-up than placebo control, in relieving pain in the hips of OA patients diagnosed according to ACR criteria and radiologically staged using the KL classification. All the injections—ultrasound, fluoroscopy, and so on—in the studies included in that meta-analysis were performed under radiological guidance. Furthermore, WOMAC and Visual Analog Scale (VAS) were generally used as the evaluation criteria. In other studies, reporting intra-articular cortisone results for hip OA, Young et al[33] examined 118 patients who received a larger total volume by adding 40 mg of triamcinolone acetonide (TAC) and 2 mL of bupivacaine or 6 mL of sterile water under fluoroscopic guidance. After 3 months, the treated patients were evaluated according to the WOMAC scores, and the result was that the patients reported significantly reduced pain compared with baseline. Margules[34] reported that following a fluoroscopy-guided injection of 40 mg/mL TAC, 198 (38.8%) of the 510 patients still responded well 8 weeks after the injection. However, in a study by Walter et al,[35] intra-articular hip injection with 80/40 mg TAC (40 mg/mL) and 3/4 mL 0.5% ropivacaine was applied to 113 patients, and an insignificant improvement was observed in the patient-reported pain scores, during the 8-week follow-up period.

In the current study, the clinical results of patients treated with cortisone were significantly improved compared with prior to the injection. This effect was more pronounced in the third month.

Table 4. Comparisons of the demographic and clinical data according to fluoroscopy-guided or blinded application.

	FLUOROSCOPY-GUIDED (N=47) MEAN ± SD	BLINDED (N=48) MEAN ± SD	*P* VALUE
Age, y	65.15 ± 10.93	61.92 ± 12.29	.165*
BMI, kg/m^2	26.74 ± 3.22	25.91 ± 2.33	.104*
ASA (stage)	2.23 ± 0.97	1.85 ± 0.83	.052*
Follow-up, mo	31.29 ± 4.52	29.53 ± 4.01	.058*
First WOMAC	70.53 ± 9.66	69.02 ± 8.70	.475*
3rd-month WOMAC	60.09 ± 6.74	59.94 ± 7.38	.641*
6th-month WOMAC	63.51 ± 8.04	60.96 ± 6.69	.082*
12th-month WOMAC	69.49 ± 8.47	68.77 ± 8.10	.660*
Improvement in WOMAC at 3 mo	10.45 ± 7.09	9.08 ± 6.30	.248*
Improvement in WOMAC at 6 mo	7.02 ± 8.87	8.06 ± 9.85	.564*
Improvement in WOMAC at 12 mo	1.04 ± 3.41	0.25 ± 4.32	.779*
KL stage on first radiograph	2.68 ± 0.62	2.65 ± 0.67	.723*
KL stage on final radiograph	2.83 ± 0.67	2.83 ± 0.69	1.000*
Gender	No. (%)	No. (%)	.208**
Female	21 (44.7)	15 (31.2)	
Male	26 (55.3)	33 (68.8)	
Side	No. (%)	No. (%)	.829**
Right	32(68.1)	31(64.6%)	
Left	15(31.9)	17(35.4)	
Treatment	No. (%)	No. (%)	.066**
Glucocorticoid	19(40.4)	29 (60.4)	
Hyaluronic acid	28(59.6)	19 (39.6)	

ASA, American Society of Anesthesiologists; BMI, body mass index; KL, Kellgren-Lawrence.
**Mann-Whitney *U* test.
** Pearson chi-square.

Viscosupplementation (VS) with HA has been safely used for many years in hip OA treatment and is stated to be as effective as VS in the knee.[36] In recent systematic reviews, non-comparative studies have shown that HA can provide satisfactory pain reduction and functional improvement. However, there is insufficient evidence to determine whether it is superior to other forms of intra-articular injection.[37] Compared with placebos, the data show little evidence of its effectiveness up to 3 months and no difference at 6 months.[38] In a meta-analysis by Lieberman et al,[39] VS was seen to make a limited but significant improvement compared with the control group. The primary meta-analysis showed a statistically significant difference in VAS scores in OA treatment with HA injections. In a study of 183 patients (KL stages 1-3) applied with HA, Schiavi et al[40] evaluated the Harris Hip Score (HHS) and VAS scores at the first, second, third, and fourth years and stated that improvements compared with baseline were only significant in the first year. Conrozier et al[41] reported that single-dose HA treatment was easily applicable, safe, and well tolerated in daily clinical practice in a USG-guided study with a maximum of 6 months of follow-up, in which they included patients with KL stage 2-3 hip OA. Eyigör et al[17] evaluated the results of HA applied with a lateral approach under fluoroscopy in 21 patients with advanced hip OA and stated that the Lequesne index and VAS pain scores decreased statistically significantly compared with the initial values at the end of the first, third, and sixth months. Dallari et al[42] reported that the combination of PRP and HA in hip OA did not lead to a more significant improvement in pain symptoms.

Migliore et al[15] evaluated VAS pain scores, Lequesne index, and the use of non-steroidal anti-inflammatory drugs (NSAIDs) at 6 and 12 months in a study of symptomatic (KL stages 1-3) patients aged ⩾40 years, and the results supported the clinical efficacy and safety of a single injection of HA for managing symptoms in patients with hip OA. However, Richette et al[43] reported that single-dose HA was ineffective in treating hip OA symptoms when compared with placebos in a series of KL stage 2-3 patients, although that study only had a follow-up period of 3 months.

In the current study, the intra-articular treatment of single-dose HA was found to be effective in the third and sixth month of follow-up. Although studies of the results of multiple repetitive intra-articular injections in the intra-articular treatment of hip OA have also been published,[26,28] the current study was planned to evaluate a single intra-articular injection for a number of reasons. First, repeated injections can result in an increased risk of local side effects that can be difficult to manage in deep joints, such as the hip.[43] Second, the technical difficulty of the injection procedure involving the use of fluoroscopy guidance and so on may limit the number of injections and cause patient discomfort.[43] Third, promising results from previous studies have indicated the advantages of a single injection of HA for the treatment of hip OA.[15,36]

Comparing cortisone versus HA results for hip OA intra-articular therapy

In a recent systematic review of studies using cortisone and HA for hip OA, a limited number of studies directly compared the clinical effect between intra-articular CS and HA injections in hip OA, but the population type and application showed heterogeneity regarding number, HA formulation, and follow-up time. The analyzed studies had a short follow-up period. The results obtained seemed to demonstrate the superiority of glucocorticoid (GC) regarding pain management compared with HA, that is, the clinical response rate.[6] In a prospective randomized controlled double-blind study by Qvistgaard et al,[28] 101 patients with hip OA were applied with a USG-assisted single injection of 40 mg Depo-Medrol and 3 injections of hyalgan. The patients treated with CS experienced a significant improvement for 3 months after the intervention, and the effect size showed a moderate clinical effect. It was reported that although a similar significant result could not be shown following treatment with HA, the effect size showed a small clinical improvement. Spitzer et al[26] conducted a randomized double-blind study comparing Hylan GF 20 (2 injections) and methylprednisolone (single injection). The WOMAC A response rates at week 4 showed that GF 20 efficacy was higher in KL grade 3 patients and Hylan GF 20 and methylprednisolone acetate (MPA) were similar in KL grade 2 patients. Hylan G-F20 was seen to provide clinically significant improvements in pain and function, comparable to that of MPA, with good safety and tolerability. Therefore, it can be concluded that it is a viable option for treating hip OA.

Atchia et al[27] also reported that MPA activity was significant for up to 8 weeks regarding the WOMAC A and total scores determined in hyaluron (durolane) and methylprednisolone studies, and HA was not superior to MPA. The results of the current study showed that patients benefit from both treatments, although the effect of cortisone was more pronounced in the third month and the HA effect in the sixth month. However, the efficacy of both drugs was determined to have disappeared within a period of 1 year.

Overall, intra-articular injections can be considered safe when administered under ultrasound or fluoroscopic guidance, and most studies have preferred image-guided methods for hip joint injections.[6-8,34-36] However, ultrasound guidance for injection into hip joints is strongly recommended by the ACR.[11] In contrast, it has also been stated that intra-articular injection of the hip can be performed using anatomical landmarks without any imaging.[19-21,44,45] The SIAS and GT are generally used as the anatomical reference points.[7,19-22,44,45] However, there is no consensus on the hip injection technique (imaging-guided or anatomical references) in the relevant literature.[21,22] Notably, non-radiological hip injections may be inaccurate and pose a danger to nearby neurovascular structures and should be performed under an image intensifier, especially in patients with high BMI, severe arthritis, and flexion deformities.[21,22,44] Similarly, there may be some risks of injection, especially under USG guidance, and therefore the intervention should be made by a trained doctor to avoid adverse events. Ultrasonography-guided guidance should be preferred because of radiation exposure and lower costs.[7,36]

Schmidt-Braekling et al[45] retrospectively evaluated 369 intra-articular hip injections administered to 331 patients using anatomical landmarks to investigate the efficacy of non-radiologically guided hip injections. It was reported that hip injections using anatomical landmarks were an effective treatment option for patients with hip OA, and those who did not respond positively had a significantly higher BMI. Singh et al[22] administered an anterior hip joint injection to 87 patients (100 hips) with symptomatic hip OA using the junction of the femoral artery and inguinal ligament. Fluoroscopy and an arthrogram were used to verify the position of the needle during the application. It was concluded that hip injections can be performed with reasonable success without radiological guidance, and experienced surgeons can perform this procedure on patients with a normal BMI in outpatient clinics. In another study, Diçaroğlu et al[21] performed fluoroscopy and arthrography on 16 patients with KL stages 2-3 to confirm the positioning of the needle using a blind method. The rate of correct positioning was reported to be significantly higher with arthrography. Wixson et al[18] performed hip injections with anterior and lateral approaches under fluoroscopy guidance. Although the lateral approach was found to be more successful than the anterior approach (100% and 96.7%, respectively), there was more radiation exposure with the lateral approach.

In the current study, when the results of injections with or without fluoroscopy assistance were compared, age, BMI, ASA, and follow-up time were higher in the fluoroscopy-assisted patients, but not statistically significant. The lower BMI of patients without fluoroscopy may have affected the results because it has been stated that injections in patients with a high BMI should be performed under radiological guidance.[21,22,45] Moreover, before the injections without fluoroscopy performed in the outpatient clinic, this procedure had been applied to at least 10 patients under operating room conditions (including those whose results could not be evaluated here). This may also have played a role in the results as experience is known to be an important factor in this procedure.[22]

Some side effects and complications related to both GC and HA have been reported.[6] The most common side effects of steroids are post-injection exacerbation, infection, local fat atrophy, tendon rupture, and/or skin hyperpigmentation or hypopigmentation. Avascular necrosis of the femoral head, increased glucose levels, and suppression of the hypothalamic-pituitary-adrenal axis are rare and more serious complications. Mild side effects experienced with HA, such as post-injection transient allergic reactions, superficial itching, and headache, are well tolerated. Rarely, more serious side effects may include severe inflammatory reactions, pseudogout, and pseudosepsis. In this study, no side effects and/or complications developed in any of the patients whose results were evaluated.

Studies related to intra-articular injection for hip OA published between 1994 and 2005 had sample sizes ranging from 22 to 104. The shortest follow-up period in those studies was 3 months and the longest was 1 year.[14] Comparative studies related to the results of intra-articular injection for hip OA (HA vs corticosteroid, HA vs local anesthetic, HA vs PRP, HA vs saline, etc) which were published between 2005 and 2019 reported sample sizes of 19 to 357 patients and follow-up periods ranging from 1 month to 7 years.[15-22,26-28,37,41-43] From the research of literature, it was observed that generally sample size had not been calculated in retrospective studies of patients with hip OA.[17-22,35,45] In the current retrospective study, sample size was calculated. The sample size and follow-up period of the current study were seen to be consistent with the literature.

Limitations and strengths of the study

First, the retrospective study design can be considered as a limitation. Some results of this study differ from those in the literature, namely, HA effectiveness and the similarity of results of blind injection. However, studies in the literature are somewhat heterogeneous in many parameters, namely, in the formulation of the drugs used (low-molecular-weight or high-molecular-weight HA), different CSs (triamnisolone, methylprednisolone, etc), the follow-up times, results evaluation criteria (VAS, WOMAC, etc), injection frequency (single injection and multiple injections), different KL OA stages, control group, placebo or not, hip injection techniques (anterior and lateral), and radiological guidance method (USG, fluoroscope, etc). All these factors may limit a robust comparison of the current study with the literature. Nevertheless, given that it has not been studied in this way before, it can be considered that the clinical results of blind/anatomically referenced intra-articular hip injection in patients with hip OA and the clinical results of the application performed with fluoroscopic verification of the needle localization can contribute to the literature. Moreover, it was seen that hip OA deteriorated significantly in all patients during the average 30 months of radiological follow-up, which supports information that hip OA is progressive[46,47] and intra-articular injections administered cannot prevent progression.[3-9,16] Finally, exercise and physiotherapy are recommended in the treatment of hip OA because of the positive effect on pain and functions.[48] However, the effects of exercise were not evaluated in this study, and this could have affected the results.

Conclusion

In symptomatic hip OA patients, intra-articular administration of CS and HA is effective for 3 to 6 months, but the effect is lost within 1 year. Also, it was observed that these treatments could not prevent the progression of OA in an average of 30 months of radiological follow-up. Furthermore, with a certain amount of experience and in selected patients, a blinded technique without radiological guidance performed in the outpatient clinic is as effective and safe as the radiologically guided technique administered in the operating room for intra-articular drug administration in the treatment of hip OA.

Declarations

Ethics approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Alanya Alaaddin Keykubat University Faculty of Medicine Clinical Research Ethics Committee (document date and number: 28.04.2021/08-02). The procedures used in this study adhere to the tenets of the Declaration of Helsinki. Informed consent was obtained from all individual participants included in the study

Consent for publication

For publication of this article, written and verbal informed consent was obtained from the patient's that their medical data would be used to the scientific study.

Author Contributions

Surgical and medical practices – A.G., M.M.T., A.A.; Concept – A.A.; Design – A.A, A.G.; Data collection and/or processing – A.G., M.M.T.; Analysis and/or interpretation – M.M.T., A.A.; Literature search – M.M.T., A.G.; Writing – A.G., M.M.T., A.A.

Acknowledgements

None.

Availability of data and materials

The data underlying this article are available in the article.

REFERENCES

1. Hawker GA. Osteoarthritis is a serious disease. *Clin Exp Rheumatol*. 2019; 37:3-6.
2. Zhang W, Doherty M, Arden N, et al.; EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). EULAR evidence based recommendations for the management of hip osteoarthritis: report of a task force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). *Ann Rheum Dis*. 2005;64:669-681. doi:10.1136/ard.2004.028886
3. Katz JN, Arant KR, Loeser RF. Diagnosis and treatment of hip and knee osteoarthritis: a review. *JAMA*. 2021;325:568-578. doi:10.1001/jama.2020.22171
4. Abramoff B, Caldera FE. Osteoarthritis: pathology, diagnosis, and treatment options. *Med Clin North Am*. 2020;104:293-311. doi:10.1016/j.mcna.2019.10.007
5. Ayhan E, Kesmezacar H, Akgun I. Intraarticular injections (corticosteroid, hyaluronic acid, platelet rich plasma) for the knee osteoarthritis. *World J Orthop*. 2014;5:351-361. doi:10.5312/wjo.v5.i3.351
6. Vilabril F, Rocha-Melo J, Gonçalves JV, Vilaça-Costa J, Brito I. Hip osteoarthritis treatment with intra-articular injections: hyaluronic acid versus glucocorticoid—a systematic review. *Acta Reumatol Port*. 2020;45:127-136.
7. Chandrasekaran S, Lodhia P, Suarez-Ahedo C, Vemula SP, Martin TJ, Domb BG. Symposium: evidence for the use of intra-articular cortisone or hyaluronic acid injection in the hip. J Hip Preserv Surg. 2015;3:5-15. doi:10.1093/jhps/hnv020
8. Colen S, Van Den Bekerom MPJ, Bellemans J, Mulier M. Comparison of intra-articular injections of hyaluronic acid and corticosteroid in the treatment of osteoarthritis of the hip in comparison with intra-articular injections of bupivacaine. Design of a prospective, randomized, controlled study with blinding of the patients and outcome assessors. *BMC Musculoskelet Disord*. 2010;11:264. doi:10.1186/1471-2474-11-264
9. Rampal S, Jaiman A, Tokgöz MA, et al. A review of the efficacy of intraarticular hip injection for patients with hip osteoarthritis: to inject or not to inject in hip osteoarthritis? *Jt Dis Relat Surg*. 2022;33:255-262. doi:10.52312/jdrs.2022.402
10. Migliore A, Paoletta M, Moretti A, Liguori S, Iolascon G. The perspectives of intra-articular therapy in the management of osteoarthritis. *Expert Opin Drug Deliv*. 2020;17:1213-1226. doi:10.1080/17425247.2020.1783234
11. Kolasinski SL. American College of Rheumatology/Arthritis Foundation guideline for the management of osteoarthritis of the hand, hip, and knee. *Arthritis Rheumatol*. 2020;72:220-233. doi:10.1002/art.41142
12. Conrozier T, Raman R, Chevalier X, et al. Viscosupplementation for the treatment of osteoarthritis. The contribution of EUROVISCO Group. *Ther Adv Musculoskelet Dis*. 2021;13:1759720X211018605. doi:10.1177/1759720X211018605
13. Bannuru RR, Osani MC, Vaysbrot EE, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. *Osteoarthritis Cartilage*. 2019;27:1578-1589. doi:10.1016/j.joca.2019.06.011
14. Fernández López JC, Ruano-Ravina A. Efficacy and safety of intraarticular hyaluronic acid in the treatment of hip osteoarthritis: a systematic review. *Osteoarthritis Cartilage*. 2006;14:1306-1311. doi:10.1016/j.joca.2006.08.003
15. Migliore A, Frediani B, Gigliucci G, et al. Efficacy of a single intra-articular HYMOVIS ONE injection for managing symptomatic hip osteoarthritis: a 12-month follow-up retrospective analysis of the ANTIAGE register data. *Orthop Res Rev*. 2020;12:19-26. doi:10.2147/ORR.S239355
16. Liao YY, Lin T, Zhu HX, Shi MM, Yan SG. Intra-articular viscosupplementation for patients with hip osteoarthritis: a meta-analysis and systematic review. *Med Sci Monit*. 2019;25:6436-6445. doi:10.12659/MSM.916955
17. Eyigör C, Pirim A, Eyigör S, Uyar M. Efficacy of intraarticular hyaluronic acid injection through a lateral approach under fluoroscopic control for advanced hip osteoarthritis. *Agri*. 2010;22:139-144.
18. Wixson MC, Jamadar DA, Moser SE, Shuchman DN. Fluoroscopically Guided Lateral Approach Hip Injection. *Fed Pract*. 2019;36:300-305.
19. Ziv YB, Kardosh R, Debi R, Backstein D, Safir O, Kosashvili Y. An inexpensive and accurate method for hip injections without the use of imaging. *J Clin Rheumatol*. 2009;15:103-105. doi:10.1097/RHU.0b013e318190fa20
20. Mei-Dan O, McConkey MO, Petersen B, McCarty E, Moreira B, Young DA. The anterior approach for a non-image-guided intra-articular hip injection. *Arthroscopy*. 2013;29:1025-1033. doi:10.1016/j.arthro.2013.02.014
21. Diraçoğlu D, Alptekin K, Dikici F, Balci HI, Ozçakar L, Aksoy C. Evaluation of needle positioning during blind intra-articular hip injections for osteoarthritis: fluoroscopy versus arthrography. *Arch Phys Med Rehabil*. 2009;90:2112-2115. doi:10.1016/j.apmr.2009.08.137
22. Singh J, Khan WS, Marwah S, Wells G, Tannous DK, Sharma HK. Do we need radiological guidance for intra-articular hip injections? *Open Orthop J*. 2014;8:114-117. doi:10.2174/1874325001408010114
23. Altman R, Alarcón G, Appelrouth D, et al. The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hip. *Arthritis Rheum*. 1991;34:505-514. doi:10.1002/art.1780340502
24. Kellgren JH, Lawrence JS. Radiological assessment of osteoarthrosis. *Ann Rheum Dis*. 1957;16:494-502. doi:10.1136/ard.16.4.494
25. Campbell MJ, Julious SA, Altman DG. Estimating sample sizes for binary, ordered categorical, and continuous outcomes in two group comparisons. *BMJ*. 1995;311:1145-1148. doi:10.1136/bmj.311.7013.1145
26. Spitzer AI, Bockow BI, Brander VA, et al. Hylan G-F 20 improves hip osteoarthritis: a prospective, randomized study. *Phys Sportsmed*. 2010;38:35-47. doi:10.3810/psm.2010.06.1781
27. Atchia I, Kane D, Reed MR, Isaacs JD, Birrell F. Efficacy of a single ultrasound-guided injection for the treatment of hip osteoarthritis. *Ann Rheum Dis*. 2011;70:110-116. doi:10.1136/ard.2009.127183
28. Qvistgaard E, Christensen R, Torp-Pedersen S, Bliddal H. Intra-articular treatment of hip osteoarthritis: a randomized trial of hyaluronic acid, corticosteroid, and isotonic saline. *Osteoarthritis Cartilage*. 2006;14:163-170. doi:10.1016/j.joca.2005.09.007
29. Tüzün EH, Eker L, Aytar A, Daşkapan A, Bayramoğlu M. Acceptability, reliability, validity and responsiveness of the Turkish version of WOMAC osteoarthritis index. *Osteoarthritis Cartilage*. 2005;13:28-33. doi:10.1016/j.joca.2004.10.010
30. Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. *J Rheumatol*. 1988;15:1833-1840.
31. Kovalenko B, Bremjit P, Fernando N. Classifications in brief: Tönnis classification of hip osteoarthritis. *Clin Orthop Relat Res*. 2018;476:1680-1684. doi:10.1097/01.blo.0000534679.75870.5f
32. Zhong HM, Zhao GF, Lin T, et al. Intra-articular steroid injection for patients with hip osteoarthritis: a systematic review and meta-analysis. *Biomed Res Int*. 2020;2020:6320154. doi:10.1155/2020/6320154
33. Young R, Harding J, Kingsly A, Bradley M. Therapeutic hip injections: is the injection volume important? *Clin Radiol*. 2012;67:55-60. doi:10.1016/j.crad.2011.07.040
34. Margules KR. Fluoroscopically directed steroid instillation in the treatment of hip osteoarthritis: safety and efficacy in 510 cases. *Arthritis Rheum*. 2001;44:2449-2450; author reply 2455. doi:10.1002/1529-0131(200110)44:10<2449:
35. Walter WR, Bearison C, Slover JD, Gold HT, Gyftopoulos S. Clinical and patient-reported outcomes after image-guided intra-articular therapeutic hip injections for osteoarthritis-related hip pain: a retrospective study. *Skeletal Radiol*. 2019;48:713-719. doi:10.1007/s00256-018-3113-3
36. Mulvaney SW. A review of viscosupplementation for osteoarthritis of the hip and a description of an ultrasound-guided hip injection technique. *Curr Sports Med Rep*. 2009;8:291-294. doi:10.1249/JSR.0b013e3181c2212f
37. Acuña AJ, Samuel LT, Jeong SH, Emara AK, Kamath AF. Viscosupplementation for hip osteoarthritis: does systematic review of patient-reported outcome measures support use? *J Orthop*. 2020;21:137-149. doi:10.1016/j.jor.2020.03.016
38. Leite VF, Daud Amadera JE, Buehler AM. Viscosupplementation for hip osteoarthritis: a systematic review and meta-analysis of the efficacy on pain and disability, and the occurrence of adverse events. *Arch Phys Med Rehabil*. 2018;99:574-583. doi:10.1016/j.apmr.2017.07.010
39. Lieberman JR, Engstrom SM, Solovyova O, Au C, Grady JJ. Is intra-articular hyaluronic acid effective in treating osteoarthritis of the hip joint? *J Arthroplasty*. 2015;30:507-511. doi:10.1016/j.arth.2013.10.019
40. Schiavi P, Calderazzi F, Pedrini MF, Tacci F, Vaienti E, Pogliacomi F. Efficacy and safety of viscosupplementation with hyaluronic acid for hip osteoarthritis: results from a cross-sectional study with a minimum follow-up of 4 years. *Acta Biomed*. 2020;91:e2020032. doi:10.23750/abm.v91i14-S.11110
41. Conrozier T, Couris CM, Mathieu P, et al. Safety, efficacy and predictive factors of efficacy of a single intra-articular injection of non-animal-stabilized-hyaluronic-acid in the hip joint: results of a standardized follow-up of patients treated for hip osteoarthritis in daily practice. *Arch Orthop Trauma Surg*. 2009;129:843-848. doi:10.1007/s00402-008-0778-4
42. Dallari D, Stagni C, Rani N, et al. Ultrasound-guided injection of platelet-rich plasma and hyaluronic acid, separately and in combination, for hip osteoarthritis: a randomized controlled study. *Am J Sports Med*. 2016;44:664-671. doi:10.1177/0363546515620383
43. Richette P, Ravaud P, Conrozier T, et al. Effect of hyaluronic acid in symptomatic hip osteoarthritis: a multicenter, randomized, placebo-controlled trial. *Arthritis Rheum*. 2009;60:824-830. doi:10.1002/art.24301

44. Kurup H, Ward P. Do we need radiological guidance for hip joint injections? *Acta Orthop Belg*. 2010;76:205-207.
45. Schmidt-Braekling T, Waldstein W, Renner L, Valle AG, Bou Monsef J, Boettner F. Ultrasound and fluoroscopy are unnecessary for injections into the arthritic hip. *Int Orthop*. 2015;39:1495-1497. doi:10.1007/s00264-014-2648-8
46. Kijowski R, Demehri S, Roemer F, Guermazi A. Osteoarthritis year in review 2019: imaging. *Osteoarthritis Cartilage*. 2020;28:285-295. doi:10.1016/j.joca.2019.11.009
47. Teirlinck CH, Dorleijn DMJ, Bos PK, Rijkels-Otters JBM, Bierma-Zeinstra SMA, Luijsterburg PAJ. Prognostic factors for progression of osteoarthritis of the hip: a systematic review. *Arthritis Res Ther*. 2019;21:192. doi:10.1186/s13075-019-1969-9
48. Hurley M, Dickson K, Hallett R, et al. Exercise interventions and patient beliefs for people with hip, knee or hip and knee osteoarthritis: a mixed methods review. *Cochrane Database Syst Rev*. 2018;4:CD010842. doi:10.1002/14651858.CD010842.pub2