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SCIENTIFIC ARTICLE

Are patients more likely to have hip osteoarthritis progression and femoral head collapse after hip steroid/anesthetic injections? A retrospective observational study

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Abstract

Objective To evaluate progression of osteoarthritis and femoral head articular surface collapse in hip steroid/anesthetic injection patients (HIPs).

Materials and methods This study was IRB-approved and HIPAA-compliant. Two musculoskeletal radiologists performed retrospective, blinded reviews of radiography for 70 HIPs (40 mg triamcinolone/4 mL 0.5% preservative-free ropivacaine) with a 3- to 10-month follow-up and two control groups: demographic-matched patients with similar hip radiograph follow-up duration but no injection; and glenohumeral joint injection patients. Discordant evaluations were adjudicated by a third, senior reader. Groups were compared using Fisher's exact and unpaired *t* tests.

Results There were 70 HIPs (mean age 67 ± 17 (range 19–92) years; 44 women, 26 men), who were followed for a mean of 6 ± 2 (3–12) months. Thirty-one (31 out of 70, 44%) of HIPs had progression of osteoarthritis after injection, versus 17 out of 70 (24%) of hip controls (HCs) and 13 out of 44 (30%) of glenohumeral injection patients (GIPs). This difference between HIPs and HCs was statistically significant ($p = 0.02$) but not that between HIPs and GIPs (0.17). Twelve (12 out of 70, 17%) HIPs had new collapse, compared with 1 out of 70 (1%) of HCs and 1 out of 44 (2%) of GIPs. This difference was statistically significant (HCs: $p = 0.002$; GIPs: $p = 0.02$).

Conclusion Hip steroid/anesthetic injection patients are more likely to demonstrate osteoarthritis progression and femoral head collapse than HC and GIPs in the injected joint 3–12 months after steroid and anesthetic injection. Further evaluation of hip injectates and the injection population is warranted.

Keywords Osteoarthritis · Steroid · Anesthetic · Injection

Introduction

Osteoarthritis is a debilitating disease of synovial joints and the most common cause of disability in the USA, affecting more than one-third of persons older than 65 years [1–3]. Although osteoarthritis is primarily degenerative, inflammation is postulated to play a role in at least some stages of disease development, and therefore intra-articular steroid injections have been used to manage osteoarthritis pain with some success, particularly in the short term (< 6 months) [3–8]. Intra-articular steroids have also been shown to decrease expression of inflammatory factors in traumatized joints of animal models [9]. However, there have been case reports on intra-articular hip steroid injections suggesting progression of osteoarthritis or the development of osteonecrosis. Yamamoto et al. described a woman with a normal MRI 1 week prior to hip steroid injection, who demonstrated rapid progression of osteoarthritis and collapse of the femoral head 3 months after the injection [10]. However, this association has not been systematically studied. The purpose of this study was to evaluate osteoarthritis progression and femoral head articular surface collapse in hip steroid/anesthetic injection patients. Our hypothesis was that these complications are more likely in hip injection patients than in control patients who did not receive an intra-articular steroid injection or patients who received steroid/anesthetic injections in their

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glenohumeral joint, another large joint with a comparable volume that is not weight-bearing.

Materials and methods

Patient cohort

A retrospective query of all hip steroid/anesthetic injections performed in two fluoroscopy suites (Siemens, Model Axiom Artis DMP, Malvern, PA and General Electric, Innova 4100, Chicago, IL, USA) in a single radiology department from 1 April 2014 to 31 March 2015 yielded 608 hip injections. All patients had previously been evaluated by a physician (Orthopedics or Primary Care) for their hip pain and were referred to the radiology department for an injection. All hip injections were performed under fluoroscopic guidance, targeting the lateral femoral head–neck junction with confirmation of intra-articular needle tip placement by injection of contrast medium (0.1–0.5 mL, iopamidol, trade name Isovue-M-300; Bracco Diagnostics, East Princeton, NJ, USA. The injectate consisted of 40 mg of triamcinolone (trade name Kenalog; Bristol-Myers Squibb Company, Princeton, NJ, USA) and 4 mL of preservative-free ropivacaine HCl 0.5% (trade name Naropin; Fresenius Kabi USA, Lake Zurich, IL, USA). Inclusion criteria were hip radiograph within 6 months before the injection and follow-up radiograph 3–12 months after the injection. Based on these criteria, 507 patients without adequate follow-up radiographs and 31 patients without pre-injection radiographs were excluded. In total, 70 patients were included in the hip injection group.

A hip control group (hips with similar duration of follow-up radiographs but without steroid injections) was identified using age- (within 5 years) and gender-matched hip radiographs performed at our institution from 1 April 2014 to 31 March 2015 with initial and 3- to 12-month follow-up radiographs. In total, 70 patients were included in the hip control group.

To study whether steroid/anesthetic injection complications affect all types of joints, a shoulder control group (glenohumeral steroid injections with 3- to 12-month follow-up radiograph) was identified using the same inclusion and exclusion criteria, except that a fluoroscopic anterior–posterior image of the shoulder before contrast medium injection from the procedure images was accepted as a substitute for a pre-injection radiograph, if a pre-injection radiograph was not available. Shoulders were selected for this control injection group because: 1, like hip joints, shoulders are also a large joint and receive the same volume and concentration of steroid/anesthetic injection mixture as hip joints; 2, unlike hip joints, shoulders are not weight-bearing; and 3, shoulder injections are a relatively common injection in our clinical practice. During the study period, 438 glenohumeral injections were performed. All shoulder injections were performed under fluoroscopic guidance from an anterior rotator interval approach targeting the medial aspect of the humeral head with confirmation of intra-articular needle tip placement by injection of contrast (iopamidol, 0.1–0.5 mL). The injectate was the same as in hip injections (40 mg triamcinolone, 4 mL 0.5% ropivacaine HCl 0.5%). Three hundred and ninety-four patients were excluded because there were no follow-up radiographs. In total, 44 injections were included.

The medical records of all subjects were reviewed. For each patient, the body mass index (BMI) was recorded for all subjects, given the known positive association between BMI and osteoarthritis [11]. For each hip injection and hip control patient, the patient's femoral neck T-score was recorded, if dual energy X-ray absorptiometry (DXA) was performed within 2 years of the initial evaluation time point, given the reported associated between osteoporosis and femoral head collapse secondary to subchondral fracture and osteonecrosis [12–14].

Image interpretation

All images were reviewed on a Picture Archiving and Communication System (PACS) workstation (Osirix software, v5; Pixmeo, Bernex, Switzerland) independently by two musculoskeletal radiologists with 6 and 5 years of experience (CYC and FJS). Discrepant reads were adjudicated by a third reader with >10 years of experience (MAB).

Radiographs of the hip and shoulder were evaluated for degree of osteoarthritis and classified into three categories, using an adaptation of the Kellgren–Lawrence (KL) grading system for the diagnosis of radiographic osteoarthritis [13]:

> Grade 1, normal/mild—doubtful or mild joint space narrowing with possible osteophytic lipping (in correspondence to KL grade 1; Fig. 1a)
> Grade 2, moderate—definite joint space narrowing and osteophytes, with or without sclerosis (KL grades 2 and 3; Fig. 1b)
> Grade 3, severe: marked joint space narrowing, including bone-on-bone appearance, with osteophytes and sclerosis (KL grade 4; Fig. 1c)

To minimize observation bias, computer-generated randomization was performed using open source software (Urbaniak, G. C., Plous, S. Research Randomizer, version 4.0., 2013). All radiographs (pre- and post-injection) were anonymized and randomly allocated into a single list using simple randomization. A numeric code was attributed to each examination, later used to decipher the

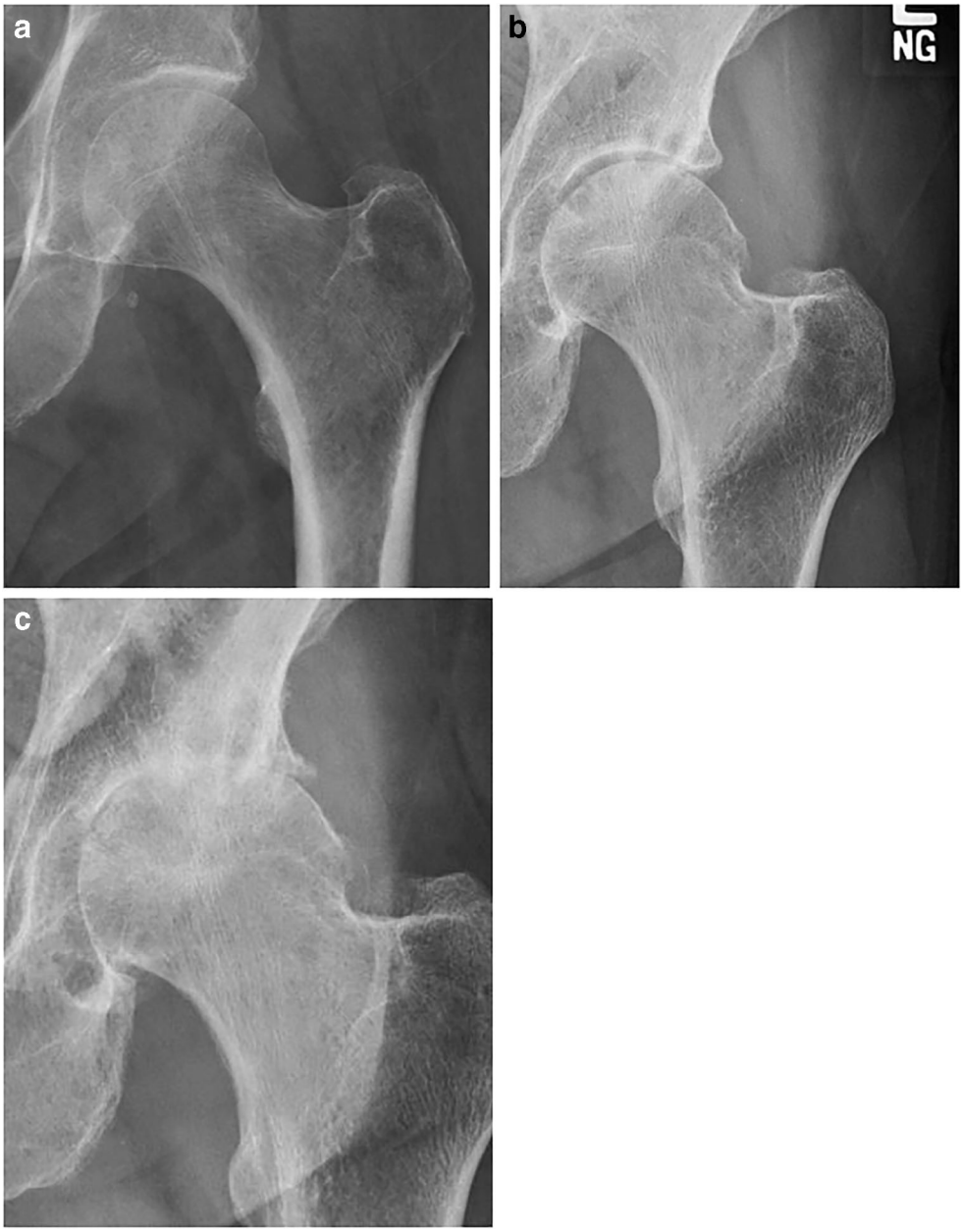

Fig. 1 Radiographs of the left hip illustrating the three grades of osteoarthritis used by the readers. **a** Grade 1 is defined as doubtful or mild joint space narrowing with possible osteophytic lipping; **b** Grade 2 is defined as definite joint space narrowing and osteophytes, with or without sclerosis; and **c** Grade 3 is defined as marked joint space narrowing, including bone-on-bone appearance, with osteophytes and sclerosis

randomized sequence once imaging analysis was concluded. Both randomization and deciphering processes were conducted by a fourth investigator (JRTV), who was not involved in imaging interpretation, to ensure proper blinding.

All readers evaluated each time point separately. For the hip injection and hip control patients, all readers were blinded to whether the patient had received an injection. For the hip injection and shoulder injection patients, all readers were also blinded to whether the time point was before or after the injection. Although the KL system is not sensitive to change, a blinded, individual timepoint evaluation was chosen over evaluating the two timepoints side by side to minimize observational bias. As the investigators knew the study aim, comparing the radiographs side by side for each patient may incline the investigator to report change.

Hip and shoulder radiographs were also evaluated for the presence of femoral/humeral head collapse, defined as loss of the normal spherical shape of the articulating surface with or without a subchondral lucent line (Fig. 2) [15, 16]. Presence of collapse was documented as a binary numerical value (0 = absent, 1 = present).

After collecting all the data, differences between the numerical ratings of osteoarthritis and collapse before and after the injection were calculated. Progression of osteoarthritis and new collapse were defined as any positive value (≥ 1).

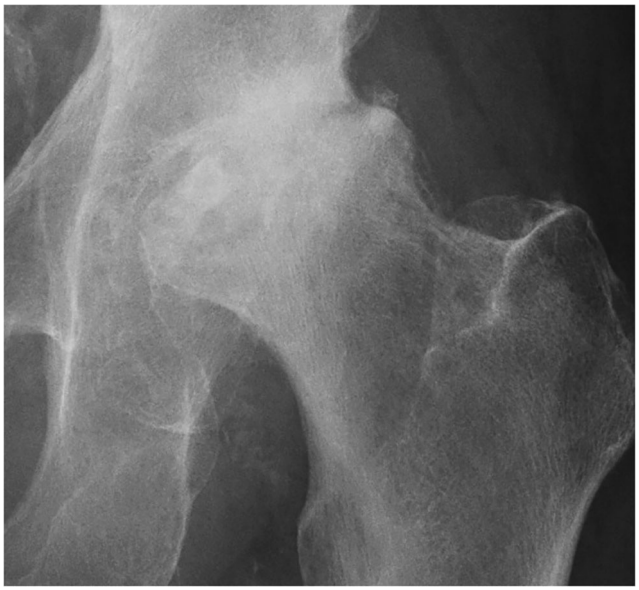

Fig. 2 Radiographs of the left hip demonstrating femoral head collapse, defined as loss of the normal spherical shape of the articulating surface with or without a subchondral lucent line

Statistical analysis

Statistical analysis was performed using JMP (version 12 Pro; SAS Institute, Cary, NC, USA). $P < 0.05$ was considered statistically significant. Two-tailed Fisher's exact test was used to compare the following variables: patient gender, femoral neck DXA T-score, severity of osteoarthritis before injection, and number of patients with collapse before injection. Unpaired *t* test was used to compare the following variables: time interval between radiographs, patient age, BMI, and femoral neck DXA T-score. $p < 0.05$ was considered statistically significant.

Inter-reader reproducibility was assessed using intraclass correlation coefficient (ICC) with 95% confidence interval (CI; MedCalc Statistical Software version 17.9.7; MedCalc, Ostend, Belgium).

Results

Patient cohort

The patient demographic information for the hip injection, hip control, and shoulder injection groups are detailed in Table 1. There were no significant differences between the groups in terms of, age, gender, BMI, DXA T-score, pre-injection severity of osteoarthritis, follow-up time, and number of patients with collapse before injection ($p > 0.05$). The hip injection patients underwent more

Table 1 Patient demographics and other characteristics for hip injection, hip control, and shoulder injection control groups

	Hip injection (A)	Hip control (B)	Shoulder injection control (C)	*p* (A vs B)	*p* (A vs C)
Number	70	70	44		
Duration between radiographic time points (months), mean ± SD (range)	6 ± 2 (3–12)	6 ± 2 (3–9)	6 ± 3 (3–12)	0.27	0.42
Age, mean ± SD (range)	67 ± 17 (19–92)	68 ± 13 (24–93)	65 ± 14 (32–95)	0.70	0.51
Gender, *n* (%)				1.0000	1.0000
Males	26 (37)	25 (36)	17 (39)		
Females	44 (63)	45 (64)	27 (61)		
Side				0.30	0.05
Left	24 (34)	31 (44)	24 (55)		
Right	46 (66)	39 (56)	20 (45)		
BMI	29 ± 6 (19–51)	29 ± 6 (18–44)	30 ± 7 (19–45)	0.90	0.69
Femoral neck DXA T-score, *n* (%) and mean ± SD (range)	29 (41) −1.0 ± 1.3 (−3 to 2.5)	25 (36) −1.0 ± 1.0 (−2.5 to 1.2)	N/A	0.93	N/A
Normal (T-score > −1)	13 (45)	13 (52)			
Osteopenia (T-score = −1 to −2.5)	10 (34)	10 (40)			
Osteoporosis (T-score ≤ −2.5)	6 (21)	2 (8)			
Pre-injection severity of osteoarthritis				0.25	0.38
None/mild	26	19	12		
Moderate	32	42	20		
Severe	12	9	12		
Pre-injection collapse	2	6	2	0.27	0.64

Table 2 Adjudicated results of hip injection patients versus hip control (no injection) and shoulder injection groups

	Hip injection (A), *n* (%)	Hip control (B), *n* (%)	Shoulder injection (C), *n* (%)	*p* (A vs B)	*p* (A vs C)
Increased osteoarthritis	31/70 (44)	17/70 (24)	13/44 (30)	0.02	0.17
New collapse	12/70 (17)	1/70 (1)	1/44 (2)	0.002	0.02

right-sided injections (66%), the shoulder injection patients had more left-sided injections (55%), and this difference approached statistical significance ($p = 0.05$).

Femoral neck DXA T-score was available for 29 out of 70 (41%) hip injection and 25 out of 70 (36%) hip control patients.

Image interpretation

The results of the blinded and adjudicated image interpretation are detailed in Table 2. The hip injection group had more patients with progression of osteoarthritis (44%) than both the hip control (24%) and the shoulder injection (30%) groups (Figs. 3, 4). This difference was statistically significant for the comparison between the hip injection and hip control groups ($P = 0.02$), but not for the comparison between the hip injection and shoulder injection groups ($p = 0.17$). The hip injection group also had more patients with new collapse (17%) than both the hip control (1%) and the shoulder injection (2%) groups, and this difference was statistically significant ($p = 0.0012$ and 0.02 respectively; Fig. 5). Source data obtained by Readers 1 and 2 prior to adjudication are available in the Appendix.

Of the hip injection patients with DXA T-scores, 13 out of 29 (45%) had normal T-scores (≥ -1), 10 out of 29

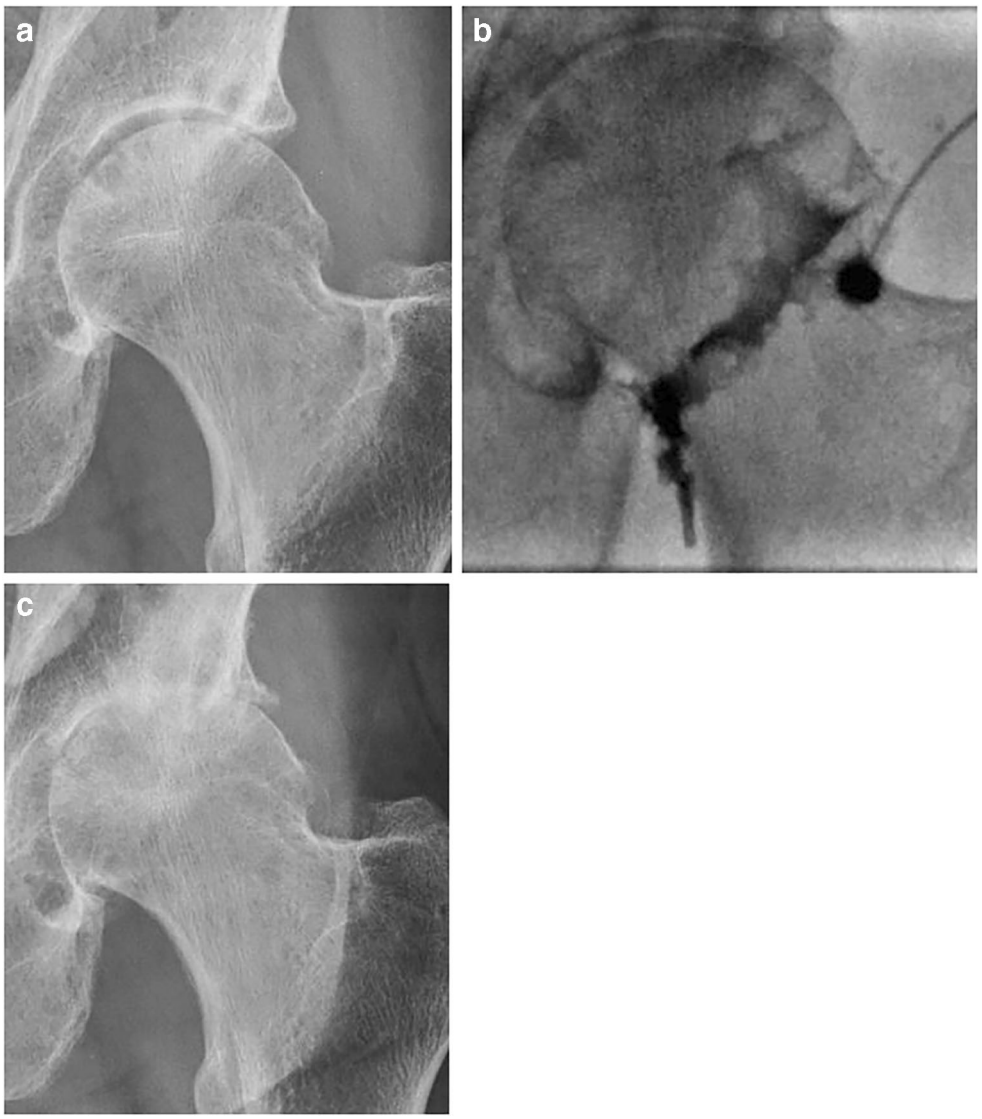

Fig. 3 A 58-year-old woman with left hip pain. **a** Frontal radiograph of the left hip 4 months before the injection demonstrates moderate joint space narrowing, bony proliferation, and subchondral cysts (grade 2 osteoarthritis). **b** Fluoroscopic image of the left hip demonstrates left hip injection. Kenalog 40 mg/mL 1 mL and ropivacaine 0.5% 4 mL were injected. **c** Frontal radiograph of the left hip 3 months after the injection demonstrates progressive, severe joint narrowing and subchondral sclerosis (grade 3 osteoarthritis). There is no femoral head collapse

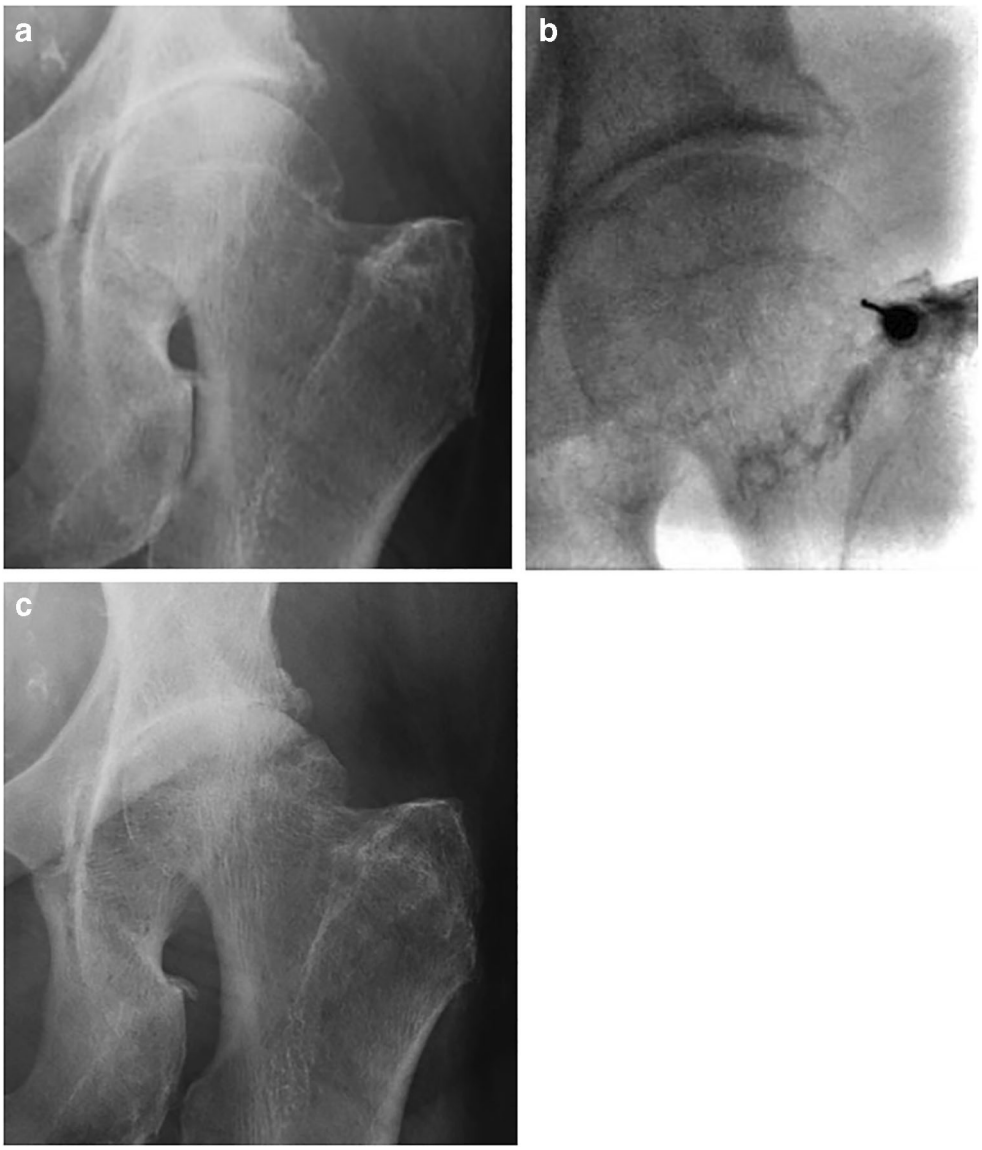

Fig. 4 A 56-year-old woman with left hip pain. **a** Frontal radiograph of the left hip 3 weeks before the injection demonstrates moderate joint space narrowing and bony proliferation (grade 2 osteoarthritis). **b** Fluoroscopic image of the left hip demonstrates left hip injection. Kenalog 40 mg/mL 1 mL and ropivacaine 0.5% 4 mL were injected. **c** Frontal radiograph of the left hip 5 months after the injection demonstrates progressive, severe joint narrowing and sclerosis of the femoral head (grade 3 osteoarthritis). There is no femoral head collapse

(34%) had osteopenia (T-score between −1 and − 2.5), and 6 out of 29 (21%) had osteoporosis (T-score ≤ −2.5; Table 1). None of the patients with normal T-scores developed new femoral head collapse, 3 out of 10 (30%) of the osteopenic patients developed new femoral head collapse, and 2 out of 6 (33%) of the osteoporotic patients developed new femoral head collapse. Of the hip control patients with DXA scores, 13 out of 25 (52%) had normal T-scores, 10 out of 25 (40%) had osteopenia, and 2 out of 25 (8%) had osteoporosis (Table 1). None of these patients developed new femoral head collapse.

Inter-rater agreement for osteoarthritis and collapse is detailed in Table 3. The κ values were 0.87 for osteoarthritis and 0.90 for femoral head collapse.

Discussion

In our study, patients who underwent steroid/anesthetic hip injections had a higher rate of osteoarthritis progression and development of femoral head collapse than patients with hip pain who did not receive an injection and patients who underwent shoulder injections.

Although we have shown an association between these events, the true relationship remains unknown as association does not always reflect causation. Hollander et al., an early pioneer of the use of intra-articular steroid injections to treat inflammatory arthritis, expressed concern for juxta-articular osteoporosis as a potential side-effect of these injections [17, 18]. Ostergaard and Halberg proposed severe juxta-articular

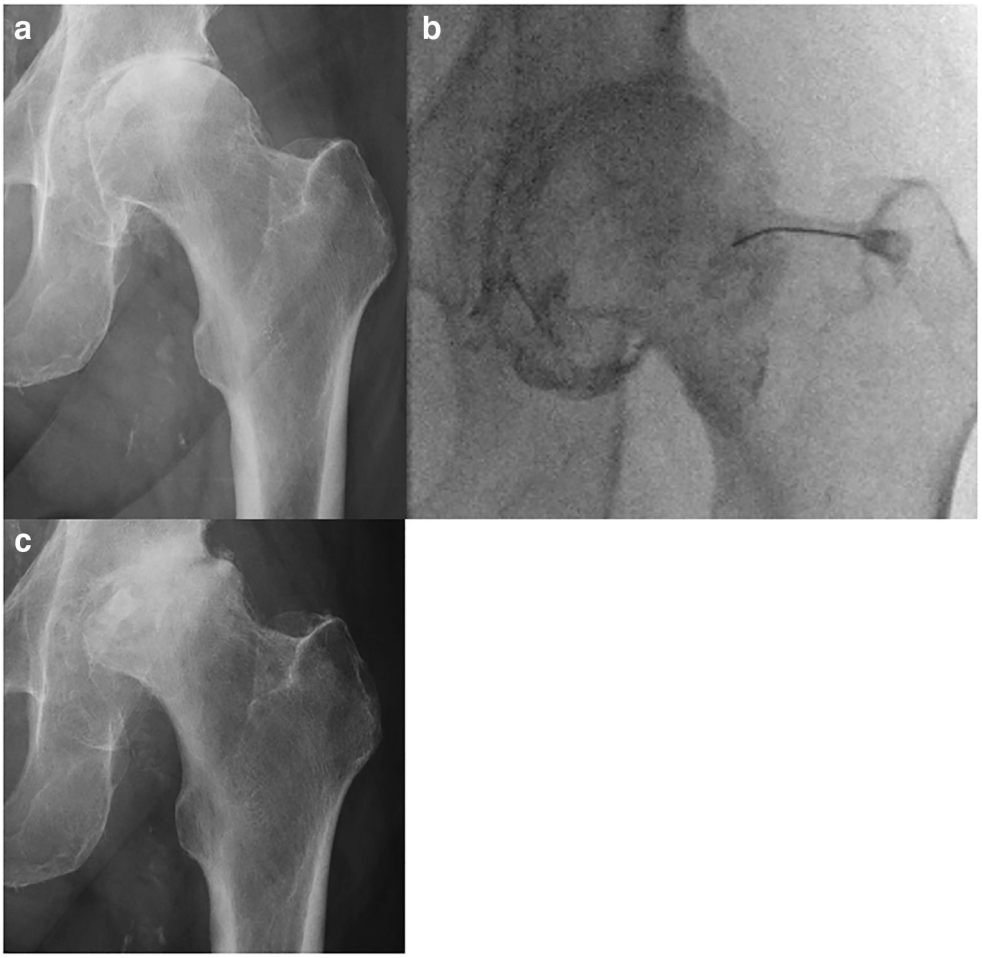

Fig. 5 A 77-year-old man with left hip pain. **a** Frontal radiograph of the left hip 2 weeks before the injection demonstrates severe joint space narrowing and subchondral sclerosis (grade 3 osteoarthritis). **b** Fluoroscopic image of the left hip demonstrates left hip injection. Kenalog 40 mg/mL 1 mL and ropivacaine 0.5% 4 mL were injected. **c** Frontal radiograph of the left hip 6 months after the injection demonstrates progressive, severe joint narrowing and collapse of the femoral head

osteoporosis as a relative contraindication for intra-articular injection, because of the risk for osteoarthritis progression [19]. However, there are no known published reports that support either hypothesis. Of note, a recent clinical trial randomizing osteoarthritis patients to steroid or saline knee injections every 3 months did show slightly greater cartilage loss (0.21 mm lost in the steroid injection group versus 0.1 mm of cartilage lost in the saline injection group) [3].

Although humeral osteonecrosis has also been observed in rheumatological patients receiving oral steroids, the rate of new osteonecrosis in shoulder injection patients was low [20]. This result suggests that the effects of steroid on the femoral head may be different than that on other articulating bones. The pathogenesis of steroid-induced osteonecrosis is multifactorial, including decreasing osteoblasts, prolonging osteoclast lifespan, osteocyte apoptosis, and an increase in marrow fat leading to decreased bone perfusion [21–26]. One possibility is that the hip joint is weight-bearing, whereas shoulders are not, making the femoral head more susceptible to fracture as a secondary effect of these mechanisms.

Table 3 Inter-rater agreement (κ) for reader 1 and reader 2

	κ (95% confidence interval)
Osteoarthritis	0.87 (0.85–0.90)
Femoral head collapse	0.90 (0.88–0.92)

The most concerning explanation for our findings would be that the injected contrast medium, steroid, and/or anesthetic are directly causing the outcome. In considering this possibility, however, we must carefully examine the exact contents of the injectates, which contain stabilizing agents and preservatives, in addition to considering potential interactions between combined medications. For example, the packaging for the triamcinolone indicates that there are multiple additives and preservatives [27, 28]. However, if the injected compounds were the sole cause of these findings, then similar results should have been observed in the shoulder injection group, which received the same injection solution, suggesting that the injectates are probably not the only risk factor. The cause is likely multifactorial: a combination of the injectates and factors specific to the hip joint compared with other joints.

The hip injection group, despite similar demographics, may be clinically different than the control hip group, because their

hip pain has been sufficiently severe to lead to an injection. Therefore, it is possible that the hip injection group is at an increased risk of osteoarthritis progression and femoral head collapse because their underlying condition is more advanced than in the control group. In this scenario, the injectate has no effect on the outcome and the steroid injection merely selects the patients who are already developing collapse. Alternatively, the steroid injection may remove the pain from underlying conditions such as osteonecrosis or subchondral fracture, and, as a result, patients may place more stress on the hip. Although there was no significant difference between the ages of the patients who did and did not develop collapse in the hip injection group, it is of interest that the youngest patient with new collapse was 56.

The actual relationship between hip steroid injections and osteoarthritis progression and femoral head collapse is likely multifactorial and may vary from patient to patient. However, our results warrant caution in injection of steroids in native hips, particularly if there is no immediate plan for arthroplasty, and also for further study of the injectates for a possible causative link.

Another entity that has been observed in the setting of steroid injection is rapidly destructive arthritis (RDA), also called rapidly progressive osteoarthritis. The imaging hallmarks of RDA include rapid joint space narrowing and chondrolysis with relative paucity of bony proliferative changes [29–31]. RDA has been previously linked to intra-articular steroid injections, femoral head osteonecrosis, and femoral head insufficiency fracture, and some reports use the terms RDA and osteonecrosis with collapse interchangeably whereas others consider them distinct entities [10, 32–36]. It is possible that the osteoarthritis progression and femoral head collapse that we are observing in this study is on the spectrum of RDA.

The limitations of our study include the retrospective study design, which prohibited a systematic collection of clinical information to ensure that the hip injection and hip control patients are similar groups in terms of clinical prognosis. A prospective study with radiographic and cross-sectional imaging before and at regular intervals after the injection would be required to establish a true causal relationship. In addition, specific injectates, including the steroid, anesthetic, and even contrast agent, would need to be studied to isolate the causative agent, if any, and to determine if this is a finding associated with a specific medication, a class of medications, or an interaction between these medications.

The strengths of our study include the evaluation by independent readers blinded to both the timepoint (first versus second) and to patient category (hip injection versus hip control). Furthermore, the KL scale is not sensitive to change, and the blinded review still demonstrated an increase in osteoarthritis in the hip injection patients. Also, there was no significant difference between the hip injection cohort and the study groups regarding most of the studied variables, including age, BMI, and hip DXA T-score. Of note, the DXA T-score was only available for 41% of the patients, and it is unknown whether the bone densitometry readings that we have are representative of the whole group.

In conclusion, hip steroid and anesthetic injection may be associated with osteoarthritis progression and new femoral head collapse. The causal relationship is unknown and further investigation is warranted.

Compliance with ethical standards

Conflicts of interest The authors declare that they have no conflicts of interest.

Ethical approval 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 the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed consent Informed consent was waived for individual participants included in the study. The study was approved by the local Institutional Review Board (IRB) and HIPAA-compliant.

Appendix

Table 4 Pre-injection severity of osteoarthritis, pre-injection osteonecrosis, and pre-injection collapse separated by reader 1 and reader 2

	Hip injection (A)		Hip control (B)		Shoulder injection control (C)		*p* (A vs B)		*p* (A vs C)	
	Reader 1	Reader 2	Reader 1	Reader 2	Reader 1	Reader 2	Reader 1	Reader 2	Reader 1	Reader 2
Pre-injection severity of osteoarthritis							0.14	0.0073	0.53	0.60
None/mild	26	28	21	14	13	14				
Moderate	31	29	42	47	19	19				
Severe	13	13	7	9	12	11				
Pre-injection osteonecrosis	8	9	13	11	4	4	0.34	0.81	0.76	0.76
Pre-injection collapse	2	1	6	6	2	3	0.27	0.12	0.64	0.30

Table 5 Hip injection patients versus hip control (no injection) and shoulder injection groups, separated by reader 1 and reader 2

	Hip injection (A), *n* (%)		Hip control (B), *n* (%)		Shoulder injection (C), *n* (%)		*p* (A vs B), *n* (%)		*p* (A vs C)	
	Reader 1	Reader 2	Reader 1	Reader 2	Reader 1	Reader 2	Reader 1	Reader 2	Reader 1	Reader 2
Increased osteoarthritis	30/70 (43)	34/70 (49)	20/70 (29)	13/70 (19)	14/44 (32)	10/44 (23)	0.11	0.0003	0.32	0.0062
New osteonecrosis	19/70 (27)	16/70 (23)	3/70 (4)	4/70 (6)	2/44 (5)	2/44 (5)	0.0003	0.0067	0.0024	0.0086
New collapse	12/70 (17)	11/70 (16)	1/70 (1)	1/70 (1)	1/44 (2)	1/44 (2)	0.0022	0.0044	0.0155	0.0274

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