Arthroscopy Association of Canada Position Statement on Intra-articular Injections for Hip Osteoarthritis

Ryan M. Degen[*,†,‡], MD, Laurie A. Hiemstra[†], MD, Joel Lobo[†], MD, Jarrett M. Woodmass[†], MD, Mark Sommerfeldt[†], MD, Moin Khan[†], MD, Sasha Carsen[†], MD, Thierry Pauyo[†], MD, Jas Chahal[†], MD, Nathan Urquhart[†], MD, John Grant[†], MD, Alexis Rousseau-Saine[†], MD, Marie-Eve Lebel[†], MD, Brendan Sheehan[†], MD, Emilie Sandman[†], MD, Allison Tucker[†], MD, Michaela Kopka[†], MD, and Ivan Wong[†], MD

[†]Arthroscopy Association of Canada.
[‡]Fowler Kennedy Sport Medicine Clinic, Western University, London, Ontario, Canada.

[*]Corresponding author: Ryan M. Degen, MD, Fowler Kennedy Sport Medicine Clinic, 1151 Richmond Street, London, Ontario, Canada, N6A 3K7 (email: Ryan.degen@lhsc.on.ca).

One or more of the authors has declared the following potential conflict of interest or source of funding: L.A.H. has received research support from Sanofi and honoraria from Pendopharm and Sanofi. B.S. has received honoraria from Sanofi. I.W. has received research support from Arthrex. AOSSM checks author disclosures against the Open Payments Database (OPD). AOSSM has not conducted an independent investigation on the OPD and disclaims any liability or responsibility relating thereto.

The Orthopaedic Journal of Sports Medicine, 10(2), 23259671211066966
DOI: 10.1177/23259671211066966

Keywords: hip; osteoarthritis; intra-articular injections; hyaluronic acid; platelet rich plasma

INTRODUCTION

Symptomatic hip and knee osteoarthritis (OA) are among the most common causes of global disability [33]. While already highly prevalent, the incidence and burden is anticipated to increase along with a concurrent increase in life expectancy of the general population and the obesity epidemic[27,38]. As such, optimal treatment strategies are required to minimize the impact of disease burden. Recently, clinical practice guidelines (CPG) for the treatment of knee OA have been established by the American Academy of Orthopedic Surgeons (AAOS), suggesting a comprehensive multimodal approach including physical therapy and injections, among other suggestions[15]. In subsequent months, the Arthroscopy Association of Canada (AAC) and Canadian Orthopaedic Association (COA) provided guidelines for the use of injections for the treatment of symptomatic knee OA based on the best-available literature[35]. However, similar recommendations for injections for the treatment of hip OA are lacking.

Recent reviews have been conducted by both the Osteoarthritis Research Society International (OARSI) [3] and the AAOS[2] regarding appropriate use of non-surgical modalities for the treatment of hip OA. The resultant position statements recommend a multimodal treatment approach. Supportive evidence is provided for the use of physical therapy and short-term non-steroidal anti-inflammatories (NSAIDs). However, the role of intra-articular injections is poorly defined. The 2017 AAOS CPG recommend the use of intra-articular corticosteroids (CS), citing strong evidence to support improved function and reduced pain. In contrast, the guidelines do not support the use of hyaluronic acid (HA), while failing to provide guidance on

the use of platelet-rich plasma (PRP) or stem cells (SC). The 2019 OARSI guidelines do not provide supportive or refutative evidence against CS, while they currently provide strong recommendations against the widespread use of PRP and SC due to poor quality evidence and a lack of standardized preparation methods.

While these position statements robustly review the literature, there have been several more randomized controlled trials, systematic reviews, and network meta-analyses published in recent years. As a result, the Arthroscopy Association of Canada (AAC) endeavored to provide an up-to-date overview of the available evidence for the use of intra-articular injections in the treatment of hip OA. In addition to summarizing the highest-available evidence, recommendations regarding each treatment are proposed by combining the best-available evidence and expert opinion. The grade of recommendation is categorized using the scale developed by Wright et al.[36] and further expanded by Stevens et al[30] (Table 1).

TABLE 1. Grades of Recommendation for Summaries or Reviews of Orthopaedic Surgical Studies and a Proposed Subscale Designed to Differentiate Evidence for Indications Receiving a Grade of Recommendation of "C"

	Description
Grades of Recommendation	
A	Good evidence (level 1 studies with consistent findings) for or against recommending an intervention
B	Fair evidence (level 2 or 3 studies with consistent findings) for or against recommending an intervention
C	Conflicting or poor-quality evidence (level 4 or 5 studies) not allowing a recommendation for or against an intervention
I	Insufficient evidence to make a recommendation
Proposed Subscale	
Cf	Representing literature "for," or in support of, a surgical intervention
Cu	Representing literature "against," or not in support of, a surgical intervention
Ce	Representing conflicting literature, some of which is in support of a surgical intervention and some of which is not in support of a surgical intervention

From Stevens MS, Legay DA, Glazebrook MA, Amirault D. The evidence for hip arthroscopy: grading the current indications. *Arthroscopy*. 2010;26(10):1370-1383.

Corticosteroids

Synthetic corticosteroids exert both anti-inflammatory and immunosuppressive effects by modulating pro-inflammatory cytokines and lymphocytes[25]. The most common types of corticosteroids utilized in intra-articular injections include particulate (or non-soluble) formulations such as methylprednisolone, betamethasone acetate, and triamcinolone acetonide and hexacetonide[24]. Intra-articular corticosteroids (CS) are a well-established modality in the non-operative management of knee OA, and have been endorsed by the AAOS, OARSI, as well as the AAC[3,15,16]. However, the utility of CS in hip OA has not been as well established. There is a paucity of high-level evidence, and concern over theoretical adverse events. While this concern is held by many clinicians, rates of these adverse events in the literature are low and no direct causality with CS has been established in prospective studies. A retrospective database review of 1471 patients who underwent fluoroscopically guided injection of triamcinolone acetate with local anaesthetic for hip OA showed an overall risk for developing rapid progression of OA to be 7%[4]. Osteonecrosis of the femoral head and the increased risk of infection following total hip arthroplasty (THA) have only been identified in case reports[23,37].

The 2017 AAOS Clinical Practice Guidelines state that "strong evidence supports the use of intra-articular corticosteroids to improve function and reduce pain in the short-term in patients with symptomatic OA of the hip"[2]. Interestingly, the 2019 OARSI Guidelines do not recommend CS in the treatment of hip OA due to the complexity of the procedure, poor safety profile, and insufficient efficacy compared to the knee[3].

Two recent systematic reviews and network meta-analyses analyzed the role of intra-articular injections in the treatment of patients with hip OA. Zhao et al.[39] reviewed 11 RCTs (1060 patients) comparing CS, hyaluronic acid (HA), and platelet rich plasma (PRP) to controls (normal saline or local anaesthetic). The authors showed that CS and HA treatments were significantly superior to controls in reducing VAS pain scores at 1 and 3 months. CS yielded the lowest pain intensity at 1 month. In contrast, a similar meta-analysis by Gazendam et al.[13] which assessed 11 RCTs (1353 patients) showed all interventions (CS, HA, PRP and placebo) provided comparable improvements in pain and functional outcomes at 2-4 and 6 months. It is important to note that only four of the RCTs evaluated in the latter study included CS as a treatment arm, whereas Zhao et al. included five studies involving CS. The study which was omitted was one of the larger RCTs (n=80), conducted by Kullenberg et al., comparing fluoroscopically guided intra-articular triamcinolone acetonide to local anaesthetic in patients with hip OA. The authors showed a significant reduction in pain, consumption of analgesics, and improved range of motion in the CS group at three and 12 week follow-up[20].

Recommendation: Intra-articular corticosteroid injections are safe and effective at reducing pain and improving function for up to three months in patients with symptomatic hip OA, with a low risk of adverse events.
Strength of Recommendation: Good - A

Hyaluronic Acid

Hyaluronic acid (HA) is a natural substance which is abundant in the fluid of synovial joints and plays an essential role in joint lubrication and shock absorbency. HA is a polysaccharide produced by a number of cells within the joint including type-B synoviocytes, fibroblasts, and chondrocytes.

As osteoarthritis progresses, the natural HA produced within the joint degrades in quality, which reduces the viscoelastic properties of the synovial fluid[17].

Viscosupplementation aims to improve or restore the physiologic function and integrity of synovial fluid by stimulating *in vivo* HA synthesis, as well as providing joint lubrication and shock absorbency[1]. Additionally, HA has significant anti-inflammatory and chondroprotective properties, which reduce pain and inflammation in the osteoarthritic joint[1]. A wide variety of HA formulations are currently available on the market, which differ in many characteristics such as molecular weight (low or high molecular weight formulations), method of production (avian derived or synthetic biofermentation), dosing, cost, degree of crosslinking, and other characteristics[31]. Significant attention has been directed in recent years to formulations that result in optimal efficacy with much of the literature available for knee osteoarthritis supporting the use of high molecular weight crosslinked formulations[1].

Current AAOS clinical practice guidelines from 2017 suggest strong evidence does not support the use of intraarticular hyaluronic acid for hip osteoarthritis given that it does not perform better than placebo for function, stiffness, and pain[2]. However, these recommendations were made with a relative scarcity of available literature at the time. Since that time, several additional publications have become available, with two network meta-analyses published in the past year evaluating the efficacy of intra-articular hip injections[13,39]. As referenced above, Zhao et al. performed a systematic review and network meta-analysis, comparing the efficacy of CS, HA, PRP and HA plus PRP[39]. They reported significant improvements in visual analogue scores at 1- and 3-months following CS and HA injections compared with the control group.

However, the primary limitation of the study by Zhao et al is that it is based on studies comparing active treatment to placebo injection and as such does not take into account the significant treatment effect from the injection itself[32]. Gazendam et al.[13] performed a network meta-analysis that evaluated the treatment effect of placebo in comparison to various intra articular hip treatments including HA. While the treatment effect for HA did exceed the minimal clinically important difference, it was not significantly better than the placebo injection itself. Furthermore, there were no differences between high and low molecular weight formulations in the literature. As such, the authors concluded that all intra-articular therapies (except HA+PRP) appeared to confer clinical improvements in pain surpassing the minimum clinically important difference. However, they are unable to recommend any particular agent over others.

It is important to note that unlike HA data with the knee, limited high-quality studies exist evaluating HA in the hip joint with all available RCT data stemming from studies with small sample sizes. As of now, available evidence is inconclusive regarding the true efficacy of HA in the hip and further large high quality randomized controlled trials are required to delineate HA efficacy.

Recommendation: HA has the potential to provide improvements in pain and functional outcomes for up to 6 months in the treatment of hip OA. However, high-level evidence remains scarce, with significant heterogeneity in available HA products. Therefore, we cannot recommend for or against the use of HA for hip OA until further high-quality clinical studies become available.

Strength of Recommendation: Cf

Platelet-Rich Plasma and Stem Cells

Platelet-rich plasma (PRP) is an autologous preparation of peripheral blood, whereby centrifugation concentrates important constituents theorized to produce a biologic healing response. The primary mechanism of action is thought to arise from the degranulation of

platelets, which releases cytokines and growth factors with potential chemotactic activity to initiate an inflammatory response and/or collagen synthesis[14,22]. Despite the theoretical mechanisms of activity, its exact indications remain to be determined.

The utilization of PRP for osteoarthritis has gained significant interest in recent years. Currently, use for knee OA remains somewhat controversial. PRP is not supported in the treatment of knee OA by the most recent clinical practice guidelines from the AAOS[15] or the AAC[16], but more recent meta-analyses and randomized clinical trials are reporting encouraging results with comparable improvements in outcome measures and better durability when compared with HA[7,9]. As a result of these encouraging results, there has been a significant increase in utilization for knee OA. The optimism surrounding PRP for knee OA has resulted in increased interest in utilization of PRP for various intra-articular hip disorders.

Specifically focusing on the use of PRP for the treatment of hip OA, there have been a few recent, randomized clinical trials reporting encouraging results. In 2016, Dallari et al. performed a randomized controlled trial evaluating the efficacy of PRP, PRP plus HA and HA alone for the treatment of symptomatic hip OA[11]. They included patients with Kellgren-Lawrence grades 1-4, with a baseline score of at least 20 points on the visual analogue scale, without any significant joint destruction or joint preservation surgery. This resulted in the randomization of a total of 111 patients into three groups: 44 patients in the PRP group, 31 patients in the PRP+HA group, and 36 patients in the HA group. At each time point (2, 6 and 12-months), patients in the PRP group demonstrated significantly lower VAS scores compared to HA and PRP+HA, while other tools including the WOMAC showed improvements at 2 and 6 months, but not at 12 months. The authors concluded that PRP had a more durable benefit out

to 12 months compared with HA and felt the combination of PRP+HA offered no clinical benefit. However, details regarding the composition of PRP and HA utilized were not included in this study.

In a similar study, Kraeutler et al. randomized 36 patients with symptomatic hip OA to receive either leukocyte-poor PRP (LP-PRP) or low-molecular weight HA (LMW-HA), evaluating conversion to total hip arthroplasty (THA) as the primary outcome, with secondary outcome measures including VAS and WOMAC[19]. They reported a significantly higher rate of THA conversion (50%) among LMW-HA patients compared with LP-PRP (15.8%; p=0.035). Additionally, they reported no significant improvements in outcome scores in the LMW-HA group, while the PRP group demonstrated improvements in WOMAC overall and functional scores to 6 weeks, and WOMAC joint scores to 6 months.

More recently, three review articles evaluating PRP have reported somewhat conflicting results. Garcia et al. performed a systematic review of PRP for hip OA or hip impingement [12]. Focusing on the results of PRP for hip OA, they reported a significant improvement in validated outcome measures out to one year. However, analysis of pooled effect sizes failed to show any significant benefit in PRP over HA at any time point. The authors concluded that the treatment of hip OA with PRP resulted in improved pain and patient reported outcomes for up to one year.

In the review mentioned earlier by Zhao et al. evaluating the efficacy of PRP, HA, CS and PRP+HA[39], they found the intensity of pain following PRP was lowest out of all injectates at 6 months. As such, the authors suggest PRP has the highest rank for long-term efficacy out to 6 months.

Similarly, Gazendam et al. performed a comparable review[13], but also included a control group consisting of an intra-articular saline injection. While none of the injectates outperformed the placebo saline injection, all were efficacious as they provided improvements in VAS at 2-4 and 6 months, which surpassed the MCID.

Recommendation: PRP injection has the potential to provide improvements in pain and functional outcomes up to one year in the treatment of hip OA. However, high-level evidence remains scarce, and significant heterogeneity exists in the optimal formulation and dosing of PRP. Therefore, we cannot recommend for or against the use of PRP for hip OA until further high-quality clinical studies become available.
Strength of Recommendation: Cf

Cellular-Based Therapies:

It is important to differentiate between bone marrow aspirate concentrate (BMAC) and multipotent stem cells. The former represents a concentrate of a bone marrow aspirate, separating it into one layer consisting of mononuclear cells (white blood cells, mesenchymal stem cells, hematopoietic stem cells and platelets) and another layer consisting of red blood cells[5]. BMAC contains only a fraction of true stem cells, estimated to be between 0.001-0.01% of all cellular components[18]. BMAC also contains a variety of growth factors, including interleukin-1 receptor antagonist, platelet-derived growth factor, transforming growth factor-beta, all of which have been shown to have anti-inflammatory and anabolic effects[18].

Stem cells, defined as undifferentiated progenitor cells, have the capacity to differentiate into multiple different cell types or to replicate themselves [5,21]. While there are several different stem cell types, the primary focus in orthopedics have been mesenchymal stem cells, or MSCs. Historically, these had primarily been identified within bone marrow, however they have also been isolated from adipose, muscle, skin, periosteum, blood and other

sources[21]. These cells are capable of differentiating into bone, cartilage, muscle or ligament, hence their appeal as an attractive option for tissue repair or tissue engineering [21].

The utilization of both BMAC and MSCs for the treatment of hip OA has been limited. Much of this relates to the evolving restrictions in place by the regulatory bodies in many countries. BMAC has been the most widely utilized, primarily due to the fact that it meets the criteria of 'minimal manipulation' as proposed by the Food and Drug Administration (FDA) and similar regulatory bodies worldwide[6]. Presently, there are two small case series available on the efficacy of BMAC in the treatment of hip OA [29,34]. Rodriguez-Fontan et al. utilized BMAC for the treatment of 15 hips with Tönnis grade I-II and 10 knees with Kellgren-Lawrence grade I-II OA[29]. They reported statistically significant improvements in outcome scores at a mean follow-up of 13.2 months, with a patient satisfaction rate of 63.2%. Additionally, 64% of patients surpassed the minimum clinically important difference (MCID). Only 2 of 15 hips (13.3%) required conversion to total hip arthroplasty, however the follow-up is likely inadequate to accurately report for this outcome. Similarly, Whitney et al. reported on the use of a single BMAC injection for the treatment of symptomatic hip OA in 16 patients (18 hips)[34]. They, too, reported significant improvements in outcome scores out to 6 months, including a numeric rating scale for pain, WOMAC score, modified Harris Hip Score (mHHS), and Hip Outcome Score-Activities of Daily Living (HOS-ADL) subscale, as well as the 12-item Short-Form (SF-12) Health Survey. They noted a persistent improvement out to 6 months, with no regression noted at that final timepoint. The authors also concluded that BMAC is effective at improving pain and function for up to 6 months for symptomatic hip OA.

MSCs have been scarcely utilized in the treatment of hip OA. In 2018, McIntyre et al. performed a systematic review of available studies where human MSCs were injected for the treatment of OA or chondral defects[26]. Of the identified case series, 14 series focused on the efficacy of MSCs for OA of the knee, ankle, and hip. Hip OA was the minority of included cases, representing only 5 of 584 patients. The authors summarized the findings of all studies, noting statistically significant improvement in at least one patient reported outcome measure with no adverse events. While they recognize the limitations within the existing literature, they conclude that MSCs appear to be safe with generally positive outcomes, but further study is required. Following this review, an additional case series was published by Dall'Oca et al., reporting on the outcomes of 6 patients with Tönnis 0-2 hip OA treated with an intra-articular MSC injection[10]. At 6 months post-injection, they noted significant improvements in mHHS, WOMAC and VAS scores, concluding that MSCs appear to provide a positive outcome but that longer duration evaluation is required.

Recommendation: There is insufficient evidence to support the use of BMAC or MSCs in the treatment of hip OA. As such, these agents should be limited to use in registered controlled trials, and we cannot recommend their use in clinical practice until higher-quality evidence is available.

Strength of Recommendation: Insufficient – I.

Combination Therapies

While combination therapy is commonly utilized in the treatment of knee OA, there is limited evidence to support their use in the treatment of hip OA. Presently, the only available literature is on the combination of CS and HA, as well as HA and PRP.

In a non-randomized study, Crook et al. reported on the outcomes comparing CS injections with CS + HA for the treatment of symptomatic hip OA[8]. This was a matched cohort

study comparing 119 patients per group, where the authors noted similar statistically significant improvements in pain from pre- to post-injection. However, the most notable finding was a significantly longer duration of benefit in the combination group compared with CS alone (128.6 ± 20.3 vs. 32.3 ± 8.6 days, p<0.001).

As discussed above, Dallari et al. included a combination PRP+HA group when comparing the efficacy of PRP and HA for the treatment of hip OA[11]. They concluded that PRP appeared to provide a significant improvement in all PROMs, with a more stable result out to 12 months compared with HA. The combination therapy of PRP+HA did not lead to a significant improvement in pain symptoms.

Recommendation: There is insufficient evidence to support the use of combination therapy in the treatment of hip OA. As such, these agents should be limited to use in registered controlled trials, and we cannot recommend their use in clinical practice until higher-quality evidence is available.
Strength of Recommendation: Insufficient – I.

Position Statement Conclusions

1. Intra-articular CS injections are safe and effective at reducing pain and improving function for up to three months in patients with symptomatic hip OA[20,28].
2. Intra-articular HA has the potential to provide improvements in pain and functional outcomes for up to 6 months in the treatment of hip OA, however higher quality evidence is required before it can be recommended for routine clinical use [13,39]
3. Intra-articular PRP injection has the potential to provide improvements in pain and functional outcomes up to 1 year in the treatment of hip OA[13,39]. However, heterogeneity in preparation systems and uncertainty regarding optimal dosage preclude recommendations for or against routine clinical use currently.

4. There is insufficient evidence to support the use of BMAC or MSCs in the treatment of hip OA
5. Rigorous, well-designed clinical trials are needed to establish the safety, efficacy, and cost-effectiveness of BMAC/MSCs before further clinical use.
6. There is insufficient evidence to support the use of combination injection therapy in the treatment of hip OA.
7. The use of injectables for hip OA should take into consideration evidence-based research and should involve a discussion with the patient regarding the efficacy, safety, and cost-effectiveness of such treatments.

References

1. Altman RD, Bedi A, Karlsson J, Sancheti P, Schemitsch E. Product Differences in Intra-articular Hyaluronic Acids for Osteoarthritis of the Knee. *Am J Sports Med.* 2016;44(8):2158-65. doi:10.1177/0363546515609599.
2. American Academy of Orthopaedic Surgeons. Management of Osteoarthritis of the Hip - Evidence-Based Clinical Practice Guideline. 2017.
3. 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(11):1578-1589. doi:10.1016/j.joca.2019.06.011.
4. Boutin RD, Pai J, Meehan JP, Newman JS, Yao L. Rapidly progressive idiopathic arthritis of the hip: incidence and risk factors in a controlled cohort study of 1471 patients after intra-articular corticosteroid injection. *Skeletal Radiol.* 2021. doi:10.1007/s00256-021-03815-7.
5. Chahla J, Mandelbaum BR. Biological Treatment for Osteoarthritis of the Knee: Moving from Bench to Bedside—Current Practical Concepts. *Arthroscopy.* 2018;34(5):1719-1729. doi:10.1016/j.arthro.2018.01.048.
6. Chahla J, La Prade RF, Mardones R, et al. Biological therapies for cartilage lesions in the hip: A new horizon. *Orthopedics.* 2016;39(4):e715-e723. doi:10.3928/01477447-20160623-01.
7. Cole BJ, Karas V, Hussey K, Merkow DB, Pilz K, Fortier LA. Hyaluronic Acid Versus Platelet-Rich Plasma: A Prospective, Double-Blind Randomized Controlled Trial Comparing Clinical Outcomes and Effects on Intra-articular Biology for the Treatment of Knee Osteoarthritis. *Am J Sports Med.* 2017;45(2):339-346. doi:10.1177/0363546516665809.
8. Crook P, Shah J, Lee K, et al. Efficacy of Intra-Articular Hyaluronic Acid and Cortisone Compared to Cortisone alone for Symptomatic Hip Osteoarthritis. *J Arthritis* 2019;08(01):1-5. doi:10.4172/2167-7921.1000278.
9. Dai WL, Zhou AG, Zhang H, Zhang J. Efficacy of Platelet-Rich Plasma in the Treatment of Knee Osteoarthritis: A Meta-analysis of Randomized Controlled Trials. *Arthroscopy.* 2017;33(3):659-670. doi:10.1016/j.arthro.2016.09.024.
10. Dall'Oca C, Breda S, Elena N, Valentini R, Samaila EM, Magnan B. Mesenchymal stem cells injection in hip osteoarthritis: Preliminary results. *Acta Biomed.* 2019;90:75-80. doi:10.23750/abm.v90i1-S.8084.
11. 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. *Am J Sports Med.* 2016;44(3):664-671. doi:10.1177/0363546515620383.
12. Garcia FL, Williams BT, Polce EM, et al. Preparation Methods and Clinical Outcomes of Platelet-Rich Plasma for Intra-articular Hip Disorders: A Systematic Review and Meta-analysis of Randomized Clinical Trials. *Orthop J Sports Med.* 2020;8(10):2325967120960414. doi:10.1177/2325967120960414.
13. Gazendam A, Ekhtiari S, Bozzo A, Phillips M, Bhandari M. Intra-articular saline injection is as effective as corticosteroids, platelet-rich plasma and hyaluronic acid for hip osteoarthritis pain: A systematic review and network meta-analysis of randomised controlled trials. *Br J Sports Med.* 2021;55(5):256-261. doi:10.1136/bjsports-2020-102179.
14. Hsu WK, Mishra A, Rodeo SRA, et al. Platelet-rich plasma in orthopaedic applications: evidence-based recommendations for treatment. *J Am Acad Orthop Surg.* 2013;21(12):739-48. doi:10.5435/JAAOS-21-12-739.
15. Jevsevar DS. Treatment of osteoarthritis of the knee: evidence-based guideline, 2nd edition. *J Am Acad Orthop Surg.* 2013;21(9):571-6. doi:10.5435/JAAOS-21-09-571.
16. Kopka M, Sheehan B, Degen R, et al. Arthroscopy Association of Canada Position Statement on

Intra-articular Injections for Knee Osteoarthritis. *Orthop J. Sports Med.* 2019;7(7):2325967119860110. doi:10.1177/2325967119860110.
17. Kosinska MK, Ludwig TE, Liebisch G, et al. Articular Joint Lubricants during Osteoarthritis and Rheumatoid Arthritis Display Altered Levels and Molecular Species. *PLoS One* 2015;10(5):e0125192. doi:10.1371/journal.pone.0125192.
18. Kraeutler MJ, Chahla J, LaPrade RF, Pascual-Garrido C. Biologic Options for Articular Cartilage Wear (Platelet-Rich Plasma, Stem Cells, Bone Marrow Aspirate Concentrate). *Clin Sports Med.* 2017;36(3):457-468. doi:10.1016/j.csm.2017.02.004.
19. Kraeutler MJ, Houck DA, Garabekyan T, Miller SL, Dragoo JL, Mei-Dan O. Comparing Intra-articular Injections of Leukocyte-Poor Platelet-Rich Plasma Versus Low–Molecular Weight Hyaluronic Acid for the Treatment of Symptomatic Osteoarthritis of the Hip: A Double-Blind, Randomized Pilot Study. *Orthop J Sports Med.* 2021;9(1):2325967120969210. doi:10.1177/2325967120969210.
20. Kullenberg B, Runesson R, Tuvhag R, Olsson C, Resch S. Intraarticular corticosteroid injection: pain relief in osteoarthritis of the hip? *J Rheumatol.* 2004;31(11):2265-8.
21. LaPrade R, Dragoo JL, Koh JL, Murray IR, Geeslin AG, Chu CR. Updates and Consensus : Biologic Treatment of Orthopaedic Injuries Abstract. *J Am Acad Orthop Surg* 2016;24(7):e62-e78.
22. LaPrade RF, Geeslin AG, Murray IR, et al. Biologic Treatments for Sports Injuries II Think Tank—Current Concepts, Future Research, and Barriers to Advancement, Part 1. *Am J Sports Med.* 2016;44(12):3270-3283. doi:10.1177/0363546516634674.
23. Laroche M, Arlet J, Mazieres B. Osteonecrosis of the femoral and humeral heads after intraarticular corticosteroid injections. *J. Rheumatol.* 1990;17(4):549-51.
24. MacMahon PJ, Eustace SJ, Kavanagh EC. Injectable corticosteroid and local anesthetic preparations: a review for radiologists. *Radiology.* 2009;252(3):647-61. doi:10.1148/radiol.2523081929.
25. Malemud CJ. Cytokines as therapeutic targets for osteoarthritis. *BioDrugs*. 2004;18(1):23-35. doi:10.2165/00063030-200418010-00003.
26. McIntyre JA, Jones IA, Han B, Vangsness CT. Intra-articular Mesenchymal Stem Cell Therapy for the Human Joint: A Systematic Review. *Am J Sports Med.* 2018;46(14):3550-3563. doi:10.1177/0363546517735844.
27. Murphy L, Helmick CG. The Impact of osteoarthritis in the United States: A population-health perspective: A population-based review of the fourth most common cause of hospitalization in U.S. adults. *Orthop Nurs.* 2012;31(2):85-91. doi:10.1097/NOR.0b013e31824fcd42.
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(2):163-70. doi:10.1016/j.joca.2005.09.007.
29. Rodriguez-Fontan F, Piuzzi NS, Kraeutler MJ, Pascual-Garrido C. Early Clinical Outcomes of Intra-Articular Injections of Bone Marrow Aspirate Concentrate for the Treatment of Early Osteoarthritis of the Hip and Knee: A Cohort Study. *PM R* 2018;10(12):1353-1359. doi:10.1016/j.pmrj.2018.05.016.
30. Stevens MS, Legay DA, Glazebrook MA, Amirault D. The evidence for hip arthroscopy: Grading the current indications. *Arthroscsopy.* 2010;26(10):1370-1383. doi:10.1016/j.arthro.2010.07.016.
31. Strauss EJ, Hart JA, Miller MD, Altman RD, Rosen JE. Hyaluronic Acid Viscosupplementation and Osteoarthritis: Current Uses and Future Directions. *Am J Sports Med.* 2009;37(8):1636-1644. doi:10.1177/0363546508326984.
32. Vannabouathong C, Bhandari M, Bedi A, et al. Nonoperative Treatments for Knee Osteoarthritis: An Evaluation of Treatment Characteristics and the Intra-Articular Placebo Effect. *JBJS Rev.* 2018;6(7):e5. doi:10.2106/JBJS.RVW.17.00167.

33. Vos T, Abajobir AA, Abate KH, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* 2017;390(10100):1211-1259. doi:10.1016/S0140-6736(17)32154-2.
34. Whitney KE, Briggs KK, Chamness C, et al. Bone Marrow Concentrate Injection Treatment Improves Short-term Outcomes in Symptomatic Hip Osteoarthritis Patients: A Pilot Study. *Orthop J Sports Med.* 2020;8(12):2325967120966162.
35. Wong I, Hiemstra L, Ayeni OR, et al. Position Statement : Arthroscopy of the Knee Joint Developed by the Arthroscopy Association of Canada (AAC) September 2017 Approved and Endorsed by the Canadian Orthopaedic Association (COA) Board of Directors January 2018. 2017;(January 2018).
36. Wright JG, Einhorn TA, Heckman JD. Grades of recommendation. *J. Bone Joint Surg. Am.* 2005;87(9):1909-10. doi:10.2106/JBJS.8709.edit.
37. Yamamoto T, Schneider R, Iwamoto Y, Bullough PG. Rapid destruction of the femoral head after a single intraarticular injection of corticosteroid into the hip joint. *J. Rheumatol.* 2006;33(8):1701-1704.
38. Young JJ, Važić O, Cregg AC. Management of knee and hip osteoarthritis: an opportunity for the Canadian chiropractic profession. *J Can Chiropr Assoc.* 2021;65(1):6-13.
39. Zhao Z, Ma J xiong, Ma X long. Different Intra-articular Injections as Therapy for Hip Osteoarthritis: A Systematic Review and Network Meta-analysis. *Arthroscopy.* 2020;36(5):1452-1464.