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Corticosteroid injections for knee osteoarthritis offer clinical benefits similar to hyaluronic acid and lower than platelet-rich plasma: a systematic review and meta-analysis

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- *Purpose:* Intra-articular corticosteroid (CS) injections for knee osteoarthritis (OA) management are endorsed by several scientific societies, while the use of hyaluronic acid (HA) and platelet-rich plasma (PRP) is more controversial. Aim of the study was to quantify and compare the clinical effectiveness of CS injections with respect to HA and PRP in patients with knee OA.
- *Methods*: The search was conducted on PubMed, Cochrane, and Web of Science following the PRISMA guidelines. Randomized controlled trials (RCTs) on the comparison of CS injections and HA or PRP injections for the treatment of knee OA were included. The minimal clinically important difference (MCID) was used to interpret the clinical relevance of the improvements at different follow-ups up to 12 months. The study quality was assessed using the Cochrane RoB-2 tool and the GRADE guidelines.
- *Results*: Thirty-five RCTs were included (3348 patients). The meta-analysis comparing CS and HA revealed no difference in terms of WOMAC improvement, while HA showed superior VAS pain improvement at long-term follow-up ($P = 0.011$), without reaching the MCID. PRP offered a superior WOMAC improvement compared to CS at short- ($P = 0.002$), mid- ($P < 0.001$, exceeding the MCID), and long-term ($P < 0.001$, exceeding the MCID) follow-ups. PRP offered a superior VAS improvement at mid- ($P < 0.001$, exceeding the MCID) and long-term ($P = 0.023$) follow-ups.
- *Conclusion*: CS injections for knee OA offer similar results to HA and PRP only at short term, while there is an overall superiority of PRP at longer follow-ups. This difference is not only statistically significant but also clinically relevant in favour of PRP.

Keywords: corticosteroids; hyaluronic acid; knee; osteoarthritis; platelet-rich plasma

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Introduction

Knee osteoarthritis (OA) is one of the most common orthopedic diseases and represents a major cause of knee pain and disability in older adults (1, 2). The prevalence of this degenerative condition is currently rising, with a heavy burden on healthcare systems worldwide (3, 4, 5, 6). Although commonly referred to as a 'wear and tear' disease, knee OA may be initiated and progressed by various mechanisms, involving complex interactions between genetic, metabolic, biochemical, and biomechanical factors, all favoring the disease progression (7, 8). Among these, inflammation plays a pivotal role in the pathophysiology of OA, with synovial membrane alterations and the release of pro-inflammatory cytokines in the whole joint environment (1). These elements induce chondrocytes to produce degradative enzymes of the extracellular matrix, thus affecting the articular surface (9). In this scenario, intra-articular corticosteroid (CS) injections have been proposed and used for over 60 years in knee OA management, relying on their anti-inflammatory properties (10, 11, 12, 13, 14).

Clinical benefits supported the use of CS injections in clinical practice, where this approach showed to provide significant pain relief and joint function improvement in knee OA patients (14, 15, 16). Scientific societies and healthcare organizations also endorsed the use of CS injections as part of a comprehensive treatment plan for knee OA. The Osteoarthritis Research Society International Guidelines (OARSI) (17), the American College of Rheumatology (ACR) (18), the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) (19), and the American Academy of Orthopaedic Surgeons (AAOS) (20) include intra-articular CS injections among the options to manage patients affected by knee OA. On the other side, the use of hyaluronic acid (HA) and platelet-rich plasma (PRP) for knee OA patients is more controversial, although the evidence supporting these products significantly increased in last years (21, 22, 23, 24, 25, 26). Recent systematic reviews and meta-analyses supported the clinical benefits provided by HA and PRP injections, but the most effective approach among the intra-articular treatment options for knee OA remains debated (26, 27). In this scenario, an updated and comprehensive meta-analysis of randomized controlled trials (RCTs) comparing CS injections with HA and PRP approaches would provide scientific evidence to clarify the clinical relevance of the benefits of these procedures and enable healthcare providers to make informed decisions regarding the most appropriate choice for the intra-articular injection therapy of knee OA.

The aim of this systematic review and meta-analysis was to quantify and compare the clinical effectiveness in terms of minimal clinically important difference (MCID) of intra-articular CS injections with respect to HA and PRP in patients affected by knee OA.

Materials and methods

Literature search and article selection

A systematic review of the literature was performed on the comparison of intra-articular CS injections versus HA or PRP for the treatment of knee OA. The study was registered on the international prospective register of systematic reviews (PROSPERO registration number: CRD42023466155). A literature search was conducted on three electronic databases (PubMed, Cochrane, and Web of Science) on July 20, 2023, with no time limitation and without any filters, using the following string: (steroid* OR corticosteroid* OR glucocorticoid* OR cortisone OR hydrocortisone OR prednisolone OR prednisone OR methylprednisolone OR triamcinolone OR dexamethasone OR betamethasone OR fludrocortisone OR deoxycorticosterone) AND (inject* OR intra-articular* OR infiltrat*) AND (osteoarthritis OR OA) AND (knee).

According to the PRISMA guidelines (28), the article selection and data extraction processes were conducted separately by two authors (A Be and A S). After the removal of duplicates, the initial title and abstract screenings were made using the following inclusion criteria: RCTs, written in English language and with no time limitation, on the comparison of intra-articular injections of CS versus HA or CS versus PRP for the treatment of knee OA. Exclusion criteria were non-randomized studies, articles written in other languages, systematic reviews, meta-analyses, narrative reviews, expert opinions, preclinical studies, and studies not reporting clinical outcomes. In the second step, the full texts of the selected articles were screened, with further exclusions according to the previously described criteria. The reference lists from the previously published relevant reviews were also screened. The screening process is detailed in Fig. 1. Two investigators independently reviewed each article (A Be and A S), and any discrepancies between them were resolved by discussion and consensus with a third author (A Bo).

Data extraction and outcome measurement

Relevant data were independently extracted from the included studies by two authors (A Be and A S). The data included authors, year of publication, number of patients, sex, age, follow-up time, CS type, HA and PRP details, dose and number of injections, Kellgren–Lawrence (KL) OA grade, and clinical outcomes. These data were collected in a database to be analyzed to the purpose of the present study.

The scores to evaluate the clinical benefit of CS, HA, and PRP injections were documented and those with at least three articles contributing to each time point evaluation were considered for the meta-analysis. Outcome analysis was performed at four different follow-ups, resulting in a very short- (≤ 6 weeks), short- (> 6 weeks and ≤ 3 months), mid- (> 3 months and ≤ 6

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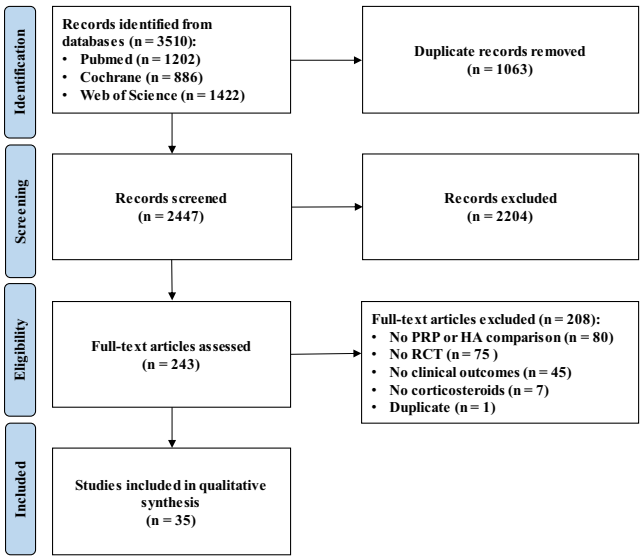

Figure 1

PRISMA flowchart of the study selection process.

months), and long-term (> 6 months and ≤ 12 months) follow-up analyses. For each outcome, the pooled effect sizes were analyzed in light of their MCID, defined as the smallest difference perceived as important by the average patient (29).

Assessment of risk of bias and quality of evidence

The risk of bias and quality of evidence of each article was assessed independently by two authors (A Be and A S), with disagreements resolved by consensus with a third author (A Bo). For the risk of bias, the Cochrane risk-of-bias tool for randomized trials version 2 (RoB 2) was used (30). RoB 2 is structured into a fixed set of domains of bias, focusing on different aspects of trial design, conduct, and reporting. Within each domain, a series of questions ('signaling questions') aims to elicit information about features of the trial that are relevant to the risk of bias. A proposed judgement on the risk of bias for each domain is generated by an algorithm, based on answers to the signaling questions. Judgement can be 'low' or 'high' risk of bias or can express 'Some concerns'. For each plotted outcome of the comparative meta-analysis, the quality of evidence was evaluated according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) guidelines. In the GRADE system, the baseline rating of RCTs is considered 'high'. Five criteria are used to downgrade one or two steps in case of 'serious' or 'very serious concerns': risk of bias in individual studies, inconsistency of results between studies, indirectness of evidence, imprecision, and publication bias. The overall quality of evidence can be graded as 'high', 'moderate', 'low', or 'very low'.

Statistical analysis

The statistical analysis and the Forest plotting were carried out according to Neyeloff *et al.* using the Meta XL tool for Microsoft Excel by an independent professional statistician (31). The analysis was carried out using random effects (DerSimonian & Laird (32)) for the weighted mean differences (MDs) of continuous variables. A statistical test for heterogeneity was first conducted with the Cochran Q statistic and I^2 metric. The presence of significant heterogeneity was considered with $I^2 \geq 25\%$. When no heterogeneity was found with $I^2 < 25\%$, a fixed effect model was used to estimate the expected values and 95% confidence intervals, otherwise a random-effect model was applied and an I^2 metric was evaluated for the random effect to check the correction of heterogeneity. A P value of 0.05 was considered significant. The comparison among groups was based on the analysis of variance of the difference between basal and follow-up scores MDs (33). All statistical analyses were carried out with Microsoft Excel 2010.

Results

Study selection and analysis

The initial search identified 3510 records: after screening of the titles, abstracts, and full texts, 35 RCTs were finally included in the systematic review, for a total of 3348 patients enrolled (62.5% women, 37.5% men, mean age 61.3 ± 6.9 years, mean BMI 28.5 ± 3.6). The details of the included studies are reported in Supplementary Table 1 (see section on supplementary materials given at the end of this article). Among the included studies, 20 compared CS with HA, 12 compared CS with PRP, while three addressed the comparison between CS, HA, and PRP. Final follow-up time ranged from 2 months to 2 years. Five studies were single-blind, 13 double-blind, one was non-blind, while the others did not report information about blinding. Since the first RCT published in 1991 the publication trend increased over time for studies comparing CS and HA, with a peak of studies between 2015 and 2019. The RCTs comparing CS and PRP were all published in the last decade and also showed and increasing publication trend (Fig. 2).

The following scores were retrieved: Visual Analog Scale (VAS) for pain, Western Ontario and McMaster University Osteoarthritis index (WOMAC) score, Knee Society Score (KSS), Knee Injury and Osteoarthritis Outcome Score (KOOS), International Knee Documentation Committee score (IKDC), 36-Item Short Form Survey (SF-36), Lequesne index for knee osteoarthritis, Lysholm Knee Scoring Scale, and Tegner Activity Score. The most employed were pain VAS (22 studies), WOMAC (18 studies), KSS (6 studies), KOOS (4 studies), SF-36 (4 studies), Lequesne (2 studies), IKDC (1 study), Lysholm (1 study), and Tegner (1 study).

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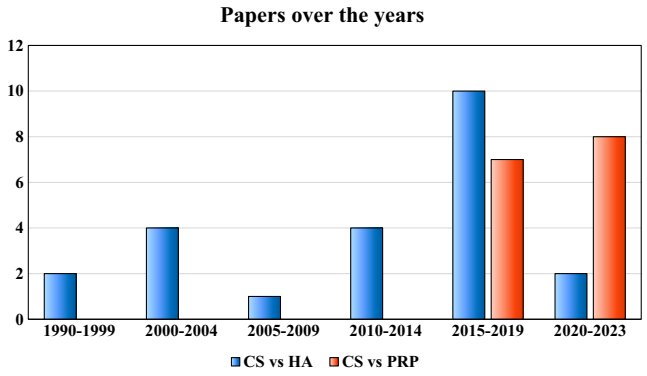

Figure 2

Number of RCTs published over time on the comparison between intra-articular corticosteroids (CS) and hyaluronic acid (HA) or platelet-rich plasma (PRP).

Corticosteroids

A total of 1553 patients received CS injections (61.4% women, 38.6% men, mean age 61.5 ± 5.5 years, mean BMI 28.5 ± 2.4). Different types of CS were injected: triamcinolone was used in 14 studies (in both acetonide or hexacetonide formulations), methylprednisolone acetate in 12 studies, betamethasone in 5 studies, and dexamethasone in 2 studies, while 2 studies did not report the corticosteroid used. In 12 studies, the CS injection was preceded by local anesthesia with either marcaine, lidocaine, or bupivacaine. Two injections were performed in two studies, three injections in five studies, and five injections in two studies, while in the other trials a single injection was performed, giving in some cases the possibility to ask for a second injection.

Hyaluronic acid

A total of 1325 patients received HA injections (62.2% women, 37.8% men, mean age 62.0 ± 6.8 years, mean BMI 28.3 ± 2.5). Different types of HA were injected: sodium hyaluronate in 11 studies, Hylan G-F 20 in five studies, cross-linked sodium hyaluronate, HYADD, Hylastan SGL-80, sodium salt of HA, and NASHA in one study each, while two studies did not report the type of HA used. Two injections of HA were administered in two studies, three injections in four studies, and five injections in six studies, while in the other trials a single injection was performed.

Platelet-rich plasma

A total of 470 patients received PRP injections (66.6% women, 33.4% men, mean age 59.8 ± 5.0 years, mean BMI 28.9 ± 2.2). PRP was autologous in all the studies. Three PRP injections were performed in 3 studies, while in the other trials a single injection was performed. PRP dosage of injection ranged from 3 mL to 8 mL. PRP was reported as leukocyte rich in two studies, leukocyte poor in two other studies, while in the remaining studies leukocyte concentration was not reported. Activation was performed in four studies, three times with sodium citrate and one time with calcium gluconate, while in the other studies no activation was performed.

Meta-analysis

Sufficient data were available for meta-analysis for WOMAC score and VAS pain. Based on previous studies, the MCID for the WOMAC score was set at 9, while the MCID for VAS pain was set at 1.37 (34).

CS vs HA

The analysis on the comparison between CS and HA was performed on 15 studies. The analysis of WOMAC improvement was available for 1156 patients in ten studies and showed no difference between the two injective products at any of the follow-ups analyzed. The analysis of VAS pain improvement was available for 1384 patients in 13 studies and showed a statistically significant difference in favor of HA at the long-term follow-up (P = 0.011, MD = −0.95, SE = 0.37), while no difference was found at the remaining follow-ups (Fig. 3). The mean difference (MD) did not exceed the 1.37 MCID.

CS vs PRP

The analysis on the comparison between CS and PRP was performed on 13 studies. The analysis of WOMAC improvement was available for 530 patients in 8 studies and showed a statistically significant difference in favor of PRP at short- (P = 0.002, MD = −5.41, SE = 1.75), mid- (P < 0.001, MD = −15.22, SE = 2.92), and long-term (P < 0.001, MD = −9.65, SE = 1.02) follow-ups (Fig. 4). The MD exceeded the nine MCID at mid- and long-term follow-ups. The analysis of VAS pain improvement was available for 668 patients in 11 studies and showed a statistically significant difference in favor of PRP at mid- (P < 0.001, MD = −1.47, SE = 0.29) and long-term (P = 0.023, MD = −1.21, SE = 0.53) follow-ups (Fig. 4). The MD exceeded the 1.37 MCID at mid-term follow-up.

Risk of bias and quality of evidence

The evaluation using the RoB 2.0 tool showed that 14 study had a 'low risk' of bias, 18 studies had 'some concerns,' and three had a 'high risk' of bias. A summary of the risk of bias assessment of the included RCTs is illustrated in Fig. 5 (35). The GRADE evaluation showed that the level of evidence of the results was low in almost all the outcomes, with only four outcomes with a moderate level of evidence. A summary of the quality of evidence assessment of the meta-analyzed outcomes is illustrated in Table 1.

Discussion

The main findings of this meta-analysis question the current support for CS injections versus other injectable

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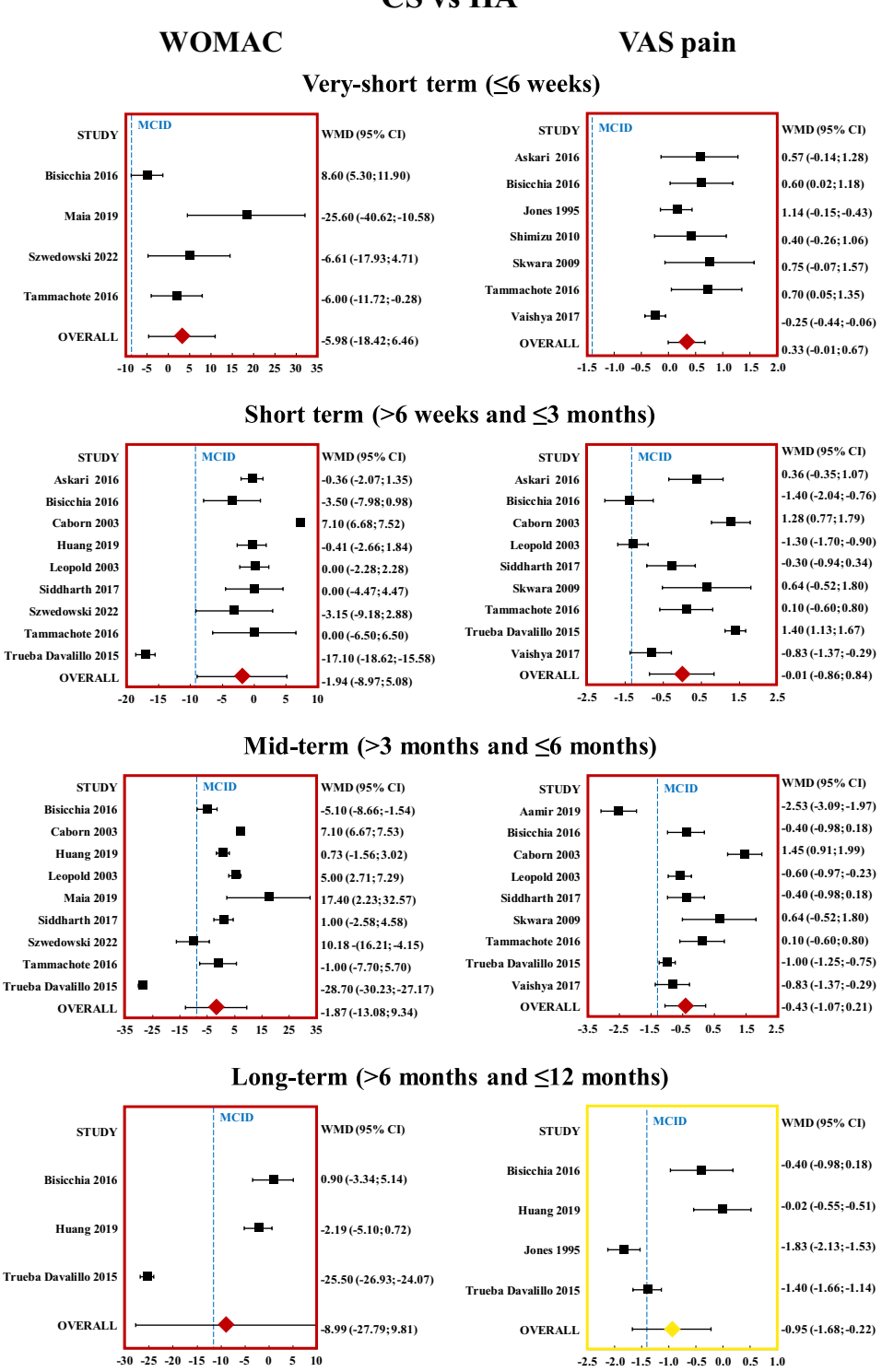

Figure 3

Forest plot of the individual studies (13, 60, 66, 67, 68, 73, 74, 78, 79, 80, 84, 85, 86, 87, 90) and pooled weighted mean difference (MD) for Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and Visual Analogue Scale (VAS) pain improvements comparing corticosteroids (CS) and hyaluronic acid (HA), including a 95% CI. No difference of WOMAC improvement was found between CS and HA at any follow-up. HA provided superior VAS improvement compared to CS at long-term follow-up. The MD did not exceed the minimal clinically important difference (MCID) value of 1.37 points. Red, not statistically significant; yellow, statistically but not clinically significant (MD < MCID); green, statistically and clinically significant (MD > MCID).

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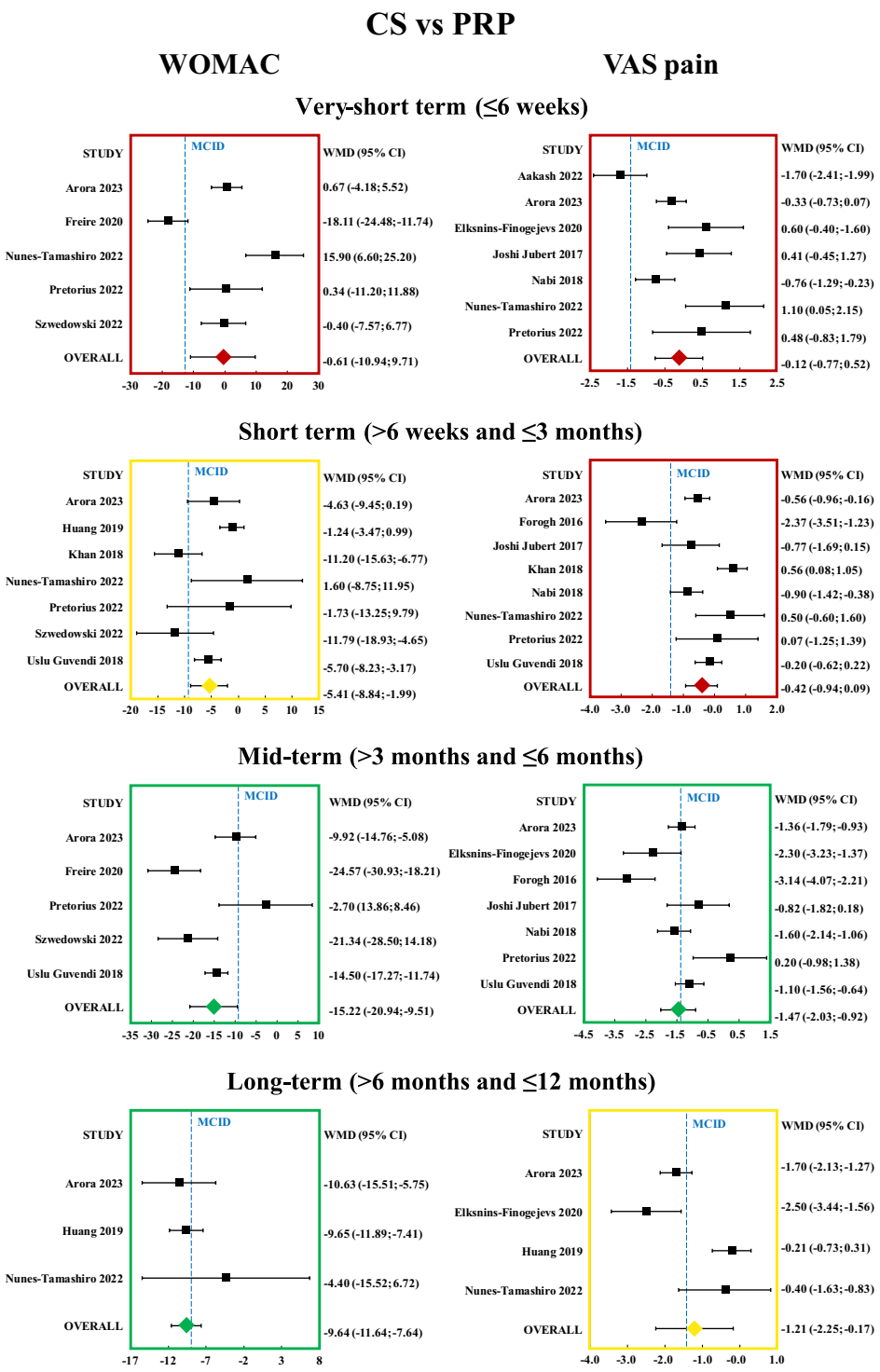

Figure 4

Forest plot of the individual studies (59, 60, 61, 62, 63, 64, 65, 67, 69, 71, 72, 75, 77) and pooled weighted mean difference (MD) for Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and Visual Analog Scale (VAS) pain improvements comparing corticosteroids (CS) and platelet-rich plasma (PRP), including a 95% CI. PRP provided superior WOMAC improvement compared to CS at short-, mid-, and long-term follow-ups. The MD exceeded the minimal clinically important difference (MCID) value of 9 points at mid- and long-term follow-ups. PRP provided superior VAS improvement compared to CS at mid- and long-term follow-ups. The MD exceeded the minimal clinically important difference (MCID) value of 1.37 points at the mid-term follow-up. Red, not statistically significant; yellow, statistically but not clinically significant (MD < MCID); green, statistically and clinically significant (MD > MCID).

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options. CS injections offers similar results to HA and PRP in terms of pain relief and functional improvement only at very short-term follow-up, while there is an overall superiority of PRP at longer follow-ups. The difference is not only statistically significant, but also clinically relevant in favor of PRP in patients affected by knee OA.

Intra-articular injective therapies represent a well-accepted conservative approach to address knee OA, especially in the early-to-moderate stages (36). Among the available alternatives, CS, HA, and PRP represent the most frequently prescribed products, but despite their widespread use in the clinical practice, the current major international societies guidelines do not provide concordant recommendations and the most appropriate intra-articular option for knee OA remains debated (17, 20, 37). CS is the option receiving more endorsement compared to HA and PRP for the management of knee OA. However, when looking at the scientific evidence, the benefits offered by CS injections seem to be lower compared to other injective approaches. The present meta-analysis provided the most updated and comprehensive evidence on the most common intra-articular options for knee OA, quantifying and comparing the benefits offered by CS in comparison to HA and PRP. Most importantly, this meta-analysis focused on the clinical relevance of the literature findings, analyzing the obtained results in light of the MCID of the scores analyzed. This represents a crucial aspect since statistically significant results do not always translate into clinically appreciable benefits for patients, and study results should always be interpreted in terms of the patient perspective (59).

The oldest and most documented alternative to CS is HA. The meta-analysis documented similar results, with negligible differences. The results of this study on the analysis comparing CS and HA outcomes showed a statistically significant difference in favor of HA only in terms of VAS pain improvement at long-term follow-up, and this improvement did not exceed the MCID, failing to prove a clinical superiority in terms of patient's perception. Moreover, no significant differences were found between the two injectable products in terms of VAS pain improvement at shorter follow-ups or in terms of WOMAC improvement at any of the follow-ups analyzed. A previous Cochrane review published by Bellamy *et al.* (38) as well as previous meta-analyses supported the equivalence between these two products or suggested a moderate superiority of HA at longer follow-ups (39, 38, 40, 41, 42). However, the strength of the current meta-analysis lies in the inclusion of a larger number of studies and even more in the interpretation of the clinical relevance of the obtained results. These results show that the two products offer similar results in terms of both entity and duration of the effects, and that the claimed superiority of HA compared to CS in terms of duration of effect on pain relief for knee OA treatment is minimal.

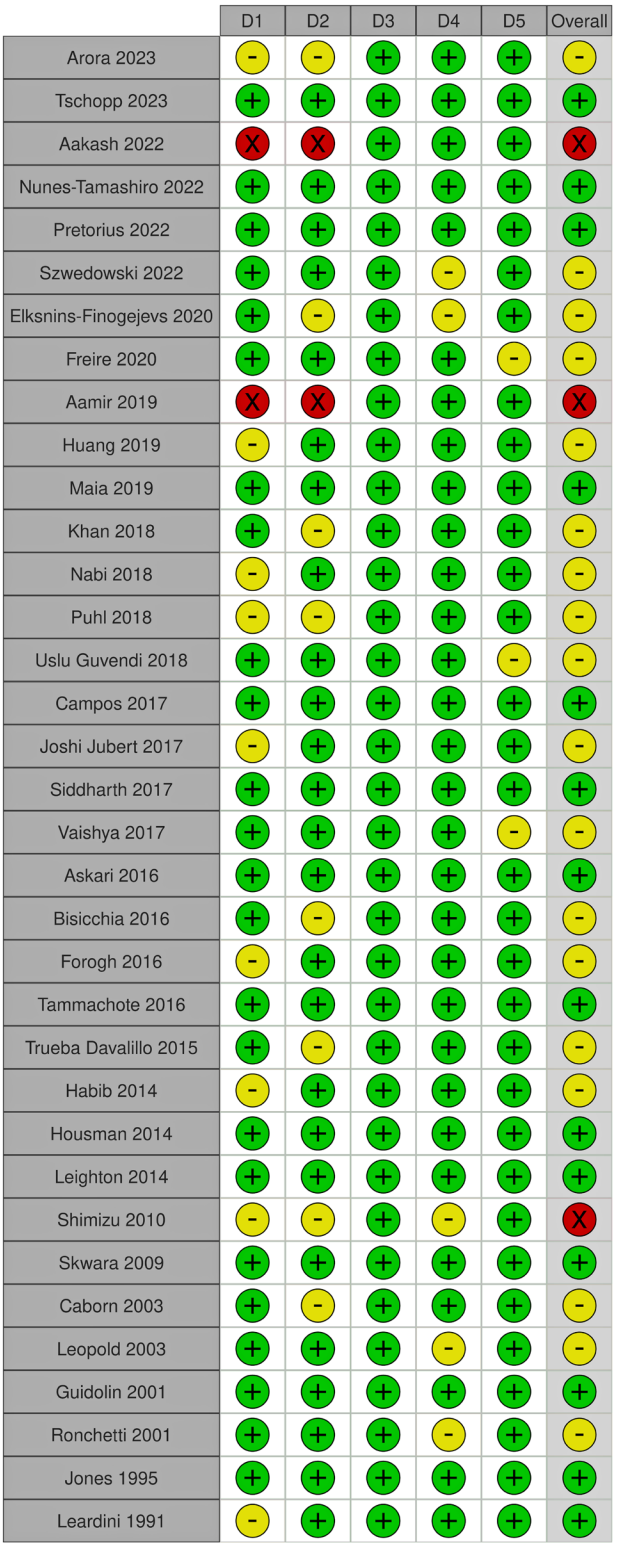

Figure 5

Cochrane risk-of-bias tool for randomized trials (13, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91) Version 2 (RoB 2.0). Green, low risk; yellow, some concerns; red, high risk.

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Table 1 GRADE evaluation.

Outcomes	RoB	Incon	Indir	Imprecision	Pub bias	Other	Quality of the evidence
CS vs PRP							
VAS							
Very short-term	No	Some	No	Some	No	No	Low : ⊕⊕◯◯
Short-term	No	Some	No	Some	No	No	Low: ⊕⊕◯◯
Mid-term	No	Some	No	Some	No	No	Low: ⊕⊕◯◯
Long-term	No	Some	No	Some	No	No	Low: ⊕⊕◯◯
WOMAC							
Very short-term	No	Some	No	Some	No	No	Low: ⊕⊕◯◯
Short-term	No	Some	No	Some	No	No	Low: ⊕⊕◯◯
Mid-term	No	Some	No	Some	No	No	Low: ⊕⊕◯◯
Long-term	No	Some	No	Some	No	No	Low: ⊕⊕◯◯
CS vs HA							
VAS							
Very short-term	No	Some	No	Some	No	No	Low: ⊕⊕◯◯
Short-term	No	Some	No	No	No	No	Moderate: ⊕⊕⊕◯
Mid-term	No	Some	No	No	No	No	Moderate: ⊕⊕⊕◯
Long-term	No	Some	No	Some	No	No	Low: ⊕⊕◯◯
WOMAC							
Very short-term	No	Some	No	Some	No	No	Low: ⊕⊕◯◯
Short-term	No	Some	No	No	No	No	Moderate: ⊕⊕⊕◯
Mid-term	No	Some	No	No	No	No	Moderate: ⊕⊕⊕◯
Long-term	No	Some	No	Some	No	No	Low: ⊕⊕◯◯

Incon, inconsistency; Indir, indirectness; Pub, publication; RoB, risk of bias.

The comparison with PRP showed different findings. The results of the analysis comparing CS and PRP outcomes showed that PRP was able to produce a statistically higher WOMAC improvement at short-, mid-, and long-term follow-ups. Similarly, the VAS pain improvement analysis identified a statistically significant difference in favor of PRP at mid- and long-term follow-ups. These improvements exceeded the MCID at mid- and long-term for WOMAC and at mid-term for VAS, demonstrating the clinical relevance of the benefits offered by PRP compared to CS. Previous meta-analyses on a lower number of studies suggested the potential of PRP to provide better results than CS by showing statistically superior results in terms of pain relief and functional improvement at intermediate and longer follow-ups but without investigating the clinical relevance of the observed findings (40, 41, 42, 43, 44). The results of the current study shed new light on the differences among these treatments in terms of effect and duration that patients could expect using CS, HA, or PRP. Looking at the obtained results, PRP seems to be a more effective injective approach for the treatment of knee OA patients.

Another aspect, beside treatment effectiveness, is important and should be considered in the clinical practice. In fact, there is an ongoing debate regarding the safety profile of intra-articular CS injections, with controversial findings reported in the current literature. At preclinical level, CS present anti-anabolic effects on healthy cartilage, raising questions about their potential damage to the cartilage joint surface (45, 46). *In vitro* studies showed deleterious effects of different CS on cartilage tissue, inducing apoptosis in human chondrocytes and aggravating the condition of the cartilage matrix already suffering from the OA environment, upregulating aggrecanases, collagenases, and metalloproteinases, and reducing lubricin production (45, 46, 47). *In vivo* studies on animal models also highlighted negative effects of CS injections on cartilage tissue, with loss of normal luster, fine fissures, cartilage thinning, matrix fibrillation, chondrocyte distribution, hypocellularity, and a decrease in the concentration of articular cartilage proteoglycans (46, 48, 49). These findings raised concerns about the risks that intra-articular CS might facilitate tissue atrophy, joint destruction, and cartilage degeneration also in the clinical setting. This was confirmed in a recent saline controlled, double-blind RCT on 140 knee OA patients with ultrasound documented synovitis receiving an intra-articular injection of 40 mg of triamcinolone every 3 months. Magnetic resonance imaging evaluation at 2 years revealed a significantly greater cartilage volume loss in patients treated with CS injections compared to saline controls (50). A study from the Osteoarthritis Initiative confirmed that intra-articular CS injections, especially repeated CS administrations, are associated with an increased risk of knee OA progression in terms of KL grade and joint space narrowing compared to controls (51). On the other hand, the clinical relevance of the joint space narrowing documented remains controversial, and a more recent study using the Osteoarthritis Initiative database and the database of the Multicenter Osteoarthritis Study found that intra-

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articular CS injections were not associated with an increased risk of knee OA progression when compared to HA injections (52). Nonetheless, considering their controversial safety profile, as well as the lack of superiority compared to HA and the lower clinical effectiveness compared to PRP, CS injections have no ground to be considered the preferred injective option for the management of patients with knee OA.

This meta-analysis presents some limitations that require consideration. First, the selected RCTs lacked standardization in data collection and reporting of outcome measures and associated follow-up timeframes, reducing the amount of data available for the meta-analysis. Second, the MCID is primarily intended as a measure of clinically significant improvement in a patient undergoing a specific intervention, and the high variability in the MCIDs reported in the literature (53) suggests some caution when considering it in regard to the mean change in a heterogeneous population. Nonetheless, the MCID is increasingly used to interpret the relevance of the difference documented in a quantitative synthesis and represents a useful tool to evaluate the clinical significance of the obtained results (54). Third, while the overall results were both statistically and clinically significant, it is still important to underline that different patients may present different risks and different treatment indications. Cartilage loss may be considered a problem in older patients with more advanced OA, while it could be a primary concern in young patients with early OA. Moreover, swollen knees and dry painful knees may present different treatment response and indication, and many other factors my influence the results and therefore the treatment choice (55, 56, 57) Future studies should investigate which patient categories could benefit the most from each individual product in order to maximize treatment efficacy and tailor the therapy to the specific patient characteristics, optimizing the management of knee OA in the clinical practice.

Despite these limitations, the present meta-analysis was able to provide valuable insights to the scientific discussion on the most suitable intra-articular injective approach to address knee OA, quantifying and comparing the clinical relevance of the benefits offered by the most used products. These findings represent an important reference for patients and physicians considering intra-articular injections, helping them having realistic expectations and optimizing the treatment indications when managing knee OA in the clinical practice.

Conclusion

This systematic review and meta-analysis provided important evidence on the clinical benefits offered by the intra-articular injection of CS compared to HA and PRP to treat OA patients. CS injections offer similar results to HA and to PRP in terms of pain relief and functional improvement at very short-term follow-up, while there is an overall superiority of PRP at longer follow-ups. This difference is not only statistically significant but also clinically relevant in favor of PRP in patients affected by knee OA.

Supplementary materials
This is linked to the online version of the paper at https://doi.org/10.1530/EOR-23-0198.

ICMJE Conflict of Interest Statement
The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the study reported.

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