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Does Hyaluronic Acid Add Benefit to Exercise Therapy in Patellar Chondromalacia? A Narrative Review of Current Evidence

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Abstract

Background:

Patellar chondromalacia is a common cause of anterior knee pain, particularly among young and physically active individuals. Conservative treatment remains the first-line approach and typically includes exercise-based physiotherapy, activity modification, and, in selected cases, intra-articular injections.

Objective:

To summarize current evidence regarding the effectiveness of physiotherapy and hyaluronic acid (HA) supplementation in the management of patellar chondromalacia.

Methods:

A narrative review of the literature was performed using PubMed database. Studies evaluating exercise therapy, rehabilitation protocols, intra-articular HA injections, and oral HA supplementation in patients with patellar chondromalacia or patellofemoral pain associated with chondral degeneration were considered.

Results:

Exercise-based physiotherapy consistently demonstrated improvements in pain and function and remains the cornerstone of conservative management. Strengthening of the quadriceps and hip musculature appears particularly beneficial. Evidence supporting intra-articular HA injections is mixed: some studies report reductions in pain and functional improvement, whereas randomized controlled trials have failed to show clear superiority over sham injection

in all patient populations. Evidence for oral HA supplementation remains limited and of lower methodological quality.

Conclusions:

Current evidence supports physiotherapy as the primary treatment modality for patellar chondromalacia. Intra-articular HA may be considered as an adjunctive option in selected patients who do not respond adequately to rehabilitation, while evidence for oral HA remains insufficient for strong recommendations. Further high-quality comparative trials are needed.

Keywords

patellar chondromalacia; patellofemoral pain; hyaluronic acid; viscosupplementation; physiotherapy; rehabilitation; exercise therapy; anterior knee pain.

1. Introduction

Patellofemoral disorders represent a common cause of anterior knee pain, particularly among adolescents, young adults, and physically active individuals (1,2). Patellofemoral pain (PFP) is clinically characterized by pain perceived around or behind the patella that is typically aggravated by activities involving increased patellofemoral joint loading, such as squatting, stair climbing, running, or prolonged sitting (1). PFP represents a substantial clinical and socioeconomic burden, with epidemiological studies demonstrating a high prevalence across both athletic and general populations (1–3). A systematic review and meta-analysis reported an annual prevalence of patellofemoral pain of approximately 22.7% in the general population and 28.9% among adolescents (3).

The terminology used to describe patellofemoral disorders has evolved considerably. Historically, the term *chondromalacia patellae* was frequently used interchangeably with anterior knee pain and patellofemoral pain syndrome (1,4). Contemporary concepts, however, suggest that these terms should not be considered synonymous (1,4). Patellar chondromalacia refers primarily to structural abnormalities of the patellar articular cartilage, whereas patellofemoral pain represents a clinical syndrome that may occur in the presence or absence of demonstrable cartilage pathology (1,5). This distinction is clinically relevant because structural cartilage abnormalities do not necessarily correlate with the presence or severity of symptoms (1,5).

Patellar chondromalacia is characterized by pathological changes involving the articular cartilage of the patella, including cartilage softening, swelling, fibrillation, fissuring, and, in more advanced cases, cartilage loss (6,7). Its pathogenesis is considered multifactorial and may involve repetitive mechanical loading, abnormal patellar kinematics, anatomical variations, patellofemoral instability, trauma, and altered neuromuscular control (6,8–10). Importantly, the relationship between cartilage abnormalities and clinical symptoms remains complex, and no single biomechanical or structural factor can adequately explain all cases (5,8–10).

Conservative management is generally considered the initial therapeutic approach for patients with symptomatic patellofemoral disorders (11,12). Current evidence places exercise-based rehabilitation and patient education at the center of treatment, with particular emphasis on strengthening the knee and hip musculature and addressing individual biomechanical and functional impairments (11–13). Contemporary consensus recommendations support exercise therapy, particularly combined hip- and knee-focused exercise, as a principal intervention for patients with patellofemoral pain (12,13).

Despite the central role of rehabilitation, pharmacological and injection-based interventions have attracted considerable interest. Hyaluronic acid (HA), administered primarily through intra-articular injection, has been proposed as a potential adjunctive treatment because of its viscoelastic, lubricating, and potentially analgesic and anti-inflammatory properties (14,15). However, clinical studies evaluating HA in patients with patellar chondral pathology have produced mixed results (16,17), and its role in the management of patellar chondromalacia remains uncertain (16–18). Evidence concerning orally administered HA is even more limited (19).

Therefore, the aim of this narrative review is to critically summarize the current evidence regarding the conservative management of patellar chondromalacia, with particular emphasis on exercise-based physiotherapy and hyaluronic acid. The review specifically examines whether HA provides additional clinical benefits when combined with an appropriately structured rehabilitation program and identifies current gaps in the evidence that warrant further research.

2. Methods

2.1. Review Design

This article was conducted as a narrative review to critically summarize and interpret the available evidence regarding the role of exercise-based rehabilitation and hyaluronic acid (HA) in the management of symptomatic patellar chondral pathology. The review was designed to address the central clinical question of whether HA may provide additional benefits when used as an adjunct to appropriately structured exercise-based rehabilitation.

The primary focus of the review was symptomatic patellar chondral pathology, including patellar chondromalacia and documented patellar cartilage lesions (1,4,6). However, because the available literature specifically involving patients with structurally confirmed patellar cartilage pathology is limited, evidence from the broader patellofemoral pain (PFP) population was also considered when directly relevant to exercise therapy, patellofemoral biomechanics, or intra-articular HA treatment (11,12,16–18). Such evidence was regarded as indirect when applied to patients with confirmed patellar chondral pathology.

Because this was a narrative review, the literature search, study selection, and evidence synthesis were not conducted as a formal systematic review or meta-analysis.

2.2. Literature Search

A literature search was performed in the PubMed/MEDLINE database from inception to August 2026. The search strategy combined controlled vocabulary, where applicable, with free-text terms related to patellar cartilage pathology, patellofemoral pain, hyaluronic acid, and exercise-based rehabilitation.

The main search concepts included:

("patellar chondromalacia" OR "patellar chondropathy" OR "patellar cartilage lesion*" OR "patellar cartilage damage" OR "patellofemoral chondral lesion*" OR "patellofemoral pain")

AND

("hyaluronic acid" OR hyaluronan OR "sodium hyaluronate" OR viscosupplementation)

AND

("exercise therapy" OR physiotherapy OR "physical therapy" OR rehabilitation OR strengthening OR "hip strengthening" OR "quadriceps strengthening" OR "movement retraining").

Additional searches were performed using treatment- and study- specific terms, including "intra-articular", "oral", "supplementation", "randomized controlled trial", "clinical trial", "systematic review", "meta-analysis", and "consensus statement".

Reference lists of key systematic reviews, randomized controlled trials, clinical practice guidelines, consensus statements, and narrative reviews were also manually screened to identify additional relevant publications.

2.3. Eligibility Criteria and Scope of Evidence

Publications were considered eligible when they addressed at least one of the following topics:

1. the pathophysiology or clinical characteristics of symptomatic patellar chondral pathology;
2. exercise-based physiotherapy or rehabilitation for patellofemoral disorders;
3. intra-articular hyaluronic acid in patients with patellar chondral pathology or patellofemoral pain;
4. oral hyaluronic acid supplementation in knee joint disorders.

Randomized controlled trials, prospective and retrospective clinical studies, systematic reviews, meta-analyses, clinical practice guidelines, international consensus statements, and relevant mechanistic studies were considered. Studies published in English were included.

Evidence was interpreted according to its directness to the primary population of interest. Studies specifically involving patients with documented patellar cartilage lesions or symptomatic patellar chondral pathology were considered direct evidence. Studies involving broader PFP populations were considered indirect evidence when applied to patients with structurally confirmed patellar cartilage pathology. Evidence from patients with knee osteoarthritis was considered indirect and was included only when necessary, particularly in the discussion of oral HA or broader mechanistic and safety considerations.

Studies were excluded when they focused exclusively on non-knee conditions, investigated surgical interventions without relevance to conservative management, or did not provide clinically relevant information regarding the interventions or outcomes addressed in this review.

2.4. Study Selection and Data Extraction

Titles and abstracts identified through the literature search were screened for relevance to the objectives and scope of the review. Potentially relevant publications were subsequently assessed on the basis of their full text. Reference lists of key publications were additionally screened manually to identify potentially relevant studies not captured by the database search.

For each relevant study, the following information was extracted where available: study design, sample size, patient characteristics, diagnostic criteria, presence and severity of structural cartilage pathology, intervention characteristics, comparator intervention, rehabilitation or exercise protocol, duration of follow-up, outcome measures, main clinical findings, structural outcomes, and reported adverse events.

Particular attention was given to randomized controlled trials evaluating intra-articular HA in patients with patellar chondral pathology or PFP, with priority given to studies involving structurally confirmed patellar cartilage lesions. Particular emphasis was placed on studies comparing HA combined with physiotherapy or exercise therapy with rehabilitation alone or sham injection.

2.5. Evidence Synthesis

A quantitative meta-analysis was not performed because of substantial heterogeneity in patient populations, diagnostic definitions, the presence or absence of structurally confirmed cartilage pathology, HA formulations and administration protocols, rehabilitation programs, outcome measures, and follow-up periods.

The evidence was therefore synthesized narratively, with particular emphasis on its directness to the primary population of interest. Studies involving confirmed patellar cartilage lesions were distinguished from those investigating the broader PFP population, while evidence derived from knee osteoarthritis populations was explicitly identified as indirect.

The findings were organized into the following themes:

1. terminology, pathophysiology, and clinical characteristics of patellar chondral pathology;
2. exercise-based rehabilitation and physiotherapy;
3. intra-articular HA and its potential mechanisms of action;
4. direct clinical evidence for HA in patellar chondral pathology and relevant evidence from PFP populations;
5. the potential additive effect of HA when combined with exercise-based rehabilitation;
6. oral HA and the limitations of indirect evidence;
7. clinical implications, limitations of the current evidence base, and future research priorities.

3. Pathophysiology and Clinical Characteristics

3.1. Pathophysiology

Patellar chondromalacia is characterized by structural alterations of the patellar articular cartilage, ranging from cartilage softening and superficial fibrillation to fissuring, thinning, and more advanced cartilage loss (20,21). Although the condition has traditionally been attributed primarily to excessive mechanical stress within the patellofemoral joint, current evidence suggests that its pathogenesis is multifactorial and involves an interaction between joint morphology, patellar kinematics, neuromuscular function, and mechanical loading (1,20,22).

The patellofemoral joint is exposed to substantial mechanical forces during activities such as squatting, stair climbing, running, and jumping (23). Patellofemoral joint mechanics are determined by the interaction between the geometry of the patella and trochlea, the surrounding ligamentous structures, and the forces generated by the quadriceps and other muscles of the lower extremity (23,24). Variations in trochlear morphology, patellar height, patellar tilt, and patellar tracking may alter the distribution of contact forces across the patellofemoral joint (24,25).

Imaging studies have demonstrated associations between patellar chondral abnormalities and altered patellofemoral morphology. In particular, trochlear dysplasia and increased patellar tilt have been associated with the presence of patellar chondromalacia (26,27). However, these morphological characteristics do not necessarily determine the severity of cartilage damage, suggesting that structural abnormalities alone are insufficient to explain the clinical presentation (26).

Muscular function represents another important component of patellofemoral biomechanics. Alterations in quadriceps strength and neuromuscular control may influence patellar motion and the distribution of joint loading (10). In addition, proximal lower-limb mechanics appear to contribute to patellofemoral loading (25). Systematic review evidence has demonstrated an association between patellofemoral pain and increased hip adduction during activities such as running and single-leg squatting (28), supporting the concept that hip and trunk function may influence the mechanical environment of the patellofemoral joint (25,28).

Importantly, the relationship between structural cartilage damage and symptoms is complex. Articular cartilage itself is aneural, and therefore cartilage lesions do not directly generate pain in the same manner as innervated tissues (20). Pain may instead arise from surrounding structures, including the synovium, subchondral bone, retinaculum, and other periarticular tissues (20). Consequently, the severity of cartilage abnormalities does not necessarily correspond to the severity of anterior knee pain (20,29). In a study of young adults with anterior knee pain, the severity of arthroscopically confirmed chondromalacia was not associated with the severity of clinical symptoms (29).

This distinction is particularly relevant when evaluating conservative treatments. An intervention that improves pain and function does not necessarily need to induce structural cartilage regeneration to produce a clinically meaningful effect (20,30). Exercise-based rehabilitation may reduce symptoms by modifying muscle strength, neuromuscular control, movement patterns, and patellofemoral loading rather than directly restoring damaged cartilage (9,12,30). Similarly, the potential clinical effects of intra-articular hyaluronic acid may involve

modulation of the joint environment and nociceptive processes rather than structural restoration of the patellar cartilage (14,15).

3.2. Clinical Characteristics

The clinical presentation of symptomatic patellar chondromalacia commonly overlaps with that of patellofemoral pain. Patients typically report anterior or retropatellar knee pain that is aggravated by activities associated with increased patellofemoral loading, including squatting, stair climbing, running, jumping, and prolonged sitting (1). Symptoms may be unilateral or bilateral and are frequently exacerbated by repetitive or high-load activities (31).

Physical examination may reveal tenderness around the patella, pain during squatting or other provocative activities, and abnormalities in patellar mobility or tracking (1,32). However, no single clinical test is sufficiently specific to establish the presence of a patellar cartilage lesion (29). This is partly explained by the multifactorial nature of patellofemoral pain and by the imperfect relationship between structural cartilage abnormalities and symptoms (1,29).

Magnetic resonance imaging (MRI) is commonly used to evaluate patellar cartilage morphology and associated patellofemoral abnormalities. MRI can demonstrate focal cartilage signal abnormalities, surface irregularity, cartilage thinning, and more advanced cartilage defects (33). Earlier MRI studies demonstrated a substantial correlation between MRI findings and arthroscopic assessment of chondromalacia, supporting its role in structural assessment (33).

Several MRI-based grading systems have subsequently been proposed to characterize the severity of patellar cartilage abnormalities (34). However, the presence of a cartilage lesion on MRI should be interpreted in the context of the patient's clinical presentation rather than considered an independent indication for treatment (1,29). Structural abnormalities may occur without substantial symptoms, and the severity of MRI abnormalities does not consistently predict pain severity or functional impairment (1,29,35).

From a clinical perspective, the distinction between structural pathology and the broader patellofemoral pain phenotype is therefore essential. Patients presenting with anterior knee pain may have demonstrable cartilage abnormalities, altered biomechanics, or predominantly functional impairments, and these factors may coexist to varying degrees (1,5,9,29). Consequently, conservative treatment should be individualized according to the patient's symptoms, functional limitations, physical findings, and contributing biomechanical factors rather than based solely on imaging findings (1,9,12).

4. Physiotherapy and Exercise Therapy

4.1. Exercise Therapy as the Cornerstone of Conservative Management

High-quality evidence supporting exercise therapy derives primarily from patients with patellofemoral pain rather than from populations with structurally confirmed patellar chondral lesions (2,12). Nevertheless, these findings are clinically relevant because symptomatic patellar chondral pathology frequently coexists with the broader patellofemoral pain phenotype (1,5). Its therapeutic rationale extends beyond direct strengthening of the quadriceps and includes

modification of lower-limb biomechanics, improvement of neuromuscular control, optimization of movement patterns, and progressive adaptation to mechanical loading(9,12,30).

Evidence from systematic reviews and meta-analyses consistently supports the clinical effectiveness of exercise therapy. A systematic review and meta-analysis by Clijisen et al. included 15 studies involving 748 participants and demonstrated that exercise therapy was associated with substantial reductions in pain and improvements in activity limitations and participation restrictions (2). Significant benefits were observed particularly during the short-term follow-up period, while improvements in functional outcomes were also observed at longer follow-up (2). However, the authors emphasized heterogeneity in exercise protocols and methodological quality across the included studies (2).

Similarly, an abridged Cochrane systematic review including 31 trials and 1690 participants found that exercise therapy was associated with clinically relevant improvements in pain and functional ability compared with control interventions (36). The review also suggested that programs combining hip and knee exercises may provide greater short-term pain reduction than knee-focused exercise alone (36). Nevertheless, the certainty of evidence was considered low or very low, largely because of methodological limitations and heterogeneity between trials (36).

More recent evidence has strengthened the position of exercise therapy within contemporary clinical practice. The 2018 international consensus statement on exercise therapy and physical interventions recommended exercise therapy, particularly programs combining hip- and knee-focused exercises, for improving pain and/or function in individuals with patellofemoral pain (12). The 2024 best-practice guide similarly identified knee-targeted with or without hip-targeted exercise, supported by patient education, as the primary intervention for patellofemoral pain (37). Additional interventions should be selected according to individual clinical presentation and patient preferences (37).

Importantly, the therapeutic effects of exercise should not be interpreted as evidence of direct cartilage regeneration. In patients with patellar chondral pathology, exercise may primarily improve symptoms and function by modifying muscle capacity, movement patterns, neuromuscular control, and patellofemoral joint loading (9,12,30). This distinction is particularly relevant when evaluating exercise therapy alongside intra-articular treatments such as hyaluronic acid.

4.2. Quadriceps Strengthening

Quadriceps strengthening has traditionally been considered a central component of rehabilitation for patellofemoral disorders. The quadriceps musculature plays a major role in controlling knee motion and contributes substantially to the mechanical environment of the patellofemoral joint (23,24). Consequently, improving quadriceps strength and endurance may enhance the patient's ability to tolerate functional and sporting activities (2,38).

However, contemporary rehabilitation strategies generally favor progressive strengthening of the quadriceps as part of a broader exercise program rather than isolated activation of the vastus medialis obliquus (12,30). Evidence from comparative studies indicates that different forms of quadriceps exercise, including open- and closed-kinetic-chain exercises, can be effective, and no single exercise modality has consistently demonstrated clear superiority (36).

A systematic review and meta-analysis of exercise therapy found that exercise programs overall provide meaningful reductions in pain and improvements in function, while the optimal combination of individual exercise modalities remains uncertain (2).

Therefore, quadriceps strengthening should be considered an important component of rehabilitation, but not as an isolated treatment targeting a presumed single muscular deficit (12,30). Exercise selection should instead be individualized according to symptoms, strength deficits, functional limitations, and tolerance to loading (12,37).

4.3. Hip-Focused Exercise

Increasing attention has been directed toward the role of proximal lower-limb musculature in the development and persistence of patellofemoral symptoms. Weakness or impaired neuromuscular control of the hip abductors and external rotators may contribute to excessive hip adduction and internal rotation during weight-bearing activities, potentially altering lower-limb alignment and patellofemoral loading (9,25,28,30).

Evidence supports the inclusion of hip-focused strengthening within rehabilitation programs. A systematic review and meta-analysis of 14 trials involving 673 participants found that combined hip and knee strengthening significantly reduced pain and improved activity compared with no training or placebo interventions (39).

A subsequent systematic review and meta-analysis comparing hip-and-knee, hip-only, and knee-only exercise programs found that combined hip-and-knee programs produced substantial improvements in pain and function (40). However, subgroup analyses did not consistently demonstrate superiority of combined programs over hip-only interventions, suggesting that the optimal exercise strategy may depend on individual patient characteristics rather than a universal requirement for a specific exercise combination (40).

These findings support a shift from a purely knee-centered rehabilitation model toward an individualized kinetic-chain approach (12,37,40). Rather than assuming that all patients with patellofemoral symptoms require identical strengthening protocols, clinicians should identify relevant proximal and distal impairments and incorporate targeted exercises accordingly (12,37).

4.4. Movement and Neuromuscular Retraining

Strengthening alone may not fully address the functional factors contributing to patellofemoral symptoms. Consequently, movement retraining has emerged as an additional component of contemporary rehabilitation, particularly in patients demonstrating excessive dynamic knee valgus, hip adduction, or other movement-pattern abnormalities (9,12,41).

A 2023 systematic review with network meta-analysis included 37 randomized controlled trials involving 1235 participants and evaluated interventions designed to modify movement patterns during weight-bearing activities. The combination of knee- and hip-focused exercises with internal feedback demonstrated the strongest effect on reducing frontal-plane knee movement, with moderate-certainty evidence. The intervention also reduced frontal-plane hip movement and increased sagittal-plane knee movement compared with hip- and knee-focused exercises alone (41).

These findings suggest that rehabilitation may benefit from incorporating movement-quality training in addition to conventional strengthening (41). Importantly, movement retraining should be individualized rather than applied universally, as not every patient with patellofemoral pain demonstrates the same biomechanical abnormality (9,12,41).

4.5. Adjunctive Physiotherapeutic Interventions

Several adjunctive interventions may be incorporated into rehabilitation programs, including patellar taping, foot orthoses, manual therapy, and movement or running retraining (12,37). Current evidence suggests that these interventions should generally be used to complement rather than replace exercise therapy (12,37).

The 2018 international consensus statement supported combined interventions and foot orthoses in selected patients, while isolated patellofemoral, knee, or lumbar mobilization and electrophysical agents were not recommended as primary interventions (12).

Similarly, the 2024 best-practice guide recommends tailoring additional interventions to the individual patient's presentation, preferences, and clinical response. Exercise therapy and education should remain the foundation of treatment (37).

Recent evidence concerning prolonged taping combined with exercise suggests potential improvements in pain; however, substantial heterogeneity between studies limits the certainty of these findings (42).

5. Does Hyaluronic Acid Provide an Additional Benefit Beyond Exercise-Based Rehabilitation?

5.1. Biological Rationale for Hyaluronic Acid as an Adjunct to Rehabilitation

Exercise-based rehabilitation remains the foundation of conservative management for patellofemoral disorders (12,37). However, persistent pain may limit a patient's ability to participate in or progress through an appropriately structured rehabilitation program. In this context, intra-articular hyaluronic acid (HA) has been proposed as a potential adjunctive intervention rather than a substitute for exercise-based treatment (18).

HA is a naturally occurring glycosaminoglycan and an important component of synovial fluid and the extracellular matrix of articular cartilage. Its proposed biological functions include lubrication of articular surfaces, modulation of the intra-articular environment, and potential effects on inflammatory and nociceptive processes (14,15). The rationale for intra-articular administration is therefore primarily symptomatic and functional rather than regenerative (14,15).

If HA reduces pain sufficiently to improve participation in progressive rehabilitation, it could theoretically enhance the effects of exercise therapy. Exercise-based rehabilitation and HA may therefore target different components of symptomatic patellofemoral disorders. Rehabilitation primarily aims to improve muscle capacity, neuromuscular control, movement patterns, and tolerance to mechanical loading, whereas HA may influence symptoms through intra-articular and nociceptive mechanisms (9,12,14,15).

Importantly, this theoretical rationale does not establish a clinical benefit. Symptomatic improvement following HA administration should not automatically be interpreted as evidence of cartilage regeneration, and a potential biological effect does not necessarily translate into an additional clinically meaningful benefit beyond an appropriately implemented rehabilitation program (14,15). The central clinical question is therefore not whether HA can improve symptoms in isolation, but whether its addition to exercise-based rehabilitation produces better outcomes than rehabilitation alone.

5.2. Direct Clinical Evidence for an Additive Effect

The available direct clinical evidence remains limited and is dominated by two randomized trials that produced apparently conflicting results.

Hart et al. conducted a prospective, randomized, double-blind, sham-controlled trial involving 86 patients with patellofemoral pain who had previously failed conservative management. Participants received either a single intra-articular HA injection or a sham injection, while both groups followed a home exercise program involving lower-extremity strengthening and flexibility exercises. At six months, both groups demonstrated significant improvements in pain and patient-reported functional outcomes. However, no significant between-group differences were identified in pain, KOOS domains, Kujala scores, quadriceps strength, or activity level (17).

These findings suggest that, in this population, the addition of a single HA injection did not provide a clinically meaningful benefit beyond continued exercise-based rehabilitation and the effects associated with a sham injection (17). Because patient selection was based primarily on patellofemoral pain rather than documented structural cartilage pathology, the findings should be considered indirect when applied to patients with confirmed patellar chondral lesions (17).

In contrast, Astur et al. investigated 70 patients with anterior knee pain and documented grade II or III patellar cartilage lesions. Patients were randomized to physical therapy alone or physical therapy combined with intra-articular HA. At three and six months, patients receiving HA in addition to physical therapy demonstrated lower pain scores and better Kujala and Lysholm functional scores than patients treated with physical therapy alone (16). No difference in MRI-based cartilage classification was observed between the groups (16).

Unlike the study by Hart et al., this trial provides more direct evidence for patients with structural patellar chondral pathology (16). Its findings suggest that HA may provide an additional symptomatic benefit when combined with physical therapy in selected patients with documented cartilage lesions (16). However, the absence of differences in MRI-based cartilage classification indicates that the observed clinical improvement was not accompanied by demonstrable structural improvement within the duration of follow-up (16).

The key characteristics and findings of these trials are summarized in Table 1.

5.3. Why Do the Available Trials Report Different Results?

The apparent discrepancy between the findings of Hart et al. and Astur et al. should not necessarily be interpreted as evidence that one intervention was effective and the other ineffective. Instead, the studies differed substantially in patient selection, diagnostic criteria, control interventions, HA protocols, and rehabilitation approaches (16,17).

The most clinically relevant difference concerns the study populations. Hart et al. primarily investigated patients with patellofemoral pain, a heterogeneous clinical syndrome in which structural cartilage pathology was not the primary basis for inclusion (17). In contrast, Astur et al. specifically enrolled patients with documented grade II or III patellar cartilage lesions (16). These populations should not be considered interchangeable.

This distinction may be particularly important because patients with patellofemoral symptoms represent a heterogeneous group. Symptoms may arise in the presence or absence of structural cartilage abnormalities and may be influenced by differences in muscle capacity, movement patterns, patellofemoral morphology, neuromuscular function, and mechanical loading (1,9,25,26,28). It is therefore plausible that the response to intra-articular HA may differ between patients with predominantly functional patellofemoral pain and those with symptomatic structural patellar cartilage lesions.

The control interventions also differed substantially. Hart et al. used a double-blind, sham-controlled design, providing a stronger basis for distinguishing a specific treatment effect from placebo or procedure-related effects (17). In contrast, the comparison between HA combined with physical therapy and physical therapy alone in the study by Astur et al. cannot isolate all potential nonspecific effects associated with an intra-articular procedure (16).

Additional differences in HA formulation, dosage, administration protocol, rehabilitation programs, baseline disease characteristics, outcome measures, and duration of follow-up further limit direct comparison between the trials (16,17). Consequently, the currently available evidence is insufficient to establish a universal additive effect of HA when combined with exercise-based rehabilitation.

5.4. Current Clinical Interpretation

Taken together, the available evidence does not support the routine addition of intra-articular HA to exercise-based rehabilitation for all patients with patellofemoral pain or patellar chondral pathology (16–18).

Exercise-based rehabilitation should remain the primary component of conservative management (12,37). Programs should be individualized according to the patient's symptoms, functional limitations, physical findings, and relevant biomechanical or neuromuscular impairments (12,37). HA should not be regarded as a substitute for progressive rehabilitation.

The evidence from Hart et al. suggests that HA does not necessarily provide additional benefit when added to exercise therapy in a broader patellofemoral pain population (17). Conversely, the findings of Astur et al. raise the possibility that patients with symptomatic and structurally documented patellar cartilage lesions may represent a subgroup in which HA could provide an additional symptomatic benefit (16).

However, this potential phenotype-dependent effect remains a hypothesis rather than an established clinical indication. The currently available studies are too limited and heterogeneous to identify which patients are most likely to benefit, which HA formulations or administration protocols should be used, or whether any observed differences are clinically meaningful over longer follow-up periods (16–18).

Therefore, intra-articular HA should not currently be considered a routine component of conservative treatment for patellar chondral pathology. If used, it should be regarded as an

adjunctive intervention in carefully selected patients rather than an alternative to active rehabilitation (12,16,17,37). Patients should also be informed that current evidence does not demonstrate cartilage regeneration and that the additional benefit of HA beyond an appropriately implemented exercise program remains uncertain (16–18).

Table 1. Comparison of the two randomized trials evaluating whether intra-articular hyaluronic acid provides additional benefit beyond rehabilitation

Characteristic	Hart et al., 2019	Astur et al., 2019
Study design	Prospective, randomized, double-blind, sham-controlled trial	Randomized controlled trial
Sample size	86 randomized; 80 completed follow-up (93%)	70 randomized; 63 patients completed follow-up (90%)
Population	Patients with clinically diagnosed patellofemoral pain	Patients with anterior knee pain and documented patellar chondropathy
Age	Mean 27.0 ± 7.7 years	Mean age of completers approximately 32 years
Definition of cartilage pathology	No structural cartilage lesion required for inclusion; radiographic OA was excluded	Grade II–III patellar cartilage lesion required for inclusion
Directness to symptomatic patellar chondral pathology	Indirect evidence	Direct evidence
Previous treatment status	Persistent symptoms despite ≥4 weeks of previous physical therapy	Not directly comparable to Hart; patients underwent study physical therapy
HA intervention	Single 6 mL intra-articular injection of hylan G-F 20 (Synvisc-One)	2 mL intra-articular HA
Control intervention	Sham procedure with needle insertion but no HA injection	Physical therapy alone
Blinding	Double-blind; outcome assessment by blinded observer	No patient blinding reported; outcome assessment performed by investigators separate from the HA injector
Rehabilitation	Both groups: standardized home strengthening and flexibility program, 4 times/week for 4 weeks	Both groups underwent physical therapy for 3 months
Primary symptom assessment	VAS pain during single-legged squat	VAS pain
Functional outcomes	KOOS, Kujala score, Tegner activity rating	Kujala and Lysholm scores
Objective/structural outcomes	Quadriceps strength and activation	MRI-based cartilage assessment; Clarke test

Follow-up	1, 3, and 6 months	3 and 6 months
Main result	Both groups improved, but HA was not superior to sham	HA + PT showed greater pain reduction and better functional scores than PT alone
Structural effect	Structural cartilage repair was not assessed as a primary outcome	No significant improvement in MRI-based cartilage classification
What does the trial answer?	Does a single HA injection outperform a sham procedure when added to a standardized exercise program in PFP? No.	Does HA + PT outperform PT alone in patients with documented grade II–III patellar lesions? Possibly yes.
Main limitation for interpreting the additive effect of HA	PFP population was heterogeneous and structural cartilage lesions were not required	No sham injection control; nonspecific effects of undergoing an injection cannot be fully separated from a specific HA effect

Footnote:

PFP - patellofemoral pain; PT - physical therapy; HA - hyaluronic acid; VAS - visual analogue scale; KOOS - Knee injury and Osteoarthritis Outcome Score; MRI – magnetic resonance imaging.

6. Oral Hyaluronic Acid

6.1. Rationale for Oral Administration

In contrast to intra-articular administration, oral hyaluronic acid (HA) supplementation has received considerably less attention in the treatment of knee disorders. The rationale for oral administration is based on the hypothesis that orally administered HA or its degradation products may be absorbed from the gastrointestinal tract and subsequently exert systemic biological effects (19,43). Experimental studies have suggested that low-molecular-weight fragments of hyaluronic acid may interact with receptors involved in immune regulation and tissue homeostasis. However, the biological mechanisms underlying the potential clinical effects of orally administered HA remain incompletely understood (43).

Importantly, the evidence supporting oral HA in patellar chondromalacia is substantially weaker than that available for intra-articular administration. A search of the available clinical literature identified no high-quality randomized controlled trials specifically evaluating oral HA in patients with symptomatic patellar chondromalacia. Consequently, evidence from other knee conditions, particularly knee osteoarthritis, should be considered indirect and should not be directly extrapolated to patients with isolated patellar chondral pathology (19).

6.2. Clinical Evidence

One of the principal randomized controlled trials evaluating oral HA in knee disease was conducted by Tashiro et al. The study included 60 patients with radiographic knee osteoarthritis classified as Kellgren–Lawrence grade 2 or 3. Participants received either 200 mg of oral HA daily or placebo for 12 months, and both groups performed daily quadriceps-strengthening exercises. Symptoms improved over time in both groups, with a tendency toward greater

improvement in the HA group. Among participants aged 70 years or younger, the HA group demonstrated significantly better Japanese Knee Osteoarthritis Measure scores than the placebo group at months 2 and 4. However, the study population consisted of patients with radiographic knee osteoarthritis rather than isolated patellar chondromalacia, limiting the applicability of these findings to the target population of the present review (44).

The simultaneous use of quadriceps-strengthening exercises in both study groups is also relevant when interpreting these findings. Because exercise therapy was provided to all participants, the study cannot determine whether oral HA provides meaningful additional benefit over an appropriately structured rehabilitation program in patients with patellar chondral pathology (44).

More broadly, the clinical evidence for HA in knee disorders is dominated by studies of intra-articular administration rather than oral supplementation. Systematic reviews evaluating intra-articular HA have demonstrated variable effects depending on patient population, study design, HA formulation, and comparator intervention (18). These findings cannot be directly generalized to oral HA because the pharmacokinetic and biological mechanisms of the two administration routes differ substantially (19,43).

6.3. Limitations of the Evidence

Several limitations prevent strong conclusions regarding oral HA in patellar chondromalacia. First, there is a lack of randomized controlled trials specifically enrolling patients with patellar chondral pathology (19,44). Second, available studies in knee osteoarthritis generally involve older populations with a different disease phenotype and pathophysiology. Third, HA preparations differ in molecular weight, formulation, dosage, and duration of treatment, making comparison between studies difficult (19).

Furthermore, the clinical relevance of small improvements observed in some studies remains uncertain. The absence of consistent evidence demonstrating improvements in validated pain and functional outcomes specifically in patients with patellar chondromalacia prevents routine recommendation of oral HA as part of evidence-based conservative treatment (19,44).

Therefore, oral HA should currently be regarded as an investigational or complementary intervention rather than an established component of conservative treatment for patellar chondromalacia. Well-designed randomized controlled trials specifically targeting younger and middle-aged patients with clinically symptomatic and structurally confirmed patellar chondral pathology are required before firm conclusions can be drawn.

7. Discussion

7.1. Clinical Implications

The findings of this review reinforce the central role of exercise-based rehabilitation in the conservative management of symptomatic patellofemoral disorders (12,37). The strongest and most consistent evidence supporting exercise therapy derives primarily from the broader patellofemoral pain population (2,12,36,37). Although the direct applicability of these findings to patients with structurally confirmed patellar chondral pathology is limited, exercise remains a rational first-line intervention because it can address modifiable impairments in muscle

capacity, neuromuscular control, movement patterns, and tolerance to mechanical loading (9,12,30).

The available evidence does not support the routine addition of intra-articular HA to exercise-based rehabilitation (16–18). The two most directly relevant randomized trials reached different conclusions, and substantial differences in patient selection and study design prevent the establishment of a clear overall treatment effect (16,17).

From a clinical perspective, the current evidence is therefore better interpreted as indicating uncertainty rather than demonstrating either universal efficacy or universal lack of efficacy (16–18). HA may have a different role in selected patients with symptomatic and structurally documented patellar cartilage lesions than in patients with the broader and more heterogeneous diagnosis of patellofemoral pain. However, this possibility remains insufficiently tested.

An important clinical consideration is that improvement in pain and function should not be equated with cartilage regeneration (16–18). The absence of a consistent relationship between structural cartilage abnormalities and symptom severity means that clinically meaningful improvement may occur without measurable changes in cartilage morphology (20,29,35). Similarly, symptomatic improvement following HA administration does not currently provide evidence that the treatment restores damaged patellar cartilage (16,17).

7.2. Limitations of the Current Evidence

Several limitations should be considered when interpreting the available evidence. First, terminology remains heterogeneous. Patellar chondromalacia, patellar chondropathy, patellar cartilage lesions, and patellofemoral pain are not synonymous, yet these populations are frequently discussed together (1,4,5,29). This complicates comparisons between studies and limits the direct extrapolation of evidence from broader PFP populations to patients with objectively confirmed cartilage pathology (1,5,29).

Second, the number of high-quality randomized controlled trials specifically investigating intra-articular HA in patellar chondral pathology is very limited. The most relevant trials differ substantially in their populations, control interventions, HA protocols, and rehabilitation programs (16,17).

Third, considerable heterogeneity exists in HA formulations and administration strategies, including differences in molecular weight, formulation, volume, dosing schedules, and the number of injections (14–18). It therefore remains unclear whether the effects observed in individual studies reflect a class effect of HA or are related to specific products or protocols.

Finally, structural and symptomatic outcomes are not consistently assessed together. Future studies should distinguish between symptomatic improvement, functional recovery, and structural changes rather than interpreting improvement in one domain as evidence of improvement in another (16,17).

7.3. Future Research Priorities

Future research should focus on improving patient phenotyping and establishing whether specific subgroups of patients with patellar chondral pathology may benefit from hyaluronic acid.

First, future randomized controlled trials should clearly distinguish patients with clinically diagnosed patellofemoral pain from those with objectively confirmed patellar cartilage lesions. Structural pathology should ideally be documented using standardized MRI criteria, while clinical diagnosis should incorporate validated measures of pain and function.

Second, future studies should directly compare standardized exercise therapy with exercise therapy combined with intra-articular HA. The rehabilitation protocol should be clearly defined and sufficiently standardized to allow the incremental effect of HA to be isolated. A sham-injection group would be particularly valuable because the placebo response associated with intra-articular procedures may be substantial (17).

Third, future studies should investigate whether the effect of HA depends on the severity or location of cartilage pathology. Patients with mild superficial cartilage abnormalities may respond differently from those with focal grade III or IV defects. Stratification according to cartilage grade, lesion location, patellofemoral morphology, and symptom duration may therefore help identify clinically meaningful phenotypes.

Fourth, further research should investigate whether HA formulation influences treatment response. Molecular weight, concentration, cross-linking, injection volume, and treatment frequency vary substantially between commercially available products. Direct comparative trials may therefore be necessary to determine whether particular formulations are more appropriate for patellar chondral pathology.

Fifth, future research should investigate the interaction between HA and rehabilitation. Rather than evaluating HA as an isolated intervention, studies should determine whether reducing pain with HA improves adherence to and progression of exercise therapy. This could provide a more clinically meaningful assessment of whether HA has a true additive effect.

Finally, oral HA requires substantially more investigation. Current evidence is limited to other joint disorders, particularly knee osteoarthritis, and cannot be directly extrapolated to isolated patellar chondromalacia (19,44). Well-designed randomized controlled trials specifically evaluating oral HA in patients with patellar chondral pathology are currently lacking.

Future studies should therefore prioritize clinically meaningful outcomes, including pain, functional capacity, return to sport, quality of life, treatment adherence, and long-term need for additional interventions, rather than relying solely on imaging-based measures of cartilage morphology.

8. Conclusions

Patellar chondral pathology is a heterogeneous condition in which structural cartilage abnormalities do not consistently correspond to symptom severity (20,29,35). Current evidence supports exercise-based physiotherapy and patient education as the foundation of conservative management, with treatment tailored to individual biomechanical and functional impairments (12,37).

The evidence for intra-articular hyaluronic acid remains limited and inconsistent. Although one randomized controlled trial demonstrated improved pain and functional outcomes when HA was added to physical therapy in patients with grade II–III patellar cartilage lesions, another

sham-controlled trial found no clinically meaningful additional benefit of HA when combined with exercise therapy (16,17). Consequently, routine use of intra-articular HA cannot currently be recommended.

Oral HA has even less supporting evidence, with no high-quality clinical trials specifically addressing patellar chondromalacia. Available evidence from knee osteoarthritis should be regarded as indirect (19,44).

The potential role of HA may therefore be best considered investigational and potentially phenotype-dependent. Further adequately powered, sham-controlled randomized trials directly comparing standardized rehabilitation with rehabilitation plus HA are required to determine whether a clinically meaningful additive effect exists.

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