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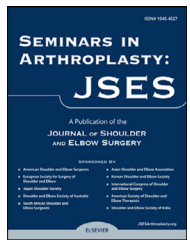

The role of conservative treatment of glenohumeral joint osteoarthritis: a systematic review

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ABSTRACT

Background: Glenohumeral joint osteoarthritis is a highly prevalent musculoskeletal disease in adults over the age of 65. The first line of treatment typically consists of nonsurgical modalities prior to consideration for definitive treatment with total shoulder arthroplasty. Within this systematic review, we aim to assess the value of conservative management of glenohumeral osteoarthritis by evaluating the quality of available research and the efficacy of nonoperative treatment on patient-reported pain scores and functional outcome measures.

Methods: A systematic review was conducted in literature published between 2000 and 2022. Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines were followed, and the electronic databases, PubMed, EBSCO Host, Medline, and Google Scholar were searched. Studies included in analysis consisted of patients receiving nonoperative management of glenohumeral joint arthritis without concomitant additional shoulder pathologies with a measured intervention and reported patient outcome measure. Two blinded reviewers screened and evaluated the data quality using the Methodological Index for Nonrandomized Studies tool.

Results: Nineteen studies were included consisting of 1879 patients with a median follow-up of 6 months. Eighteen studies included intra-articular injections including hyaluronic acid, corticosteroid, bone marrow aspirate, leukocyte-poor platelet-rich plasma, and autologous-conditioned serum injections. Each study reported symptomatic improvement following injection. Hyaluronic acid was the most commonly used (13 of 18 studies) agent with multiple studies demonstrating temporary improvement in pain and function. Four studies reported the outcomes of noninjectable modalities including physical therapy, bracing, and radiofrequency ablation. Two studies demonstrate that injections combined with physical therapy can lead to greater improvement in Constant score and range over motion for a greater period of time.

Conclusion: Conservative treatment modalities can be effective in lowering pain scores and improving functional outcome scores in patients with glenohumeral osteoarthritis. The

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effect of each individual modality may be most effective when combined with other treatments. However, these benefits appear to be short-term. Additional studies are necessary to further determine the long-term efficacy and establish guidelines for the mainstay of first-line therapy in the management of glenohumeral joint osteoarthritis.

Level of evidence: Level IV; Systematic Review

Glenohumeral joint osteoarthritis (GHOA) is one of the most common musculoskeletal diseases in the world with studies reporting that between 16.1% and 20.1% of adults older than 65 years of age have radiographic evidence of it.[19,27] GHOA results in degeneration of the joint space, deterioration of shoulder function, and overall lower quality of life.[5] The definitive treatment for GHOA is often total shoulder arthroplasty (TSA). However, TSA is not without its complications. Importantly, in young and active patients with GHOA, TSA often has less than acceptable results in providing long-term symptom relief.[8,21,33] As with many treatments in orthopedics, the recommended first line of therapy consists of a multitude of nonsurgical modalities prior to consideration for arthroplasty.[1]

The 2022 Guidelines from the American Academy of Orthopaedic Surgeons recommend initial nonoperative care for GHOA, including a combination of nonsteroidal anti-inflammatory medicines and physical therapy. There are mixed recommendations on the various types of intra-articular injections.[1] Importantly, the data supporting these modalities is sparse, and the recommendations are mainly based on results seen in the knee or hip osteoarthritis (OA) literature. To better understand the current evidence evaluating the efficacy of conservative management of GHOA, a systematic review was conducted to survey the current literature. Within this systematic review, we aim to: (1) evaluate the quality of research; and (2) evaluate the efficacy of nonoperative treatment on pain scores and functional outcomes in GHOA.

Methods

Literature search

A systematic literature review was performed in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analyses 2009 guidelines.[25] A comprehensive literature review was conducted using PubMed, EBSCO Host, Medline, and Google Scholar to identify all studies that evaluated the outcomes of nonoperative treatment of GHOA between 2000 and 2022. The search queried the aforementioned databases using the following terms: ("Glenohumeral osteoarthritis" OR "Glenohumeral arthritis" OR "shoulder arthritis" OR "osteoarthritis") AND ("nonpharmacologic" OR "weight loss" OR "exercise" OR "diet" OR "physical therapy" OR "Massage" OR "joint manipulation" OR "phonophoresis" OR "electrical stimulation" OR "acupuncture" OR "pharmacologic" OR "medication" OR "Acetaminophen" OR "NSAIDs" OR "Nonsteroidal anti-inflammatory drugs" OR "Antidepressants" OR "Nortriptyline" OR "Duloxetine" OR "corticosteroid" OR "opioids" OR "morphine" OR "supplements" OR "Glucosamine" OR "chondroitin" OR "topical" OR "Diclofenac" OR "ketoprofen" OR "Topical capsaicin" OR "Topical Cannabis" OR "CBD oil" OR "injectable" OR "Corticosteroid" OR "Methylprednisolone" OR "triamcinolone" OR "Viscosupplementation" OR "hyaluronic acid" OR "Orthobiologics" OR "PRP" OR "Bone-marrow aspirate" OR "Mesenchymal stem cells" OR "nerve block" OR "Nerve ablation").

Study eligibility and selection

Following the identification of studies based on the search criteria above, the title and abstract screening was completed by two authors (A.K. and M.E.) while being blinded to each other's results. Studies were considered based on the following inclusion criteria: (1) full manuscript was written in English; (2) studies that included subjects older than the age of 18; (3) patients receiving nonoperative treatment for GHOA; and (4) studies that reported an outcome. The exclusion criteria included: (1) studies that reported on pathologies other GHOA; (2) studies that reported on GHOA in addition to another shoulder pathology; (3) narrative reviews, systematic reviews, case reports and animal studies; (4) patients under the age of 18; and (5) any duplicate studies among databases.

Data extraction and analysis

A collaborative online spreadsheet was utilized for data extraction. Two reviewers performed the extraction, and the findings were compared for verification. We utilized a systematic checklist to compile study characteristics including the author, year, study design, patient demographics, treatment type, and outcomes, when available.

Risk of bias in individual studies

Using the Methodological Index for Nonrandomized Studies (MINORS) tool, the two reviewers (A.K. and M.E.) independently assessed the quality of the included studies.[32] The MINORS tool assigns a score from 0 to 16 to noncomparative studies based on eight criterion categories and 0 to 24 for comparative studies related to article design, outcomes evaluated, and follow-up. Each criteria item received a score of 0 if it was not recorded, 1 if it was reported but was unclear, and 2 if it was adequately documented. Disagreements were discussed, and a third independent reviewer (E.H.) was consulted to achieve consensus.

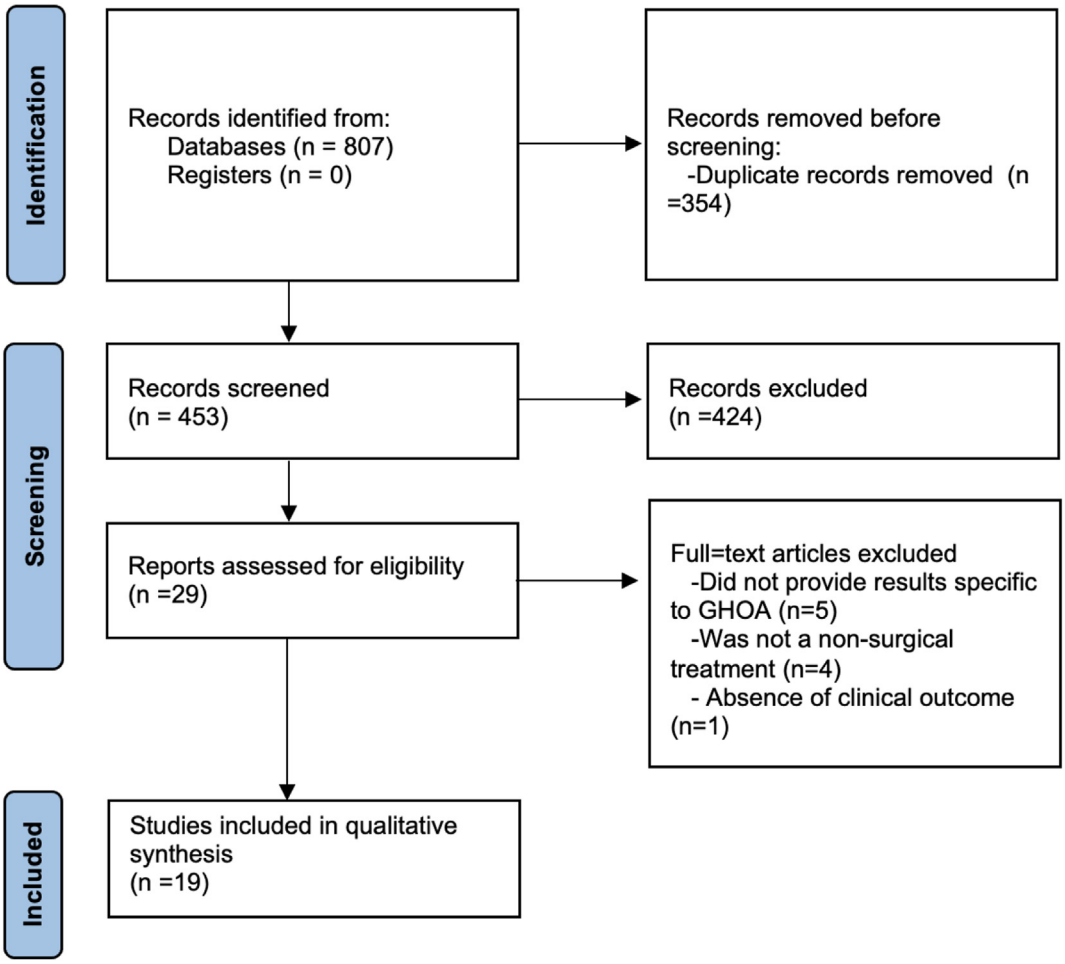

Figure 1 – PRISMA diagram for study inclusion. *PRISMA*, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Study selection

In accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines, two reviewers independently assessed the eligibility of each article for inclusion in our review. Disagreements were discussed, and a third independent reviewer was consulted to achieve consensus. The initial query yielded 807 publications, which were then screened for appropriate studies that aligned with the purpose of our review. After removing duplicates and reading each abstract, we selected 30 studies for further consideration. The full text of each article was then reviewed, 19 of which fulfilled our inclusion criteria. A thorough review of each study's reference list did not yield any additional articles (Fig. 1).

Results

Study selection

The final analysis included 19 studies (Table I).[7,10,13-18,20,22-24,26,29-31,34-36] Overall, a total of 1879 patients with 982 males (52.3%) and 897 females (47.7%) were included. The median follow-up period was 6 months. There were 10 prospective studies, 2 retrospective studies, 6 randomized controlled trials (RCTs), and 1 case series. The mean MINORS score was 14.4 ± 2.63.

Eighteen studies evaluated the impact of injections on glenohumeral joint GHOA (Table II). Hyaluronic acid (HA) (13/19) was the most frequent type of injection studied, followed by corticosteroid injection (7/19) and other types of injections (3/19), including bone marrow aspirate (BMA), leukocyte-poor platelet-rich plasma, and autologous conditioned serum. All of the studies reported that the injectable therapies resulted in symptom improvement.

The efficacy of hyaluronic acid injections on outcomes in glenohumeral joint OA

Out of the 19 identified studies, thirteen evaluated HA injection. HA was administered in different amounts across the studies. Brander et al reported that two injections of HA at 14 days apart led to clinically significant improvement in visual analog scale (VAS) pain scores from 53.3 mm at rest to 23.6 mm suggesting an improvement of VAS scores by 29.7 mm at 6 months.[7] Noël et al[26] and Porcellini et al[29] reported similar results where two HA injections led to an improvement in VAS scores by 24.1 mm and 28.4 mm, respectively. In a high-quality

Table I – Characteristics of articles included in final analysis.

Author, year	Study design	Conservative method used	Sample size (N)	Sex (%male)	Minors score
Brander et al, 2010[7]	Prospective open-label pilot investigation	HA (Hylan G-F 20)	36	N/A	15
Di Giacomo et al, 2017[14]	RCT	HA (Hyalubrix) and PT	78	41%	N/A
Di Giacomo et al, 2015[13]	Prospective longitudinal study	HA (Hyalgan) and PT	61	43%	20
Dwyer et al, 2021[10]	RCT	Bone Marrow Aspirate and CSI	25	68%	N/A
Guo et al, 2016[15]	Prospective longitudinal study	NSAIDs, CSI, sodium hyaluronate, education, PT and bracing	129	47%	12
Hashemi et al, 2018[16]	RCT	Intra-articular botox and CSI	50	48%	N/A
Kim et al, 2022[17]	Retrospective Study	CSI	275	46.20%	13
Kirschner, 2022[18]	RCT	HA, leukocyte-poor PRP	70	45.70%	N/A
Kwon et al, 2013[20]	RCT	HA (Sodium Hyaluronate)	300	55%	N/A
McKee et al, 2019[22]	Prospective longitudinal study	Nonanimal HA	41	N/A	13
Merolla et al, 2011[23]	Retrospective Study	HA (Hylan G-F 20) and CSI	84	27%	20
Metzger et al, 2021[24]	Prospective longitudinal observational study	CSI	29	52%	13
Noël et al, 2009[26]	Prospective longitudinal study	HA (Hylan G-F 20)	33	55%	14
Porcellini et al, 2015[27]	Prospective longitudinal study	HA (HYADD 4-G)	41	73%	14
Silverstein et al, 2007[30]	Case series	HA (Hylan G-F 20)	27	63%	12
Simon et al, 2021[31]	Prospective longitudinal study	Autologous conditioned serum (Orthokine) Injections	40	65%	14
Tortato et al, 2022[34]	RCT	HA (Hylan G-F 20) and CSI	77	13%	N/A
Tran et al, 2022[35]	Prospective Pilot study	Cooled Radiofrequency Ablation	12	75%	13
Weil et al, 2011[36]	Prospective Cohort Study	HA (Euflexxa)	27	51.90%	14

RCT, Randomized Controlled Trial; *HA*, hyaluronic acid; *PT*, physical therapy; *CSI*, corticosteroid injection; *NSAIDs*, nonsteroidal anti-inflammatory drugs; *PRP*, platelet-rich plasma.

study with a large patient population, Kwon et al demonstrated that HA injections in GHOA patients without any concomitant pathology resulted in a significant improvement of 19.88 mm in VAS scores; however, this improvement is not statistically different when compared to those who received a placebo phosphate-buffered saline (PBS), which saw an increase in VAS score by 16.29 mm.[20]

In a prospective study, Di Giacomo et al compared patients who received 5 HA injections (1 injection every 15 days) with patients who performed only physical therapy.[14] They saw that HA injections led to an improvement in forward elevation by 18°, improvement by 7.6° in external rotation and improvement by 13.4° in the Constant score at a mean follow-up of 5.2 months.[14] Those in the physical therapy group also experienced statistically significant improvements, albeit to a lesser extent, where forward elevation, external rotation, and Constant score improved by 7.8°, 4.5°, and 8.2 points, respectively.[14] Di Giacomo et al validated this prospective study by performing an RCT study of 78 patients, half of whom would receive HA injections with physical therapy while the other half received physical therapy in isolation.[13] Those who received combination therapy saw an improvement in the Constant score, forward elevation, and external rotation by 16.2, 14.2°, and 3.2°, respectively which was similar to those in physical therapy alone 10.2, 8.9°, and 2.2°.[13] The Constant score improvement was statistically better in the combined therapy group.[13] These results suggest that combination therapy is likely a more efficacious treatment providing greater and perhaps longer-lasting relief of pain compared to physical therapy alone.[13]

Silverstein et al suggest that HA injections can provide pain relief (improvement in VAS scores by 24 mm), improvement in patient-reported outcomes (simple shoulder test [SST], University of California-Los Angeles), and sleep quality at 6 months following 3 weekly intra-articular HA injections without an adverse event.[30] A similar result was seen by McKee et al[22] who reported an improvement in VAS score by approximately 20 mm at 6 months, which is similar to the findings in the RCT conducted by Kwon et al[20] (Table II). Weil et al demonstrated that one HA injection per week for 3 weeks led to statistical improvement in VAS score, range of motion, and Western Ontario and McMaster Universities Osteoarthritis Index scores at 26 weeks.[36]

The efficacy of corticosteroid injections on outcomes in glenohumeral joint OA

Corticosteroid injections were the second-most frequently cited injectable therapy. Kim et al reported on time to surgical intervention following corticosteroid injection and found that a third of patients underwent shoulder arthroplasty within 3 to 8 years following the injection.[17] Metzger et al reported that a corticosteroid injection provides clinically significant improvements in pain level, for up to a year, with the first four months showing the greatest improvement.[24]

Comparative studies of injection therapy in GHOA

In a retrospective study, Merolla et al reported that corticosteroid injections resulted in a symptomatic improvement for one month, while HA injections showed benefit for up to 6 months.[23] Those who received corticosteroid injections saw an improvement in VAS score (0-10 scale) by 1.83, but at longer follow-up, this effect was lost. However, the HA group saw a

Table II – Outcomes of the articles discussing different types of injections.

Author, year	Preoperative treatment VAS score	Postoperative treatment VAS score	Follow-up period	Outcomes
Brander et al, 2010[7]	53.3 ± 14.8 mm	6 weeks: 30.3 ± 29.8 mm 3 mo: 33.3 ± 26.4 mm 6 mo: 23.6 ± 23.4 mm	6 mo	Clinically (≥20% improvement) and statistically significant improvements ($P < .001$) in VAS pain were seen at 6 weeks, 3 mo, and 6 mo suggesting two Hylan G-F 20 injections can improve pain and function.
Di Giacomo, 2017[14]	N/A	N/A	6 mo	The combination of three IA HA injections with a physical therapy program was more effective in lowering pain compared to physical therapy alone. No difference was seen in the ROM between the two groups.
Di Giacomo et al, 2015[13]	N/A	N/A	5.2 mo	Physical therapy alone improved pain, elevation, and external rotation, however when five-injection HA treatment was coupled with physical therapy the benefits were stronger and longer-lasting in individuals with GHOA degree I, II, or III.
Dwyer et al, 2021[10]	BMA: 4.5 ± 2.3 CSI: 4.8 ± 1.8	BMA: 3.0 ± 2.8 CSI: 5.1 ± 3.2	12 mo	Patients with GHOA treated with BMA have superior changes in disability/symptom (QuickDASH) and general health-status (EQ-5D-5L) scores at 12 mo post injection, but not in shoulder-related quality of life (WOOS) outcomes measures, when compared to patients treated with CSI.
Guo et al, 2016[15]	67.07 ± 20.88 mm	34.15 ± 12.15 mm	3 y	Following an initial increase at 3 mo, SST and VAS started to decrease at 6 and 12 mo, and this trend was maintained during the 3-y follow-up. Conservative treatment should be followed for at least 12 mo before deciding for shoulder arthroplasty, according to the findings of this study.
Hashemi et al, 2018[16]	N/A	12 weeks: Botox 2.75; CSI: 4.24. The VAS scores were significantly decreased for both interventions at all timepoints.	12 weeks	IA Botox or CSI resulted in reduced pain and increased range of motion in people with GHOA. However, Botox injections resulted in higher pain reduction at week 12 and an increase in range of abduction, internal rotation, and external rotation.
Kim et al, 2022[17]	N/A	N/A	8 y	Around one-third of GHOA patients who received an IA CSI went on to have shoulder arthroplasty within 3 to 8 y following the injection.
Kirschner, 2022[18]	N/A	N/A	1 y	Both HA and leukocyte-poor PRP injections resulted in considerable improvements in pain and function in individuals with GHOA. There was no significant difference in the outcome between HA and leukocyte-poor PRP injections.

Kwon et al, 2013[20]	N/A	Improved by 19.88 mm	26 weeks	HA injections in GHOA patients without any concomitant pathologies resulted in a significant improvement in VAS scores compared to the control.
McKee et al, 2019[22]	70.9 ± 13.7	6w: 50.7 ± 24.6 mm 12w: 44.1 ± 26.0 mm 18w: 46.4 ± 27.9 mm 26w: 50.0 ± 26.8 mm	6 mo	A single HA injection may be effective over a period of six months in reducing pain in GHOA.
Merolla et al, 2011[23]	HA: 6.1 ± 0.91 CSI: 6.25 ± 1.67	HA: 3.65 ± 0.90 CSI: 5.94 ± 1.58	6 mo	The benefit from CSI lasted for one month. However, IA injections of Hylan G-F 20 were successful in lowering pain in GHOA for up to six months.
Metzger et al, 2021[24]	5.8	N/A	1 y	For up to a year, patients reported statistically and clinically significant reductions in their pain, with the first four months showing the greatest improvement after receiving CSI.
Noël et al, 2009[26]	61.2 ± 16.2 mm	37.1 mm	3 mo	In individuals with GHOA, one or two IA injections of Hylan GF 20 can alleviate pain.
Porcellini et al 2015[29]	66.1 mm	37.7 mm	6 mo	For up to six months after the first injection, two IA injections of HA, given one week apart, can dramatically reduce pain and improve shoulder functioning.
Silverstein et al, 2007[30]	54 mm	30 mm	6 mo	Patients with GHOA who received hylan G-F 20 saw considerable pain relief and improvements in their ability to do everyday activities up to 6 mo after the first injection.
Simon et al, 2021[31]	4.8 ± 2.2	3.7 ± 2.4	3 mo	In patients with GHOA, IA autologous conditioned serum injections improved function, lowered pain, and had a mean time to arthroplasty of 3.1 ± 1.7 y.
Tortato et al, 2022[34]	Severe OA: HA: 8.6, CSI: 9.1 Nonsevere OA: HA: 8.1, CSI: 8.3	Severe OA: 1 week HA: 8, CSI: 6.5 1 mo: HA: 7.5, CSI: 6 3 mo: HA: 7.4, CSI: 7 6 mo: HA: 7.25, CSI: 8.9 Nonsevere OA: 1 week: HA: 7, CSI: 4.8 1 mo: HA: 5, CSI: 4.1 3 mo: HA: 5, CSI: 6.2 6 mo: HA: 4.9, CSI: 7.8	6 mo	Both HA and CSI resulted in the reduction of pain and higher patient satisfaction, but patients that got HA had greater and longer-lasting outcomes.
Weil, 2011[36]	56.37 ± 16.62 mm	Significantly decreased ($P < .0011$). However, exact mean and SD cannot be determined	26 weeks	High molecular weight hyaluronate treatment of GHOA reduces pain, stiffness, and range of motion.

VAS, visual analog scale; *ASES*, American Shoulder and Elbow Surgeons; *WOOS*, Western Ontario Osteoarthritis of the Shoulder; *OA*, osteoarthritis; *HA*, hyaluronic acid; *CSI*, corticosteroid injection; *PRP*, platelet-rich plasma; *ROM*, range of motion; *IA*, intra-articular.

Table III – Outcomes of the articles discussing other types of conservative treatments.

Author, year	Preoperative treatment VAS score	Postoperative treatment VAS score	Follow-up period	Outcomes
Di Giacomo, 2017[14]	N/A	N/A	6 mo	The combination of three intra-articular HA injections with a physical therapy program was more effective in lowering pain compared to physical therapy alone. No difference was seen in the ROM between the two groups.
Di Giacomo et al, 2015[13]	N/A	N/A	5.2 mo	Physical therapy alone improved pain, elevation, and external rotation, however when five-injection HA treatment was coupled with physical therapy the benefits were stronger and longer-lasting in individuals with GHOA degree I, II, or III.
Guo et al, 2016[15]	67.07 ± 20.88 mm	34.15 ± 12.15 mm	3 yr	Following an initial increase at 3 mo, SST and VAS started to decrease at 6 and 12 mo, and this trend was maintained during the 3-y follow-up. Conservative treatment should be followed for at least 12 mo before deciding for shoulder arthroplasty, according to the findings of this study.
Tran et al, 2022[35]	8.8 ± 0.6	2.2 ± 0.4	6 mo	Patients' VAS and ASES scores improved dramatically after cooled radiofrequency ablation. There were no major complications, and no patients required re-treatment or shoulder arthroplasty within 6 mo following the procedure.

HA, hyaluronic acid; *ROM*, range of motion; *GHOA*, glenohumeral osteoarthritis; *SST*, simple shoulder test; *VAS*, visual analog scale; *ASES*, American Shoulder and Elbow Surgeons.

larger interval improvement in VAS score from 6.1 points to 3.37 points before that effect plateaued to 3.65 points at the 6-month point.[23]

Kirschner et al[18] and Tortato et al[34] compared HA with leukocyte-poor platelet-rich plasma and corticosteroid injection in their RCTs. Kirschner et al demonstrated that HA and leukocyte-poor platelet-rich plasma injections resulted in similar outcomes and resulted in improvements in pain and function.[19] Both types of injections resulted in a significant improvement in Shoulder Pain and Disability Index, American Shoulder and Elbow Surgeons, and numerical rating scale pain scores and no significant between-group differences at any time point up to 12 months postinjection.[19] Tortato et al demonstrated that while corticosteroid is able to achieve a similar reduction of pain and higher patient satisfaction compared to HA, it was short-lasting.[36] Of those that received HA injections, 76% experienced pain improvement (VAS score) at the first month, and 71% had improvement after 6 months. Although more patients (82%) experienced improvement in pain at the first month after a corticosteroid injection compared to an HA injection, 32% showed improvement at 6 months.[36]

Hashemi et al, in an RCT of 50 patients, demonstrated that both Botox and corticosteroid injections result in an improvement in VAS scores and the range of motion in individuals with GHOA.[16] There was no statistical difference between the two groups in terms of improvement in range of motion, but Botox injections had a statistically better improvement in VAS compared to corticosteroid injections. Botox injections had a VAS score of 2.75 points compared to 4.24 points in those that received corticosteroid injections at 12 weeks.[16] Dwyer et al compared BMA and corticosteroid injections in their RCT and demonstrated that BMA resulted in a statistically significant better improvement in disability (change of 17.0 vs. 2.3, $P < .006$ in QuickDASH score) and general health status (change of 2.5 vs. −7.3, $P < .032$ in EuroQOL 5-dimensions 5-level questionnaire) scores at 12 months postinjection, but not in shoulder-related quality of life (change of 398.0 vs. 86.2, $P < .07$ in Western Ontario Osteoarthritis of the Shoulder) outcomes measures or VAS scores (change of 3.0 vs. 5.1, $P < .09$) when compared to patients treated with corticosteroid.[10]

Simon et al demonstrated that autologous conditioned serum (Orthokine) injections can improve functional outcomes, reduce VAS scores (VAS pain 4.8 points at baseline to 3.7 points at 3 months), and 53% of their patients with symptomatic and radiographic OA at an average of 3.6 ± 1.0 years did not go on to arthroplasty.[31]

The impact of other types of conservative treatments on glenohumeral OA

There were four studies that reported the outcomes of noninjectable conservative treatment of glenohumeral OA (Table III). Guo et al, in a prospective study, reported on

heterogeneous combinations of different conservative treatments including physical therapy, nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroid and sodium hyaluronate injections, education, and bracing. They demonstrated a significant improvement in both VAS pain and SST scores after 3 years. The VAS pain score improved from 67.07 ± 20.88 mm to 34.15 ± 12.15 mm, and the SST score improved from 4.72 ± 2.20 to 7.51 ± 1.86.[15] Tran et al in a prospective pilot study evaluated the use of cooled radiofrequency nerve ablation (C-RFA) in conservative treatment of GHOA. The study includes a total of 12 patients experiencing chronic shoulder pain from moderate to severe GHOA.

Patients received anesthetic blocks on the axillary, lateral pectoral, and suprascapular nerves to assess eligibility for C-RFA treatment. Those who reported a minimum of 50% pain reduction based on the subjective Likert scale within 15-20 minutes after the nerve block screening were selected for the C-RFA procedure, scheduled 3-4 weeks later. After six months post-C-RFA, significant improvements were observed in VAS scores, which decreased from 8.8 to 2.2 points, and American Shoulder and Elbow Surgeons scores, which increased from 17.2 to 65.7 points. Moreover, no major complications were reported.[35]

Discussion

A systematic review of the literature was conducted to understand the efficacy of nonsurgical treatment in the management of glenohumeral joint OA (GHOA). Overall, we found few studies that evaluated the efficacy of these treatments in GHOA with the most frequently studied modality being injectable therapies. Our review found that these conservative treatment modalities can be effective in lowering VAS pain scores and improving functional outcomes. These outcomes may be more effective when combined with other treatments; however, improvements may be limited to the short-term with only few studies demonstrating durable efficacy beyond 6 months.

Based on the available literature, glenohumeral joint injections of HA may achieve more robust improvements in functional outcomes and pain scores when compared with other injectables such as corticosteroids.[23,34] HA is a naturally occurring polysaccharide within the synovial fluid and articular cartilage and helps to provide lubrication, nutrition, and stabilization to articular surfaces by forming strong biomechanical bonds among the various components of the joint.[9] Several studies have suggested that HA injections are well tolerated and provide reductions in pain,[6,13,20] albeit these studies are limited by short follow-up periods with conflicting results, such as those cited in the study by Kwon et al.[20] In this particular study, the authors found that HA led to a statistically significant improvement of VAS score by 19.88 mm; however, when compared to those who received placebo (PBS), this was not a statistically significant difference.[20] The remainder of studies reporting on HA injections also reported an improvement in VAS pain scores by approximately 20 mm (range: 19.8 mm-29.7 mm) at 6 months.

The impact of placebo injections within the context of intra-articular injections should be appreciated from the results of this review. Multiple studies emphasize the need to have further RCTs to show that clinical improvement can be derived from HA or other similar injectable medications.[37] For example, a study by Bannuru showed that placebos have differential effects and, in some cases, within the context of knee OA can have greater therapeutic benefits than injectable medicine.[4] This underscores the need for future prospective trials that are both double-blinded and controlled for differential placebo effects and the impact of co-interventions. For instance, the study by Di Giacomo compared pain scores between those who received HA injections with concomitant enrollment in a physical therapy (PT) program and those who only received PT.[13] Although they showed that the combination of intra-articular HA with PT was more effective compared to PT alone, a more robust analysis would have included an injectable placebo, such as PBS, to make certain that the improvements seen are not due to a placebo effect.[38]

A few studies in our review assessed the clinical utility of other intra-articular injectables such as corticosteroids, Botox injections, autologous conditioned serum, and leukocyte-poor platelet-rich plasma. Of the seven included studies that assessed corticosteroids, different doses and types of corticosteroids were used, which may have impacted the heterogeneity of their results regarding treatment efficacy. Further studies are needed to analyze the optimal dose and frequency of these injections.[2] Of note, one study assessed autologous conditioned serum and reported good results in pain relief.[31] This may be driven by autologous conditioned serum's ability to elicit a rapid increase in interleukin-1Ra, which is associated with the synthesis of anti-inflammatory cytokines that contribute to chondro-protective effects, a finding confirmed in animal models of horses, rabbits, and dogs.[11,12,28] Large-scale prospective trials comparing the efficacy of autologous conditioned serum with HA in the glenohumeral joint are lacking but necessary, as a previous report by Baltzer et al on knee OA suggested that autologous conditioned serum was more effective in improving the quality of life of patients across all follow-up time points compared to those receiving HA injections.[3]

There were a limited number of studies that observed the relationship between other types of conservative treatments and their outcomes in patients with GHOA. The majority of studies included in this study observed the combined effect of different types of conservative treatments on glenohumeral OA, but not each individual treatment on its own. In addition, it is unknown whether the severity of GHOA either radiographically or functionally has an influence on the success of different forms of conservative treatments. If certain severity or classifications of GHOA are unresponsive to one form of conservative treatment, alternative forms of treatments should be employed in order to save cost and resources for both the patient and the healthcare system. In addition, a first-line medication in the treatment or pain control of OA is NSAIDs. However, Guo et al was the only study that evaluated the efficacy of NSAIDs in the treatment of OA.[15] Given the multiple side effects and contraindications of NSAIDs, it is important that the efficacy of NSAIDs be critically evaluated to properly weigh the benefits and risks of this treatment

modality. Future studies should seek to evaluate these treatments in isolation and in combination to determine which strategy is the most appropriate use of healthcare resources in the management of GHOA.

C-RFA is among the newer forms of treatment being evaluated for the management of GHOA. C-RFA presents itself as an alternate option for managing symptomatic GHOA in cases where conventional treatments have proven ineffective, the patient is unsuitable for surgery, or when the patient elects against surgical intervention. In the study by Tran et al, the physicians ablated the suprascapular, axillary, and lateral pectoral nerves; however, it is possible to ablate a single nerve based on the specific area in which the patient is experiencing pain.[35] There were no adverse events associated with the procedure, and none of the patients experienced any motor dysfunction or nerve palsy at the 6-month follow-up.[35] Even though the study by Tran et al did not report any complications with C-RFA treatment, there are some limitations and concerns related to the procedure.[35] The standard RFA probe used in C-RFA raises the temperature of surrounding tissue to over 100°C, resulting in denatured proteins forming a thrombus that interferes with the electrical current of the probe limiting the size of the ablation lesion.[35] One of the feared complications of C-RFA is neuropathic arthropathy, a complex condition involving motor and sensory neuropathy, vascular issues, and soft tissue damage.[35] Loss of joint sensation can lead to ongoing trauma, initiating a cycle of constant injury, bone resorption, and osseous hypertrophy.[35] Currently, a large prospective trial with long-term outcomes is necessary to know the incidence and clinical course of this and other potential complications following C-RFA.

Our analysis is characterized by broad search terms, rigorous methodological assessment, and *a priori* determination of inclusion and exclusion criteria. We systematically extracted study characteristics and outcomes, which reduces the risk of a reporting bias. However, the results of our qualitative assessment must be considered in light of this study's limitations. Firstly, different types of HA were administered (high vs. low molecular weight) with varying dosing regimens. Additionally, the included studies utilized different scales to assess pain and functional outcomes, which limited our ability to perform a meta-analysis. Thirdly, the articles included in our study had a mean MINORS score of 14.4 ± 2.63, which is relatively a low score and limits the generalizability of our results. Finally, only 19 studies met our inclusion/exclusion criteria, underscoring the need to further study nonoperative treatment of glenohumeral joint OA.

Conclusion

Among injectable therapies, HA injections showed promising results, with several studies reporting significant improvements in VAS pain scores and functional outcomes. HA injections appeared to provide more robust and longer-lasting relief compared to corticosteroid injections, although further research is needed to understand the optimal dosing and long-term effects. Additionally, autologous conditioned serum and leukocyte-poor platelet-rich plasma demonstrated potential benefits but require more investigation. Regarding noninjectable conservative treatments, physical therapy showed promise in improving pain and range of motion in GHOA patients. However, the impact of physical therapy in isolation and its efficacy in different GHOA severity levels require further exploration.

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