Non-Operative Management of Shoulder Osteoarthritis:

Current Concepts

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Abstract

Glenohumeral osteoarthritis (OA) is one of the most common causes of shoulder pain. Conservative treatment options include physical therapy, pharmacological therapy, and biologic therapy. Patients with glenohumeral OA present shoulder pain and decreased shoulder range of motion (ROM). Abnormal scapular motion is also seen in patients as adaptation to the restricted glenohumeral motion. Physical therapy is performed to (1) decrease pain, (2) increase shoulder ROM, and (3) protect the glenohumeral joint. To decrease pain, it should be assessed whether the pain appears at rest or during shoulder motion. Physical therapy may be effective for motion pain rather than rest pain. To increase shoulder ROM, the soft tissues responsible for the ROM loss need to be identified and targeted for intervention. To protect the glenohumeral joint, rotator cuff strengthening exercises are recommended. Administration of pharmacological agents is the major part next to physical therapy in the conservative treatment. Main aim of pharmacological treatment is the reduction of pain and diminution of inflammation in the joint. To achieve this aim NSAIDs are recommended as first-line therapy. Additionally, the supplementation of oral vitamin C and vitamin D can help to slow down cartilage degeneration. Depending on the individual comorbidities and contraindications, sufficient medication with good pain reduction is
thus possible for each patient. This interrupts the chronic inflammatory state in the joint
and in turn enables pain-free physical therapy. Biologics such as platelet-rich plasma,
bone marrow aspirate concentrate, and mesenchymal stem cells have gathered increased
attention. Good clinical outcomes have been reported, but we need to be aware that
these options are helpful in decreasing shoulder pain but neither stopping the
progression nor improving OA. Further evidence of biologics needs to be obtained to
determine their effectiveness. In athletes, a combined approach of activity modification
and physical therapy can be effective. Oral medications can provide patients with
transient pain relief. Intra-articular corticosteroid injection, which provides longer term
effects, must be used cautiously in athletes. There is mixed evidence for the efficacy of
hyaluronic acid injections. There is still limited evidence regarding the use of biologics.
Current Concepts

- Physical therapy can be useful in the management of glenohumeral OA.
- NSAIDs are the first-line treatment to reduce pain.
- The supplementation of oral vitamin C and vitamin D can help to slow down cartilage degeneration.
- There is mixed evidence for the efficacy of hyaluronic acid injections in the management of glenohumeral OA.
- Biologics such as platelet-rich plasma, bone marrow aspirate concentrate, and mesenchymal stem cells have gathered increased attention, but no conclusive evidence of their efficacy for glenohumeral OA.

Future Perspectives

- There remain many unanswered questions regarding the use, indication, safety, and efficacy of biologics. Further large-scale randomized trials need to be performed to determine the efficacy of biologics in glenohumeral OA.
Glenohumeral osteoarthritis (OA) is one of the most common causes of shoulder pain in clinical practice. Population-based studies suggest that 16.1% to 20.1% of adults older than 65 years have radiographic evidence of glenohumeral OA [1]. If the patients are young and/or athletes, initial management of glenohumeral OA should focus on non-operative options. A combined approach of activity modification and physical therapy can be effective. Standard conservative treatments include medication such as anti-inflammatories, physical therapy, and corticosteroid injections. Corticosteroid injections are reported to be effective in many cases but there are concerns regarding tendon and chondral toxicity [2]. Until recently, the second-line treatment was believed to be surgical treatment such as arthroplasty. Biologic injections such as platelet rich plasma (PRP) and mesenchymal stem cells (MSCs) have gathered increased attention over the past 2 decades. In fact, newer injection options are now being increasingly used. In this current concept article, we review non-operative management of the glenohumeral OA focusing on standard conservative treatments as well as the latest practice based on the available evidence.

For this study, neither study approval nor ethics approval was required.
Physical Therapy and Exercise

Clinical presentation

In patients with glenohumeral OA, shoulder range of motion (ROM) is frequently limited in various directions rather than in specific directions. The loss of shoulder ROM can be caused by pain, decreased flexibility of soft tissues, and glenoid deformity related to OA. Muscle weakness can occur by disuse due to pain. Previous studies evaluated muscle atrophy in patients with glenohumeral OA by comparing muscle area with healthy subjects [3, 4]. These studies showed that patients with glenohumeral OA had decreased muscle area of the supraspinatus [4], but not the deltoid muscle compared with the healthy subjects [3]. Alterations in shoulder kinematics are frequently observed in patients with glenohumeral OA. Fayad et al. [5] examined the scapulothoracic and glenohumeral motions during arm elevation of the affected and unaffected shoulders in patients with glenohumeral OA. They found increased scapular external rotation and decreased glenohumeral elevation on the affected side.

Management principles

Physical therapy for patients with glenohumeral OA is performed in order to (1) decrease pain, (2) increase shoulder ROM, and (3) protect the glenohumeral joint. First,
we should assess whether pain appears at rest and/or during shoulder motion. To improve shoulder ROM loss, we need to identify the soft tissues affecting the ROM loss. If the muscle weakness and/or imbalance of the rotator cuff are found, interventions to the muscles are recommended. However, excessive strengthening exercise should be avoided as it may cause exacerbation of symptoms.

Assessment

Muscle strengths of the shoulder girdle muscles are evaluated with manual muscle testing [6]. However, manual muscle testing is prone to interobserver variability [7]. Hand-held dynamometer is useful tool for clinicians to quantitatively evaluate muscle strength and verify intervention effect. Several previous studies proposed reliable clinical assessment methods for scapular position/motion. The clinical methods are divided into visual observation and objective assessment. Visible alterations in scapular position and motion patterns have been termed “scapular dyskinesis”. The current recommendation for clinical assessment of scapular dyskinesis is the use of dynamic scapular dyskinesis test (SDT) [8, 9]. Objective assessment of scapular position and motion is conducted with a digital inclinometer. For the assessment of
scapular upward rotation, the inclination angle of the digital inclinometer aligned along the scapular spine is measured [10].

**Management**

* a. *ROM and stretching exercises*

We start from performing active shoulder ROM-exercise within the pain-free range. If the pain becomes mild, we perform passive shoulder ROM-exercise.

1. Shoulder flexion/abduction

   The pectoralis major and latissimus dorsi are the primary tissues responsible for decreased shoulder flexion/abduction. For the pectoralis major, the clavicular and sternal regions are stretched by passive shoulder horizontal extension at 90° of shoulder abduction, and the abdominal region is stretched by passive shoulder horizontal extension at 135° of shoulder abduction [11]. The latissimus dorsi is stretched by passive contralateral rotation and bending of the trunk, with shoulder maximally elevated [12].

2. Shoulder extension/adduction

   The anterior deltoid and supraspinatus are the primary tissues responsible for decreased shoulder extension/adduction. The anterior deltoid is considered to be...
stretched by passive shoulder extension. The supraspinatus is stretched by passive shoulder adduction in shoulder extension [13].

3. Shoulder external rotation (ER)

The coracohumeral ligament and subscapularis are the primary tissues responsible for decreased shoulder ER. The coracohumeral ligament is stretched by passive shoulder ER in shoulder adduction [14]. The subscapularis (the inferior portion) is stretched by passive shoulder ER at 90° of shoulder flexion or abduction, or passive horizontal extension [15].

4. Shoulder internal rotation (IR)

The posterior capsule and infraspinatus and teres minor are the primary tissues responsible for decreased shoulder IR. For the posterior capsule, the superior portion of the posterior capsule is stretched by passive shoulder IR at 30° of shoulder extension, whereas the middle and inferior portions of the posterior capsule stretched by passive shoulder IR at 30° of abduction [16]. For the infraspinatus and teres minor, both muscles are stretched by passive shoulder IR at 90° of abduction [13].

b. Joint mobilization

Joint mobilization is a therapeutic approach to improve joint play and accessory motion, resulting in pain relief and increased ROM. A structured exercise program
combined with joint mobilization has been shown to decrease pain and improve
function in patients with various shoulder disorders [17].

**c. Muscle strengthening exercise**

Full-can exercise as well as prone ER exercise are an optimal exercise to strengthen
supraspinatus as these exercises produce high activity of the supraspinatus with less
activity of the deltoid muscle. Side-lying ER exercise has been used for strengthening
the infraspinatus and teres minor (Figure 1A) [18]. IR exercise in the belly-press test
position is effective in strengthening the subscapularis (Figure 1B).

**Pharmacological Therapy (Table 1)**

**Corticosteroids**

The most common use of corticosteroids in glenohumeral OA is intra-
articular injection (Figure 2). However, an intra-articular injection is often applied for
patients with shoulder pain of all etiologies to reduce an acute state of inflammation in
the joint. Nevertheless, an injection of corticosteroids can affect the cartilage negatively
and even hasten the progression of glenohumeral OA [19]. In a recent meta-analysis of
randomized controlled trails Shanthanna et al [20] demonstrated that injections with
corticosteroids provided no additional benefit compared to injections consisting of only
local anesthetic agents. At the same time, the number of injections performed should be limited to a maximum of three to prevent an increased risk of infection and further side effects [21]. Besides intra-articular injections, oral prescription of corticosteroids is also possible. While some positive effects on the reduction of symptoms have been mentioned, there is no effect on the progress of joint degeneration [22].

**Non-Steroidal Anti-Inflammatory drugs (NSAIDs)**

Most commonly-used pharmacological therapy is based on non-steroidal anti-inflammatory drugs (NSAIDs). By inhibition of cyclooxygenase (COX)-1 and COX-2 enzymes the synthesis of prostaglandins is reduced and leads to reduction of inflammatory processes with concomitant analgesic effects. An improvement of symptoms was reported by up to 67% of patients with shoulder pain [23]. Compared to acetaminophen, NSAIDs demonstrated an increased pain reduction in OA [24]. Due to a poorer side effect profile of unselective COX inhibitors, selective COX-2 inhibitors are used especially for elderly patients and patients with comorbidities. Besides the oral application, the usage of topical NSAIDs is also a common part of therapy. Because of their good pain reduction and anti-inflammatory effect, NSAIDs are recommended as first-line therapy in the conservative treatment of shoulder OA [25].
Oral vitamins

The National Institute of Health and Care Excellence (NICE) UK guidelines report the administration of oral vitamins as optional part for the treatment of shoulder OA [26]. In particular vitamin C (ascorbic acid) and vitamin D showed positive effects on the development of cartilage. The chondroprotective mechanism of vitamin C is based on the antioxidant impact and the reduction of apoptosis. To our knowledge there is no clear evidence for the effects of vitamin C on glenohumeral OA, nevertheless recent results in hip and knee OA can be adopted to the glenohumeral joint.

Naturopathic remedies

Naturopathic drugs are often requested by patients with skepticism towards conventional oral medication and can be used as additional therapeutic part in the treatment of glenohumeral OA. Various remedies act via identical receptors as conventional drugs (e.g., NSAIDs), but do not reach identical potency. Two of the most commonly-used remedies are Boswellia serrata preparations and avocado-soybean unsaponifiables (ASU). Boswellia serrata remedies act via direct inhibition of 5-lipoxygenase, which is a key enzyme in the production of leukotrienes and thus has a
direct influence on inflammatory mediators [27]. Liu et al [28] showed in their systematic review a sufficient pain reduction with clinical importance by admission of collagen hydrolysate, passion fruit peel extract, Curcuma longa extract, Boswellia serrata extract, curcumin, pycnogenol and L-carnitine.

Biologics (Table 2, 3)

Platelet rich plasma (PRP) injections: Basic science

PRP consists of a sample of autologous blood with platelet concentrations, which is produced through the separation of whole blood by centrifugation. The proposed mechanism is that PRP initiates the body’s own repair processes, modulates inflammation, delivers growth factors, and attracts and activates MSCs, which promote a healing environment and reduce shoulder pain [30]. Especially, platelets possess biologically active growth factors, which have the potential to reduce joint inflammation, decrease cartilage breakdown, and promote tissue repair.

PRP injections: clinical outcomes
There have been few clinical studies evaluating the use of PRP injections to treat glenohumeral OA. There is one paper by Eliasberg et al. [31] reporting complications following biologic injections.

**Bone marrow aspirate injections: Basic science**

Bone marrow aspirate injections are becoming increasingly popular as a treatment for glenohumeral OA. Secretion of cytokines and growth factors through a paracrine mechanism plays a role [32]. This paracrine activity is thought to stimulate angiogenesis and have anti-inflammatory properties [33]. MSCs are harvested from bone marrow, adipose, umbilical or placental tissue sources.

**Bone marrow aspirate injections: Clinical outcomes (Figure 3)**

The number of studies on the use of cell-based therapies, especially autologous bone marrow aspirate injections, to treat symptomatic knee OA has grown recently. On the other hand, clinical evidence to treat glenohumeral OA is not enough. Centeno et al. [34] observed preliminary encouraging results following bone marrow concentrate injections for shoulder OA.
Adipose tissue is another major source of cells, considering that it can be easily accessed and harvested and that few complications have been reported with the procedure. Multiple mechanisms have been proposed for how adipose-derived stem cells (ASCs) may improve shoulder pain and function. Immunomodulatory and anti-inflammatory properties secondary to a paracrine secretion of growth factors and cytokines likely contribute [32].

Adipose-derived stem cells injections: Clinical outcomes

There are two studies reporting stromal vascular fraction (SVF) outcomes on shoulder pain in patients with rotator cuff tears. There are few reports investigating the effect of ASCs injections in patients with glenohumeral OA.

Amniotic membrane and umbilical cord

The amnion is a natural, biodegradable tissue that exhibits low immunogenicity and stimulates new vascularization. Amniotic membrane (AM) and umbilical cord (UC) are well known to have anti-inflammatory properties and have been shown to promote healing in various orthopedic indications. In case series by Ackley et al. [35], 10
patients that received injection of 50 mg AM/UC for partial rotator cuff tears. Follow-
up MRI scans did not demonstrate any significant change in rotator cuff tear size. This
small case series provides preliminary data for use of cryopreserved AM/UC particulate
matrix in patients with partial rotator cuff tears.

Non-operative management in the athletes

Patient Education/Activity Modification

When managing an athlete with glenohumeral OA, an important initial step is
to educate the patient on both the arthritic process, as well as the long-term outlook on
their condition and how it may impact their athletic career [40]. This can help the
athletes make decisions regarding their treatment options, and to set expectations for
their symptoms and function. Activity modification may alleviate some symptoms;
however, complete immobilization of the shoulder can lead to shoulder stiffness and
should be avoided [41]. Limiting extremes of ROM, as well as avoiding activities that
involve weight bearing in the upper extremity, may prevent exacerbations of pain.

Physical Therapy
Physical therapy can be useful in the management of glenohumeral OA. Patients with minor radiographic changes and limitations in ROM and strength benefit most [40]. Physical therapy programs should incorporate joint mobilization techniques (active, active-assisted, and passive) [42], as well as stretching involving the rotator cuff, surrounding musculature, and the joint capsule. After improvements in mobility and stretching are obtained, strength training can be added with a focus on the deltoid and the scapular girdle [42]. Additionally, aerobic exercise has been shown to be beneficial. While the data regarding the benefits of physical therapy in patients with glenohumeral OA is limited, the consensus is that in young patients who elect to proceed with non-operative options as well as in older patients who are not surgical candidates, physical therapy can be particularly helpful in optimizing function and managing symptoms [43].

Viscosupplementation

Hyaluronic acid makes up a significant proportion of synovial fluid and its content within the joint results in the viscoelasticity of synovial fluid. Favorable results have been reported that hyaluronic acid injection prolongs the symptom improvement compared to corticosteroid [44, 45]. However, the American Academy of Orthopaedic
Surgeons (AAOS) makes a recommendation against the use of hyaluronic acid injections in the treatment of glenohumeral OA based on studies, which failed to demonstrate a significant benefit of hyaluronic acid on the symptoms of glenohumeral OA [43]. High-quality evidence needs to be established.
References


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Figure legends

Figure 1. Strengthening exercise for the infraspinatus, teres minor, and subscapularis

To strengthen the infraspinatus and teres minor (A), the patient in the side-lying position on the unaffected side externally rotates the shoulder with the elbow at the side against resistance. To strengthen the subscapularis (B), the patient in a supine position internally rotates the shoulder at 30° of abduction against resistance.

Figure 2  Corticosteroid glenohumeral injection

A: Positioning for posterior approach to ultrasound guided glenohumeral injection. B: Color flow doppler confirming injection within the glenohumeral joint space.

Figure 3  Bone marrow aspiration technique from posterior iliac crest

A: Local anesthesia injected along track to the iliac crest. B: Insertion of Trocar needle and BMA cannula. C: Removal of Trocar needle. D: Syringe attached to BMA cannula with aspiration of bone marrow from the iliac crest.
Table 1. Overall recommendations of pharmacological treatment [29]

<table>
<thead>
<tr>
<th>Application form</th>
<th>Drug</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systematic</td>
<td>Acetaminophen</td>
<td>Recommended</td>
</tr>
<tr>
<td></td>
<td>NSAIDs</td>
<td>Recommended</td>
</tr>
<tr>
<td></td>
<td>Opioids</td>
<td>Not recommended</td>
</tr>
<tr>
<td></td>
<td>Duloxetine</td>
<td>Recommended</td>
</tr>
<tr>
<td></td>
<td>Glucosamine</td>
<td>Not recommended</td>
</tr>
<tr>
<td></td>
<td>Pine bark extract</td>
<td>Inconclusive</td>
</tr>
<tr>
<td></td>
<td>Vitamin D</td>
<td>Not recommended</td>
</tr>
<tr>
<td></td>
<td>Omega-3</td>
<td>Not recommended</td>
</tr>
<tr>
<td></td>
<td>Avocado-soybean unsaponifiable (ASU)</td>
<td>Inconclusive</td>
</tr>
<tr>
<td></td>
<td>Boswellia serrata</td>
<td>Inconclusive</td>
</tr>
<tr>
<td></td>
<td>Curcuma</td>
<td>Inconclusive</td>
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<tr>
<td>Topical</td>
<td>NSAIDs</td>
<td>Recommended</td>
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<tr>
<td></td>
<td>Capsaicin</td>
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</tr>
<tr>
<td>Intraarticular</td>
<td>Corticosteroids</td>
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<tr>
<td></td>
<td>Hyaluronic acid</td>
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Table 2. Biologic therapy

<table>
<thead>
<tr>
<th>Biologic Therapy</th>
<th>Preparation/Location</th>
<th>Active</th>
<th>Mechanism</th>
<th>Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet Rich Plasma</td>
<td>Autologous blood through centrifugation produces increased concentration of platelets</td>
<td>Alpha granules within platelets become activated they contain proteins and growth factors (platelet-derived growth factor (PDGF), TGF-B, and platelet factor 4, in addition to fibrinogen, albumin, and IgG) [36-37]</td>
<td>Promote less inflammatory joint environment by reducing proinflammatory mediators (COX) and promoting upregulation of anti-inflammatory mediators. They also inhibit MMPs catabolic effects [36]</td>
<td>Multiple studies shown improvement with LP-PRP in knee OA some studies have shown improvement with LP-PRP in glenohumeral OA</td>
</tr>
<tr>
<td>Cell Therapies: Bone</td>
<td>Cell components harvested through bone marrow aspiration and then undergo centrifugation</td>
<td>The cell layers of interest include connective tissue stem and progenitor cells and hematopoietic stem cells</td>
<td>Hypothesized to result in tissue regeneration through stem and progenitor cell differentiation by recruitment of local progenitor cells and limiting inflammation through high levels if IL-1 and IL-1B antagonism [32, 38]</td>
<td>Limited data, one study compared BMAC and CSI found BMAC was preferred [38]</td>
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</tr>
<tr>
<td>Biologic Therapy</td>
<td>Mechanism</td>
<td>Preparation Time</td>
<td>Data in Shoulder OA</td>
<td></td>
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<tr>
<td>-----------------------------</td>
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<td></td>
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<tr>
<td>Platelet Rich Plasma</td>
<td>Growth factors reduce pro-inflammatory cytokines and slow catabolic pathways</td>
<td>~30 minutes</td>
<td>Limited, small studies and case reports</td>
<td></td>
</tr>
<tr>
<td>Bone Marrow Aspirate Concentrate</td>
<td>Recruit local progenitor cells and antagonize local inflammatory mediators</td>
<td>~1 hour</td>
<td>Limited, small studies</td>
<td></td>
</tr>
<tr>
<td>Mesenchymal Stem Cells</td>
<td>Anti-inflammatory and anti-catabolic effects through secretory process</td>
<td>~24 hours</td>
<td>Limited, small studies</td>
<td></td>
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</tbody>
</table>
Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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