Ankle osteoarthritis constitutes a large burden to society and is a leading cause of chronic disability in the United States. Most commonly, it is post-traumatic, occurs in younger individuals, and is associated with obesity. This entity presents similarly to osteoarthritis of the other joints, with the typical nonspecific symptoms of stiffness, swelling, and pain. Radiographic investigation includes four weight-bearing standard views: antero-posterior and lateral foot, mortise view of the ankle, and a specialized view of the hindfoot. In this review, we covered epidemiology, anatomy and biomechanics, etiology, pathology, differential diagnoses, symptoms, physical examination, appropriate radiological investigation, as well as current treatment options and algorithms. Non-operative treatment options include weight loss, physical therapy, bracing, orthoses, pharmacologic treatments, corticosteroid injections, viscosupplementation, and biologic
Although ankle osteoarthritis (OA) occurs in only 1% of the world’s population, it is a leading cause of chronic disability in the United States and Canada. In a cross-sectional study of 130 patients who had end-stage ankle arthritis, the physical disability was shown to be two standard deviations higher than that of the general population (30 vs. 52; p<0.05), which is similar to end-stage osteoarthritis of the hip joint, end-stage kidney disease, or heart failure. Agel et al. administered a Musculoskeletal Functional Assessment (MFA) survey to 426 patients who had ankle arthritis and 123 patients who did not, and they demonstrated significantly worse mean MFA scores in ankle arthritis patients (40 vs. 9 points; p<0.05).

Primary ankle osteoarthritis usually afflicts an older population (mean age, 65 years), but it is not as common as post-traumatic osteoarthritis, which can present in patients in their early 20s (mean age, 58 years). In a statewide Iowa database, the symptomatic ankle osteoarthritis was estimated to have an incidence of 1,516 and a prevalence of 22,125 cases. Using 2015 United States Census Bureau Iowa State data (3,123,899 individuals) and the United States (321,773,631 individuals) data, we can extrapolate the national incidence to approximately 156,000 and the prevalence of approximately 2,279,000 cases. The lifetime cost of treating a single patient who has ankle arthritis is approximately $50,000, and utilizing an average life expectancy of 79 years, the annual cost of ankle osteoarthritis treatment in the United States is approximately $1.5 billion.

Various non-operative and surgical treatment methods have been investigated and developed for the treatment of this disease. Similar to osteoarthritis of other joints, early disease is treated non-operatively with physical therapy, pharmacotherapy, injections, and orthoses. In more severe cases, operative treatment can be utilized. However, due to the younger mean age in this population of patients, and their long life expectancy, a non-operative treatment is desired. Therefore, the aim of this review is to provide an up-to-date, evidence-based guide for the diagnosis and treatment of ankle osteoarthritis. We discuss the epidemiology, anatomy, biomechanics, etiology, as well as the pathology of ankle osteoarthritis, and update the readership on recent advances in diagnosis and treatment of this disease.

INTRODUCTION

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1. EPIDEMIOLOGY OF ANKLE ARTHRITIS

Primary idiopathic osteoarthritis of the ankle is a rare phenomenon (approximately 9% of total arthritis incidence) with secondary (13%) and post-traumatic osteoarthritis being more common (78%). According to one study, approximately 6 to 13% of all osteoarthritis involves the ankle. Some patient populations have a higher risk of developing this condition. In a study of 1,411 adults, Frey et al. demonstrated that overweight and obese individuals (body mass index [BMI] ≥ 25 kg/m²) have a 1.5 times increased likelihood of developing ankle osteoarthritis (p<0.05, 95% CI 0.986 to 2.274). In a comparative study of female ballet dancers and the general population (27 vs. 38 subjects respectively), van Dijk et al. demonstrated that the female ballet dancers had a higher risk of developing ankle arthritis (11 of 27 vs. 0 of 38; p=0.043). In a cadaver study, Muehleman et al. demonstrated that of the 1,060 extremity pairs, knee arthritis was much more common than in the ankle; however,
they did not observe any cases of ankle arthritis that were not associated with ipsilateral knee disease.18 Interestingly, they noted that the earliest signs of ankle degeneration were in a 28-year-old patient. In addition, only 1 to 3% of ankles had more severe OA of the ankle than the knee. There was no difference in the severity of disease between obese and non-obese subjects (p>0.05).10 However, this is a cadaver study, and several other studies have demonstrated that obesity is a risk factor for the development of ankle OA.5,11,12

2. ANATOMY AND BIOMECHANICS

The ankle, also known as the talocrural joint, is a synovial hinge-type joint composed of the tibia, fibula, and talus, which allows for dorsiflexion and plantarflexion movements in the sagittal plane.11 The medial side of the joint is formed by the medial malleolus of the tibia, and the lateral side of the joint is formed by the lateral malleolus of the fibula. The axis of rotation is oblique to both sagittal and frontal planes (approximately 8 to 10° from the transverse plane) (Fig 1).14 Normal range of motion (ROM) is 0 to 30° for dorsiflexion and 0 to 55° for plantarflexion.14 The articular surfaces are located on the distal inferior aspect of the tibia (plafond) and fibula proximally, and the talar dome distally.11 The articular surface area is smaller when compared to the hip and knee joint, but the cartilage resistance is higher.11 Shepherd and Seedhom measured the thickness of 11 stets of cadaver joints and demonstrated that the cartilage in the ankle joint was thinner (1.0 to 1.2mm vs. 1.69 to 2.0mm; pp<0.001), more uniform, and had a higher compressive modulus when compared to the knee joint.12

Normally, the ankle joint has approximately 3mm width between the tibia and talus, a medial space of approximately 3 to 4mm, and a lateral space of 5mm.16 In osteoarthritis, cartilage deterioration and loss secondary to trauma, poor biomechanics, infection, or inflammatory changes results in the narrowing of these spaces and denudation of the subchondral bone surfaces.8 This may lead to altered gait patterns in these patients.15 In a study of 15 patients with and 15 patients without ankle arthritis, Valderrabano et al. demonstrated reduced total plantar flexion movement (-37.5%), total inversion movement (-28.4%), total adduction movement (-19.8%), as well as maximal plantar flexion movement (-13.8%), and maximal adduction movement (-44.4%) in ankle arthritis patients when compared to the normal subjects.18 In addition, cadence (-9.1%), walking speed (-16.2%), stride time (+9.4%), step time (+13.2%), stride length (-6.7%), and step length (+7.2%) were different from normal subjects.17

3. ETIOLOGY OF ANKLE OSTEOARTHRITIS

A history of ankle trauma or recurrent instability which results in irreversible cartilage damage are the most common etiologies of ankle osteoarthritis.6 In a study of 639 patients that presented with Kellgren-Lawrence grade 3 or 4 ankle arthritis at a large academic center, Saltzman et al. identified the etiology of the disease based on the medical history, physical examination, and imaging.19 Of these patients, 445 (70%) were identified to be post-traumatic, 76 (12%) due to rheumatoid disease, and 46 (7%) were idiopathic (primary) osteoarthritis. Most of the patients that were diagnosed with post-traumatic ankle arthritis had a prior rotational ankle fracture in the past. Half of the patients diagnosed with primary osteoarthritis had malalignment of the hindfoot, which could have been the predisposing reason for the development of the degenerative joint disease.19

In a similar study, Valderrabano et al.1 identified 390 patients (406 ankles) who presented to a single institution and classified them into post-traumatic arthritis (n=318, 78%), secondary arthritis (n=52; 13%), and primary osteoarthritis (n=36; 9%). The most common traumatic injuries were identified to be fractures of the malleoli (157), tibial plafond (58), talus (9), tibial shaft fractures (20), and ankle ligamentous injuries (65). Secondary osteoarthritis cases included rheumatoid arthritis (22), hemochromatosis (11), hemophilia (6), clubfoot (4), osteonecrosis of the talus (3), osteochondrosis dissecans (3), and post-infectious arthritis (3). Patients who had primary osteoarthritis were significantly older than the post-traumatic and secondary cohorts (65 vs. 58 and 57 years; p<0.05). Those who had secondary osteoarthritis, had significantly higher pain scores than post-traumatic and primary cohorts (7.0 vs. 6.9 and 6.1 points). The primary osteoarthritis cohort had the highest range of motion (28°) when compared to the other two cohorts (22 for post-traumatic and 20 points for secondary; p<0.05). Patients with secondary osteoarthritis had the lowest American Orthopaedic Foot and Ankle Society (AOFAS) scores (32 vs. 38 and 38 points; p<0.05). Similar radiographic alignment was found between the three groups (p<0.05).

4. PATHOLOGY OF ANKLE OSTEOARTHRITIS

Ankle osteoarthritis is similar to knee and hip osteoarthritis in pathologic findings of subchondral bone changes, such as sclerosis, cyst formation, bone attrition, bone marrow lesions, and osteophytes.20 Typical histological findings in ankle osteoarthritis include necrotic chondrocytes, irregularity of tidemark, thinning, fragmentation, and fibrillation of thinned cartilage, subchondral cysts with mucoid fluid, and usually no inflammatory findings.21 The presence of magnetic resonance imaging (MRI)-visible bone marrow lesions may possibly be due to bone marrow necrosis, fibrosis, and trabecular abnormalities. These are usually found in the same area as bone cysts, and there may be an association between these two findings.32,33 Subchondral cysts contain fibrous connective tissue, adipocytes, and osteoblasts, and may occasionally be continuous with the joint space.34 In addition, secondary inflammation of the joint may occur.25,56 A commonly used histological scale modified for the ankle by Mushlem et al. classifies the degree of cartilage degeneration into four grades: 1) minimal fibrillations, shallow pits or grooves but no changes in articular surface geometry; 2) deep fibrillations and fissuring, flaking, pitting and/or blistering, early marginal hyperplasia and, possibly small osteophytes; 3) extensive fibrillations, fissuring, obvious osteophytes and 30% or less of the articular cartilage surface eroded down to the subchondral bone; 4) prominent osteophytes and greater than 30% of the articular surface eroded down to the
Current Concepts in Osteoarthritis of the Ankle: Review

5. Differential Diagnoses

Patients who present complaining of ankle pain may be examined closely because there are many structures surrounding the ankle joint that may be the source of pain. These include the subtalar joint, the peroneal tendon, the Achilles tendon insertion, and others [10]. Therefore, a radiographic finding of talo-fibular joint degeneration, which is present in many elderly patients, should not be the only deciding factor in diagnosing ankle osteoarthritis. This can be diagnosed clinically; therefore, other differential diagnoses must be considered when evaluating the patient. These include inflammatory arthropathies, such as rheumatoid arthritis, infectious mono-arthritis (gonococcal vs. non-gonococcal), gout, and osteonecrosis. A thorough clinical exam, as well as serological inflammatory markers, can help narrow the differential diagnoses. Osteonecrosis may present with symptoms typical of arthritis before overt joint destruction is observed. Lyme disease is a rare entity associated with this joint. Even rarer phenomena, which may affect the ankle joint and present clinically as osteoarthritic pain, are sarcoid periarthritis, juxtaarticular benign or malignant neoplasms (or tumors in the synovium or other soft tissues of the joint), myelodysplastic and leukemic disorders which may present as acute arthritis, and plant-thorn synovitis. Some other conditions which may result in ankle arthritis include joint dysplasias and joint dislocations, and may present as acute arthritis, and plant-thorn synovitis. Some other conditions which may present as acute arthritis, and plant-thorn synovitis.

6. Symptoms of Ankle Osteoarthritis

Ankle osteoarthritis presents similarly to other joints, with the typical nonspecific symptoms of stiffness, swelling, and pain, typically described as aching within the talo-talar joint. The pain may be localized or general, may be time and weight-bearing dependent, and in severe disease, may occur at rest and during the night. The diagnosis of ankle osteoarthritis may be clinically determined, without a need for laboratory or radiologic confirmation, especially in the at-risk populations such as age >60 years, female gender, and obesity. Symptoms that are frequently encountered in patients who have ankle osteoarthritis include: joint pain that is activity-related (as the joint fills with fluid), insidious onset with slow progression, exacerbation with weight-bearing, relieved by rest in early stages of the disease, and increasing intensity during the night as the disease progresses. There may be associated morning stiffness, described as being a "deep pain" with "crunching, clicking noises," which may be relieved by heat.

7. Physical Examination

The physical exam performed on a patient with ankle pain can help discern when osteoarthritis is the etiology. The patient is asked to wear shorts and remove footwear for adequate exposure. Footwear can then be examined for wear patterns which can indicate abnormal contact of the foot with the ground. Early lateral, proximal, and mid-shoe wear can indicate a supination deformity; while wear on the medial border indicates a pronation deformity. Therefore, a radiographic finding of tarsal coalition noted along with any localized swelling that could indicate injury. Evaluate for skin discoloration, ulcers, callous, signs of infections, and lack of hair which can signify circulatory changes. Palpation is then performed with focus given to the malleoli, talocrural joint line, Achilles tendon, peroneal tendons, posterior talofibular ligament (PTFL), calcaneofibular ligament (CFL), anterior talofibular ligament (ATFL), and anterior inferior talofibular ligament (AITFL). Ankle osteoarthritis patients typically have tenderness to palpation over the joint line, but care should be provided to perform a full palpation exam to prevent missing other potential pain generators. Further palpation can be performed of the sinus tarsi, calcaneus, cuboid, navicular, talus, posterior tibials, anterior tibials, and plantar fascia based on pain location and symptom profile. Ankle motion is then evaluated. Active dorsiflexion, planatarflexion, inversion, and eversion is performed and compared to the other side. Normal ankle dorsiflexion is 0 to 20°, plantarflexion 0 to 50°, inversion 0 to 35°, and eversion 0 to 15°, respectively. Passive motion is then evaluated. Along with dorsiflexion, plantatarflexion, inversion, and eversion, evaluation of pronation and supination can be performed passively. In ankle osteoarthritis, range of motion can be limited throughout all planes due to pain, but with increased...
restriction of dorsiflexion and plantarflexion. Inversion and eversion is mostly motion of the subtalar joint which can become restricted and painful in conditions of subtalar arthritis and tarsal coalitions. A complete physical exam of the ankle concludes with a lower extremity neurovascular exam along with evaluation of the ipsilateral knee and hip.

8. APPROPRIATE RADIOLOGICAL INVESTIGATION

X-ray findings
Conventional radiographs are usually the next step after physical examination of the ankle. Radiographic investigation includes four weight-bearing standard views: antero-posterior and lateral foot, mortise view of the ankle, and a specialized view of the hindfoot (Saltzman view). For the specialized view of the hindfoot, patients stand on a radiolucent platform facing the film with the medial border of their feet parallel and their knees in extension. A 3 mm x 2 mm x 6 cm lead strip is placed perpendicular to the longitudinal axis of the feet at the most posterior aspect of the heel. The X-ray cassette is positioned at 20° ankle form vertical. Only weight-bearing radiographs should be performed because non-weight-bearing films are often misleading.

In osteoarthritis, radiographs usually demonstrate increased bone density (subchondral sclerosis), flattening of the subchondral surface (bone attrition), and bone marrow lesions. These findings may be due to increased bone turnover and remodeling. It is important to measure radiographic ankle alignment including medial distal tibial and anterior distal tibial angles as well as the apparent movement of the arm in order to continuously monitor for any changes. Several ankle osteoarthritis classification systems have been created including Kellgren-Lawrence, Dijk et al., Takakura et al., Giannini et al., Cheng et al., Cedell et al., and Krause et al.

Magnetic resonance imaging findings
In some patients, MRIs may be used to identify the early osteochondral lesions that may commonly lead to osteoarthritis. In a study of 78 patients (79 ankles) who had ankle arthritis, Gatlin et al. performed 3.0 Tesla MRIs and arthroscopic examinations with Outerbridge osteoarthritis classifications of the ankles and demonstrated a sensitivity of 0.714 and a specificity of 0.738 for the detection of grades 3 and 4 articular cartilage defects. Other studies have demonstrated similar findings. However, standard MRI sequences do not always adequately allow for quantification of early degenerative changes. Quantitative T2-mapping is an MRI technique which can quantify cartilage water content and collagen fiber orientation. Increased T2 relaxation times have been shown to be linked to the development of osteoarthritis. In addition, recently developed three-dimensional isotropic MRI imaging has higher signal-to-noise ratio and may better define the stability of osteochondral fragments and provide more information on early changes of cartilage damage. Thermore, magnetic resonance arthrography can be used to identify cartilage lesions and osteochondral lesions of the tibia and talus.

Computed tomography findings
Computed tomography (CT), specifically, single-photon emission computed tomography (SPECT-CT), may be useful in the evaluation of the extent of the degenerative changes in the ankle joint. In a study of 20 patients with ankle pain, Pagenstert et al. found that the inter-observer reliability for SPECT-CT was 0.86 (95% CI 0.81 to 0.88). Paul et al. performed a SPECT-CT on six consecutive patients who had end-stage ankle osteoarthritis and underwent a total ankle arthroplasty (TAA) and correlated the imaging findings with historical findings at SPECT-positive and SPECT-negative areas of tibial and talus subchondral bone and cartilage. The authors demonstrated increased osteoblast-mediated bone formation (p=0.011) in the absence of functional osteoclasts, indicating a pathologic bone-remodeling process in end-stage osteoarthritis.

9. CURRENT TREATMENT OPTIONS AND ALGORITHMS

Search strategies
The literature review was conducted utilizing three electronic databases: PubMed, EBSCO Host, and SCOPUS. This search was performed December 12 to 14, 2017 by two authors (HK and AK). We evaluated studies published between January 1, 1989 and December 31, 2016 using the following search terms: osteoarthritis [title], ankle [title], weight loss [title], physical therapy [title], assistive devices [title], brace [title], orthoses [title], viscosupplementation [title], hyaluronic acid [title], corticosteroid injection [title], biologics [title], stem cell [title], amniotic [title], PRP [title], surgical [title], arthroplasty [title], and arthrodesis [title]. Other search terms included: “ankle osteoarthritis treatment”, “non-operative treatment”, “surgical treatment”, “ankle arthritis”, “arthrodesis”, and “allograft transplant”. We included all relevant reports on non-operative and operative treatment options; non-peer-reviewed literature and manuscripts in languages other than English were not reviewed. We attempted to include as many Level I and II studies; however, all studies thought to be relevant to our topic were included. The initial search resulted in 372 titles (Fig. 2). After duplicate removal (64 studies) and title and abstract screening (255 unrelated reports removed), 53 full-text articles were assessed for eligibility. A total of 16 reports were excluded (nine irrelevant to this topic and seven in languages other than English). Citation lists from all included reports were reviewed and an additional nine studies were identified. This yielded a total of 46 studies, including 16 on non-operative (two physical therapy/weight loss, two braces and orthoses, two corticosteroid injections, one biologic agent, and nine hyaluronic acid) and 30 on operative treatments of ankle osteoarthritis (18 total ankle arthroplasty/arthrodesis, six osteochondral allograft transplant, two arthroscopic treatments, one interposition ankle arthroplasty, and three arthrodesis).

Non-operative
Non-operative treatment options can be successful in the early stages of the disease. These include physical therapy, weight loss, assistive devices, pharmacologic treatments, corticosteroid injections, viscosupplementation, and biologic options. Most of the studies investigating these treatment options have low levels of evidence. Viscosupplementation is the only treatment option which has been carefully evaluated utilizing randomized clinical trials.
Physical therapy, weight loss, and assistive devices

Physical therapy is commonly prescribed as the first treatment option for ankle osteoarthritis. However, it is also important to stress to these patients the importance of weight loss, which is often overlooked. In a study of 142 sedentary, overweight, and obese adults, Messier et al. demonstrated that for each pound of weight lost, there was a four-fold reduction in the load exerted on the knee joint.51 This load reduction is predicted to be even more marked at the ankle joint.51 In addition, 25% of body weight can be offloaded from the involved ankle using a single-point cane.52 In addition to weight loss programs, physical strengthening of lower extremity muscles is important. In a study of 20 patients who had post-traumatic ankle arthritis, Shih et al. demonstrated that gait and muscle strength deteriorated as the disease progressed.53 Specifically, the dorsiflexor and plantar flexor muscles had decreased strength.53 Physical therapy and weight loss programs can be prescribed alone or in combination with nonsteroidal anti-inflammatory drugs (NSAIDS) and assistive devices.54-56

Two studies have evaluated the use of braces and orthoses in patients who have ankle osteoarthritis,57,55 (Table I). Wu et al. enrolled 11 subjects into a gait lab study and demonstrated that rocker sole and solid-ankle cushion-heel (SACH) limited forefoot joint excursion during level walking (30 vs. 24˚; p<0.01), stair climbing, and stair descending, and it decreased ankle motion.57 In a similar study, Huang et al. performed a gait lab analysis of ankle foot orthoses (AFOs), rigid hindfoot orthoses (HFO-Rs), and articulated hindfoot orthoses (HFO-As), and demonstrated superiority of HFO-Rs in ankle joint motion restriction (p<0.001) while allowing for the most forefoot motion.55,58

Corticosteroid injections

We found only two studies that investigated the use of corticosteroid intra-articular injections for ankle osteoarthritis (Table I).59,60 In a study of 12 patients, Ward et al. administered a single 40mg/ml methylprednisolone acetate injection and at one-year mean latest follow up, there was a mean increase in FAOS score of three points.59 In a similar study, Ali et al. injected a single dose of 40mg triamcinolone in 28 ankles with osteoarthritis.60 The authors demonstrated that the visual analog score (VAS) decreased from eight points at baseline to six points at the final follow up of six months. These studies have demonstrated that corticosteroid injections can provide short-term symptom relief with minimal side effects, but they have not been shown to stop disease progression.54,55

Biological agents

Biologic options include platelet-rich plasma (PRP), amniotic, or stem cells; however, data on these treatment options is limited for ankle arthritis and more prospective randomized clinical trials are needed (Table I).59 In a study of 20 ankles (20 patients) who had Kellgren-Lawrence stage 2 to 3 ankle arthritis, Fukawa et al. performed two weekly intra-articular injections of 2ml of PRP and demonstrated improvements in VAS pain scores (60 vs. 42 points; p<0.001), Japanese Society for Surgery of the Foot (JSSF) scores (52 vs. 66 points; p<0.001), and Self-Administered Foot Evaluation Questionnaire (SAFE-Q) scores (47 vs. 56 points; p<0.001) at a final follow up of 24 weeks.61

Potential role of hyaluronic acid

There are four studies prospectively evaluating the safety and efficacy of hyaluronic acid injections (Table II). In a study of 21 patients who had Kellgren-Lawrence grade II ankle arthritis, Luciani et al. administered three weekly doses of hyaluronic acid. At the latest follow up of 18 months, there was a significant improvement in the mean Ankle Osteoarthritis Scale (AOS) pain score (45 to 34 points; p<0.05), AOS disability score (49 to 33 points; p<0.001), and VAS pain scores (6.6 to 4.6 points; p<0.0005).62 In a similar study, Mei-Dan et al. performed five weekly ankle injections of hyaluronic acid in patients with Kellgren-Lawrence grade II to IV ankle arthritis with resulting decreases in the mean VAS pain score from 5.29 to 3.05 points (p<0.001), and the mean VAS stiffness score from 5.61 to 3.33 points (p<0.001).63 In addition, the patients...
experienced improvement in mean ROM by 15° and in the Ankle-Hindfoot Scale score by a mean of seven points.63 In a study of 93 patients who had Kellgren-Lawrence grade I or II ankle arthritis, Sun et al. administered five weekly doses of intra-articular hyaluronic acid and demonstrated improvements in the mean AOS scores from 1.9 to 2.6 points (p<0.001) and the mean AOFAS score from 64 to 78 points (p<0.001) at the final mean follow up of six months.64 Local self-limited adverse events occurred in only 6.7%.64 In a similar study, Sun et al. performed intra-articular injections of hyaluronic acid in 50 patients with Kellgren-Lawrence grade II or III ankle arthritis and demonstrated improvements in the mean AOS score from 5.5 to 3.2 points (p<0.05) and the mean AOFAS Ankle-Hindfoot Score from 60.5 to 76.7 points (p<0.05).65 In addition, acetaminophen use dropped from 16 to seven tablets/week (p<0.005).65 Three prospective randomized controlled trials compared the efficacy of hyaluronic acid and normal saline ankle injections for the treatment of ankle arthritis (Table II). Salk et al. stratified 22 patients who had Kellgren-Lawrence grade II to IV ankle arthritis into two cohorts: three weekly injections of hyaluronic acid or saline.46 At the final mean follow up of six months, more patients in the hyaluronic acid cohort (five patients) had >30mm of improvement on the AOS scale when compared to baseline (one patient). In a similar study, Karatosun et al. stratified 30 patients (43 ankles) who had Kellgren-Lawrence grade III ankle arthritis into two cohorts: single 2.5ml injections of hyaluronic acid or normal saline.47 At the final mean follow up of 12 weeks, the overall group of patients demonstrated improvements in AOFAS (p=0.006) and AOS (p=0.013) scores; however, there was no significant difference between the two cohorts (p>0.05).47 Three studies compared various dosages and regimens of intra-articular hyaluronic acid injections (Table III).69-71 Mei-Dan et al. studied 16 patients with stage II, III, and IV osteoarthritis, in which intra-articular injections of 25 mg of sodium hyaluronate were injected into arthritic

**Table I**

<table>
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<tr>
<th>Author</th>
<th>Year</th>
<th>N</th>
<th>OA grades</th>
<th>Study Design</th>
<th>Outcomes</th>
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<tr>
<td>Wu et al.57</td>
<td>2004</td>
<td>11</td>
<td>N/A</td>
<td>Gait lab analysis of rocker sole and solid-ankle cushion-heal (SACH) heels during level walking, stair climbing, and stair descending.</td>
<td>SACHs limited forefoot joint excursion during level walking (30 vs. 24 degrees; p&lt;0.01), stair climbing, and stair descending and decreased ankle motion.</td>
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<td>Huang et al.55</td>
<td>2006</td>
<td>13</td>
<td>Gait lab analysis of custom-made ankle-foot orthosis (AFO), rigid hindfoot orthosis (HFO-R), and articular hindfoot orthosis (HFO-A).</td>
<td>AFO and HFO-R had the most hindfoot motion restriction (p&lt;0.001). However, HFO-R was superior in sagittal plane forefoot motion (p=0.01), and side-slope conditions (p&lt;0.02).</td>
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<tr>
<td>Ward et al.59</td>
<td>2008</td>
<td>12</td>
<td>N/A</td>
<td>Single-dose methylprednisolone acetate 40mg/ml. No control cohort. Latest follow up at 1 year.</td>
<td>Mean increase in FAOS of 3 points.</td>
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<td>Ali et al.60</td>
<td>2016</td>
<td>28</td>
<td>Triamcinolone 40mg, no control cohort, latest follow up at 6 months.</td>
<td>The mean VAS pain score improved from 8 to 6 points. Five patients had to undergo another injection at 6 months.</td>
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<td>Fukawa et al.61</td>
<td>2017</td>
<td>20</td>
<td>2 to 4*</td>
<td>Weekly 2ml PRP for 2 weeks. Latest follow up at 24 weeks.</td>
<td>VAS pain scores (60 vs. 42 points; p&lt;0.001), Japanese Society for Surgery of the Foot (JSSF) scores (52 vs. 66 points; p&lt;0.001), and Self-Administered Foot Evaluation Questionnaire (SAFE-Q) scores (47 vs. 56 points; p&lt;0.001).</td>
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*Takakura classification system37
ankles. There was an improvement of 20% in range of motion after 4-, 8-, 11-, 17-, and 32-week follow ups, as well as a statistically significant reduction in pain measured by visual analog score and ankle-hindfoot scores.\(^69\) Witteveen et al. stratified 26 patients who had stage II arthritis (grade by van Dijk et al.)\(^38\) to receive single injections of hyaluronic acid of 1, 2, or 3ml, or three weekly doses of 1ml.\(^71\) In a similar study, Witteveen et al. stratified 55 patients who had stage II osteoarthritis (van Dijk et al.) into two cohorts: those receiving a single 2ml injection and those receiving two weekly 2ml injections of hyaluronic acid.\(^71\) Overall, the mean VAS pain score decreased from 68 to 34 points (p<0.001). Patients who received one injection had a mean change of -43 vs. -24 points in the other cohort (p<0.001). The mean OA disability score decreased by -28 and -16 points (p<0.008) in the single- and two-injection cohorts. The overall Patient global assessment (PGA) scores

<table>
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<th>Author</th>
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<td>2008</td>
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<td>KL* II</td>
<td>Weekly x 3</td>
<td>18 months</td>
<td>There was a significant improvement in AOS** pain (45 to 34; p&lt;0.05), AOS disability (49 to 33; p&lt;0.001), and VAS pain scores (6.6 to 4.6; p&lt;0.0005) from baseline to 18 months.</td>
</tr>
<tr>
<td>Mei-Dan et al.(^66)</td>
<td>2010</td>
<td>16</td>
<td>KL II-IV</td>
<td>Weekly x 5</td>
<td>32 weeks</td>
<td>The mean VAS pain score decreased from 5.29 to 3.05, p&lt;0.001. The mean VAS stiffness score decreased from 5.61 to 3.33, p&lt;0.001. Improvement in ROM*** (15 degrees, 20%) and in Ankle-Hindfoot Scale score by 7 points.</td>
</tr>
<tr>
<td>Sun et al.(^64)</td>
<td>2006</td>
<td>93</td>
<td>KL I or II</td>
<td>Weekly x 5</td>
<td>6 months</td>
<td>The mean AOS score improved from 1.9 to 2.6 (p&lt;0.001). The mean AOFAS score improved from 64 points to 78 points (p&lt;0.001). No significant difference in ROM. Local adverse events occurred in 6.7%. Acetaminophen consumption dropped significantly p&lt;0.001.</td>
</tr>
<tr>
<td>Sun et al.(^65)</td>
<td>2015</td>
<td>50</td>
<td>KL II or III</td>
<td>Weekly x 3</td>
<td>6 months</td>
<td>The mean AOS score improved from 5.5 to 3.2 (p&lt;0.05). The mean AOFAS Ankle-Hindfoot Score improved from 60.5 to 76.7 (p&lt;0.05). Acetaminophen use dropped from 16 to 7 tablets/week (p&lt;0.005). Patients demonstrated improvement in 4 balance tests (p&lt;0.05).</td>
</tr>
<tr>
<td>Randomized Controlled Studies</td>
<td></td>
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<tr>
<td>Salk et al.(^67)</td>
<td>2006</td>
<td>22</td>
<td>N/A</td>
<td>HA: Weekly x 5 Control: NS, weekly x 5</td>
<td>26 weeks</td>
<td>At 6 months, more patients in HA group (5 patients) had &gt;30mm of improvement on AOS as compared to baseline (1 patient).</td>
</tr>
<tr>
<td>Karatosun et al.(^68)</td>
<td>2008</td>
<td>43 (30 patients)</td>
<td>KL III</td>
<td>HA: N=19, Weekly x 3 Control: N=24, Home-based exercise therapy x 6 weeks</td>
<td>12 months</td>
<td>AOFAS Ankle-Hindfoot Score: both groups improved significantly from baseline (HA 62 to 90, p&lt;0.001; Control 72 to 88 p&lt;0.001), but no difference between the cohorts at the final follow up.</td>
</tr>
<tr>
<td>DeGroot et al.(^69)</td>
<td>2012</td>
<td>56</td>
<td>N/A</td>
<td>HA: Single injection 2.5ml Control: Single injection NS 2.5ml</td>
<td>12 weeks</td>
<td>AOFAS and AOS improved at the final follow up for both cohorts, but there was no significant difference between the two groups.</td>
</tr>
</tbody>
</table>

*KL – Kellgren-Lawrence osteoarthritis grade; **AOS–Ankle Osteoarthritis Score; ***ROM – range of motion
improved from 65 to 35 points (p<0.001) at three months. The mean PGA scores for the single-injection cohort improved from 55 to 21 points (p<0.001) and for the two-injection cohorts from 42 to 27.2 points (p<0.001). The mean SF-36 score improved from 36 to 45 points (p<0.001) at 6 months.

In summary, patients who present with mild ankle arthritis should be prescribed non-operative modalities beginning with physical therapy, pharmacotherapy, and assistive devices if deemed needed. As the disease progresses, corticosteroid injections may be utilized, however, they tend to provide only limited symptom relief. The most evidence-based non-operative treatment option is viscosupplementation with hyaluronic acid, which may provide longer symptom relief than intra-articular corticosteroids.

### Operative Treatment

#### Total ankle arthroplasty vs. ankle arthrodesis

Many studies have compared the safety and efficacy of ankle arthrodesis (AA) and total ankle arthroplasty (TAA) (Figs. 3 and 4). A recent systematic review by Maffulli et al. compiled 21 level 1 to 3 studies at a minimum mean follow up of six months.\(^7\) The authors demonstrated that although TAA has become an increasingly more common treatment for end-stage ankle osteoarthritis, the revision rates for this procedure are significantly higher than for AA (OR 2.28; 95% CI 1.63 to 3.19; p<0.0001). Although, the success of TAA has been improving over the past several years, the authors do not recommend its routine use. Of note, the Coleman Methodology Score for this review was 42.5, demonstrating that the overall mean quality of the studies was poor.\(^7\) Many studies have compared the survivorship, range of motion, functional outcomes, and quality of life in these patients.

One Level II and five Level III studies have reported on the survivorship and failure rates of total ankle arthroplasty (TAA) and the ankle arthrodesis (AA) in
patients who had end-stage ankle arthritis (Table IV). Overall, four of the six studies demonstrated a higher failure rate in patients who underwent TAA. In addition, Suhoo et al. showed that patients treated with TAA had an increased risk of major revision surgery in patients treated with TAA (HR, 1.93, 95% CI, 1.50 to 2.49).

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Level</th>
<th>N</th>
<th>Follow up (months)</th>
<th>Revision Rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saltzman et al.</td>
<td>2009</td>
<td>II</td>
<td>224</td>
<td>24</td>
<td>12/158 (8%) in TAA and 7/66 (11%) in AA</td>
</tr>
<tr>
<td>Younger et al.</td>
<td>2016</td>
<td>III</td>
<td>687</td>
<td>57</td>
<td>124/474 (26%) in TAA and 10/213 (5%) in AA</td>
</tr>
<tr>
<td>Daniels et al.</td>
<td>2014</td>
<td>III</td>
<td>388</td>
<td>66</td>
<td>48/232 (17%) in TAA and 7/89 (7%) in AA</td>
</tr>
<tr>
<td>Krause et al.</td>
<td>2011</td>
<td>III</td>
<td>161</td>
<td>39</td>
<td>12/114 (11%) in TAA and 2/47 (4%) in AA</td>
</tr>
<tr>
<td>Saltzman et al.</td>
<td>2010</td>
<td>III</td>
<td>71</td>
<td>50</td>
<td>3/37 (8%) in TAA and 4/23 (17%) in AA</td>
</tr>
<tr>
<td>SooHoo et al.</td>
<td>2007</td>
<td>III</td>
<td>5,185</td>
<td>60</td>
<td>Increased risk of major revision surgery in patients treated with TAA (HR, 1.93, 95% CI, 1.50 to 2.49)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Range of motion</th>
<th>Level</th>
<th>N</th>
<th>Follow up (months)</th>
<th>Revision Rates</th>
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</thead>
<tbody>
<tr>
<td>Jastifer et al.</td>
<td>2015</td>
<td>II</td>
<td>77</td>
<td>ROM 18° TAA vs 10° AA</td>
</tr>
<tr>
<td>Braito et al.</td>
<td>2014</td>
<td>II</td>
<td>141</td>
<td>ROM 17° TAA vs 12° AA</td>
</tr>
<tr>
<td>Singer et al.</td>
<td>2013</td>
<td>II</td>
<td>34</td>
<td>ROM 18° TAA vs 13° AA</td>
</tr>
<tr>
<td>Hahn et al.</td>
<td>2012</td>
<td>II</td>
<td>18</td>
<td>ROM 18° TAA vs 15° AA</td>
</tr>
<tr>
<td>Rouhani et al.</td>
<td>2012</td>
<td>II</td>
<td>20</td>
<td>ROM 23° TAA vs 16° AA</td>
</tr>
<tr>
<td>Piriou et al.</td>
<td>2008</td>
<td>II</td>
<td>24</td>
<td>ROM 22° TAA vs 16° AA</td>
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</table>

<table>
<thead>
<tr>
<th>Functional Outcomes</th>
<th>Level</th>
<th>N</th>
<th>Follow up (months)</th>
<th>Revision Rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jastifer et al.</td>
<td>2015</td>
<td>II</td>
<td>77</td>
<td>AOFAS* 81 TAA vs. 72 points AA</td>
</tr>
<tr>
<td>Daniels et al.</td>
<td>2014</td>
<td>II</td>
<td>388</td>
<td>AOS** 25 TAA vs. 34 points AA</td>
</tr>
<tr>
<td>Braito et al.</td>
<td>2014</td>
<td>II</td>
<td>141</td>
<td>AOFAS 71 TAA vs. 68 points AA</td>
</tr>
<tr>
<td>Singer et al.</td>
<td>2013</td>
<td>II</td>
<td>34</td>
<td>AOS 33 TAA vs. 32 points AA</td>
</tr>
<tr>
<td>Rouhani et al.</td>
<td>2012</td>
<td>II</td>
<td>20</td>
<td>AOFAS 78 TAA vs. 67 points AA</td>
</tr>
<tr>
<td>Esparragozza et al.</td>
<td>2011</td>
<td>II</td>
<td>30</td>
<td>MFA 37 TAA vs. 40 points AA; p=0.12</td>
</tr>
<tr>
<td>Benich et al.</td>
<td>2017</td>
<td>II</td>
<td>273</td>
<td>MFA 37 TAA vs. 40 points AA; p=0.12</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Level III</th>
<th>N</th>
<th>Follow up (months)</th>
<th>Revision Rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dalat et al.</td>
<td>2014</td>
<td>III</td>
<td>54</td>
</tr>
<tr>
<td>Schuh et al.</td>
<td>2012</td>
<td>III</td>
<td>41</td>
</tr>
<tr>
<td>Krause et al.</td>
<td>2011</td>
<td>III</td>
<td>161</td>
</tr>
<tr>
<td>Saltzman et al.</td>
<td>2010</td>
<td>III</td>
<td>71</td>
</tr>
</tbody>
</table>

AOFAS – American Orthopaedic Foot and Ankle Society score; AOS – Ankle Osteoarthritis Scale; MFA – Musculoskeletal Function Assessment; *SF-36 PCS – Short Form-36 Physical Component Score; ** FAOS QOL – Foot and Ankle Outcome Score Quality of Life; BP – Buechel-Pappas score.
In summary, the survivorship of ankle arthroplasty has been shown to be superior to total ankle arthroplasty. Although, the range of motion, functional outcomes, and quality of life measures were superior in total ankle arthroplasty patients, the difference was small and does not justify routine use of this procedure in light of high revision rates. Further study in this area is needed.

### Osteochondral total ankle allograft transplantation

Several studies have reported on fresh osteochondral total ankle arthroplasties for the treatment of ankle osteoarthritis (Table V). At the mean follow up of five years, both cohorts demonstrated significant improvements in AOFAS scores from baseline (allograft: 75 vs. 53 points; p<0.05; TAA: 80 vs. 29 points; p<0.05). Similar findings were demonstrated in spatio-temporal parameters (stance time, swing time, stride length, cycle time, and speed) (p<0.05). In a similar study, Bugbee et al. performed osteochondral allograft transplantation on 26 ankles with osteoarthritis and, at the mean 41 months of follow up, there were six failures (23%). The mean AOFAS score improved from 27 to 78 points, p<0.0005. The authors demonstrated a significant correlation between low degree of distal tibial slope and better clinical outcomes (p=0.049).

### Novel surgical treatment options

Several studies describe arthroscopic synovectomy and debridement of the ankle joint as a potential treatment for osteoarthritis; however, the evidence is lacking. This technique appears to be most effective in patients who have ankle impingement. Arthroscopic techniques can also be used for ankle arthrodesis. Several other novel operative techniques have been explored, such as interposition ankle arthroplasty using acellular dermal matrix. In a study of four patients who had end-stage ankle arthritis Carpenter et al. utilized acellular dermal matrix and

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### Table IV (continued)

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Level</th>
<th>N</th>
<th>Follow up (months)</th>
<th>Revision Rates</th>
</tr>
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<td><strong>Level II</strong></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Daniels et al.</td>
<td>2014</td>
<td>II</td>
<td>388</td>
<td>66</td>
<td>SF-36 PCS 37 vs. 39 points</td>
</tr>
<tr>
<td>Braito et al.</td>
<td>2014</td>
<td>II</td>
<td>141</td>
<td>6</td>
<td>FAOS QOL 42 vs. 43 points</td>
</tr>
<tr>
<td>Hahn et al.</td>
<td>2012</td>
<td>II</td>
<td>18</td>
<td>12</td>
<td>SF-36 78 vs. 68 points</td>
</tr>
<tr>
<td>Esparragozza et al.</td>
<td>2011</td>
<td>II</td>
<td>30</td>
<td>25</td>
<td>SF-36 60 vs. 46 points</td>
</tr>
<tr>
<td>Slobogean et al.</td>
<td>2010</td>
<td>II</td>
<td>107</td>
<td>12</td>
<td>SF-6D 0.73 vs. 0.73 points</td>
</tr>
<tr>
<td>Saltzman et al.</td>
<td>2009</td>
<td>II</td>
<td>224</td>
<td>24</td>
<td>BP*** function 19 vs. 21 points</td>
</tr>
<tr>
<td>Benich et al.</td>
<td>2017</td>
<td>II</td>
<td>273</td>
<td>36</td>
<td>SF-36 38 vs. 40 points; p=0.55</td>
</tr>
<tr>
<td><strong>Level III</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Pedowitz et al.</td>
<td>2016</td>
<td>III</td>
<td>68</td>
<td>34</td>
<td>SF-12 PCS 47 vs. 45 points</td>
</tr>
<tr>
<td>Dalat et al.</td>
<td>2014</td>
<td>III</td>
<td>54</td>
<td>52</td>
<td>SF-36 63 vs. 56 points</td>
</tr>
<tr>
<td>Saltzman et al.</td>
<td>2010</td>
<td>III</td>
<td>71</td>
<td>57</td>
<td>SF-36 33 vs. 45 points</td>
</tr>
</tbody>
</table>

AOFAS – American Orthopaedic Foot and Ankle Society score; AOS – Ankle Osteoarthritis Scale; MFA – Musculoskeletal Function Assessment; *SF-36 PCS – Short Form-36 Physical Component Score; ** FAOS QOL – Foot and Ankle Outcome Score Quality of Life; BP – Buechel-Pappas score.
demonstrated improved AOFAS scores at the mean 12-month follow up when compared to baseline (35 vs. 89 points; p=0.003). Another treatment option that has been investigated, specifically for post-traumatic ankle arthritis, is arthrodiastasis; however, the evidence for its use is limited.103–106 This procedure is performed by placing Kirschner wires above (tibia) and below (calcaneus) the ankle joint with external tensioning by threaded rods.107 In a study of 57 patients who had end-stage ankle arthritis, Marijnissen et al. performed a joint distraction arthrodiastasis and demonstrated a 38% decrease in the mean pain score (p≤0.0001), 69% increase in mean function score (p<0.0001), and a mean increase in clinical condition of 120% (p<0.0001) at one year follow up.107 However, several other studies have demonstrated high failure rates (21.7%) and decreased function over time.106,105 Similar findings were demonstrated in spatio-temporal parameters (stance time, swing time, stride length, cycle time, and speed) (p<0.05).

In summary, current evidence suggests that for patients who have severe ankle arthritis and who have failed non-operative treatment, ankle arthrodesis remains the safest and most efficacious treatment option. However, there have been marked advances in the designs and techniques of total ankle alloplasty as well as osteochondral allograft transplantation which may be a good alternative for certain patient populations. Other surgical treatment options do not have enough supporting evidence to justify routine clinical use.

**CONCLUSION**

The incidence of ankle arthritis continues to increase, and it tends to occur in younger patient populations when compared to hip or knee arthritis. Patient work up starts with a careful physical examination and four weight-bearing radiographic views. Advanced imaging options, such as three-dimensional MRI and SPECT-CT, may be useful in early stages of the disease. Early treatment options include physical therapy, pharmacotherapy, and bracing. Corticosteroid injections may be used to temporarily relieve arthritis symptoms. For patients who have moderate to severe disease, surgery may be indicated. However, current surgical treatment
options are either associated with a large number of complications (TAA) or they severely restrict ankle range of motion (ankle arthrodesis), which is undesirable in this young and active patient population. Another non-operative treatment option which can be used in moderate to severe disease is visco-supplementation with hyaluronic acid. This treatment modality has the most evidence-based support and has been shown to be safe and efficacious. In

### Authors’ Disclosures


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All other authors have no conflicts of interest to disclose.

### References


