Topical Review

AMERICAN ORTHOPAEDIC FOOT & ANKLE SOCIETY®

Foot & Ankle Orthopaedics
2020, Vol. 5(4) 1-9

DOI: 10.1177/2473011420970463
journals.sagepub.com/home/fao

Arthrofibrosis of the Ankle

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Abstract

Arthrofibrosis is a common, but often overlooked, condition that imparts significant morbidity following injuries and surgery to the foot and ankle. The most common etiologies are related to soft tissue trauma with subsequent fibrotic and contractile scar tissue formation within the ligaments and capsule of the ankle. This leads to pain, alterations in gait, and ankle dysfunction. Initial treatment often includes extensive physical therapy, however, if severe enough surgical options exist. Although the literature regarding ankle arthrofibrosis is scarce, this review article provides a greater understanding of the pathogenesis of arthrofibrosis and describes the current and future therapeutic options to treat fibrotic joints.
Level of Evidence: Level V, expert opinion.

Keywords: arthrofibrosis, review article

Introduction

Limited joint motion can have a profound effect on a patient's daily life. Although the etiology of motion loss is multifactorial, arthrofibrosis has more recently been investigated as a key cause. Arthrofibrosis is defined as joint pain and stiffness that does not allow functional range of motion and is commonly due to adhesions, scarring, and contracture of the joint.[34,36] Motion-limiting arthrofibrosis has been reported throughout the body, including the knee, shoulder, wrist, and elbow.[33,34,39,68] There is far less literature, however, regarding arthrofibrosis of the ankle.

In the ankle, this condition is mostly commonly due to an inciting trauma. Utsugi et al[63] reported arthrofibrosis in 73% (24/33) of patients who sustained an ankle fracture, whereas Thomas et al[60] found it to be present in 40% (20/50) of patients similarly sustaining ankle fractures. Clinically, arthrofibrosis is characterized by pain, diminished range of motion, stiffness, and difficulty with performing daily activities due to impaired gait and abnormal ankle function. Early preventive strategies are critical for minimizing the risk of developing arthrofibrosis, including bracing and splinting the ankle in a neutral position to prevent an equinus contracture.[36,45] Once fibrosis has developed, conservative and operative management have been shown to improve function.[11,20,36] In part because of the limited current evidence, this entity has rarely been discussed despite the significant impact it can have on a patient's recovery. Therefore, the purpose of this article is to review the current literature on arthrofibrosis of the ankle.

Etiology

A variety of factors contribute to causing arthrofibrosis. A few common causes are infection, trauma, and surgery.[4,62,64] Following the inciting event, fibrous scar tissue may develop in the anterior capsule, posterior capsule, or both. Common surgeries reported to lead to fibrosis of the

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anterior ankle capsule include open reduction and internal fixation (ORIF) of fractures (73% of ankle fractures), open debridement of anterior osteophytes, and ankle arthroplasty (22.1% of ankle arthroplasties).[9,25,36,51,63] Posterior ankle capsular arthrofibrosis may occur following posterior ankle impingement surgery or following posterior approach to the ankle for ORIF.[36] However, cause and effect are unclear and initial pathology may predispose to increased fibrosis after these procedures. Prolonged immobilization after trauma or surgery may also play a role in the development of arthrofibrosis, particularly if the ankle is immobilized in equinus.[24] Inflammation, whether caused by trauma, systemic disease, surgery or infection, is implicated as a root cause of arthrofibrosis of all joints. The role that the inflammatory cycle plays is being increasingly explored by the basic science community.[62] In particular, the role of cytokines such as interleukin-1 (IL-1) and IL-6, is being investigated since they are frequently upregulated in the setting of infection and lead to cell migration, adhesion, and increased matrix metalloproteinase activity.[62]

The direct causes of decreased ankle range of motion can be further categorized into either extra-articular or intra-articular pathology. Potential extra-articular pathologies causing ankle stiffness and restricted motion include soft tissue infections, tendon adhesions, or muscle contractures around the ankle.[64] Depending on the muscle or tendon, patients will predominantly have limitations in either plantarflexion or dorsiflexion. Conversely, examples of intra-articular pathology are adhesive capsulitis and intra-articular fractures. Adhesive capsulitis of the ankle is a rarely reported condition that is often preceded by a traumatic injury.[11,22,38,49] The condition typically involves the development of intra-articular adhesions, and therefore limits both ankle plantarflexion and dorsiflexion.[11,38]

Pathophysiology

Following an inciting event, a synovial inflammatory response is activated. There is proliferation of fibroblasts and a significant deposition of extracellular matrix proteins.[35,36,61] The excess extracellular matrix may then impair blood flow by increasing the distance of the tissue to blood vessels, and thus oxygen delivery to the injured tissue is reduced, resulting in local hypoxia.[14] Deprivation of oxygen triggers the release of inflammatory cytokines, primarily transforming growth factor-beta (TGF-beta) and platelet-derived growth factor (PDGF).[62] These cytokines, in turn, signal a cascade of events resulting in scar tissue formation. In normal healing responses, TGF-beta and PDGF levels decrease over time. However, in patients with arthrofibrosis following injury or infection, these cytokines are dysregulated and continue to be expressed at elevated levels. This overexpression leads to elevated alpha-smooth muscle actin expression in fibroblasts; increased collagen type VI synthesis, which is thought to normally serve as an anchoring element between collagen I/III fibrils and basement membranes; and prolongation of the inflammatory response resulting in fibrous tissue hyperplasia.[36,39,61,67] Additionally, as demonstrated in patients following total knee arthroplasty, reactive oxygen and nitrogen species initiate and sustain the arthrofibrotic response by inducing protein and DNA modifications.[17] Interestingly, other studies have reported an association with human leukocyte antigens (HLAs), suggesting a genetic predisposition to the development of arthrofibrosis.[55] Specifically, HLA-Cw*07 was found significantly less often in patients with primary arthrofibrosis following ACL reconstruction than in the general population ($P = .022$). The opposite effect was seen for HLA-Cw*08, which was found in 17.6% of the study group but only in 3.8% of the control group ($P = .045$). A significant difference was also seen for HLA-DQB1*06, with 23.5% of the patients possessing this allelic variant as opposed to 48.6% of the control group ($P = .048$). However, a statistical bias cannot be excluded given the relatively small number of 17 patients reviewed.[55] A very recent study attempted to uncover evidence of a genetic predisposition for fibrosis in musculoskeletal tissues.[13] They demonstrated that 22% of gene variants were between the lung and the hand, specifically idiopathic pulmonary fibrosis and Dupuytren disease. These genes included *ADAM*, *HLA*, *CARD*, *EIF*, *TGF*, *WNT*, and *ZNF* genes. Despite these shared genetic variations, the authors concluded that there remains limited information about genetic variants associated with fibrosis in other MSK regions.[13] Although bony deformities or arthritic changes may cause bony impingement and altered biomechanics, this review will focus on arthrofibrosis independent of mechanical impingement. These factors should, of course, be carefully evaluated for in any clinical scenario.

Clinical Features and Diagnosis

The clinical manifestations of arthrofibrosis may include joint pain, swelling, stiffness, and decreased range motion. First, distinguishing between stiffness and diminished range of motion is important. Although these 2 terms are often used interchangeably, there are distinct differences between them. Stiffness is a symptom reported by the patient. A patient may report joint stiffness even if there is no objective sign of decreased range of motion. Vega et al[64] reported that some patients may refer to the feeling of stiffness as a similar to having a "mass-occupying feeling" in the ankle. In the ankle, stiffness often suggests the presence of impinging scar tissue within the joint. Diminished range of motion is an objective finding defined as a deficit in degrees of motion from the expected normal or in comparison to the contralateral, uninjured side.[64] Potential extra-articular factors, such as muscle contractures, may also contribute to decreased range of motion. Peri-articular causes of diminished range of motion typically involve the capsule and ankle ligaments.[38,64]

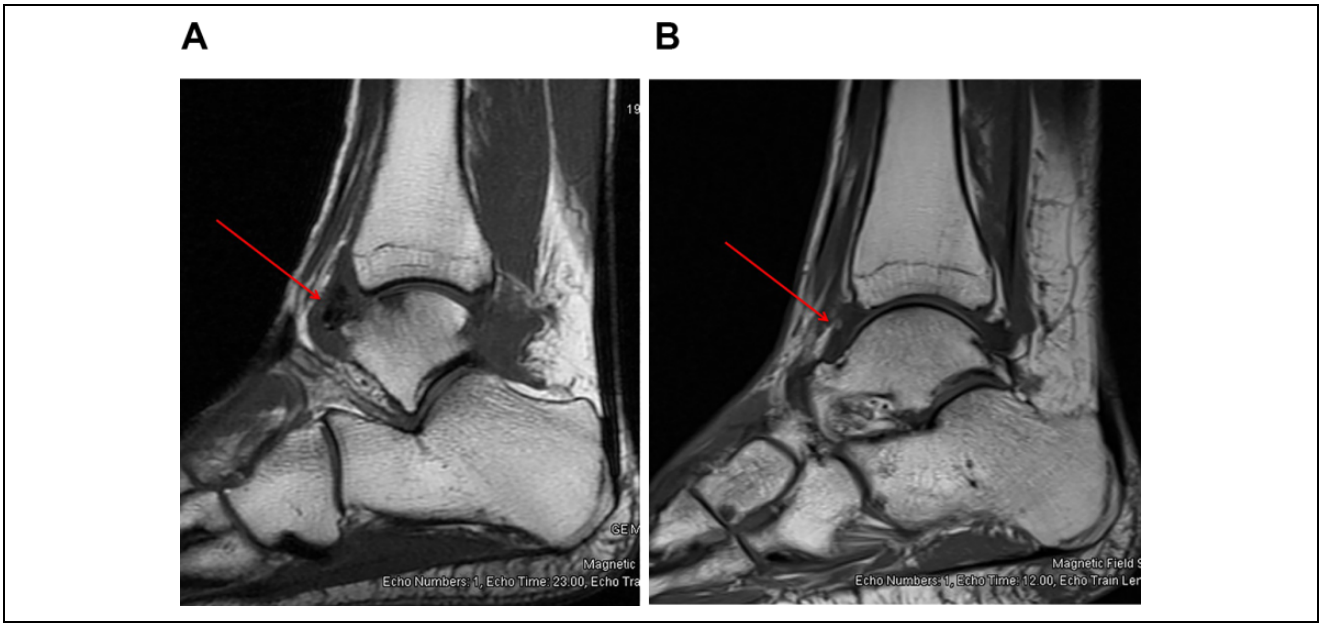

Figure 1. Magnetic resonance images demonstrating (A) fibrotic tissue at the anterior ankle joint line (red arrow) and (B) dense fibrotic tissue extending along the capsule of the joint (red arrow).

As with any patient encounter, a careful history must be obtained. Patient complaints regarding pain and limitations in activities of daily living such as difficulty navigating stairs or sloped surfaces suggest arthrofibrosis. All patients should be asked about prior trauma or surgeries, as intra-articular fibrous tissue formation occurs commonly after an ankle fracture or dislocation. In 2007, one study graded ankle arthrofibrosis according to the extent of intra-articular fibrous tissue detected by arthroscopy. This was present in 73% of patients who had undergone ankle fracture ORIF.[63] Other studies demonstrated that arthrofibrosis occurs in more than 20% of patients who underwent total ankle replacement.[9,25,26] Providers should also elicit a history of coexistent medical diseases including juvenile arthritis, infectious diseases, and particularly hemophilic arthropathy. Hemophilic arthropathy is a condition most associated with arthrofibrosis and loss of motion in the knee, ankle, and elbow joints.[56] Patients commonly develop synovial fibrosis and musculotendinous shortening, resulting in joint contracture and diminished motion.[56] The prevalence of knee, ankle, and elbow joint contractures in patients with severe hemophilia has been reported to be between 50% and 95%, with the most common deformities being knee and elbow flexion contractures as well as ankle equinus.[2,56]

Following the history, a thorough physical examination should be performed. In the absence of bony deformity or severe arthritic changes, a careful inspection of both lower extremities is performed to identify potential extra-articular causes of joint dysfunction such as tendon adhesions and muscle or fascia contractures.[64] After inspection, palpation of the ankle should be done as patients with arthrofibrosis often present with tenderness to palpation of the joint margins. It is important to observe the patient both standing and walking as they will often present with an altered gait. Abnormal gait, as manifest by shortened stride and early heel lift-off, occurs when patients cannot achieve a minimum of 5 to 10 degrees of dorsiflexion.[10] Lastly, intra-articular injection of a local anesthetic may assist in diagnosis. There is a higher likelihood of extensive ankle arthrofibrosis and structural pathology if only a few milliliters can be injected or if there is dense fibrous tissue in the anterior ankle, which may be felt on needle insertion.[36,57]

Imaging studies may be used to diagnose arthrofibrosis and to plan treatment. Plain radiographs and computed tomography (CT) should be obtained to detect other causes of joint motion restriction such as bony incongruity, arthritis, malunion, nonunion, and loose bodies. Dynamic radiographic sequences, or fluoroscopy, can more objectively record the degree of motion loss, particularly in relation to the contralateral side.[42] One of the more common imaging methods used for diagnosing ankle arthrofibrosis is magnetic resonance (MR) imaging.[36] Typical imaging findings consist of capsular and pericapsular thickening (>3 mm) and scarring that is best demonstrated on proton-density MR images (Figure 1).[36] The signal intensity of the capsular thickening on proton-density–weighted MR images correlates with the stage of arthrofibrosis. Less commonly, ultrasonography can also be used to detect arthrofibrosis. Findings will demonstrate hypoechoic capsular thickening and pericapsular scars.[36]

Finally, fluoroscopic-guided arthrography can be used to confirm the diagnosis. Patients with arthrofibrosis typically demonstrate decreases in joint capacity, obliteration of normal joint recesses and high back flow.[21,38]

Treatment Options

Early detection of motion loss as well as the underlying etiology of ankle dysfunction, whether it be intra- or extra-articular in origin, is crucial to the management of ankle stiffness. Once defined, management usually follows a stepwise approach starting from conservative therapies to more aggressive treatments.

Nonoperative Management

Conservative treatment begins with physical therapy. Range of motion exercises have been shown to increase strength and motion as one gradually increases intensity. Care should be taken to discourage overly aggressive therapy, in particular passive range of motion, as this can increase the risk of inflammation and fibrosis.[62]

Another option for the treatment of arthrofibrosis is dynamic splinting with prolonged, passive stretching. The premise of dynamic splinting is to deliver a low load and prolonged duration of passive stretching with measurable dynamic tension to stretch the connective tissue. Furthermore, dynamic splinting involves splint application that allows a patient to achieve 6 to 8 hours of passive stretching each day. When used as home therapy, the combination of dynamic splinting and prolonged passive stretching has demonstrated to be a safe and efficacious treatment for lower extremity joint contractures with minimal risk of adverse events.[18] A systematic review by Furia et al[18] reported that mean ankle range of motion was improved between 9 and 31 degrees with the use of dynamic splints. They also found that the degree of improvement was directly and linearly related to the number of hours that stretching was performed. Although the conclusion that dynamic splinting serves as an effective treatment for ankle arthrofibrosis is only based off of one study, the authors believe that these devices can be particularly useful because the effort required to comply with the protocol is relatively low and can be performed without direct supervision.

Adjunctive intra-articular corticosteroid injections may also be used to help alleviate arthrofibrosis, although at a low success rate. One study reported only a 20% long-term response rate.[11] Joint manipulation under anesthesia can be a useful modality but supportive data in the foot and ankle is sparse.[7,16] Lastly, other adjunctive modalities such as continuous passive motion, whirlpool therapy, and ultrasound stimulation have not been reported in the literature.

Operative Management

If conservative measures fail to improve patient symptoms, surgical treatment is sometimes considered. The procedure depends on the cause of decreased joint motion. Extra-articular issues such as muscle, tendon, or fascial contractures or adhesions may require open or percutaneous release or lengthening procedures. Large osteophytes causing mechanical impingement should be removed as well. The literature is scant with regard to evaluating surgical management of ankle arthrofibrosis and is limited to reports, discussed below, which have evaluated various open and arthroscopic techniques.

Arthroscopy has been advocated as a minimally invasive strategy. The current literature, however, does not robustly support arthroscopic release. The most compelling compilation of objective outcome measurements was by Glazebrook et al[20] in their 2009 systematic review. They cautiously recommended arthroscopic treatment of arthrofibrosis as they found only Level IV studies supporting its use. Still, 5 of the 6 studies reviewed demonstrated positive outcomes for majority of patients.[1,6,11,38,50,63] Lui et al[38] found that the mean dorsiflexion increased from 1 to 19 degrees and plantarflexion increased from 16 to 39 degrees following arthroscopic debridement and release, whereas Cui et al[11] found that range of motion increased by 6.7 degrees. Both studies demonstrated an improvement in patient outcome scores including American Orthopaedic Foot & Ankle Society (AOFAS) scores (63.8 to 88.6) and Foot Function Index scores. Utsugi et al[63] showed no benefit in measured range of motion but did note an increase in AOFAS scores from 90.3 to 97 in patients following ankle arthroscopy. Amendola et al[1] reported that 9 of 14 patients benefited from arthroscopic debridement, and the mean score on an unvalidated visual analog scale for function (0 = worst, 10 = no pain) improved from 3.1 to 5.3. Similarly, Parisien and Vangsness found clinical improvement in 2 of 3 patients following arthroscopy.[50] Bonnin and Bouysset, however, did not show improvement in 6 patients following arthroscopic debridement for post-traumatic ankle stiffness.[6]

Ankle arthroscopy can be performed both anteriorly and posteriorly depending on the location of scarring and deficit in motion. Anterior arthroscopy allows easy access to the anterior plafond and both the medial and lateral gutters, although access of the posterior ankle can be limited by joint distraction and portal placement. The posterior approach allows easier access to the posterior capsule and tendons.[37] Postoperatively, active and passive range-of-motion exercises should be initiated as soon as possible in order to achieve the best outcomes.[38,64]

Open debridement is another option. Postoperative arthrofibrosis can be treated with open arthrolysis, Achilles tendon lengthening, and/or gastrocnemius recession with good pain relief and increased range of motion reported.[28] Similar to arthroscopic treatments, there are few reports on outcomes following open procedures. There is some encouraging literature in the total ankle arthroplasty for open debridement. In Gross and colleagues' retrospective study of surgical treatment of bony and soft-tissue impingement in total ankle replacements, they demonstrated improvement in all pre- to postoperative assessments.[23] Of note, there were no significant differences in pain relief, rates of repeat debridements, and functional improvement between the arthroscopic and open debridement groups. AOFAS hindfoot

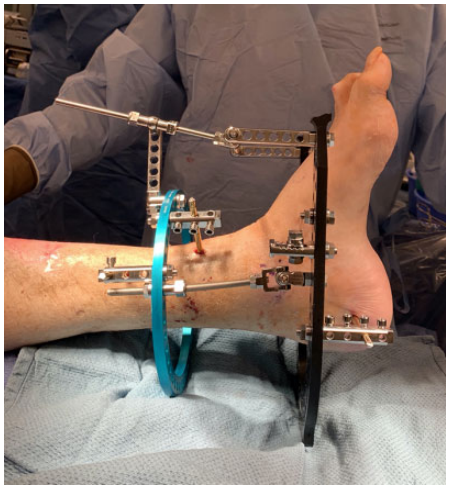

Figure 2. Hinged external fixator allowing for gradual stretching and correction of equinus.

scores improved from 42.3 to 66.1, visual analog scale pain score declined from 7.3 to 3.1, SF-36 increased from 41.4 to 58.2, and SMFA scores decreased from 49.7-30.9. Among the patients who were followed over 1 year postoperatively, 84% remained pain-free at 26.6 months.

Finally, in the foot and ankle, gradual correction with external fixation is often considered for correction of soft tissue contractures and arthrofibrosis. Circular external fixation has been used as a treatment method for many secondary ankle and foot pathologies that result in rigidity. This technique provides for gradual correction of deformity or maintenance of a static position during treatment, often while enabling functional use of the limb. Although external fixation is not recognized as a primary treatment of arthrofibrosis, it has been employed to treat contracture as well as arthrosis that may be present concomitantly. Gradual correction by this method can allow joint realignment and soft tissue lengthening without traditional releases or extensive incisions (Figure 2).[12,27,32,46] Complications commonly include pin tract infection, but this is often preferable to the morbidity of larger, open procedures.[27,32]

Ankle joint distraction arthroplasty was introduced in 1978 as an alternative to arthrodesis and arthroplasty.[31] This technique involves temporarily unloading the joint with an external fixator with the goal of improving joint diastasis and range of motion.[30,41,43,48,52,58] Adjunctive procedures to address soft tissue contracture about the ankle or hindfoot, bony limb malalignment, osteophytosis, nerve compression, and intra-articular pathology can be performed concurrently.[48,52,58] There is an improved arc of motion after treatment that is more functional, even though the overall range of motion may not change.[48,52,58] Short- and midterm results have been good in patients with severe arthritis, with reduced ankle satisfaction by 8-10 years.[40,43,48]

Arthrofibrosis of the ankle and subtalar joints frequently results in asymmetric contracture, resulting in joint incongruity.[11,36,63] Contractures (eg, ankle equinus) can be safely managed with hinged or multiplanar external fixation and gradual correction.[27,29,32,46] This method uses the concept of distraction histogenesis, whereby soft tissue lengthening occurs in response to gradual stretching.[27,59] It is a less invasive alternative to traditional methods, and neurovascular (eg, tarsal tunnel decompression) and soft tissue releases may be performed concomitantly.[32,46] Distraction histogenesis is frequently sufficient to treat diagnoses such as equinus contracture, but the addition of osteotomies can allow reorientation of the foot to a more plantigrade position if arthrofibrosis is too severe.[27,32]

Prevention

Because arthrofibrosis most commonly occurs following trauma or surgery, preventive strategies begin directly after the provoking incident. These tactics include postoperative pain control, early passive and active range of motion exercises, and ongoing communication between therapists and physicians to ensure appropriate rehabilitation.[8,44,54] The importance of active and passive range-of-motion ankle exercise programs supervised by a physical therapist cannot be overstated. In 2000, Shaffer and colleagues showed that after 8 weeks of cast immobilization after open reduction and internal fixation of ankle fractures, patients experienced significant decreases in muscle performance, functional ability, and fatigue resistance. However, 10 weeks of mobilization with physical therapy can successfully return patients to normal functional performance.[54] This highlights the need for rigid internal fixation of fractures, which can then allow more rapid return to motion activities to potentially decrease the risk of arthrofibrosis. The authors' protocol following ORIF includes splinting for 2 weeks followed by boot for 4 weeks, then nighttime padded ankle foot orthosis postoperatively. Physical therapy at 6 weeks is prescribed if needed for better range of motion, strengthening, etc.

One preventive strategy that can be overlooked is proper casting and splinting technique. As one molds the cast or splint, the ankle must be held in a neutral position until the plaster or fiberglass hardens to minimize the risk of developing contractures.[24] Maintaining optimal foot position is also paramount during treatment of wounds and for soft tissue coverage procedures. If the splinted ankle is positioned in plantarflexion and immobilized for prolonged periods of time, patients are at increased risk for muscle and joint stiffness. Splint in equinus for short term may be tolerated and resolved with stretching. However, if prolonged immobilization occurs, contractures may become chronic. It is therefore important to limit the duration of immobilization and initiate range of motion exercises early after discontinuation. In more serious cases of contractures, the patient may benefit from physical therapy after the removal of the immobilizing device. Lastly, it is best practice to keep the ankle neutral until the splint/cast hardens

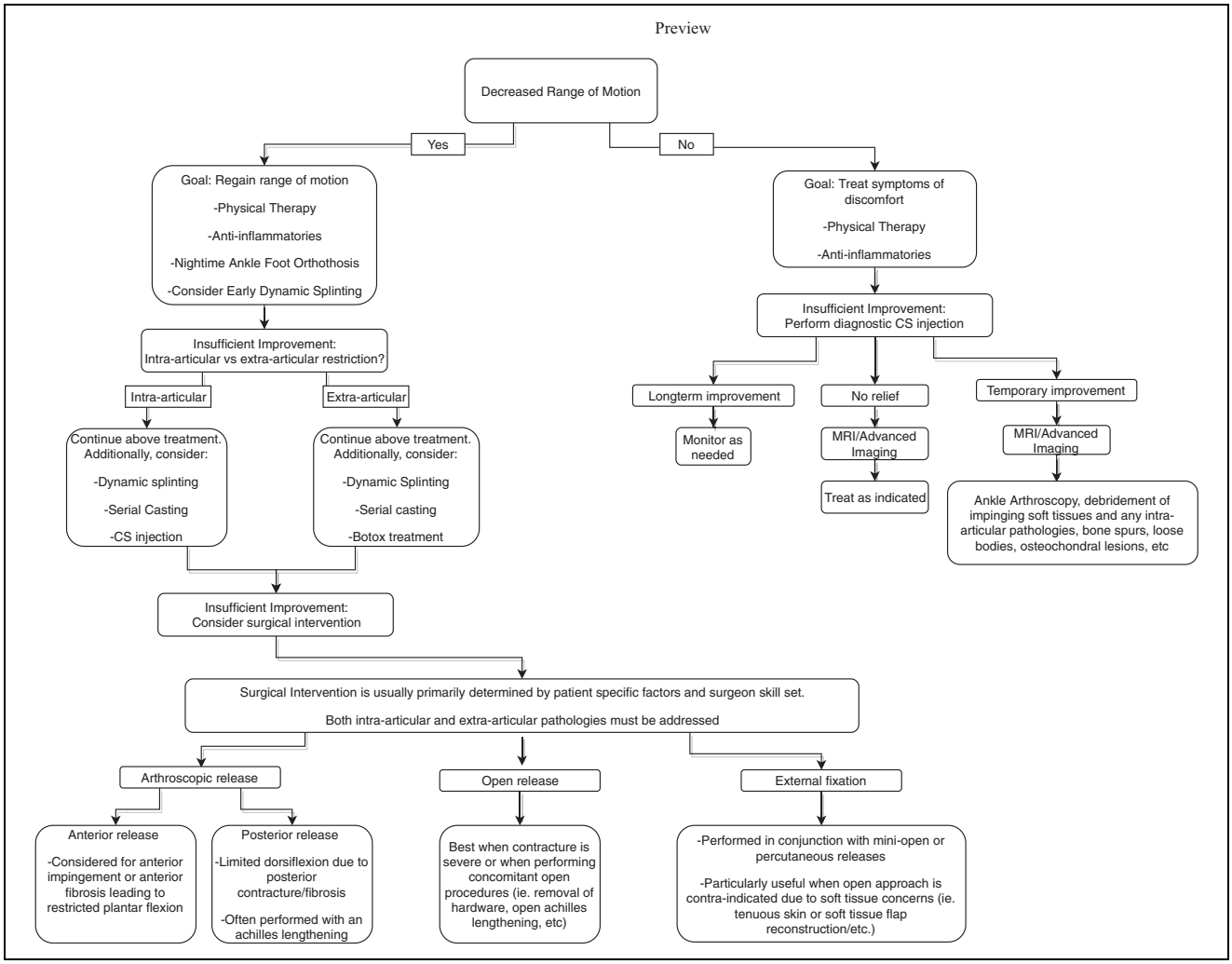

Figure 3. Treatment algorithm for ankle arthrofibrosis.

and to place the entire foot on a relatively flat surface to ensure the ankle is not immobilized in equinus. The exception is if equinus is desired (ie, after Achilles repair) in which case it should be maintained for as short a period of time as possible. Nevertheless, more studies are needed to develop a better understanding of the prevention of ankle arthrofibrosis.

Future Treatments

Current treatments as described above have limitations. Therefore, the advent of pharmacologic agents that can successfully address excess fibrous tissue from the ankle joint are promising. Two agents with antifibrotic effects have recently emerged and have the potential to effectively treat arthrofibrosis: anakinra and relaxin.

Anakinra is an interleukin-1 antagonist. Interleukin-1 plays an integral role in the inflammatory cascade, promotes pro-fibrotic mediators, and stimulates fibroblast proliferation and chemotaxis.[5,8,19] In a pilot study, intra-articular injection of anakinra was given to 8 patients with knee arthrofibrosis. A majority of patients (75%) reported improvement in range of motion and pain.[8] Although the cohort of patients was small, anakinra may be a promising agent for ankle or other joint arthrofibrosis.

Relaxin is a versatile endogenous neurohormone. Though traditionally viewed as a pregnancy hormone only secreted by the corpus luteum, it has been subsequently established that relaxin is also produced in the heart, endometrium, mammary gland, placenta, and prostate.[15,66] Although much of the recent literature has investigated the cardiovascular effects of relaxin in the setting of heart failure,[66] relaxin possesses multiple other properties, including antifibrotic effects.[3,53] Its antifibrotic effect profile may offer a pharmacologic intervention to target arthrofibrosis.

Recently, a rat model of shoulder arthrofibrosis has been produced via prolonged immobilization, and this has been shown to render lasting effects on in vivo kinematics.[47,65] This novel animal model provides a basis on which researchers can begin testing new pharmacologic therapies.

Conclusion

Arthrofibrosis is a common, but overlooked, condition that imparts significant morbidity following injuries and surgery to the foot and ankle. The most common etiologies are related to soft tissue trauma with subsequent fibrotic and contractile scar tissue formation within the ligaments and capsule of the ankle. This leads to pain, alterations in gait, and ankle dysfunction. The most critical component of treatment is most likely attempting prevention by providing appropriate splinting and physical therapy. However, when arthrofibrosis occurs, there are effective treatments including physical therapy and dynamic splinting. When conservative treatment fails, open or arthroscopic procedures as well as management with external fixation may be effective (Figure 3). Although surgery may be beneficial, there are currently few studies on which to guide expectations. The future, however, is hopeful and there may be new treatment options that can be used to treat fibrotic joints without the need for surgical intervention.

Ethics Approval

Ethical approval was not sought for the present study because it was a topical review.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. ICMJE forms for all authors are available online.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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