JOINTS 2024; 2: e1197

Category: Narrative Review

MANAGEMENT STRATEGIES FOR ANKLE SPRAINS: A NARRATIVE REVIEW

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ABSTRACT – Ankle sprains are among the most common musculoskeletal injuries encountered in both athletic and general populations, presenting a significant challenge in orthopedic and sports medicine. This review explores the complexities of managing ankle sprains, emphasizing the critical need for a personalized approach that considers the injury's severity, the patient's unique factors, and anticipated long-term outcomes. While conservative management, epitomized by the Rest, Ice, Compression, and Elevation (RICE) protocol, bracing, and physiotherapy, serves as the cornerstone for treating most sprains, this review underscores instances where surgical intervention may be warranted. Particularly, grade III sprains and cases exhibiting persistent instability or functional impairment despite conservative measures are highlighted as potential candidates for surgery. Advances in surgical techniques and rehabilitation protocols offer promise for enhancing treatment efficacy, with a focus on minimizing complications and expediting return to activity. This review advocates for ongoing research to further refine management strategies, aiming to optimize outcomes for patients with ankle sprains. Through a nuanced understanding of treatment modalities and patient-specific considerations, healthcare professionals can tailor interventions to best support recovery and prevent recurrent injury, aligning treatment objectives with patients' lifestyles and activity levels.

KEYWORDS: Ankle sprain, Sports injury, Rehabilitation, Ankle surgery.

INTRODUCTION

Ankle sprains rank among the most common musculoskeletal injuries, impacting individuals across various demographics and physical activity levels. They present an estimated incidence rate of 11.6 per 1,000 people and a prevalence of 11.9%[1], positioning them as the predominant trauma in athletes, accounting for 10-30% of all sports-related injuries[2,3]. Typically, the highest incidence of ankle sprains occurs from the second to the third decade of life, with it being particularly prevalent among individuals aged 18 to

34 years[2]. The significant incidence of ankle sprains in both athletes and the general population highlights a major public health issue, given their potential to cause chronic pain, instability, and reduced quality of life if not appropriately managed[3]. Despite their frequency, finding the optimal management strategy for ankle sprains, which includes immediate care, rehabilitation protocols, and preventive measures, remains a significant area of ongoing research and debate within the medical community.

This narrative review seeks to consolidate current evidence regarding the diagnosis, classification, and treatment of ankle sprains to offer a comprehensive guide for their effective management. Through the examination of the most recent research findings and consensus guidelines, we aim to introduce evidence-based practices that can inform clinical decision-making and enhance patient outcomes. Ultimately, we strive to highlight the pathway to improved recovery for those affected by ankle sprains, thereby reducing the likelihood of chronic issues and elevating the standard of care provided.

ANATOMY AND MECHANISM OF INJURY

The talocrural joint, or ankle joint, is a complex hinged synovial joint formed by the articulation of three bones: the tibia and fibula (of the lower leg) and the talus (of the foot). The stability of this joint is fortified by various ligaments, categorized into lateral, medial, and syndesmotic ligaments:

Lateral ligaments: these include the anterior talofibular ligament (ATFL), the calcaneofibular ligament (CFL), and the posterior talofibular ligament (PTFL). The ATFL, the most frequently injured ankle ligament, connects the fibula to the talus at the front of the joint and is particularly vulnerable to sprains when the foot is inverted and plantarflexed[1]. Being the weakest, this ligament is typically the first to be affected in a sprain, with subsequent injuries to the CFL and PTFL[4]. The CFL, attaching the fibula to the calcaneus, provides lateral stability, particularly when the ankle is dorsiflexed. The PTFL, the strongest of the three, connects the fibula to the talus at the back of the joint and prevents excessive rotation. Injuries can extend beyond the lateral complex to involve the subtalar, syndesmotic, or medial areas[2], often implicating the interosseous, syndesmotic, or deltoid ligaments. Such sprains might also accompany injuries to adjacent tendons, cartilage damage, and bone bruises[2].

Medial ligament: often referred to as the deltoid ligament, this is a multifaceted ligamentous structure providing medial stability. It connects the medial malleolus to multiple tarsal bones and resists excessive eversion of the foot. This ligament is composed of deep and superficial layers, which include the tibionavicular, tibiocalcaneal, and posterior tibiotalar ligaments. The deltoid ligament is less frequently injured due to its strength and the less common mechanism of injury.

Syndesmotic ligaments: these include the interosseous tibiofibular ligament, which lies between the tibia and fibula, and the anterior and posterior tibiofibular ligaments that stabilize the distal tibiofibular syndesmosis. This complex also mitigates force transmission from the ankle to the knee.

Ankle sprains are caused by excessive force applied to the ligaments, resulting in their stretching, partial tears, or complete ruptures. It is essential to understand that the term ‘sprained ankles’ does not refer to a specific diagnosis but to the mechanism of injury, which typically involves:

- Inversion sprains: the most common type, where the foot rolls inward, exerting undue stress on the lateral ligaments. The ATFL is especially vulnerable in this context[2].
- Eversion sprains: less common; these sprains occur when the foot rolls outward, affecting the medial or deltoid ligament.
- High ankle sprains (syndesmotic sprains): resulting from a forceful outward twisting of the foot, these injuries impact the syndesmotic ligaments and generally require a longer recovery period due to the complexity of the structures involved[5]. Syndesmotic injuries account for 20% to 25% of all ankle injuries[6] and are associated with prolonged disability and an increased risk of chronic pain and instability.

Classification

Ankle sprains manifest in a spectrum of ligamentous injuries, ranging from mild stretching to complete tears. These injuries are typically categorized into three grades, reflecting the extent of ligament damage. This grading system is pivotal for devising appropriate management strategies and forecasting recovery outcomes. Variability in ankle sprains arises from the injury mechanism (high- *vs.* low-energy impacts), foot positioning, and the rotational force exerted on the joint and its stabilizing ligamentous structure[7]. Minor injuries (grades I and II) involve stretching or microscopic tearing of the stabilizing ligaments, whereas a severe injury (grade III) impacts the syndesmotic structures. However, none of these classification systems has been validated for their prognostic utility, nor are they widely used as a reference in treatment decisions or comparative clinical trials.

- Grade I (mild): characterized by ligament stretching without evident macroscopic tearing, manifesting as mild swelling or tenderness without mechanical instability or functional loss. Typically, only the ATFL is implicated. Grade I sprains involve minor stretching and microscopic tears of ligament fibers, presenting with minimal tenderness and swelling and no significant functional impairment or mechanical instability. Patients may report minor pain at the injury's onset, with negligible impact on function. A physical examination might reveal mild tenderness at the affected ligament site, generally without significant swelling or bruising.
- Grade II (moderate): caused by partial macroscopic tearing of the ligaments, resulting in moderate swelling, ecchymosis, and tenderness, alongside mild to moderate instability and a slight restriction in movement. Patients typically experience moderate pain during weight-bearing activities and ambulation. The ATFL, possibly along with the CFL, is affected. This classification pertains to a partial ligament tear, inducing abnormal joint laxity. Affected individuals experience moderate discomfort, swelling, and bruising, coupled with functional limitations and mild to moderate instability. Physical examinations are likely to reveal heightened tenderness, ecchymosis, and positive outcomes in stability assessments like the anterior drawer test.
- Grade III (severe): resulting from a complete rupture of the ligaments, characterized by intense swelling, ecchymosis, tenderness, and pain.

In standard classification, each ligament's injury severity is assessed individually[5,8]. Based on the anterior drawer (AD) and talar tilt (TT) tests, grade I injuries present negative clinical results (AD and TT); grade II injuries exhibit a positive AD test, and grade III injuries show positive results in both AD and TT tests[7,8].

Lacerda et al[9] conducted an exhaustive review to catalog and evaluate the existing formal classification systems for lateral ankle sprains and to assess the reliability and validity of each. They observed that accurately determining a sprain's severity and classification from an initial assessment is challenging, especially given the existence of 26 different classification systems. These systems generally employ a three-grade scale to denote increasing severity from 1 to 3, with the distinction between stretching, partial tearing, or complete ligament rupture being a common parameter[9].

CLINICAL ASSESSMENT

Upon arrival at the emergency room (E.R.) with an ankle injury, a thorough clinical assessment is essential. This begins with obtaining the patient's history and conducting a physical examination, focusing on the injury mechanism, localized pain, swelling, and the patient's ability to bear weight. Clinical tests, such as the AD test and TT test, are employed to assess ligament integrity. However, their utility may be limited in the acute phase due to pain and swelling, making repeat evaluations crucial for more accurate information[10].

Van Dijk et al[10] highlighted the significance of anatomical surface palpation, hematomas, and a positive AD test within the first 48 hours, showing a 71% sensitivity and a 33% specificity. A clinical evaluation five days post-trauma indicated increased sensitivity (96%) and specificity (84%), emphasizing the necessity of a short-term secondary outpatient evaluation. Ferreira et al[11] recommend a delayed evaluation between the 4th and 14th-day post-injury to gain a comprehensive understanding of the injury type, ligament laxity, and any associated injuries, with MRI recommended for severe cases or when an additional injury is suspected.

Delahunt et al[12] suggest that clinical stability tests to assess AFL should be conducted between the 4th and 6th-day post-injury for improved specificity and sensitivity. They note that post-injury pain on palpation or stress is indicative of an ATFL injury, employing a similar method for assessing PC ligament injuries.

Van den Bekerom et al[13] and Vuurberg et al[5] advocate for a delayed clinical examination to achieve a more precise diagnosis, noting that effective management of initial swelling can enhance the sensitivity and specificity of clinical tests upon reevaluation. They also mention that while ultrasound is a sensitive method for detecting injuries, it lacks specificity and highly depends on the technician's skill and the equipment's quality. MRI is strongly recommended due to its superior sensitivity and specificity in detecting such injuries. According to Van den Bekerom et al[13], the lack of pain over the ATFL often suggests the absence of an acute rupture, while localized pain, particularly when accompanied by a resolving hematoma, strongly indicates an acute rupture[14]. The anterior drawer test's sensitivity is recorded at 73%, with a specificity of 97%, figures that markedly increase to 98% sensitivity and 84% specificity when combined with palpation pain at the ATFL and the presence of a hematoma. Chen et al[15] stress that an increase in laxity, as observed by the examiner compared to the uninjured ankle, indicates a positive result for the AD test. Validation studies[15,16] for this test show a sensitivity range of 80% to 95% and a specificity range of 74% to 84% for detecting ligament ruptures.

For syndesmosis injuries, Tourné et al[16] noted that up to 20% of these injuries were initially undiagnosed, highlighting the necessity for early and precise reassessment. Various diagnostic tests, such as the stress test, cotton test, and peroneal translation, are crucial in identifying these injuries, as suggested by Alonso et al[17].

Within the medial compartment, Alshalawi et al[18] identify tenderness upon deltoid ligament palpation as a primary sign of injury, with additional pain on the medial side suggesting rotational instability.

Imaging

- X-rays are fundamental in the diagnosis and management of ankle and foot injuries, serving as the primary tool for ruling out fractures. The Ottawa Ankle Rules (OAR), established in 1992, guide the use of radiographs for ankle and midfoot injuries to reduce unnecessary radiation exposure and healthcare costs[18,19]. Although only about 13% of such examinations reveal clinically relevant fractures, the decision to employ X-rays often results from factors such as long wait times in emergency departments, patient requests, or adherence to routine practices[19]. The OAR effectively minimizes the need for unnecessary radiographs, thereby reducing patient exposure to ionizing radiation and conserving medical resources. The criteria recommend X-rays for patients experiencing pain at the posterior edge or tip of the malleolus or who cannot bear weight immediately post-injury or walk a few steps in the ER. Additionally, foot X-rays are advised for bone pain at the base of the fifth metatarsal or the navicular bone. Exclusion criteria for the OAR include children under the age of 5, patients with neurological disorders affecting the legs, those with an altered sensorium or communication inability, pregnant patients, or cases of penetrating trauma (Figure 1)[20-22].

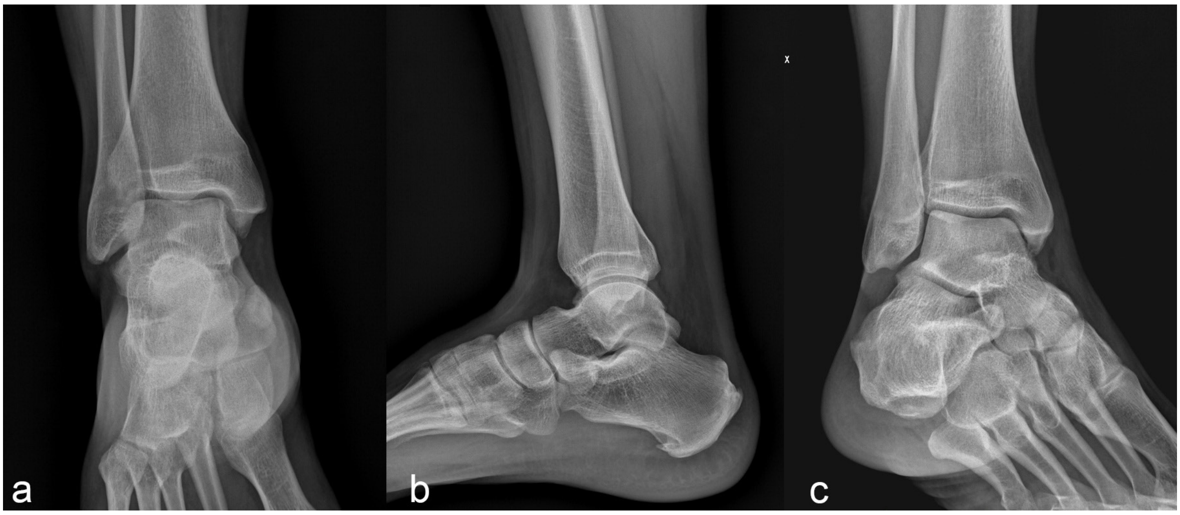

Figure 1. Basic exam to take in ER in case of Ottawa Ankle Rules positive and negative exclusion criteria. Three standard ankle views: anteroposterior (**a**), latero-lateral (**b**) and the Mortise view (**c**).

- Computed Tomography (CT) scans are recommended for persistent pain despite negative initial X-ray results, particularly when occult fractures are suspected or when malalignment is observed, which may indicate syndesmotic or ligamentous injuries. CT scans provide a detailed view of bone structures, which is invaluable for identifying complex fractures and evaluating alignment issues not visible on standard X-rays[23].
- Magnetic Resonance Imaging (MRI) is the most sensitive imaging modality for detecting occult fractures and injuries to ligamentous structures, including the anterior tibiofibular and deltoid ligaments, syndesmosis lesions, and cartilage damage. Its ability to offer detailed images of both bone and soft tissue is essential for accurately diagnosing the full extent of ankle sprains and ensuring proper management (Figure 2)[24].

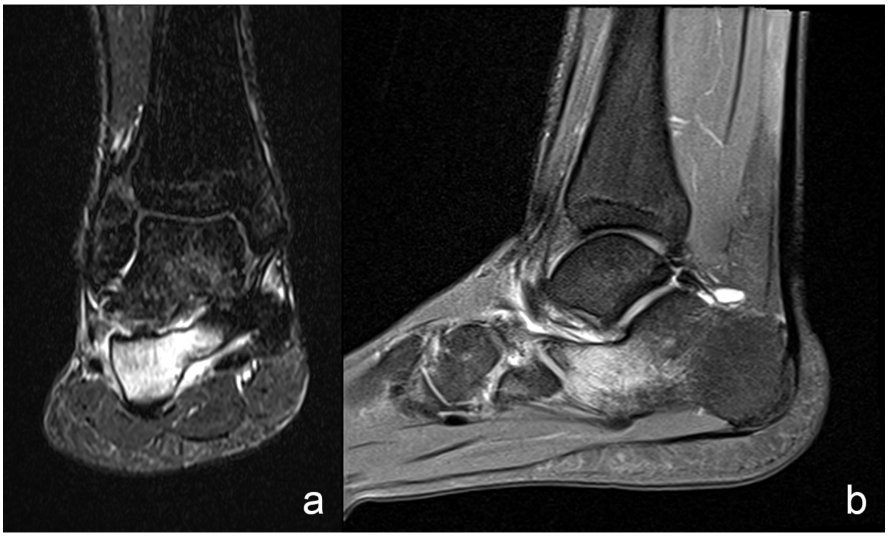

Figure 2. Ankle MRI showing calcaneus edema in a spongy bone fracture, in coronal (**a**) and sagittal (**b**) views.

- Ultrasound imaging is particularly effective for assessing soft tissue structures, such as the peroneal tendons and their retinaculum. As a non-invasive technique providing dynamic assessment and real-time images of the affected area, ultrasound is invaluable for diagnosing tendon injuries and other soft tissue abnormalities in the ankle region[25].
- Stress radiographs are employed to diagnose syndesmotic instability, and they offer crucial insights into the injury's functional impact on ankle stability. By applying stress in specific ways and capturing radiographic images, healthcare providers can assess the degree of separation and instability in the syndesmosis, aiding in treatment decision-making. These imaging techniques collectively provide a comprehensive approach to diagnosing ankle injuries and formulating an effective treatment[26].

Therefore, in scenarios encountered in the E.R. (Figure 3):

1. Patients meeting OAR criteria without exclusions should receive an X-ray in three standard views. Additional specific views may be required depending on the suspected injury.
2. Patients not meeting OAR criteria without exclusions do not require further assessment.
3. Patients not meeting OAR criteria but with exclusions should undergo standard radiographs as the chosen examination.

For persistent pain within the first three weeks post-trauma despite negative initial X-rays, further examinations, such as CT scans, are advisable, particularly if bone injury is suspected. MRI is recommended for detecting occult fractures, bone marrow edema, cartilage lesions, and evaluating ligament or syndesmosis lesions, while ultrasound can assess soft tissue injuries. Stress radiographs may help diagnose syndesmotic instability, providing valuable management information[27].

MANAGEMENT STRATEGIES

Management strategies for ankle sprains, especially inversion sprains, which are among the most prevalent ankle injuries, require a detailed approach that considers the injury's severity and individual patient factors. Differentiating between stable injuries (grade I) and more severe injuries, such as partial or complete ligament ruptures (grades II and III), is critical in selecting the most appropriate treatment method.

A functional conservative treatment regimen is typically advised, corresponding with the biological tissue healing phases:

1. The inflammatory phase (first two weeks): the primary goals are to reduce inflammation and alleviate pain. The Rest, Ice, Compression, and Elevation protocol (RICE) is recommended to minimize swelling and discomfort. Nonsteroidal anti-inflammatory drugs (NSAIDs) are also beneficial for pain management during this phase.
2. The proliferative phase (from the third week after injury to up to three months): attention shifts to promoting healing and preventing further injury. This phase involves gradually reintroducing weight-bearing activities, supplemented by protective bracing or taping to aid recovery. Physiotherapy exercises designed to improve range of motion, strength, and proprioception are critical for restoring functional stability.

Type of lesion – adults or children above 5 years of age	X-ray	CT scan	MRI	US
OAR +, exclusionary criteria -	YES	NO	NO	NO
OAR -, exclusionary criteria -	NO	NO	NO	NO
OAR -, exclusionary criteria +	YES	YES	NO	NO

Type of lesion – adults or children above 5 years of age	CT scan	MRI	US	X-ray	Stress X-ray
Persistent pain for 1 to 3 weeks after trauma, exclusionary criteria -, first X-ray -	YES	YES	OCCASIONALLY REQUIRED IN CHILDREN	OCCASIONALLY REPEATED	OCCASIONALLY REQUIRED
Exclusionary criteria -, X-ray showing fracture or osteochondral lesion	YES	YES	NO	BRODEN VIEW	NO
X-ray -, signs of dislocation, syndesmotic or ligaments injury	YES	YES	NO	LEG X-RAY (MAISONNEUVE'S FRACTURE)	YES

Figure 3. Algorithm to adopt to avoid unnecessary diagnostic exams and to prevent neglecting occult fractures after an ankle sprain.

3. The remodeling phase (up to one year): this final phase focuses on strengthening the ankle and enhancing its functional capabilities. Advanced balance and proprioception exercises are vital for returning the ankle to its pre-injury state or better. This phase also includes sport-specific training and activities tailored to the individual's lifestyle, ensuring a complete return to activity.

Conservative management is the foremost approach for the majority of ankle sprains, given its efficacy across various injury scenarios. Surgical intervention is typically reserved for instances where conservative treatment is unsuccessful or in cases of chronic instability, aiming for a definitive resolution to the instability and potentially averting long-term issues such as osteoarthritis. The choice between a conservative management strategy and surgical intervention depends on several factors, including:

- Patient's age: the recovery process may differ between younger, more active individuals and older patients, influencing the treatment approach.
- Activity level before injury: individuals with a high activity level or athletes might need a more robust rehabilitation plan to regain their former activity levels.
- Previous treatment outcomes: the effectiveness or failure of previous treatments for ankle injuries can inform future management plans.
- Degree of ankle instability and severity of the injury: significant instability and severe injuries might necessitate considering surgical options earlier.
- Patient preference: the treatment choice can significantly be influenced by the individual's preferences, expectations, and lifestyle.
- Unsuccessful conservative management or presence of chronic instability: should conservative treatments fail to improve the condition or if chronic instability persists, surgical intervention may be required to address the root causes and reestablish stability.

Conservative Treatment

Conservative management forms the basis for treating most ankle sprains, particularly for grade I and II injuries. The main objectives are to alleviate pain, diminish inflammation, and support healing while preserving the ankle's functional integrity.

Functional Treatment Guidelines[28] highlight the importance of nurturing the natural healing process. Prompt care is crucial in the initial stages to reduce inflammation and swelling, which sets the stage for effective tissue healing and rehabilitation[28,29].

RICE Model: Combines Rest, Ice (cold application), Compression (using devices like tubigrip or manually applied pressure), and Elevation to decrease inflammation, swelling, and pain. This creates an ideal healing environment by minimizing inflammation, swelling, hemorrhage, pain, and cellular metabolism[30,31]. Moreover, it is vital to prevent further damage in the initial weeks (1-3 weeks) after a ligament injury to protect the affected ligament and support conservative management. The reduction of pain and inflammation around 10 to 21 days post-injury indicates the start of the maturation phase, where collagen forms and envelops the wound in scar tissue[32]. During this phase, introducing controlled mobilization exercises is key for the healing of ligaments. Ideally, immobilization should end before this phase to avoid adverse effects on the tendons, muscles, bones, joints, and neighboring healthy ligaments[33]. Progressive controlled muscle exercises and joint movement therapy align collagen fibers along stress lines, improving the ligaments' structural and mechanical performance[34].

Besides exercise-based therapy, other treatments like short waves, temperature-contrast baths, ultrasound, cryotherapy, NSAIDs, and advanced methods such as interference or diadynamic current therapy may speed up healing and recovery[35]. Electrical muscle stimulation (EMS) or electro-galvanic stimulation might help prevent calf muscle atrophy, enhancing muscle coordination and joint range of motion. Yet, the effectiveness of these methods requires more research.

Other components include:

- Bracing and immobilization: for acute sprains, especially grades I and II, bracing supports and prevents further injury. Early mobilization is shown[36] to enhance recovery compared to prolonged immobilization. The use of non-weight-bearing techniques or crutches varies with the injury's severity and patient symptoms. Grade II and III sprains often benefit from 48 to 72 hours of unloading[11]. Immobilization can reduce pain and swelling more quickly; however, early mobilization and proprioception exercises generally improve functional outcomes more rapidly. It is therefore necessary to remove the immobilization after 5-7 days, the time expected for the clinical re-evaluation of the patient[11]. Regarding the type of immobilization to be used, no significant difference has been found in the literature[37] between treatment with taping and other external supports, such as soft braces, semi-rigid braces, and braces with laces, with regards to pain, swelling, functionality, mobility, patient satisfaction and return to sport. No significant differences were found[38], even between adhesive taping and cast knee socks in terms of swelling and functionality. Considering the absence of significant differences in the result, the application of temporary braces or taping is certainly more practical and immediate. Plaster immobilization for two weeks, which is often still offered in some emergency rooms, is undoubtedly obsolete.
- Drugs: while NSAIDs' effectiveness is established, opioids administered in the emergency department have shown[39] lower pain levels at 4 hours and 5-day follow-ups. However, concerns about opioid abuse and misuse persist[40], especially among teenagers and young adults, who are at risk of future abuse[41,42]. It is crucial to use NSAIDs judiciously, as some inflammation is beneficial for the healing process[43].

Surgical Treatment

Surgical intervention for ankle sprains is generally reserved for grade III injuries or cases where conservative management fails to resolve persistent instability or functional impairments. The goal of surgery is to repair or reconstruct the injured ligaments to restore ankle stability and function. The decision to opt for surgery considers various factors, including the patient's activity level, professional demands, and the degree of ankle instability[44].

Although conservative management is recommended for most ankle sprains, including grades I and II, the approach to managing grade III sprains is more controversial[45]. Studies[43,45], including a Cochrane meta-analysis, indicate no definitive superiority of surgical over conservative treatment for grade III injuries, with a consensus against routine surgical intervention.

However, evidence[44] suggests that surgical treatment of acute injuries may offer greater objective stability and a lower recurrence rate than conservative treatment, albeit with an increased risk of complications. Surgical intervention is typically suggested for professional athletes to reduce the risk of chronic ankle instability[45].

Research by Pihlajamäki et al[46] indicates that surgery can lower the recurrence rate, though it is associated with a higher incidence of grade II osteoarthritis among athletes who undergo surgical treatment. Similarly, Takao et al[47] found that isolated functional treatment had a 10% failure rate and a slower return to full sports activity compared to combined functional and surgical treatment. The need for surgery should be evaluated on a case-by-case basis, considering factors like the type of sport, the athlete's expectations, and the timing of the injury relative to the season and the athlete's career.

Several stabilizing techniques have been described for the treatment of lateral ankle ligament injuries and ankle instability. Among these, anatomical repairs provide a reattachment of the native remnant, restoring ankle stability and preserving physiological function[48,49]. For this reason, the open anatomic ligament repair, also known as the Broström procedure, has been preferred over reconstruction procedures, and it is widely considered the gold standard treatment[48,49].

In recent years, arthroscopic treatment of ankle instability has evolved and gained widespread popularity. The potential for addressing both the instability and any intra-articular associated pathology arthroscopically has deemed ankle arthroscopy as the emerging gold standard and preferred technique for many surgeons[50]. Potential advantages of the arthroscopic technique are less invasiveness, minimized postoperative pain, a faster recovery, and the ability to treat concomitant intra-articular pathology during the same procedure[50].

The all-arthroscopic ankle ligament repairs aim to restore ankle stability by reattaching injured ligament remnants through suture anchor/s[51]. Several studies reported[49,50] excellent clinical results, and recently, all-inside ligament repair has been reported to have superior clinical outcomes compared to open repair. Additionally, in the last few years the same arthroscopic technique was developed to repair deltoid ligament injuries in medial or ankle multiligamentous instability with excellent clinical results reported in the literature[52].

Rehabilitation and Return to Activity

Post-treatment rehabilitation, whether following conservative or surgical approaches, is essential. It encompasses phases from initial rest and protection to strength training, proprioception exercises, and sport-specific activities. Successful rehabilitation focuses on achieving pain-free mobility, restoring strength and balance, and ensuring confidence in the ankle's stability – key criteria for a safe return to sport or activity[53]. Before allowing a return to active participation, an assessment ensures readiness for full sporting activities. This includes the ability to run and perform high-speed maneuvers without pain, achieving 90% strength in the affected ankle compared to the unaffected side, and unrestricted and painless ankle motion. A successful rehabilitation program incorporates a clear management plan, routine monitoring, and follow-ups to facilitate patient progress and guide them through suitable exercises for their recovery stage[5].

CONCLUSIONS

This review has elucidated the intricate nature of managing ankle sprains, emphasizing the necessity of a detailed approach that takes into account the severity of the injury, individual patient factors, and the prospects for long-term recovery. Conservative treatment stands as the primary method for the majority of sprains, yet surgical intervention can provide significant advantages in specific instances, particularly for individuals with high athletic requirements or enduring instability. Future research and progress in surgical methodologies and rehabilitation practices promise to enhance the strategies for ankle sprain management and improve patient outcomes across the board.

Acknowledgments:

The authors sincerely acknowledge all the collaborative authors in the Foot and Ankle group of SIAGASCOT:
Bertelli Angelo, Buda Roberto, Cortese Fabrizio, De Angelis Gian Mauro, De Guttry Giacomo, Del Prete Armando, Delmastro Elena, Lijoi Francesco, Lughi Marcello, Martinelli Niccolò, Mercurio Michele, Terzaghi Clara, Zanini Antonio.

Conflict of Interest:

The authors declare that they have no conflict of interest to disclose.

Authors' Contributions:

A.P. and M.G. participated in the drafting and critical revision of the manuscript. A.M. contributed extensively to the study's methodology development and was instrumental in the acquisition of data. Additionally, M.B. played a key role in interpreting the data and provided substantial input in the writing and editing of the manuscript. M.G. was deeply involved in the data analysis and interpretation. D.M. contributed significantly to the drafting of the manuscript, particularly in the discussion and conclusion sections.

Ethics Approval and Informed Consent:

Not applicable.

Availability of Data and Materials:

Data are available on reasonable request to the corresponding author.

Funding:

None.

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