Diagnosis, treatment and prevention of ankle sprains: update of an evidence-based clinical guideline

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ABSTRACT

This guideline aimed to advance current understandings regarding the diagnosis, prevention and therapeutic interventions for ankle sprains by updating the existing guideline and incorporate new research. A secondary objective was to provide an update related to the cost-effectiveness of diagnostic procedures, therapeutic interventions and prevention strategies. It was posited that subsequent interaction of clinicians with this guideline could help reduce health impairments and patient burden associated with this prevalent musculoskeletal injury. The previous guideline provided evidence that the severity of ligament damage can be assessed most reliably by delayed physical examination (4–5 days post trauma). After correct diagnosis, it can be stated that even though a short time of immobilisation may be helpful in relieving pain and swelling, the patient with an acute lateral ankle ligament rupture benefits most from use of tape or a brace in combination with an exercise programme.

New in this update: Participation in certain sports is associated with a heightened risk of sustaining a lateral ankle sprain. Care should be taken with non-steroidal anti-inflammatory drugs (NSAIDs) usage after an ankle sprain. They may be used to reduce pain and swelling, but usage is not without complications and NSAIDs may suppress the natural healing process. Concerning treatment, supervised exercise-based programmes preferred over passive modalities as it stimulates the recovery of functional joint stability. Surgery should be reserved for cases that do not respond to thorough and comprehensive exercise-based treatment. For the prevention of recurrent lateral ankle sprains, ankle braces should be considered as an efficacious option.

INTRODUCTION

A lateral ankle sprain (LAS) is a frequently incurred musculoskeletal injury, with a high prevalence among the general population and individuals who participate in sports.[1 2] About 40% of all traumatic ankle injuries occur during sports. For indoor sports, an incidence of 7 LAS per 1000 exposures has been reported.[3] Despite the high prevalence and incidence of LAS injuries, it has been reported that only approximately 50% of individuals who incur a LAS seek medical attention.[4] A large proportion of individuals who sustain a LAS will develop chronic ankle instability (CAI).[5–7] CAI may be defined as persistent complaints of pain, swelling and/or giving way in combination with recurrent sprains for at least 12 months after the initial ankle sprain,[8–11] which in turn may lead to (long-term) absenteeism from work and sports. Treatment costs in combination with sick leave lead to a high socioeconomic burden.[4 7 12] Additionally, associations with joint degeneration and osteochondral lesions have been reported over time.[13] Adequate diagnosis, treatment and prevention of injury recurrence could forestall the development of long-term injury-associated symptoms and hence substantially reduced the associated socioeconomic burden.

Despite the increasing number of published studies on this topic, heterogeneity in treatment strategies persists worldwide. This necessitated the development of an international evidence-based clinical guideline.[14] Since the publication of this guideline, additional studies have been undertaken and published on this topic.

In order to provide an update of the multidisciplinary clinical guideline, a multidisciplinary guideline committee was formed. The committee included health professionals who were directly involved in the care of patients with LAS in clinical practice or research environments and included general practitioners, emergency physicians, musculoskeletal radiologists, occupational physicians, orthopaedic surgeons, rehabilitation physicians, physical therapists, athletic trainers, sports massage therapists, sports physicians and trauma surgeons. This clinical guideline incorporates the most recently published peer-reviewed literature on the topic of LAS injury. The aim of this updated evidence-based clinical guideline is to facilitate uniformity of diagnosis and treatment of acute LAS injury, with the primary purpose of reducing the long-term injury-associated symptoms resulting from this prevalent injury.

The multidisciplinary guideline committee developed this update in order to assist all healthcare professionals, in both primary and secondary care settings, involved in the care of patients who have sustained an acute LAS injury. These include general practitioners, emergency physicians, musculoskeletal radiologists, occupational physicians, orthopaedic surgeons, rehabilitation physicians, physical therapists, athletic trainers, sports massage therapists, sports physicians, trauma surgeons and other professionals involved in lower extremity musculoskeletal injuries. This updated Clinical Practice Guideline (CPG) will enable these healthcare

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professionals to benefit from and implement the most up-to-date evidence-based recommendations concerning LAS.

MATERIALS AND METHODS

The initial guideline was constrained in its recommendations due to limitations in available published literature, limiting assessment by means of meta-analyses.[14] Due to the considerable number of new studies on LAS, it was decided by the guideline committee that an update of the original document was warranted.

Search and data collection

To provide updated recommendations on the diagnosis and treatment of acute LAS injuries and the prevention of injury recurrence, a search was performed to identify all potential relevant articles published from January 2009—the search date of the initial guideline—up to September 2016 (online supplementary appendix 1). The search was performed in Embase, MEDLINE, Cochrane and PEDro using the database-specific search translation on the topics of predisposing and prognostic factors, diagnostics, treatment, prevention and return to work and sports. For each subtopic addressed in this guideline, an individual search was performed, which is available in the appendix. All searches consisted of the common terms 'ankle sprain', 'ankle injury' and their database-specific synonyms, combined with topic specific terms such as 'prevention' and all available synonyms. To ensure all relevant articles were identified, the current search results were combined with the articles identified by the initial guideline and references of all relevant articles were checked for possibly missed inclusions.

Inclusion and exclusion criteria

Studies were deemed eligible for inclusion if they included individuals aged at least 16 years with acute LAS. Studies published in Dutch, English, German, French, Spanish, Danish or Swedish were all eligible for inclusion. Narrative reviews, case reports and cadaveric analyses were excluded. Additional exclusion criteria were reported medial ankle involvement, fractures or other concomitant injuries/pathology and CAI. In addition to the original search, a manual search of all reference lists of included studies was performed to identify relevant articles that may not have been identified by the search strategy. There were no inclusion or exclusion criteria formed regarding outcome measures. In addition to including all outcomes assessed in the previous guideline (see the individual searches in online supplemenatry appendix 1), all other outcomes concerning risk/prognostic factors, diagnostics, treatment, prevention and work/sports resumption were included. If multiple follow-up time points were included in the assessment, the latest postintervention assessment was included.

Data selection

After duplicate removal all studies were screened by two researchers (GV and AH/BFWvdD) independently using the Rayyan[15] screening tool as advised by the Dutch Cochrane Society. Disagreements among the researchers who performed the initial screening were resolved in a consensus meeting. Subsequently, the same pair of researchers assessed full texts independently, followed by another consensus meeting to resolve disagreements. If disagreement persisted, the senior author (GMMJK) was consulted to reach consensus. To avoid loss of original data for systematic reviews, all the included studies were manually checked for eligibility and relevant data.

Table 1 Classification of methodological quality of individual studies

Classification of studies	Intervention	Diagnostic accuracy of research	Damage or side effects, aetiology, prognosis*
A1	Systematic review of at least two independently conducted studies of A2 level		
A2	Randomised double-blind comparative clinical research of good quality and sufficient sample size	Research relative to a reference test (a 'golden standard') with predefined cut-off points and independent assessment of the results of a test, on a sufficiently large series of consecutive patients who all have had the index and reference test	Prospective cohort study of sufficient sample size and follow-up duration adequately controlled for 'confounding' and selective follow-up is sufficiently excluded
B	Comparative research, but not with all the features as mentioned under A2 (this includes patient control research, cohort study)	Research relative to a reference test, but not with all the attributes that are listed under A2	Prospective cohort study, but not with all the features as mentioned under A2 or retrospective cohort study or patient monitoring research
C	Not comparative research		
D	Opinion of experts		

*This classification only applies to situations in which due to ethical or other reasons controlled trials are not possible to perform. If these are possible, then the classification applies to interventions.

Evidence and guideline quality

Quality of evidence of included articles was classified in order of scientific value (tables 1 and 2). Recommendations were based on the best available evidence. Statements formed by evidence from multiple studies, and the summarised level of evidence of the full statement was provided. The same was done for the level of evidence of the recommendations.

As this guideline concerns an update, as recommended by the EQUATOR-network, the CheckUp list was used for this guideline to help emphasise new information and changes implemented in this updated CPG.[16] Additionally, theAppraisal of Guidelines for Research & Evaluation (AGREE) II criteria were followed in order to ensure complete reporting of methods and results and improve transparency and quality.

Data extraction

All outcomes that were described by at least two of the included studies were extracted for the meta-analyses (online

Table 2 Level of evidence of conclusions

Evidence level	Conclusions based on
1	Research of level A1 or at least two examinations of level A2 performed independently of each other with consistent results
2	One examination of level A2 or at least two examinations of level B, performed independently of each other
3	One examination of level B or C
4	Opinion of experts

Table 3 Results of treatment strategies for acute LAS*

Treatment strategy	Effect	Studies	Patients (N)	(S) MD/RR (95% CI)	In favour of
RICE versus control	Swelling (in mL)	1 RCT	44	MD −47.00 (−65.07 to 28.93)	RICE
	Swelling (in mm)	1 RCT	32	MD −2.30 (−3.86 to 0.74)	RICE
	ROM	1 RCT	44	MD 3.00 (−1.35 to 7.35)	None
NSAIDs versus placebo	Pain	1 RCT	60	RR 0.51 (0.38 to 0.68)	NSAIDs
		5 RCTs	942	MD −5.42 (−6.91 to 3.93)	
	Swelling (in mm)	3 RCTs	455	MD −0.94 (−1.35 to 0.52)	NSAIDs
	ROM restriction	1 RCT	51	RR 0.85 (0.50 to 2.40)	None
	Complications	3 RCTs	641	RR 1.17 (0.79 to 1.74)	None
Immobilisation versus functional support	Pain	10 RCTs	571	RR 0.68 (0.54 to 0.85)	Immobilisation
	Swelling	7 RCTs	520	RR 0.68 (0.44 to 1.04)	None
	ROM restriction	3 RCTs	390	RR 1.42 (0.91 to 2.21)	None
	Satisfaction	5 RCTs	347	RR 1.83 (1.09 to 3.07)	Functional support
	PROMs	3 RCTs	336	MD −2.59 (−3.66 to 1.53)	Functional support
	No return to work	3 RCTs	214	RR 2.13 (0.90 to 5.05)	Functional support
	Days until return to work	8 RCTs	837	MD 7.80 (3.07 to 12.52)	Functional support
	No return to sports	8 RCTs	654	RR 1.34 (0.88 to 2.03)	None
	Days until return to sports	3 RCTs	195	MD 4.88 (1.50 to 8.25)	Functional support
Manual mobilisation versus control	Pain	3 RCTs	120	MD −1.20 (−1.68 to 0.72)	Mobilisation
	ROM increase	5 RCTs	161	MD 5.14 (5.01 to 5.26)	Mobilisation
Exercise therapy	Pain	2 RCTs	166	RR 0.92 (0.78 to 1.08)	None
		4 RCTs	287	MD −0.05 (−0.21 to 0.11)	None
	Objective instability	4 RCTs	251	RR 0.68 (0.49 to 0.95)	Exercise
	Subjective instability	3 RCTs	174	RR 0.80 (0.64 to 1.00)	Exercise
	Days until return to work	4 RCTs	231	MD 0.76 (−0.33 to 1.85)	None
	Days until return to sports	2 RCTs	156	MD −2.61 (−4.05 to 1.16)	Exercise
Surgery versus conservative	Pain	14 RCTs	1553	RR 0.75 (0.56 to 1.00)	Surgery
	Swelling	12 RCTs	1423	RR 0.88 (0.58 to 1.32)	None
	ROM restriction	7 RCTs	746	RR 1.95 (1.16 to 3.28)	Conservative
	Complications	14 RCTs	1614	RR 5.01 (2.33 to 10.77)	Conservative
	No return to sports	4 RCTs	409	RR 0.68 (0.35 to 1.35)	None

*For details, analyses and figures, see online supplementary appendix 3.
Control, same therapy without intervention therapy; NSAID, non-steroidal anti-inflammatory drug; RCT, randomised controlled trial; RICE, Rest Ice Compression Elevation; ROM, range of motion; RR, relative risk; (S) MD, (standardised) mean difference; PROM, Patient Reported Outcome Measure.

supplementary appendix 3). If outcomes concerned the same variable and were measured similarly (eg, pain on an 11-point Likert scale), they were pooled using Review Manager (RevMan; V.5.3, The Nordic Cochrane Centre, Copenhagen, The Cochrane Collaboration, 2014). Data that could not be pooled were assessed qualitatively.

Formulation of recommendations

Individual topics were assigned to the appropriate coauthors depending on their field of expertise in order to formulate recommendations based on the collected evidence. They subsequently received the corresponding studies to enable them to write the corresponding paragraph according to the method section predefined content to ensure uniformity. Results of these diagnostic, treatment and preventive recommendations were provided with the corresponding levels of evidence of the included conclusions. Aspects such as potential harm of interventions, patients' perspective, costs and logistics were carefully considered when formulating the final recommendations. Recommendations were explicitly mentioned under 'Recommendations'; including the full recommendation based on all the available evidence and including a statement about whether this recommendation changed since this update.

In addition to recommendations on diagnostics, an overview of treatment and prevention strategies is provided in tables 3 and 4 by pooling the data of studies assessing the same treatment/preventive measure (number of patients (N); relative risk (RR) or mean difference (MD) and 95% CI).

New information was explicitly mentioned under *'What's new?'*.

Implementation

To ensure implementation of a multidisciplinary view in this CPG in all phases of rehabilitation after sustaining a LAS, the guideline committee consisted of an emergency medicine physician, epidemiologists, general practitioner, musculoskeletal radiologist, orthopaedic surgeons, movement scientists, physiotherapists and rehabilitation specialist (see affiliations). All members, apart from the two senior supervisors (RAdB and GMMJK), participated either in the search and selection of evidence or in reading, extracting and implementing data into this CGP. Apart from full review by all coauthors, the two senior authors additionally functioned as external reviewers by means of full detailed review to ensure this CPG was compliant with the AGREE II criteria and to optimise quality, assess applicability in clinical practise and feasibility of results.

Terminology

- functional treatment: treatment during which the function of the joint (ie, freedom of movement) is retained;

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Table 4 Checklist: essential information for healthcare professionals during referral of patients with lateral ankle sprain

Medical discipline	Diagnostic phase	Acute treatment phase	Guidance phase
General for each healthcare professional	Time of accident Trauma mechanism Age, weight, profession, hobby Man, woman Ability to walk after trauma Therapy until visit Concomitant symptoms and damage	(Differential) diagnosis Time schedule and treatment plan Advise follow-up visit Duration of rest When normal weight bearing allowed What to do with deviant drift of symptoms	Diagnosis Result of treatment Advise on activities of daily living and sports participation Medication Recommendations to prevent recurrence
Emergency physician		Thrombosis prophylaxis yes/no?	Not involved in the guidance phase
Radiologist		Fracture yes/no Concomitant pathology Not involved in treatment plan	Not involved in the guidance phase
Orthopaedic and trauma surgeon		Fracture yes/no Treatment options Thrombosis prophylaxis yes/no?	Therapy/treatment
Sports physician, general practitioner		Thrombosis prophylaxis yes/no?	Advise follow-up visit
Sports masseur, physical therapist			Therapy Advise follow-up visit
Medical officer, insurance medical officer, rehabilitation physician			Time schedule and treatment plan/result Advise follow-up visit Prognosis Reintegration protocol

- functional support: support such as tape or brace, preserving joint motion, but limiting extreme joint positions such as maximum inversion;
- functional outcome: outcome of treatment that leads to improvement of function such as pain reduction or range of motion (ROM) increase enabling patients to return to their preinjury level of activity and participation.

RESULTS

To systematically evaluate and summarise all available evidence concerning LAS, a broad literature search was undertaken specifically related to the following areas: (1) predisposing and prognostic factors; (2) diagnostics, (3) treatment, (4) prevention and (5) return to work/sport. This search resulted in the identification of a total of 10 067 studies. After title and abstract screening and reading full texts, a total of 194 articles were eligible for inclusion in this guideline (online supplementary appendix 2). All fields of evidence with regard to relevant diagnostic tools, reliability of diagnostics, different treatment modalities and their efficacy, as well as prevention interventions including their cost-effectiveness will in turn be discussed. Recommendations will be provided based on the available level of evidence (tables 1 and 2).

Predisposing factors

Predisposing factors are defined as factors that increase the risk of sustaining a LAS. Risk factors for LAS can be classified as either intrinsic (patient-related factors, eg, proprioception) or extrinsic (eg, sports or environmental characteristics). An important aspect that should be considered by clinicians when addressing predisposing factors is whether they can be modified or not. Modifiable risk factors may be targeted by (preventive) treatment.

Intrinsic risk factors

There are a number of intrinsic risk factors, which substantially heighten the risk of sustaining a LAS. These include limited dorsiflexion ROM,[17–19] reduced proprioception[18 20–23] and (preseason) deficiencies in postural control/balance (positive single-leg balance test (RR 2.54, 95% CI 1.02 to 6.03)[20–22 24–28] (level 1). In addition, other modifiable risk factors which heighten the risk of sustaining a LAS include body mass index (BMI) and high medial plantar pressures during running[28–33] (level 3). Concerning BMI, included results are conflicting as to whether a higher or lower BMI increases the risk of incurring a LAS. Our meta-analysis showed a greater risk of sprains in patients with a lower BMI (mean difference (MD) −0.08, 95% CI −0.14 to –0.02)[23 34] (level 2). Additional factors that may contribute to an increased risk are reduced strength,[18 20–23 35] coordination,[25] cardiorespiratory endurance,[25] limited overall ankle joint ROM and decreased peroneal reaction time[18 20–23] (level 3).

Concerning non-modifiable risk factors, females have a higher risk of sustaining a LAS compared with males (RR 1.25, 95% CI 1.17 to 1.34)[29 36] (level 3). Despite a history of LAS being described as a strong predictor, pooling results lead to a non-significant risk ratio (RR 1.44, 95% CI 0.96 to 2.16)[18 21 22 37–39] (level 2). Additional factors correlated to an increased risk of sustaining a LAS are physical characteristics such as greater height, ankle joint configuration, foot posture index, anatomical abnormalities in ankle and knee alignment and multiple clinical defects[28–33] (level 3).

What's new: An increase in available data made it possible to identify female sex as well as potentially a lower BMI being risk factors for ankle sprains. Additionally, a recommendation is provided which was missing in the original guideline.

Recommendation (new): When treating patients with an acute LAS, modifiable risk factors such as deficiencies in proprioception and ROM should be identified and if possible included in a prevention and/or rehabilitation programme to mitigate the risk for recurrent sprains (level 3).

Extrinsic risk factors

Irrespectively of patients' wish to switch sports, the main modifiable extrinsic risk factor for LAS appears to be the type of sport practised. The highest incidence of LAS was found for aeroball, basketball, indoor volleyball, field sports and climbing.[29 40 41]

The incidence of LAS was dependent on the level of participation.[29 40 41] In volleyball, landing after a jump is the most important risk factor[41 42] (level 2). Playing soccer on natural grass (vs artificial turf: RR 0.53, 95% CI 0.48 to 0.59)[43–45] as well as being a defender (42.3% of all sprains)[46 47] increased the incidence of LAS (level 2). Concerning shoe wear, high heels (9.5 vs 1.3 cm) heighten the risk of incurring a LAS[48] (level 3).

The only non-modifiable factor was sex. Despite girls having an increased risk of LAS compared with boys, in-competition risk for LAS is higher in boys (RR 3.42, 95% CI 3.20 to 3.66) compared with girls (RR 2.71, 95% CI 2.48 to 2.95)[36] (level 3).

What's new: The new search resulted in a significant increase in data. The subsequent performed meta-analyses made it possible to identify the size of the increased risk of playing soccer on natural grass, the risk associated with being a defender and the risk while playing sports at a competitive level. New recommendations are provided concerning the high impact of sport.

Recommendation (new): Extrinsic risk factors, although outside of the patient, may provide a significant increase in the risk at sustaining a LAS. Healthcare professionals involved in treating patients who sustain a LAS should take notice especially of the type of sport practised but also of other extrinsic risk factors, as modifications may lower the risk at future sprains and other ankle injuries (level 2).

Prognostic factors

Following an acute LAS, pain decreases rapidly within the first two weeks after injury.[49] However, a substantial proportion of patients report long-term unresolved injury-associated symptoms. At a follow-up of 1–4 years, 5%–46% of patients still experience pain,[49–51] 3%–34% of patients experience recurrent sprains[49–51] and 33%–55% of patients report instability.[49 51] Additionally, a higher physical workload load may be associated with an increased risk of recurrent sprains (RR 1.09, 95% CI 0.52 to 1.19; RR 0.96, 95% CI 0.36 to 1.2) and ankle instability (RR 1.16, 95% CI 0.71 to 1.18; RR 1.10, 95% CI 0.57 to 1.19).[51] Even clinical signs of anterior impingement were found in 25% of patients, of which 82% were radiographically confirmed[50] (level 3).

Despite initial treatment consisting of taping/bracing and physical rehabilitation, up to 40% of individuals who have sustained a LAS develop CAI.[52] This may indicate that not all factors contributing to the success or failure of rehabilitation are known. Some of the known unfavourable prognostic factors identified for the development of CAI were an inability to complete jumping and landing within 2 weeks after a first-time LAS, deficiencies in dynamic postural control,[53] altered hip joint kinematics[54] and lack of mechanical stability/increased ligament laxity 8 weeks after an ankle sprain.[55 56] Other factors that may influence the prognosis are sports participation at a high level,[57] being a young male,[52] increased BMI[52] and greater body height[52] (level 3). Finally, acute postural balance impairments persisting after LAS may also contribute to the development of CAI.[58] Due to the neuromuscular origin of some of these prognostic factors, physical therapy might be helpful to improve physical impairments after a LAS and prevent progression to CAI.[59 60] Based on the limited evidence concerning the risk factors for developing CAI following an ankle sprain, further research on prognostic factors is required and may provide additional and more uniform insights.[61 62]

What's new: Over the past years more data have become available on negative prognostic factors that may indicate slow or incomplete rehabilitation. This enabled us to modify the previous recommendation, which lacked a conclusion due to insufficient evidence.

Recommendation (modified): Following acute LAS, adequate attention should be directed towards the patient's current level of pain, their workload and level of sports participation. These may all negatively influence recovery and increase the risk of future injury recurrence. Hence, they should be addressed early in the treatment process (level 3).

Table 5 Clinical decision rules in acute lateral ankle sprain[67 73 74 78 214–216]

Ottawa ankle rules		Bernese ankle rules	
Pain on the dorsal side of one or both malleoli		Indirect fibular stress	
Palpation pain at the basis of the metatarsal bone V		Direct medial malleolar stress	
Palpation pain of the navicular bone		Compression stress of the midfoot and hindfoot	
Inability to walk at least four steps			
Sensitivity 86%–99%; specificity 25%–46%		Sensitivity 69%–86%; specificity 40%–45%	
PPV 24%–48%; NPV 97%–99%			
Reproducibility 45%		Reproducibility 48%	
Leiden ankle rules		**Utrecht ankle rules**	
Deformity/instability/crepitating	5	Deformity/instability/crepitating	4
Weight bearing*	3	Weight bearing/axial compression*	2
Pulseless/weak posterior tibial artery†	2	Pain on palpation/swelling	
Pain and palpation malleoli/metatarsal V‡	2	Pain on palpation/swelling	
Swelling malleoli/metatarsal V	2	Tibia	1
Swelling/pain in Achilles tendon	1	Fibula	1
Age divided by 10		Achilles tendon	1
Radiographs required if	>7	Base of fifth metatarsal	1
Sensitivity 88%; specificity 57%		Haematoma/haemarthrosis	1
		Age divided by 10	
		Radiographs required if	≥8
		Sensitivity 59%; specificity 84%	

*Inability to bear weight was defined as the inability to walk four steps. Axial compression pain was defined as pain on application of axial compression.
†Positive in case of a marked difference with the contralateral side.
‡Of the posterior edge (6 cm) of both the lateral and the inability to walk four steps. Axial and medial malleolus and the base of the fifth metatarsal bone.
NPV, negative predictive value; PPV, positive predictive value.

Diagnostics

In case of a severe ankle sprain, a fracture should be excluded by proper use of the Ottawa ankle rules (OAR), and if indicated, conventional radiographic imaging should be undertaken (table 5). Since only 15% of patients with LAS, who are examined using a radiograph, are diagnosed with an ankle fracture, the OAR have been developed to rule out a fracture.[63] The OAR are an accurate and valid tool, which can be used with patients who have a suspected ankle/foot fracture within 1 week after the initial trauma (level 1).[63–67] A high incidence of less serious traumas may lower the predictive value of the OAR in clinical practice.[68 69] To avoid unnecessary use of radiographs, the OAR are recommended as a primary physical examination tool to rule out the likelihood of foot/ankle fractures by emergency physicians, general practitioners or physiotherapists[63 70–73] (level 1). The Bernese ankle rules (BAR) have been developed as response to the high rate of unnecessary radiographs based on

OAR findings. However, the sensitivity of the BAR is too low to promote clinical use[74] (level 2).

In general, ankle ligament injuries are classified into three grades representing increasing injury severity: grade I, mild ankle sprain; grade II, moderate sprain/microligament lesions; and grade III, severe sprain/full ligament lesion.[75] In cases where a haematoma is present, accompanied by pain on palpation around the distal fibula and/or a positive anterior drawer test, a rupture of the lateral ankle ligaments likely exists. The sensitivity (84%) and specificity (96%) of physical examination using the anterior drawer test are optimised if clinical assessment is delayed for between 4 and 5 days post injury[68 69 76 77] (level 2). Ultrasonography has similar sensitivity (92%) but lacks specificity (64%) compared with delayed examination, and additionally depends on the availability of an experienced technician and equipment.[69 78] In case of suspicion of high-grade ligament injuries, osteochondral defects, syndesmotic injuries and occult fractures, an MRI can be performed[78] because of its excellent sensitivity (93%–96%) and specificity (100%) for visualising these injuries.[79–83] Poor availability of MRI in combination with the high prevalence of ankle sprains limits the use of MRI in acute settings, but in case of persisting symptoms it may be used to diagnose underlying joint damage. In case of suspicion of complete uncomplicated rupture of the anterior talofibular ligament, an MRI is not needed as the sensitivity and specificity of delayed physical examination are sufficient.[69] Other diagnostic modalities are stress radiographs and arthrography. Due to the limited diagnostic value of stress views in combination with pain in the acute setting while stressing the ligaments, these are regarded as obsolete and should not be used. As arthrography is an invasive procedure and its sensitivity and specificity are equal to delayed physical examination, it is also not recommended as a diagnostic tool in the acute setting[78] (level 2).

What's new: To ensure readability, the OAR were included in this diagnostics section. To make sure this guideline provides a complete overview of the many decision rules which the OAR belong to, table 5 was added including the parametric properties of the most popular clinical decision rules. The recommendation includes a short summary by providing an overview of the most important diagnostic steps, which was missing in the previous guideline.

Recommendation (new): Regarding the clinical assessment of damage to the anterior talofibular ligament, the sensitivity (84%) and specificity (96%) of assessment using the anterior drawer are optimised if clinical assessment is delayed for between 4 and 5 days post injury. In case of a suspected fracture, the OAR should be applied (level 2).

Treatment

Rest Ice Compression Elevation (RICE)

RICE is a conservative treatment method that has not been rigorously investigated, and the efficacy of this combination is questionable. The individual elements of ice and compression have been the subject of numerous scientific investigations; however, there is little scientific support for their efficacy in reducing injury-associated symptoms following acute LAS.

The limited available evidence showed that the efficacy of cryotherapy for reducing acute LAS injury-associated symptoms is unclear (33 randomised controlled trials (RCTs), n=2337)[84 85] (level 1). There are no indications that the isolated use of ice can increase function, as well as decrease swelling and pain at rest among individuals who have sustained an acute LAS (27 RCTs, n=1670)[84 86–90] (level 2). In combination with exercise therapy, cryotherapy has a greater effect on reducing swelling compared with heat application (one RCT, n=30)[86] (level 2). The combination of cryotherapy and exercise additionally results in significant improvements in ankle function in the short term, allowing patients to increase loading during weight bearing compared with standard functional treatment (one RCT, n=101)[91] (level 3).

Evidence regarding the efficacy of compression therapy after acute LAS is also inconclusive (three RCTs, N=86)[87–89] (level 2).

As a combined therapeutic modality, the use of RICE plus multimodal physiotherapy compared with RICE alone provides no additional benefits. Both treatments provide pain reduction, increase patient function and reduce ankle swelling (one RCT, n=28)[92] (level 2).

Regarding the individual effects of rest and elevation after LAS, no evidence was available.

What's new: No new statements could be made based on the newly identified studies. The increased evidence indicates that the individual aspects of RICE are not effective, apart from cryotherapy, if provided in combination with exercise therapy.

Recommendation (modified): There is no evidence that RICE alone, or cryotherapy, or compression therapy alone has any positive influence on pain, swelling or patient function. Therefore, there is no role for RICE alone in the treatment of acute LAS (level 2).

Non-steroidal anti-inflammatory drugs

NSAIDs are commonly prescribed for patients who have sustained an acute LAS, with the primary purpose of reducing pain. Pooling the results of current studies shows that the use of oral or topical NSAIDs results in less pain in the short term (<14 days) without significantly increasing the risk of adverse events compared with placebo (26 RCTs, n=4225)[93–97] (level 1) (table 3). However, studies that included other NSAIDs instead of a placebo were excluded from this review[98–102]; additionally, the included participants were relatively young and healthy and thus potentially less prone to side effects. A comparison between selective NSAIDs (celecoxib 200 mg two times daily) and non-selective NSAIDs (ibuprofen, naproxen or diclofenac) (four RCTs, n=1490) concluded that celecoxib was non-inferior to non-selective NSAIDs for the primary outcome of pain following an acute LAS injury. Adverse events did not occur more frequently[99 103–105] (level 1). Diclofenac showed superior results at days 1 and 2 compared with piroxicam (two RCTs, n=201) and ibuprofen (one RCT, n=60) for reducing pain during motion in patients with mild-to-severe acute ankle sprains and equal adverse event rates[98 101] (levels 2 and 3). Contradicting results have been reported on the effect of diclofenac for pain during rest, swelling and inflammation,.[98 101] No differences in effect were seen when comparing a fixed dosage (500 mg two times daily) to an as-needed naproxen dosage (one RCT, n=135, MD_{pain} −0.13 (−0.38 to 0.12))[106] (level 3). Despite dose differences, paracetamol (cq. acetaminophen) seems to be equally effective as NSAID usage (three RCTs, n=450) for pain (one RCT, n=86, MD 1.80, 95% CI −1.42 to 5.02), swelling (two RCTs, n=186, MD −0.07, 95% CI −0.29 to 0.14) and ROM (one RCT, n=100, MD 0.70, 95% CI −0.62 to 2.02)[107–109] (level 1). Opioid analgesics are equally effective for pain relief, but lead to significantly more side effects (two RCTs, n=869)[100 110] (level 2). The use of NSAIDs may delay the natural healing process as the inflammation suppressed by NSAIDs is a necessary component of tissue recovery.[111]

Besides these commonly prescribed analgesics, other pharmaceutical treatment modalities were described: venotonic drugs did not result in enhanced outcomes for pain and swelling compared with paracetamol and RICE[112] (level 2); platelet-rich plasma injections were not superior for pain and functional outcomes compared with placebo injections (one RCT, n=37)[113] (level 3), and topically applied Traumeel (one RCT, n=449)[114] (level 2) was not superior compared with diclofenac topical gel for ankle oedema, pain and function. Periarticular hyaluronic acid injections compared with placebo (two RCTs; n=158) did show a positive effect on pain, nor did they result in a quicker time to return to sport or reduced prevalence of recurrent sprains[115 116] (level 2).

What's new: Based on the search results concerning treatment, the committee agreed on implementing a topic on NSAIDs. Over the past years much research has been undertaken on NSAIDs in relation to musculoskeletal injuries, and in many countries they are available without prescription. However, before recommending NSAIDs, their effect in the specific context of an ankle sprain had to be assessed.

Recommendation (new): NSAIDs may be used by patients who have incurred an acute LAS for the primary purpose of reducing pain and swelling. However, care should be taken in NSAID usage as it is associated with complications (level 2) and may suppress or delay the natural healing process.

Immobilisation

A minimum of 4 weeks in a lower leg cast following an acute LAS results in less optimal outcomes compared with functional support and exercise strategies with a duration of 4–6 weeks[117118] (22 RCTs, n=2304) (level 1). More recent evidence (three RCTs, n=694) showed that a short period (<10 days) of immobilisation with a plaster cast or rigid support can be of added value in the treatment of acute lateral ligament injury as it decreases pain and oedema and improves functional outcome[119–122] (level 2).

What's new: Despite the inclusion of new recent studies, there were no new findings.

Recommendation (not changed): Use of functional support and exercise therapy is preferred as it provides better outcomes compared with immobilisation. If immobilisation is applied to treat pain or oedema, it should be for a maximum of 10 days after which functional treatment should be commenced (level 2).

Functional treatment

Functional support

Functional supports in the form of an ankle brace or tape are often used following acute LAS. These external supports differ from rigid immobilisation and allow the patient to load the damaged tissues in a protected manner. Treatment with any type of real ankle support was more effective compared with treatment with less adequate support such as a compression bandage or a tubigrip[5 122] (level 2). Wearing compression stockings beyond the acute phase is not helpful in the treatment of acute lateral ankle ligament injury[123] (level 3). The success of functional treatment is, however, dependent on the severity of the injury. For example, if a sprain is complicated by a ligament avulsion fracture results may be inferior to those in patients with isolated ligament injury.[124]

The superiority of one external support over another is debated rigorously in the literature.[125–127] A meta-analysis (n=892) showed a lace-up brace or a semi-rigid brace should be preferred to the use of an elastic bandage[125] (level 1). Use of an ankle brace results in better outcome compared with other types of functional treatment such as sports tape (non-elastic) or kinesiotape (elastic), without showing any side effects.[128] Based on a small systematic review (n=276), it can be concluded that kinesiotape is unlikely to provide sufficient mechanical support in unstable ankles[129] (level 1).

What's new: New evidence emphasises that the use of external supports (ie, braces) is preferred over immobilisation. Additionally, the preferred time frame during which the use of external support is advised is outlined. Overall, the core message of this section remains unchanged.

Recommendation (modified): Use of functional support for 4–6 weeks is preferred over immobilisation. The use of an ankle brace shows the greatest effects compared with other types of functional support (level 2).

Exercise

Among patients who seek professional healthcare following an acute LAS, exercise therapy is often an integral component of the treatment administered. Exercise therapy programmes mainly consist of neuromuscular and proprioceptive exercises. Exercise therapy programmes that are initiated early following an acute LAS injury have established efficacy. They can reduce the prevalence of recurrent injuries[130–132] (10 RCTs, n=1284) (RR 0.62, 95% CI 0.51 to 0.76), as well as the prevalence of functional ankle instability[131 133] (3 RCTs, n=174) (RR 0.80, 95% CI 0.64 to 1.00). Furthermore, they are associated with a quicker time to recovery and enhanced outcomes[130 133–136] (level 1). Including supervised physiotherapy has shown to have some benefit in patients with a severe ankle sprain compared with a mild LAS as measured by PROMs,[60] and whence compared with a home exercise programme[137 138] (level 1). Additionally, supervised exercise therapy may lead to improvements in ankle strength[138] and proprioception,[138] faster return to work[139] and sport,[134] compared with performing the exercise programme without supervision or guidance (level 1). Many articles, however, contradict these findings, concluding that there is no effect from the addition of supervised exercise therapy to conventional treatment alone (two RCTs, n=130)[140 141] (level 2) nor an improvement of postural balance after exercise therapy[131 142] (level 1).

What's new: New evidence has become available on the specific effects of different types of exercise/rehabilitation programmes; especially the beneficial effect of exercise therapy on preventing recurrent sprains, reducing the risk of functional instability and expediting the recovery of ankle joint function.

Recommendation (modified): Exercise therapy should be commenced after LAS to optimise recovery of joint functionality. Whether exercise therapy should be supervised or not remains unclear due to contradictory evidence and requires further research (level 1).

Manual mobilisation

Manual joint mobilisation can provide a short-term increase in ankle joint dorsiflexion ROM following acute LAS[131 143–147] (12 RCTs, n=427) (level 1). Additionally, joint mobilisation has been reported to decrease pain[143] (level 1). Manual therapy combined with exercise therapy resulted in better outcomes compared with exercise therapy alone[137] (level 3).

What's new: Despite findings by the previous version of this guideline that manual mobilisation only results in short-term treatment effects, current evidence shows added value of manual mobilisation when used in combination with exercise therapy.

Recommendation (modified): A combination with other treatment modalities, such as exercise therapy, enhances the efficacy of manual joint mobilisation and is therefore advised (level 3).

Surgical therapy

Surgical therapy for acute lateral ligament injuries has been performed abundantly until it was recognised that conservative treatment provides equal effects and that not all patients require surgery in order to resolve complaints[148–151] (level 1). Nowadays, surgery is mainly reserved for patients who have chronic instability after a LAS and who have not responded to a comprehensive exercise-based physiotherapy programme. Long-term effects of surgical treatment in cases of acute lateral ligament injury correspond with those of functional treatment. Surgery seems superior at decreasing the prevalence of recurrent LAS, which is important as recurrent LAS in turn may increase the risk for the subsequent development of osteoarthritis (one RCT, n=51)[13] (level 2). There is limited evidence for longer recovery times, higher incidences of ankle stiffness, impaired ankle mobility and complications in patients who received surgical treatment (20 RCTs, n=2562)[150] (level 1). More recent studies show that outcomes in terms of recovery of ankle activity and instability are significantly better for surgical treatment than for functional treatment (12 RCTs, n=1413)[152] (level 1). As a previous sprain is a predictor for recurrent ankle sprains, this may be related to increased ligament laxity. This laxity is resolved during surgery. Based on this indirect evidence, it may be suggested that surgical therapy helps prevent recurrent ankle sprains. However, a large percentage (60%–70%) of individuals who sustain a LAS respond well to non-surgical treatment programmes,[149] and therefore treating all patients with LAS would mean unnecessary exposure to an invasive intervention for many patients, not to mention costs (level 1).

What's new: New evidence supports the rationale for being reserved with the recommendation of surgery for all patients following LAS. This lead to refinement of the recommendation regarding surgery.

Recommendation (modified): Despite good clinical outcomes of surgery after both chronic injuries and an acute complete lateral ligament rupture, functional treatment is still the preferred method as not all patients require surgical treatment. This also helps to avoid unnecessary exposure to invasive (over) treatment and unnecessary risk of complications[149 152] (level 1). However, treatment decisions have to be made on an individual basis. In professional athletes, surgical treatment may be preferred to ensure quicker return to play.[151]

Other therapies

Other treatment modalities less frequently used do not always show a treatment effect. For example, no effect on pain, oedema, function and return to play has been shown for ultrasound[153 154] (level 1), laser therapy[155] (level 1), electrotherapy[156–158] (level 1) and shortwave therapy[159–163] (level 2) in the treatment of acute LAS. Evidence on acupuncture is inconclusive concerning the therapeutic effect due to large heterogeneity between studies[164 165] (level 1). A small cohort study indicated that local vibration therapy may be effective in patients with LAS by increasing dorsiflexion and eversion and decreasing perceived ankle stiffness,[166] while another study indicated the possible beneficial effect of Bioptron light therapy in addition to cryotherapy[167] (level 3).

What's new: Acupuncture, vibration therapy and Bioptron light therapy were added to the present update. Concerning the other identified therapies, new evidence did not change previous statements.

Recommendation (not changed): As no strong evidence exists on the effectiveness of these treatment modalities, they are not advised in the treatment of acute LAS (level 2).

Communication between professionals

Since there are various disciplines involved in the care for patients with LAS, it is preferable to make working arrangements at a regional level on indications for referral, division of tasks and what information is provided by healthcare professionals. The different disciplines involved in primary and secondary care are emergency physicians, sports masseurs and physical therapists, sports physicians and general practitioners, orthopaedic and trauma surgeons, radiologists, medical officers for occupational medicine and rehabilitation physicians. Within referral between healthcare professionals, optimal communication is preferred. What information should be communicated between healthcare professionals depends on the phase of LAS; the diagnostic phase, the treatment phase and the guidance phase.[14 168–170]

What's new: The checklist and statements from the previous version of this guideline were not subject to change. The most important factor remains communication.

Recommendation (not changed): To refine communication between healthcare professionals involved in the treatment of patients with LAS, a communication check list is recommended (table 4).[14 168–170]

Prevention

Functional support

The use of brace or tape reduces the risk of both recurrent (RR 0.30, 95% CI 0.21 to 0.43) and first-time ankle sprains (RR 0.69, 95% CI 0.49 to 0.96), especially in those who participate in sports[4 125 171 172] (level 1). Kinesiotape may also have a preventive effect in patients who have already sustained a LAS due to its effects on postural control[171] (five RCTs, n=276) (level 1). The use of a brace or tape is a personal choice and based on practical usability and costs. Associated adverse events are rare.[4 125 171 172] Ankle brace or tape usage has not shown any beneficial effects on proprioceptive acuity in patients who sustained recurrent ankle sprains or those who have functional ankle instability (eight RCTs, n=152) (level 1). This conclusion was consistent when the two aspects of proprioception, sense of movement and joint position, were considered separately.[129] No differences in prevention of recurrent sprains were found between different types of tape and brace as support.[117 172 173]

What's new: In addition to updating the risk ratios by including new studies, a risk ratio is provided for the preventive effect of tape and brace for first-time ankle sprains. Additionally information on the effect on proprioception and adverse events was included. This new evidence did not change the previous recommendation.

Recommendation (not changed): Both tape and brace have a role in the prevention of recurrent LAS despite limited evidence on mechanisms that leads to these beneficial effects (level 1). The choice of usage should depend on personal preferences.

Exercise therapy

Coordination and balance training have been shown to prevent recurrent ankle sprains.[4] The assessment of the effect of exercise therapy as in neuromuscular training (mainly proprioception) has shown a positive effect towards prevention of LAS[132 139 173–175] and especially recurrent LAS. A meta-analysis (two RCTs, n=130)

Table 6 Results of prevention therapy

Preventive measure	Effect	Studies	Patients (N)	(S)MD/RR (95% CI)	Results in favour of
Immobilisation versus functional support	Recurrent sprains	11 RCTs	844	RR 1.17 (0.86 to 1.59)	None
Functional support	Recurrent sprains	6 RCTs	2307	RR 0.30 (0.21 to 0.43)	Functional support
	First-time sprains	4 RCTs	2933	RR 0.69 (0.49 to 0.96)	Functional support
	Sprains in mixed injured –non-injured groups	6 RCTs	6108	RR 0.39 (0.25 to 0.95)	Functional support
	Muscle activity	1 RCT	60	MD 1.13 (–1.48 to 3.75)	None
	Stability	1 RCT	62	MD –0.44 (– 0.70 to –0.18)	Functional support
Exercise therapy	Recurrent sprains	10 RCTs	1284	RR 0.62 (0.51 to 0.76)	Exercise
	First-time sprains	1 RCT	173	RR 0.45 (0.15 to 1.37)	None
	Sprains in mixed injured –non-injured groups	13 RCTs	8021	RR 0.60 (0.51 to 0.70)	Exercise
Surgery	Recurrent sprains	12 RCTs	1437	RR 0.72 (0.55 to 0.94)	Surgery

Immobilisation: cast; exercise therapy: physical therapy, strength training, proprioceptive training; functional support: brace, tape; surgery, anatomic repair or reconstruction; walker boot.
RCTs, randomised controlled trials; RR, relative risk; (S) MD, standardised mean difference .

illustrated that exercise therapy had a protective effect compared with usual care on preventing recurrent LAS (RR 0.62, 95% CI 0.51 to 0.76). Usual care was defined as 'any form of rehabilitative treatment used by the athlete, without any interference from the authors' (cited from Hupperets *et al*).[176] This effect is even larger in athletes (RR 0.38, 95% CI 0.23 to 0.62)[38 177] (level 1). When exposing athletes with recurrent sprains to proprioceptive training, to improve joint position sense, their risk of recurrence of LAS is reduced to the same level as healthy controls[4 42 177–180] (level 3). Exercise therapy such as coordination and balance training mainly seem to be effective for recurrent ankle sprains up to 12 months after the initial sprain,[4 131 176 181] but not on first-time ankle sprains[21 38 175 182] (level 1).

What's new: More positive effects of different training programmes have become available, strengthening the recommendation of the previous guideline.

Recommendation (not changed): For this reason, it is advised to start exercise therapy, especially in athletes, as soon as possible after the initial sprain to prevent recurrent LAS. Exercise therapy should be included into regular training activities as much as possible as home-based exercise (level 1). The preventive effect of exercise therapy for first-time LAS lacks evidence (table 6).

Footwear

No evident conclusions exist on the role of footwear in the prevention of ankle sprains (level 2). Wearing low-fitted or high-fitted shoes did not show any difference in preventive effect (three RCTs, n=3410)[4 172 183] (level 1). Despite the lack of evidence, some authors prefer high-fitted shoes,[73 117] whereas other authors describe a preference of low-fitted shoes[120] (level 1). Possibly shoes being new is of greater importance compared with the height of the shaft of the shoe in preventing ankle sprains.[4] Also, no difference in LAS incidence is seen when wearing sports shoes with or without a cushioned column.[91]

What's new: New evidence corresponded with the evidence found in the previous guideline.

Recommendation (not changed): Due to the inconclusiveness of evidence, no recommendations can be made concerning shoe wear (level 1).

Resuming work

To facilitate return to work, discrimination between different degrees of injury can support the initial treatment and identification of the prognosis in relation to return to work[184] (level 4). Additionally, a schedule for work resumption (table 7), which takes into account all task requirements, may assist in optimisation of the reintegration process[185 186] (level 3). Two systematic reviews stated wearing a brace provided better functional outcome compared with no brace, without limiting return to work (two RCTs, n=157)[125 128] (level 2). Immediate post-traumatic mobilisation and functional treatment also seem to have a positive effect on the treatment of acute LAS and lead to shorter sick leave and faster return to work compared with immobilisation[131 187–189] (level 1).

What's new: With the current focus on productivity and socioeconomic burden, return to work is of substantial importance. Based on new available evidence, table 7 was expanded and the advice on return to work was further specified.

Table 7 Return to work and sports[185 186]

Degree of inversion injury	Time from injury (weeks)	Restrictions	Overall tips and tricks
Distortion (depending on degree of pain/subjective limitation/severity)	2	Mostly sitting work Not exceeding 10 kg of lifting Limit standing and walking position on uneven surfaces	▶ Phased rehabilitation focusing on work/sport-specific tasks ▶ Scheduled progression of work activities ▶ Work-hardening and functional capacity evaluation ▶ Recognition of the emotional aspect of the situation ▶ Involvement of an occupational physician and therapist
	3–4	Return to full work and sports depending on task requirements	
Partial or total rupture of ligaments	3–6	Mostly sitting work Not exceeding 10 kg of lifting Limit standing and walking position on uneven surfaces	
	6–8	Return to full work and sports depending on task requirements and result of physiotherapy	
In case of surgery	2	Non-weightbearing cast and crutches	
	3–6	Weight bearing as tolerated Sedentary work resumed in case of weight bearing	
	>6	Cast is replaced by a brace	
	12–16	Return to physically demanding job and sports	

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Recommendation (modified): To speed up return to work, a brace and immediate functional treatment in combination with a return to work schedule are advised (level 3).

Sport resumption

LAS may lead to multiple problems such as proprioception disturbances. These disturbances seem to originate from the central nervous system above the level of the spinal reflex (level 2) and may result in functional instability.[190–192] Additionally, delayed response time of the peroneal muscle has been detected, possibly due to traction injury of the peroneal nerve.[193] However, motor-unit insufficiencies seen after a LAS seem to last shorter than those after other lateral ankle injuries not based on an inversion trauma mechanism[178 193–195] (level 2). Strength deficits are present following LAS. For these reasons, early functional treatment is advised and should address proprioception, muscle response time and muscle strength,[196–200] enabling early return to sport participation[187 188] (level 2).

What's new: In addition to the many new and varying types of rehabilitation programmes, recent results showed that supervised exercise provides better outcomes compared with non-supervised training.

Recommendation (modified): Supervised exercises focusing on a variety of exercises such as proprioception, strength, coordination and function will lead to a faster return to sport in patients after a LAS[134] and are therefore recommended (level 1).

Cost-effectiveness

Costs of injury

Estimated societal costs of ankle sprains, as reported in the literature, vary between €360[201] and €1100[202] per individual (level 2). This disparity in reported costs is due to, among others, variations in healthcare system, population, and type and severity of injury. Although most patients with ankle sprain do not receive supervised rehabilitation[203] (level 3), these values indicate that ankle sprains have a substantial financial impact on society. Additionally, added to these costs in the short term, patients with ankle sprain are at risk of developing chronic conditions, which in turn may lead to subsequent costs. Consequently, optimised treatment and prevention will provide economic benefits in addition to clinical effects for the individual.

Diagnostics

The OAR provide a valid and reliable cost-effective tool to diagnose fractures after an ankle sprain[203] (level 3). In 1995, it was shown that implementing the OAR as opposed to existing hospital protocols resulted in cost savings between €7.01 and €30.96 per patient[204] (level 3). More recently, implementation of the OAR through emergency department nurses has been shown to be a cost-effective method to diagnose and manage ankle sprains[205] (level 3). As an alternative to the OAR, the low-risk ankle rule provides a cost-effective tool to diagnose paediatric ankle fractures, with an estimated reduction in required radiographs of around 60%[206] (level 3).

Treatment

Functional treatment is clinically the treatment strategy of choice for ankle sprains. No full cost-effectiveness studies are known to compare functional treatment against immobilisation as treatment. In regards to indirect costs, a functional approach (3–5 days of rest, ice, compression and elevation with early weight bearing, after which active exercise is commenced) leads to the fastest resumption of work and daily life activities compared with any other kind of treatment[207] (level 3). For protection, ankle support may be indicated to facilitate return to work. A semirigid brace is suggested to be the most cost-effective option compared with taping[208] (level 3).

Prevention

Preventive efforts against first-time and recurrent ankle sprains have shown high cost benefits[208] (level 3). Both neuromuscular training and ankle braces have been proven beneficial as a preventive investment due to lower societal costs, mainly achieved through reduced indirect costs[209] (level 2). Comparisons between measures have indicated bracing to be superior to taping[210] and neuromuscular training[211] as a preventive option (level 1). Of note is that the latter statement is only valid for the preventive value of bracing. Neuromuscular training has been associated with clinical benefits other than prevention alone, which should also be considered[212] (level 1) (table 8).

DISCUSSION

After an acute LAS it is important to first exclude the presence of any fractures. To this end the OAR can be used, having a high sensitivity and specificity. Subsequently, functional treatment in the form of exercise and functional support (ie, brace or tape) is preferred over immobilisation. Still a short time of immobilisation may help diminish complaints of pain and swelling in case of a lateral ligament injury. In case of ROM restriction, mobilisation therapy may provide help, but combination with exercise therapy is advised. Surgery should be reserved for patients with lateral ligament ruptures to avoid unnecessary invasive treatment and risk of complications. In the prevention of ankle sprains, functional support is effective in patients with both first-time and recurrent LAS, but seems most effective in preventing recurrent sprains. Exercise therapy, however, has only shown a significant preventive effect for recurrent ankle sprains. For first-time LAS, there was mainly a lack of evidence as studies did not explicitly name whether their included population had previously suffered a LAS or not. Additionally, this may be explained by a lack of research on exercise in a population who has never suffered a LAS as exercise is mostly commenced after injury during rehabilitation.

Overall there is no clear evidence on the role of other forms of therapy such as (high-fitted and low- fitted and sports) shoe wear, vibration and electrostimulation therapy in the treatment and prevention of (recurrent) LAS. There are no conclusions on acupuncture since there were no studies that involved a sham acupuncture group. On the exact role of BMI, we cannot provide any conclusive recommendations. Whereas a lower BMI seems to increase the risk of sustaining an initial ankle sprain, a higher BMI seems to be a prognostic factor for persistent complaints and incomplete recovery.

Apart from the side effects reported for NSAIDs usage and complications resulting from surgery, no complications have been reported for functional support devices such as tape or brace.[213] This is despite some known adverse effects such as rashes, which may need more detailed reporting in articles studying such devices.

By development of this CPG on ankle sprains, all current evidence is considered to provide insight into the best evidence-based practice. To ensure readability, all information was categorised, summarised and recommendations provided separately explicating the effectiveness per treatment or preventive modality. Overall, this guideline provides strong evidence per treatment and preventive modality by combining multiple RCTs

Table 8 Final recommendations per intervention modality

Modality	Recommendation	Level of evidence
Predisposing factors	In the treatment of patients with LAS, modifiable risk factors should be identified and, if possible, addressed.	2–3
Prognostic factors	Assessed of prognostic factors during the rehabilitation process in order to address negative modifiable factors.	3
Diagnostics	Late physical examination is advised to come to conclusions on the severity of the ligament damage.	2
RICE	RICE is not advised as treatment modality after a LAS.	2
NSAIDs	NSAIDs may be used to reduce pain and swelling.	2
Immobilisation	Immobilisation should not be used in the treatment of a LAS.	2
Functional support	Functional support is preferred over immobilisation, especially the use of a brace.	2
	For prevention, both tape and brace may be used. Choice of modality should always be based on patient preferences.	1
Exercise	Exercise therapy should be started as soon as possible to recover joint functionality.	1
	For recurrent ankle sprains, exercise should be included in regular training activities as much as possible.	1
Manual mobilisation	Manual mobilisation is only advised in combination with other treatment modalities to enhance the treatment effect.	3
Surgery	Surgery is only advised for patients that require quick recovery, such as professional athletes, or whose complaints are not resolved by conservative treatment to avoid unnecessary invasive treatment on patients that would just as well recover from conservative treatment.	1
Other therapies	Based on current evidence, other modalities than the once mentioned above are not advised.	2
Interprofessional communication	A communication checklist should be used to ensure communication errors.	1
Footwear	No recommendations can be made concerning footwear due to inconclusiveness of evidence.	1
Work resumption	Immediate functional treatment and a return to work schedule are advised to minimise work absenteeism.	3
Sport resumption	Supervised exercises are advised with the focus on proprioception, strength, coordination and function.	1

LAS, lateral ankle sprain; NSAIDs, non-steroidal anti-inflammatory drugs; RICE, Rest Ice Compression Elevation.

showing consistent results. The AGREE II reporting guidelines have been used in an attempt to optimise the quality of this CPG.

Provided evidence may, however, be influenced by publication bias, indicated by the limited amount of evidence on negative effects or treatment without any clinical effect. Level of evidence and bias assessment using GRADEpro were not possible due to the large amount of included studies. As an alternative, each statement was provided with a level of evidence according to tables 1 and 2. There is also the effect of selection bias. Ankle sprains are very common, and many people sustaining LAS do not seek medical advice. Therefore, the effect of 'no intervention' on the outcome after LAS remains unknown. Most contradictory results were found in small studies showing both positive and negative effects, levelling out to a neutral MD or RR. Additionally, most studies only included injured patients, whereas there is some conflict in the evidence of certain preventive measures in patients with first-time LAS. For this, more research is needed to enable adequate comparison between preventive effects based on a history of ankle sprains, preferably within the same study group. The best available evidence has been included in this guideline. However, the preferred approach by both patients and healthcare professionals in the diagnostic process, treatment and prevention of LAS has not. This is due to a lack of evidence on subjective data, apart from patient satisfaction after undergoing a certain treatment. More evidence on this topic may help identify the best treatment strategy per patient.

By including all steps that may be encountered by a patient from the moment of sustaining an ankle sprain up to full recovery, this guideline also includes all procedures considered and possibly performed by healthcare professionals. Thus, this guideline has a clinical focus and may provide support for all healthcare professionals encountering patients with ankle sprain irrespective of the phase of rehabilitation the patient is in. Many of the steps addressed in this guideline are steps in daily clinical practice, whether they are proven effective or not. There is a need for a clear policy that can be implemented worldwide. By updating the guideline on ankle sprains, the first step is taken towards such a policy. Further awareness regarding this guideline, to enable healthcare providers to follow the state-of-the-art recommendations, must be raised by means of scientific publication, scientific referral, congresses and raising awareness among the various professional associations.

Future perspectives and research

This update provides the most recent evidence on diagnostics, treatment and prevention for acute LAS. As more evidence has become available, often of a higher evidence level, this enabled the use of meta-analyses where there was a lack of evidence in the initial guideline. However, not all recommendations were supported by meta-analysis. Also, some recommendations lack evidence from RCTs. A future update might be required if enough new studies become available. Thus this guideline may be updated after 5–10 years to ensure content and recommendations remain up to date using the same methodology and search strategy. If relevant new treatment methods, preventive techniques or other aspects are identified, these will receive appropriate attention depending on their importance for patients who sustained a LAS. In a future update, the methodological quality may be included to formulate conclusions based on the quality and reliability of results, as may be done using the GRADEpro tool.

Future research is required in the field of different functional treatment and prevention strategies, identifying superiority between different types of support and training and for which specific subpopulations these are effective (eg, recurrent or first-time LAS). Additional research may be performed on preferences of patients and healthcare professionals: what do patients prefer on forehand before undergoing treatment and what were their experiences? Which treatments do healthcare professionals prefer and is this dependent on injury severity, and so on, as this may contribute to formulating future recommendations.

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