Ankle Sprains in General Practice
Diagnosis and treatment of persistent complaints

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Ankle Sprains in General Practice: Diagnosis and treatment of persistent complaints

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Chapter 1

General introduction

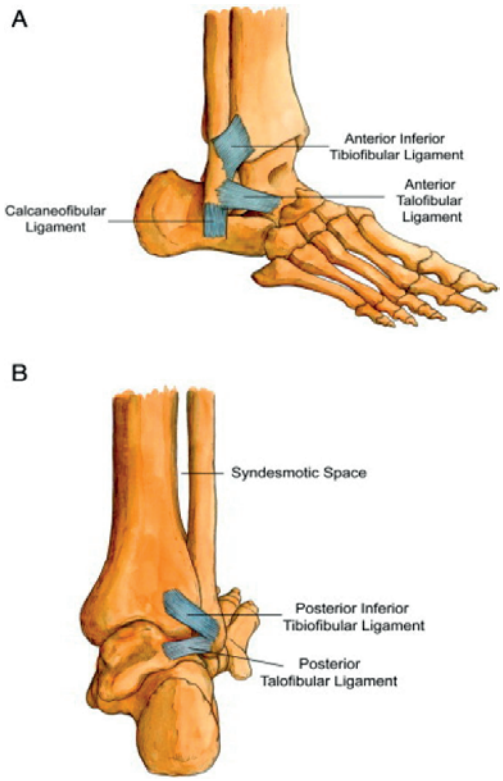
GENERAL INTRODUCTION

In The Netherlands ankle sprains are the most common injuries of the musculoskeletal system.[1] Approximately 680.000 people sustain an acute ankle sprain yearly, where about 290.000 people seek medical care. From these, 130.000 patients visit the general practitioner and 87.000 the physical therapist, while 26.000 patients ask for help at the emergency department of a hospital.[2] Often, in 200.000 people, sprains are due to a sports related injury.[2] The incidence of an ankle sprain in general practice is 8 per 1.000 patients per year, is higher in male than female and higher in younger people.[3] The incidence of a fracture after an ankle sprain is 5% in general practice and up to 20% in emergency departments of hospitals.[3] More than 75% of the ankle injuries are cause by an inversion sprain, leading to a strained or ruptured lateral ankle ligament, often caused by participating in sports.[4, 5] In 33 of 44 sports reviewed, the ankle was the most common site of injury.[5] In the Netherlands annual costs for sport-related ankle sprain are estimated to be € 187 million and persisting complaints are expected to lead to more costs as a result of productively loss and healthcare costs.[6]

In general practice, conservative treatment is mostly used after an ankle sprain, consisting of functional interventions as early mobilization, instructions in use of the ankle, weight bearing, application of ice (RICE), sometimes together with physiotherapy treatment and additional support for the injured ankle (tape, bandage or brace). Mean absenteeism of work after functional treatment for an ankle sprain is about 2,5 weeks.[7] After 6 weeks, 90% of patients has resumed work and up to 90% of patients participating in sports, return to sports at the same level as before the injury in 12 week time.[3] Although in most patients conservative treatment leads to full recovery (ranging from 36% to 85%), persistent complaints have been reported in different studies ranging up to 34%.[7] Patients that have persistent complaints experience either pain, function loss, swelling, a feeling of giving-way, instability, or limitations in daily activities and sports participation or a combination of these. In high risk sports recurrence of ankle sprains is seen up to 80%.[8, 9] When these complaints persist for more than 6 months, the term chronic (lateral) ankle complaints or chronic ankle instability is often used.[10] Regarding these data, we may conclude that an ankle sprain is not an innocent injury and often leads to chronic complaints in general population.[11] It has even been suggested that a single ankle sprain, besides pain and recurrence, can lead to persistent complaints predicting future degenerative cartilage lesions.[12, 13] The longer-term consequence of an ankle sprain can be cartilage damage and lead to early osteoarthritis and result in a poor quality of life and high costs.[13, 14]

Anatomy

More than 75% of the ankle injuries are caused by an inversion sprain, leading to damage at the lateral ankle ligament complex.[3] Most commonly, the anterior talofibular ligament complex generally gets strained or ruptured.[4] Other structures that may be injured caused by an ankle sprain are the calcaneofibular ligament (CFL), the posterior talofibular ligament (PTFL), peroneal tendons, joint capsule, talus and the proprioceptive nerve endings within the surrounding soft tissue. Sometimes damage of syndesmosis or metatarsal V is found.[4]



Anatomy of the ankle: lateral and posterior view

Purpose of the study

Up to 2010 it was still unclear which treatment options were most effective after an acute ankle sprain. We therefore aimed to assess the evidence for the different treatment options after acute ankle sprain. These results were used in the present practical guideline of the Dutch College of General Practitioners on the treatment of acute ankle sprains (edited in 2012).[3] Initial treatment for a lateral ankle sprain is, according to these guidelines, mostly conservative and consists of functional interventions that include

early mobilization with instruction for rest, ice, time period and way of walking, continued weight bearing, and sometimes physiotherapy, together with external support for the ankle (tape, bandage or brace). An identified gap in knowledge was emphasized in the same guideline with respect to evidence on diagnosis and the treatment options for chronic complaints after an ankle sprain. Therefore, we studied systematically the effectiveness of the different types of interventions used for chronic ankle complaints after a lateral ankle sprain.

Regarding diagnosis and treatment of persistent complaints of patients after an lateral ankle sprain, despite the many treatment options applied and available, it is not known whether these persistent complaints are associated with structural changes or abnormalities in the ankle caused by the trauma. Identification of structural abnormalities possibly associated with persistent complaints could provide help in prognosis and choice of treatment for patients with persistent complaints after a lateral ankle sprain in general practice. Radiography is generally regarded as a reliable method for detection of fractures, sclerosis, or osteophytes, but is not suitable for assessment of soft tissue, bone marrow edema, or lesions of cartilage and ligaments. These can be assessed more directly and accurately using magnetic resonance imaging (MRI). Therefore, we aimed to investigate the association between persistent complaints after a lateral ankle sprain and possible structural abnormalities found on radiography and MRI. Further, we studied the impact of a lateral ankle sprain on persistent complaints.

OUTLINE OF THIS THESIS

Chapter 2 presents the results of a systematic review on the effectiveness of adding supervised exercises to conventional treatment compared to conventional treatment alone in patients with acute lateral ankle sprains. **Chapter 3** presents a systematic review on the effectiveness of treatments in case of persistent complaints after an ankle sprain. In **Chapter 4** the results of an observational case control study in primary care are presented investigating the association between persistent complaints after an ankle sprain and structural abnormalities seen by radiography and MRI. In **Chapter 5** we compared the structural abnormalities seen on MRI in subjects with a previous lateral ankle sprain between the injured ankle and the contralateral ankle. The aim of the cross-sectional study, presented in **Chapter 6**, was to determine possible associations between patient history and physical examination and early signs of osteoarthritis on MRI in patients with a previous ankle sprain. In **Chapter 7** the impact of a lateral ankle sprain on functioning, the effect on physical health and the use of medical resources was investigated in patients with persistent complains after an ankle sprain. **Chapter 8** presents the potential differences in the center of pressure (COP) during gait and single leg

stance between patients with persistent complaints and patients without complaints after an ankle sprain. Finally in **Chapter 9** the main findings of the different studies on the course of chronic ankle complaints are presented, the results will be interpreted in view with existing literature and methodological issues will be discussed. Implications for further research and clinical practice of the general practitioner will be given.

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Chapter 2

Effectiveness of additional supervised exercises compared with conventional treatment alone in patients with acute lateral ankle sprains: A systematic review

R.M. van Rijn, J.M. van Ochten, P.A.J. Luijsterburg, M. van Middelkoop, B.W Koes, S.M.A. Bierma-Zeinstra

British Medical Journal 2010; 341: c5688

ABSTRACT

Objective: To summarise the effectiveness of adding supervised exercises to conventional treatment compared with conventional treatment alone in patients with acute lateral ankle sprains

Design: Systematic review

Data sources: Medline, Embase, Cochrane Central Register of Controlled Trials, Cinahl and reference screening.

Study selection: Included studies were randomized controlled trials, quasi-randomized controlled trials, or clinical trials. Patients were adolescents or adults with an acute lateral ankle sprain. The treatment options were conventional treatment alone or conventional treatment combined with supervised exercises. Two reviewers independently assessed the risk of bias, and one reviewer extracted data. Because of clinical heterogeneity we analysed the data using a best-evidence synthesis. Follow-up was classified as short term (up to two weeks), intermediate (two weeks to three months), and long term (more than three months).

Results: 11 studies were included. There was limited to moderate evidence to suggest that the addition of supervised exercises to conventional treatment leads to faster and better recovery, and a faster return to sport at short-term follow-up than conventional treatment alone. In specific populations (athletes, soldiers and patients with severe injuries) this evidence was restricted to a faster return to work and sport only. There was no strong evidence of effectiveness for any of the outcome measures. Most of the included studies had a high risk of bias, with few having adequate statistical power to detect clinically relevant differences.

Conclusion: Additional supervised exercises compared to conventional treatment alone have some benefit for recovery and return to sport in patients with ankle sprain, though the evidence is limited or moderate and many studies are subject to bias.

The results of the present systematic review suggest that further high-quality RCTs should be conducted to determine the effectiveness of additional supervised treatment especially in specific populations such as athletes and patients with severe injuries.

INTRODUCTION

Lateral ligament ankle sprains are one of the most commonly encountered musculoskeletal injuries,[1] with up to 23.000 and 5000 occurring daily in the United States and the United Kingdom respectively.[1, 2] In the Netherlands approximately 600.000 people sustain an ankle injury each year, 120.000 of which are the result of sporting injuries, and of these it is estimated that 43.000 present for medical care.[3, 4] Each year general practitioners in the Netherlands see around 125.000 patients with an ankle sprain, with an incidence of 8 per 1000 patients per year.[5] A recent systematic review evaluated the clinical course of conventionally treated acute ankle sprains and found that after 1 year follow-up 5%-33% of the patients still experienced pain and instability, 34% reported at least one re-sprain, and 15%-64% reported that they had not recovered fully from their initial injury.[6] Despite the large societal effect of these injuries and considering the commonly encountered poor clinical course, the optimal treatment and rehabilitation has yet to be established.

As part of a formal rehabilitation protocol, balance training and coordination exercises could reduce proprioceptive deficits, symptoms of giving way, and risk of re-injury, and improve postural control.[7-9] Different reviews have shown that functional treatment of the ankle (defined as the use of an elastic bandage, tape, lace-up ankle support or semi-rigid ankle support) results in a quicker return to sports and work compared with immobilisation, that there is no evidence that surgery is better than functional treatment or immobilisation, and that a semi-rigid ankle support is preferable to the use of an elastic bandage or tape.[10-12]

Protection of the ankle by means of functional treatment (elastic bandage, tape, lace-up ankle support or semi-rigid ankle support) is needed to avoid stress to the scar tissue in the inflammatory phase of tissue healing. In the subsequent phases, the proliferative phase and the maturation phase, the emphasis lies on the alignment and strengthening of the newly formed collagen fibers.[13] Physical therapists use this knowledge about tissue healing to construct an exercise programme.[14] The effectiveness of supervised exercises as administered by a physical therapist, however, is uncertain. We carried out a systematic review is to examine the effectiveness of conventional treatment (non-surgical treatment such as immobilisation, non-supervised treatment involving exercise instructions or use of external support) combined with supervised exercises with conventional treatment alone for the rehabilitation of acute lateral ankle sprains. As the effectiveness can differ between populations[15, 16] and can depend on the type of conventional treatment used, the severity of the injury, or the exposure to activities associated with a high risk for (re-) sprains, we also evaluate the added value of supervised exercises in specific populations as well as by type of conventional treatment.

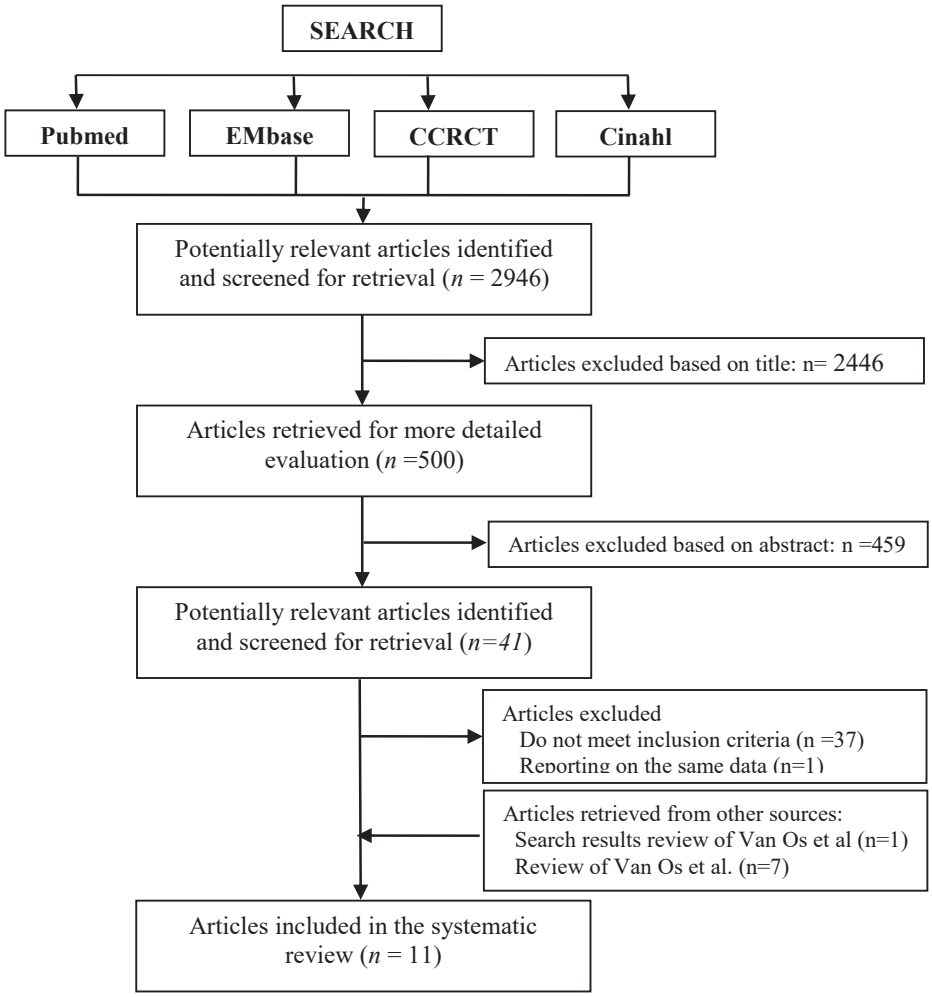

Figure 1. Flow chart of the selected articles. CCRCT = Cochrane Central Register of Controlled Trials

METHODS

Literature search

As starting-point for our review we identified all included references of an earlier review by van Os et al.[17], which covered the same topic with a literature search until March 2004. We then searched MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials and Cinahl, from March 2004 to July 2010, using the search strategy as supplied by van Os et al (Appendix 1).[17]

Two reviewers (RMvR and PAJL) independently selected the articles, initially based on title and abstract. For final inclusion the articles had to fulfil all of the following criteria: 1)

the adolescent and adult subjects in the study had to have an acute lateral ankle sprain, 2) at least one of the treatment options consisted of a conventional treatment (defined as either immobilisation, such as in a plaster cast, non-supervised treatment involving exercise instructions or use of external support), 3) at least one of the treatment options consisted of conventional treatment combined with supervised exercises, 4) the study design had to be either a randomised controlled trial, a quasi-randomised controlled trial, or a controlled clinical trial and 5) studies involving post-surgical treatment or treatment of recurrent ankle injuries or chronic instability were excluded. The help of a native speaker was obtained for studies published in languages other than English, German or Dutch. A consensus method was used to resolve disagreements. Finally, the references of all included studies were checked for possible relevant articles.

Assessment of risk of bias

Pairs of reviewers (from RMvR, JvO and MvM) independently assessed the risk of bias of the included studies, using the Cochrane collaboration's tool (RMvR assessed all studies, except the study of which he is the first author; RMvR was not involved in any decision regarding this trial).[18] We adapted this tool for our review to give five domains, with 11 items in total (Appendix 2). Each item was rated as 'yes', 'no', or 'unsure'. Disagreements were resolved in a consensus meeting. Studies with 6 or more points were regarded as having a low risk of bias. The interpretation of the risk of bias tool was pre-tested in two studies that focused on the effectiveness of physical therapy treatment in patients with low back pain (a condition outside the scope of this review).

Data extraction

One reviewer (RMvR) extracted relevant data from the included studies. Study characteristics extracted were information on target population (age, gender, setting, injury grade, sample size), treatment, outcome measures, and duration of follow-up. Outcome measures extracted, if present, were pain, instability (feeling of 'giving way'), re-sprain, return to sport and work, recovery and functional scores. In case of uncertainty about the extracted data from the included studies a second reviewer (MvM) was consulted.

The core findings in each article were expressed as estimates, relative risks (RR) or effect sizes (ES), with corresponding 95% confidence interval. Where possible, these measures were directly extracted from the article. For articles in which this information was not presented, these measures were calculated if enough data was available. Outcome measures were presented according to follow-up time, and therefore grouped into the following categories: 1) Short-term (within 2 weeks of randomization), 2) Intermediate-term (between 2 weeks and 3 months follow-up, and 3) long-term (more than 3 months follow-up).[6]

Table 1. Results of the risk of bias assessment of the individual studies with scores per item. + = yes; - = no; ? = unsure

	1.Adequate randomization?	2. Allocation concealed?	3. Patient Blinded?	4. Care provider blinded?	5. Outcome assessor blinded?	6. Drop-out rate described?	7. Intention-to-treat analysis?	8. Groups similar at baseline?	9. Co-interventions avoided?	10. Compliance acceptable?	11. Timing of outcome assessment similar?	Total Score
Basses et al.[22]	+	?	-	-	-	+	?	-	?	+	?	3
Brooks et al.[23]	?	?	-	-	-	-	?	?	+	?	+	2
Holme et al.[24]	+	?	-	-	-	+	+	+	?	?	+	4
Hultman et al.	-	?	-	-	-	-	?	?	?	?	+	1
Karlsson et al.[21]	?	?	-	-	-	+	?	?	?	?	-	1
Nilsson.[25]	?	?	-	-	-	+	+	?	-	?	-	2
Oostendorp.[26]	?	?	-	-	-	?	?	?	?	?	+	1
Reinhardt et al.[27]	?	?	-	-	-	+	?	?	?	?	+	2
Roycroft et al.[28]	?	?	-	-	-	-	?	?	?	?	+	1
Van Rijn et al.[20]	+	+	-	-	-	+	+	?	?	+	+	6
Wester et al.[29]	+	?	-	-	-	-	?	?	+	?	+	3

Data analysis

Our main comparison was any conventional treatment versus conventional treatment with additional supervised exercises. Our secondary objective was to evaluate the results of the main comparison in vulnerable populations with a high risk for (re-)sprains (such as athletes[15]) or with increased risk for slower improvement (such as those with a severe injury[16]). Finally, we classified results by type of conventional treatment. When studies were clinically homogenous concerning population, intervention and outcome measures, we statistically pooled data. In cases of clinically heterogeneity we analysed the data using a best-evidence synthesis.[19] This rating system consists of 4 levels of scientific evidence based on the quality of the studies: 1) strong evidence; provided by generally consistent findings in multiple randomised controlled trials assessed as having low risk of bias, 2) moderate evidence; provided by generally consistent findings in one RCT assessed as having low risk of bias, and one or more RCTs assessed as having high risk of bias or by generally consistent findings in multiple RCTs assessed as having high risk of bias, 3) limited or conflicting evidence; only one randomised controlled trial (either assessed as having low or high risk of bias) or inconsistent findings in multiple RCTs, and 4) no available evidence; no randomised controlled trials.

RESULTS

Literature search

Our search resulted in 2946 potentially relevant articles. From titles and abstract we identified 41 articles. Of these, four articles met our inclusion criteria after reviewing full text. Multiple publications were found, reporting on the same data, for Van Rijn et al..[16, 20] We used information from both publications for the assessment of methodological quality and data extraction, but only the first or most prominent publication was used for citation of these studies. We also went through the original search results of an earlier review of Van Os et al.[17] on the same topic and found one additional article.[21] Combined with the articles already included in the review of Van Os et al.[17] a total of 11 articles were included in this review. (Figure 1)

Assessment of risk of bias

Figure 2 shows the overall assessment of risk of bias, and table 1 shows the assessment in individual studies. The initial agreement of the reviewers on the total assessment of risk of bias was 80.2% (97 of 121 items). Any initial disagreements were solved in a consensus meeting. Ten studies were assessed as having high risk of bias[21-29] and one study was assessed as having low risk of bias.[20] The most prevalent shortcomings were found in the items about blinding (patient, care provider and outcome assessor), allocation concealment and similarity of treatment groups at baseline.

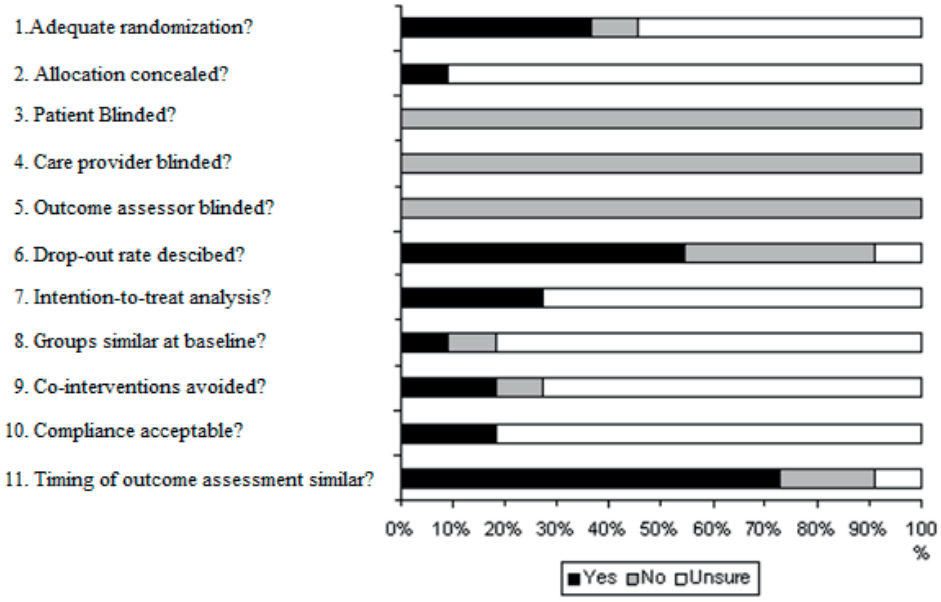

Figure 2. Results of risk of bias assessment. Frequency of scores (%) .

Included studies

Table 2 shows the characteristics of the included studies. Conventional treatment in the included studies consists of a variety of therapies, namely: no treatment, ice application, partial immobilisation (tape, brace, or bandage), complete immobilisation (plaster cast), a home exercise program, instructions for early ankle mobilisation, or a combination of these treatments. Supervised exercises consist of visits to a physical therapist in which the patients focused on strength, mobility and balance exercises whether or not combined with the use of a balance or wobble board. As, the included studies were considered too heterogeneous to perform a meta-analysis, we refrained from pooling and performed a best evidence synthesis (Table 3). Also, the contrast between the types of conventional treatments was too small to execute an analysis grouped by type of treatment. For that reason, we describe the results of the main comparison per outcome measure, but evaluated the results, were possible, by distinguishing between high-risk populations. Six studies included a vulnerable population consisting of patients active in sports more than two hours a week[29], patients who sustained an ankle sprain during sport[24, 26], patients active in sports at a recreational or competitive level[21], recruits and professional soldiers[27], and patients with a severe injury[20]. Table 4 presents the results of the studies per outcome measure classified by duration of follow-up.

Table 2. Characteristics of the included studies

Author	Study population	Conventional treatment	Supervised treatment
Basset et al.[22]	47 (52) patients with an acute ankle sprain (first-time or recurrent) recruited from 4 physical therapy clinics in middle to low socioeconomic suburbs: 60% male; mean age 30±12.4 yr; injury grade: 38% mild, 51% moderate, 11% severe; re-sprain 55%	Home based intervention program - Small home program of no more than 4 simple activities - Equipment such as strapping tape, Tubigrip for compression, Thera-band resistance bands, and wobble boards. - Treatment booklet; information about structure of the ankle, ankle sprains, diary grids, progress sheets, adherence-enhancing, and the 3 treatment phases: 1. Acute (36-48 hrs): RICE, and active ankle movements within the limits of pain 2. Mobilizing (10-14 days): mobilizing and strengthening exercises, calf and heel stretches, ankle strapping/taping 3. Strengthening (10-14days): Thera-band resistance, body-weight resistance in standing, one-leg standing, standing on wobble board, weight bearing activities, ankle strapping	Clinic based intervention program - Small home program of no more than 4 simple activities - Physical therapist treated symptoms, and supervised the activities/exercises of a 3 phase physical therapy program: 1. Acute (36-48 hrs): RICE, and active ankle movements within the limits of pain 2. Mobilizing (10-14 days): mobilizing and strengthening exercises, calf and heel stretches, ankle strapping/taping 3. Strengthening (10-14days): Thera-band resistance, body-weight resistance in standing, one-leg standing, standing on wobble board, weight bearing activities, ankle strapping
Brooks et al.[23]	102 (241) patients with inversion injury, with a talar tilt <15°, who attended the local emergency department: age 12-65 yr	Treatment groups: 1. No treatment, no support or only a minimal bandage 2. Double Tubigrip support to wear during daytime and advised to remove in bed at night 3. Ankle completely immobilized in a below-knee plaster-of-Paris cast, but patients were encouraged to bear weight as soon as possible	First day or within 48 hr of presentation: - iced foot bath, mobilization, instruction in normal gait. Second or third visit: - wobble board exercises Treatment was considered complete when the patient could tolerate 10 minutes on the wobble board

Table 2. Characteristics of the included studies (continued)

Author	Study population	Conventional treatment	Supervised treatment
Holme et al.[24]	71 (92) patients, all recreational athletes, with an ankle sprain sustained during sports who attended the local emergency department: 62% male; mean age 26.5 yr; injury grade: 30% mild, 53% moderate, 17% severe	Information regarding early ankle mobilization, including strength, mobility, and balance exercises	Information regarding early ankle mobilization, including strength, mobility, and balance exercises, combined with supervised group physical therapy rehabilitation (1hr, twice weekly): - comprehensive balance exercises on both legs - figure-of-eight running - standing on a balance board and catching a ball - standing on the outside of the feet - standing on the inside of the feet with open and closed eyes
Hultman et al.[30]	65 (115) with an ankle sprain who attended emergency department: 54% male; mean age 35 (18-65) years	Examination of the ankle, initial weight-unloading with crutches, elastic wrap, and verbal and/or written information from the attending physician or nurse about mobilization and early weight-bearing, followed by two visits to the physiotherapist (6 weeks, 3 months): - early range of motion training - weight-bearing on injured ankle - balance and strength training - instructions for home-exercises	Examination of the ankle, initial weight-unloading with crutches, elastic wrap, and verbal and/or written information from the attending physician or nurse about mobilization and early weight-bearing, followed by four visits to the physiotherapist (baseline, 3 weeks, 6 weeks, 3 months): - early range of motion training - weight-bearing on injured ankle - balance and strength training - instructions for home-exercises
Karlsson et al.[21]	84 (86) consecutive patients, active in sports on recreational or competitive level, with ligament ruptures of the ankle: 66% male; mean age 22 (16-38) yr; injury grade: 59% moderate, 41% severe	Elastic wrapping, partial weight bearing and crutches until the pain subsided	Functional treatment - compression pads - early weight-bearing Range of motion training - dorsal and plantar flexion - supination proprioceptive training - standing on one leg with eyes closed - walking along zig-zag lines Strength training - rubber cords - weight boots

Table 2. Characteristics of the included studies (continued)

Author	Study population	Conventional treatment	Supervised treatment
Nilsson[25]	118 (180) patients with injury to the lateral ankle ligaments (classified as 'rupture'or 'no rupture'), occurred within the last 6 hr, who attended the local emergency department: 59% male; mean age 33.6 (15-66) yr	Elastic wrapping only (n=59)	Elastic wrapping and cryotherapy combined with physiotherapy starting on the 5th day after injury: - limbering exercises of the ankle - ultrasound treatment to the lateral side of the ankle - coordination exercises - strengthening exercises of the fibular muscles (n=59) Each session lasted 45 min, and was given daily until patient was symptom free or had received 10 treatments.
Oostendorp[26]	24 (24) patients with inversion injury of the ankle, sustained during volleyball, basketball, handball or soccer, who attended physical therapy practices: 67% male; mean age 22.1 (15-30) yr	Cryotherapy, compression bandage and minimal weight bearing followed by 6wk tape bandage	Cryotherapy, compression bandage and minimal weight bearing followed by 6wk tape bandage combined with a standardized progressive training program (3 physical therapy sessions a week, daily home exercises): stability exercises - disturbance in balance - variation in posture - visual control) isometric strengthening exercises - manual resistance
Reinhardt et al.[27]	72 (80) patients, consisting of recruits and professional soldiers, with acute ankle sprain: mean age 22.6 yr	Early functional treatment: - Aircast-brace - non-weight bearing - cryotherapy - elevation for 3-5 days	Early functional treatment: - Aircast-brace - non-weight bearing - cryotherapy - elevation for 3-5 days 6 physical therapy sessions: - proprioceptive training (balance board, rough terrain) - limbering exercises - strengthening exercises - home exercises (n=47)

Table 2. Characteristics of the included studies (continued)

Author	Study population	Conventional treatment	Supervised treatment
Roycroft et al.[28]	43 (98) patients with inversion injurie of the ankle who attended the local emergency department: injury grade: 47.5% mild, 52.5% moderate	Wool and elastoplasts bandage or plaster of Paris backslab, none weight bearing (n=37)	Immediate active treatment (RICE) and full weight bearing, after 24 hr referred to physical therapy: - ultrasound - taping - tubigrip support - mobilization and rehabilitation (n=43)
Van Rijn et al.[20]	102 (107) patients with an acute lateral ankle sprain, who attended the GP or local emergency department: 58% male; mean age 37.0 yr; injury grade 42% mild, 40% moderate, 4% severe, 14% unknown	Early ankle mobilization, home exercises, early weight bearing, and tape, bandage or brace (n=53)	Early ankle mobilization, home exercises, early weight bearing, and tape, bandage or brace Progressive training program supervised by a physiotherapist (max. 9 ½hr sessions, within 3 months): - balance exercises - walking - running - jumping (n=49)
Wester et al.[29]	48 (61) patients, active in sports >2 hr/week, with a primary ankle sprain who attended the local emergency department: 60% male; mean age 25 (±7.2) yr; injury grade: moderate	Compression bandage for 1 wk, leg elevation and immobilization for 2 days, avoiding activities straining the lateral ligaments, and return to sports activities was not permitted until ADL were possible without pain.	Compression bandage for 1 wk, leg elevation and immobilization for 2 days, avoiding activities straining the lateral ligaments, and return to sports activities was not permitted until ADL were possible without pain, 12 wk training program (15 min/day), using a wobble board

EFFECTIVENESS OF SUPERVISED EXERCISES

Pain

Four studies described pain as an outcome measure, three had a high risk of bias[25, 26, 29], and one had a low risk of bias.[20] Pain was measured with a visual analogue scale[20, 26], or by presenting the number of patients reporting pain.[25, 29] Two studies measured pain intensity on several occasions (at rest, during walking, and during sports)[20, 29], whereas the other studies did not specify pain intensity. Conventional treatment was similar in three out of four studies. Oostendorp[26] used a more reserved policy in the first week of rehabilitation with cryotherapy, compression bandage and minimal weight bearing, whereas the other studies promoted early ankle mobilisation or early weight bearing. Oostendorp[26] also assessed the effect of additional supervised exercises at intermediate follow-up, whereas the other studies found no significant difference between treatment groups. Therefore, the evidence of effectiveness is conflicting. None of the studies that described pain as an outcome measure found a significant difference between treatment groups at short-term[25, 29] and long-term[20, 25, 26] follow-up, resulting in moderate evidence of no effectiveness.

In a subgroup of studies of athletes, we found conflicting evidence of effectiveness (intermediate-term) and moderate evidence of no effectiveness (short- and long-term) was found.[26, 29] There was also limited evidence of effectiveness in patients with severe injuries at intermediate follow-up.[20]

Instability

Five studies, four with high risk of bias[25-27, 29] and one with a low risk of bias[20], presented instability as an outcome measure to evaluate the effectiveness of additional supervised exercises. Four studies use a questionnaire to measure instability or the 'feeling of giving way'. [20, 25, 27, 29] One study did not provide information measuring instability[26]. All studies provided the number of patients reporting instability. Conventional treatment was similar in three of five studies. Oostendorp[26] and Reinhardt et al.[27], used a more reserved policy in the first week of rehabilitation by prescribing cryotherapy, compression bandage or aircast brace, and minimal weight bearing, whereas the other studies promoted early ankle mobilisation or early weight bearing as much as pain allowed. We could not calculate relative risks from the study of Wester et al,[29] though they reported a significant difference in the number of patients with instability at long-term follow-up. No differences were found in the other studies concerning instability.[20, 25, 29] Therefore, the evidence for effectiveness was conflicting at long-term follow-up. None of the studies that described instability as an outcome measure found a significant difference between treatment groups at intermediate-term follow-up[20 26 27], resulting in moderate evidence of no effectiveness.

In a subgroup of studies of athletes or soldiers there was moderate evidence of no effectiveness in the intermediate and conflicting evidence of effectiveness in the long-term.[26, 27, 29] There was limited evidence of effectiveness in patients with severe injuries at intermediate follow-up.[20]

Table 3. Results of the best evidence synthesis

Outcome	Follow-up	Studies	Effectiveness #	Best evidence synthesis
Pain	Short-term	2 HR RCT[25 29]	No, No	Moderate evidence no effectiveness
	Intermediate-term	2 HR RCT[26 29] 1 LR RCT[20]	Yes, No No	Conflicting evidence
	Long-term	2 HR RCT[25 26] 1 LR RCT[20]	No, No No	Moderate evidence no effectiveness
Instability	Short-term	-	-	No available evidence
	Intermediate-term	2 HR RCT[26 27] 1 LR RCT[20]	No, No No	Moderate evidence no effectiveness
	Long-term	3 HR RCT[25 26 29] 1 LR RCT[20]	Yes, No, No No	Conflicting evidence
Recovery	Short-term	1 HR RCT[28]	Yes	Limited evidence effectiveness
	Intermediate-term	1 LR RCT[20]	No	Limited evidence no effectiveness
	Long-term	1 LR RCT[20]	No	Limited evidence no effectiveness
Function	Short-term	2 HR RCT[22 30]	No, Yes	Conflicting evidence
	Intermediate-term	-	-	No available evidence
	Long-term	1 HR RCT[21]	No	Limited evidence no effectiveness
Re-sprain	Short-term	-	-	No available evidence
	Intermediate-term	1 HR RCT[27] 1 LR RCT[20]	No No	Moderate evidence no effectiveness
	Long-term	3 HR RCT[24 25 29] 1 LR RCT[20]	Yes, No, No No	Conflicting evidence
Return to work	Short-term	5 HR RCT[21 23 25 27 30]	NA, Yes, NA, Yes, No	Conflicting evidence
	Intermediate-term	1 HR RCT[26]	No	Limited evidence no effectiveness

Table 3. Results of the best evidence synthesis (continued)

Outcome	Follow-up	Studies	Effectiveness #	Best evidence synthesis
	Long-term	1 HR RCT[26]	No	Limited evidence no effectiveness
Return to sport	Short-term	2 HR RCT[21 27]	Yes, NA	Limited evidence effectiveness
	Intermediate-term	1 HR RCT[26]	Yes, No*	Conflicting evidence
	Long-term	1 HR RCT[26]	No	Limited evidence no effectiveness

HR = High risk of bias; LR = Low risk of bias; RCT = Randomized controlled trial; NA = Not applicable, due to incomplete data

#: No effectiveness = No difference of effectiveness between treatment groups; Yes effectiveness = Effectiveness of conventional treatment combined with supervised exercises compared to conventional treatment alone

*: One study described two follow-up moments (6 and 12 weeks) measuring 'return to sport' which are part of the intermediate term follow-up. No differences between treatment groups were found at 6 weeks, whereas a statistically significant difference was found at 12 weeks follow-up in favor of supervised exercises

Re-sprain

Five studies, one with low risk of bias[20] and four with high risk of bias[24, 25, 27, 29], reported the number of re-sprains sustained during intermediate and long-term follow-up. In three of these studies the study participants were recreational athletes, patients who were active in sports over two hours of a week, and recruits or professional soldiers.[24, 27, 29] Conventional treatment was similar in four out of five studies. The studies of van Rijn et al.[20], Holme et al.[24], Nilsson[25] and Wester et al.[29] promoted early ankle mobilisation or early weight bearing as much as pain allowed, whereas the study by Reinhardt et al.[27] prescribed a more preserved policy (cryotherapy, compression bandage, minimal weight bearing). Holme et al.[24] found significantly fewer re-sprains in the group treated with early ankle mobilisation combined with supervised balance exercises. The other studies found no difference between the treatment groups regarding the number of re-sprains, resulting in conflicting evidence for effectiveness at long-term follow-up.[20, 25, 29] None of the studies showed a difference between treatment groups in the number of re-sprains reported at intermediate follow-up. Therefore, there is moderate evidence of no effectiveness. In a subgroup of studies in which participants were athletes or soldiers, there was moderate evidence of no effectiveness in the intermediate-term and conflicting evidence for effectiveness in the long-term.[24, 27, 29] There was also limited evidence for no effectiveness of additional supervised exercises at long-term follow-up regarding the number of re-sprains in patients with severe injuries.[20]

Recovery

Two studies described recovery as an outcome measure to determine the effectiveness of additional supervised exercises.[20, 28] Recovery was measured with a visual analogue scale[20] or by calculating the mean period in days to recovery.[28] Conventional treatment differed between studies; a wool and elastoplast bandage or a plaster of Paris backslab with non-weight bearing[28] versus early ankle mobilisation and early weight bearing with externally protection of tape, bandage or brace.[20] We could not calculate the effect size in the study by Roycroft et al., which had a high risk of bias.[28] Patients receiving active treatment, however, reported a significantly shorter recovery period compared to patients receiving conservative treatment at short term-follow-up (11.9 days versus 18.6 days).

At intermediate-term and long-term follow-up only one study (with a low risk of bias) reported on recovery, but found no differences between treatment groups.[20] There is therefore limited evidence for effectiveness at short-term follow-up and limited evidence for no effectiveness at intermediate-term and long-term follow-up.

van Rijn and colleagues also performed a subgroup analysis in patients with severe injuries. In this population they found limited evidence for effectiveness at short-term follow-up and limited evidence for no effectiveness at intermediate and long-term follow-up.

Table 4. Results of the individual studies per outcome measure classified by duration of follow-up.

Author	Outcome	Follow-up	Conventional treatment	Supervised treatment	RR *or* ES (95% CI)
Pain					
Short term					
Nillson[25]	Pain, *n (%)*	7 days	38 (64.4)	31 (52.5)	RR 0.82 (0.60-1.11)
Wester[29]	Pain, *n (%)*				
	At rest	1 wk	7 (29)	12 (50)	RR 1.71 (0.82-3.60)
	Walking	1 wk	20 (83)	20 (83)	RR 1.00 (0.78-1.29)
	Sports	1 wk	23 (96)	23 (96)	RR 1.00 (0.89-1.13)
Intermediate-term					
Oostendorp[26]	Pain (VAS 0-100), *mean (SD)*	6 wk	25 (5)	18 (7)	ES 1.11 (0.25-1.97)*
		12 wk	15 (7)	9 (8)	ES 0.77 (-0.06-1.60)
Van Rijn[20]	Pain (VAS 0-10), *mean (SD)*				
	At rest[#]	3 mth	0.4 (1.0)	0.3 (1.2)	ES 0.14 (-0.28-0.56)
	Walking flat[#]	3 mth	0.4 (1.0)	0.4 (1.3)	ES 0.04 (-0.38-0.47)
	Walking rough[#]	3 mth	1.3 (1.7)	0.8 (1.3)	ES 0.30 (-0.13-0.72)
	Subgroup AFS≤40 (severe)				
	At rest	8 wk	1.5 (2.6)	0.5 (1.0)	ES 0.50 (-0.03-1.03)
	Walking flat	8 wk	1.2 (1.9)	0.6 (1.2)	ES 0.37 (-0.16-0.90)
	Walking rough	8 wk	3.1 (2.4)	1.7 (1.9)	ES 0.64 (0.10-1.17)*
	Subgroup AFS>40 (mild)				
	At rest	8 wk	0.6 (1.5)	0.2 (0.7)	ES 0.31 (-0.27-0.89)
	Walking flat	8 wk	0.5 (1.5)	0.3 (0.6)	ES 0.17 (-0.41-0.75)
	Walking rough	8 wk	1.5 (2.3)	1.1 (1.7)	ES 0.19 (-0.39-0.77)

Table 4. Results of the individual studies per outcome measure classified by duration of follow-up. (continued)

Author	Outcome	Follow-up	Conventional treatment	Supervised treatment	RR *or* ES (95% CI)
Wester[29]	Pain, *n (%)*				
	At rest	6 wk	0 (0)	1 (4)	NA
		12 wk	1 (4)	0 (0)	NA
	Walking	6 wk	5 (21)	6 (25)	RR 1.20 (0.42-3.41)
		12 wk	1 (4)	1 (4)	RR 1.00 (0.07-15.08)
	Sports	6 wk	18 (75)	18 (75)	RR 1.00 (0.72-1.39)
		12 wk	7 (29)	4 (17)	RR 0.57 (0.19-1.70)
Long-term					
Nillson[25]	Pain, *n (%)*	3-6 mth	19 (32.2)	18 (30.5)	RR 0.95 (0.56-1.62)
		3 yr	8 (15.7)	5 (9.4)	RR 0.60 (0.21-1.72)
Oostendorp[26]	Pain (VAS 0-100), *mean (SD)*	24 wk	10 (6)	6 (4)	ES 0.76 (-0.07-1.59)
Van Rijn[20]	Pain (VAS 0-10), *mean (SD)*				
	At rest[#]	12 mth	0.3 (0.8)	0.3 (0.9)	ES 0.02 (-0.44-0.48)
	Walking flat[#]	12 mth	0.2 (0.7)	0.3 (0.9)	ES -0.10 (-0.56-0.36)
	Walking rough[#]	12 mth	0.8 (1.4)	0.9 (2.1)	ES -0.05 (-0.51-0.41)
	Subgroup AFS≤40 (severe)				
	At rest	12 mth	0.4 (0.8)	0.3 (0.9)	ES 0.12 (-0.41-0.64)
	Walking flat	12 mth	0.2 (0.7)	0.3 (1.0)	ES -0.11 (-0.64-0.41)
	Walking rough	12 mth	1.0 (1.5)	0.9 (2.3)	ES 0.05 (-0.47-0.57)
	Subgroup AFS>40 (mild)				
	At rest	12 mth	0.1 (0.6)	0.4 (0.9)	ES -0.39 (-0.98-0.19)
	Walking flat	12 mth	0.3 (0.8)	0.1 (0.5)	ES 0.29 (-0.29-0.87)
	Walking rough	12 mth	0.8 (1.5)	1.0 (2.1)	ES -0.11 (-0.69-0.47)
Instability					
Intermediate term					
Oostendorp[26]	Fear of giving way, *n (%)*	6 wk	8 (67)	3 (25)	RR 0.38 (0.13-1.08)
		12 wk	5 (42)	2 (17)	RR 0.40 (0.10-1.67)
Reinhardt[27]	Instability, *n (%)*	3 mth	5 (15)	2 (4)	RR 0.28 (0.06-1.36)
Van Rijn[20]	Instability, *n (%)*	3 mth	32 (65)	34 (64)	RR 1.02 (0.76-1.36)
	Instability (VAS 0-10), *mean (SD)* *Subgroup AFS≤40 (severe)*				
	Walking flat	8 wk	1.4 (1.6)	0.3 (0.8)	ES 0.86 (0.31-1.40)*
	Walking rough	8 wk	2.8 (2.1)	1.6 (1.6)	ES 0.63 (0.10-1.17)*
	Subgroup AFS>40 (mild)				
	Walking flat	8 wk	0.7 (1.2)	0.4 (0.9)	ES 0.27 (-0.31-0.86)
	Walking rough	8 wk	1.6 (2.1)	1.2 (1.4)	ES 0.22 (-0.37-0.80)
Long-term					
Nilsson[25]	Instability, *n (%)*	3-6 mth	12 (20.3)	14 (23.7)	RR 1.17 (0.59- 2.30)
		3 yr	12 (23.5)	7 (13.2)	RR 0.56 (0.24-1.31)
Oostendorp[26]	Fear of giving way, *n (%)*	24 wk	5 (42)	1 (8)	RR 0.20 (0.03-1.47)
Van Rijn[20]	Instability, *n (%)*	12 mth	26 (53)	30 (57)	RR 1.06 (0.75-1.52)

Table 4. Results of the individual studies per outcome measure classified by duration of follow-up. (continued)

Author	Outcome	Follow-up	Conventional treatment	Supervised treatment	RR *or* ES (95% CI)
	Instability (VAS 0-10), *mean (SD)*				
	Subgroup AFS≤40 (severe)				
	Walking flat	12 mth	0.4 (0.8)	0.4 (1.6)	ES 0.00 (-0.52-0.52)
	Walking rough	12 mth	1.4 (1.5)	1.4 (2.5)	ES 0.00 (-0.52-0.52)
	Subgroup AFS>40 (mild)				
	Walking flat	12 mth	0.3 (0.7)	0.5 (1.5)	ES -0.17 (-0.75-0.41)
	Walking rough	12 mth	0.7 (1.3)	1.5 (2.6)	ES -0.39 (-0.98-0.19)
Wester[29]	Instability, *n (%)*	230 days	6 (25)	0 (0)	NA
Re-sprain					
Intermediate term					
Reinhardt[27]	Re-sprain, *n (%)*	3 mth	4 (12)	1 (2)	RR 0.18 (0.02-1.55)
Van Rijn[20]	Re-sprain, *n (%)*	3 mth	14(27)	10(23)	RR 0.86 (0.43-1.75)
	Subgroup AFS≤40 (severe)	8 wk	10 (36)	6 (21)	RR 0.60 (0.25-1.43)
	Subgroup AFS>40 (mild)	8 wk	2 (8)	7 (33)	RR 4.14 (0.97-17.95)
Long-term					
Holme[24]	Re-sprain, *n (%)*	12 mth	11 (28.9)	2 (6.9)	RR 0.24 (0.06-0.99)*
Nilsson[25]	Re-sprain, *n (%)*	3-6 mth	5 (9)	6 (10)	RR 1.20 (0.39-3.72)
		3 yr	9 (18)	9 (17)	RR 0.96 (0.42-2.23)
Van Rijn[20]	Re-sprain, *n (%)*	12 mth	16(31)	13(29)	RR 0.94 (0.51-1.73)
	Subgroup AFS≤40 (severe)	12 mth	12 (43)	9 (32)	RR 0.75 (0.38-1.49)
	Subgroup AFS>40 (mild)	12 mth	5 (20)	8 (38)	RR 1.90 (0.73-4.95)
Wester[29]	Re-sprain, *n (%)*	230 days	13(54)	6(25)	RR 0.46 (0.21-1.01)
Recovery					
Short-term					
Roycroft[28]	Mean recovery period (days)		18.6	11.9	NA
Intermediate term					
Van Rijn[20]	Recovery (VAS 0-10), *mean (SD)*	3 mth	7.8 (2.4)	8.2 (2.4)	ES 0.17 (-0.22-0.55)
	Subgroup AFS≤40 (severe)	8 wk	6.6 (2.0)	7.2 (2.1)	ES 0.29 (-0.24-0.82)
	Subgroup AFS>40 (mild)	8 wk	7.7 (2.3)	7.0 (2.9)	ES -0.27 (-0.85-0.32)
Long-term					
Van Rijn[20]	Recovery (VAS 0-10), *mean (SD)*	12 mth	8.6 (1.9)	8.3 (2.8)	ES -0.13 (-0.51-0.26)
	Subgroup AFS≤40 (severe)	12 mth	8.7 (1.6)	8.4 (2.4)	ES -0.15 (-0.67-0.38)
	Subgroup AFS>40 (mild)	12 mth	8.7 (2.1)	9.2 (1.9)	ES 0.24 (-0.34-0.83)
Function					
Short-term					
Basset[22]	LLTQ recreational, *mean (SD)*	10-14	8.2 (7.2)	12.0 (10.1)	ES -0.43 (-1.02-0.17)
	LLTQ ADL, *mean (SD)*	days	1.8 (3.9)	2.3 (3.6)	ES -0.13 (-0.72-0.46)
	Motor activity scale, *mean (SD)*	10-14 days	5.7 (1.1)	5.1 (1.3)	ES 0.49 (-0.11-1.09)
		10-14 days			

Table 4. Results of the individual studies per outcome measure classified by duration of follow-up. (continued)

Author	Outcome	Follow-up	Conventional treatment	Supervised treatment	RR *or* ES (95% CI)
Hultman[30]		FAOS	NA	NA	NA
Long-term					
Karlsson[21]	Excellent functional results, *n (%)*	12-24 mth	34 (87)	41 (91)	RR 0.78 (0.23-2.70)
Return to work					
Short term					
Brooks[23]	Days off work (days), *n*		I 5.1/ II 7.5 / III 14.0	6.0	NA
Hultman[30]	Days off work (days), *mean (SD)*		6.1 (7.4)	4.6 (6.1)	ES 0.22 (-0.34-0.77)
Karlsson[21]	Mean sick leave (days), *mean (SD)*		10.2 (6.8)	5.6 (4.2)	ES 0.82 (0.37-1.27)*
Nilsson[25]	Mean sick leave (days)		12.7	11.5	NA
Reinhardt[27]	Return to work (days), *mean (SD)*		8.7 (3.1)	5.7 (3.1)	ES 0.96 (0.49-1.43)*
Intermediate term					
Oostendorp[26]	Return to work, *n (%)*	6 wk 12 wk	10 (85) 11 (88)	10 (86) 11 (91)	RR 1.00 (0.70-1.43) RR 1.00 (0.79-1.27)
Long-term					
Oostendorp[26]	Return to work, *n (%)*	24 wk	11(91)	11(94)	RR 1.00 (0.79-1.27)
Return to sport					
Short-term					
Karlsson[21]	Return to sports activity (days), *mean (SD)*		19.2 (9.5)	9.6 (4.8)	ES 1.29 (0.82-1.76)*
Reinhardt[27]	Return to sports (days)		13.8	11.7	NA
Intermediate term					
Oostendorp[26]	Return to sports training, *n (%)*	6 wk 12 wk	7 (62) 11(88)	4 (30) 5(43)	RR 0.57 (0.22-1.45) RR 0.45 (0.23-0.91)*
Long-term					
Oostendorp[26]	Return to sports training, *n (%)*	24 wk	11(96)	9 (74)	RR 0.82 (0.57-1.18)

Function

Three studies, all with high risk of bias, used some sort of functional score to evaluate the effectiveness of additional supervised exercises.[21, 22, 30] Basset et al.[22] presented the results of two functional scores: the Lower Limb Task Questionnaire (LLTQ) and the motor activity scale. The task questionnaire consisted of two subscales: the recreational activity scale, which measures strenuous activities such as running, jumping and cutting, and the activities of daily living scale, which measures less demanding activities such as walking, getting up from a chair, and carrying. The motor activity scale measures motor performance on six activities that involve running, walking, and hopping. Karlsson et al.[21] presented a scoring scale for functional results consisting of categories as instability, pain, swelling, stiffness, work and sport activities, stair climbing, running, and support. Hultman et al.[30] presented the results of the Foot and Ankle Outcome Score (FAOS), which is a 42-item questionnaire consisting of five subscales: pain, symptoms, activities of daily living, sports and recreation function, and ankle-related quality of life. As Hultman et al. standardised treatment in both groups after six weeks we only report the results only until that time. In one study participants were patients who were active in sports on recreational or competitive level.[21] Conventional treatment differs between the studies: RICE (rest, ice, compression and elevation) followed by mobilising and strengthening exercises[22] versus elastic wrapping, partial weight bearing and crutches until pain subsided.[21, 30]

At short term follow-up, Basset and colleagues found no significant differences for both functional scales between the treatment groups.[22] Though we could not calculate effect sizes from the study of Hultman et al.[30], patients who received early physiotherapy treatment reported significant improvements on all subscales of the foot and ankle outcome score (FAOS) compared with patients who received conventional treatment at short term-follow-up. At long-term follow-up, Karlsson et al. found no difference in functional results between the two treatment groups.[21] Consequently, there is conflicting evidence at short-term follow-up and limited evidence for no effectiveness at long-term follow-up.

The study of Karlsson et al., which is the only study in which the participants were athletes, found no difference in the number of patients with excellent functional results between both treatment groups at long-term follow-up.[21] Therefore, there is limited evidence for no effectiveness of additional supervised exercises at long-term follow-up.

Return to work

Seven studies, all with high risk of bias, described time to return to work as an outcome measure to evaluate the effectiveness of treatment.[21, 23, 25-27, 30] In two of these, effect sizes could not be calculated due to insufficient data.[23 25] Conventional treatment differs between the studies. The studies of Oostendorp[26], Reinhardt et al.[27] and Karlsson et

al.[21] prescribed a more preserved policy (cryotherapy, compression bandage, minimal weight bearing until pain subsided). Nilsson[25] and Hultman et al.[30] promoted early ankle mobilisation or early weight bearing as much as pain allowed. In the study of Hultman et al.[30] this treatment was followed by two visits to the physiotherapist at 6 weeks and 3 months follow-up. Brooks et al.[23] divided conventional treatment in three groups; 1) no treatment or minimal bandage, 2) tubigrip, and 3) complete immobilisation in a below-knee plaster-of-Paris cast.

Three studies included a more specific study population; patients who were active in sports on recreational or competitive level[21, 26], and recruits or professional soldiers[27]. Reinhardt et al.[27] and Karlsson et al.[21] demonstrated a faster return to work for patients receiving early functional treatment and supervised balance and strengthening exercises compared to patients receiving conventional treatment at short-term follow-up, while Hultman and colleagues found no differences between treatment groups at short-term follow-up concerning return to work.[30] One study evaluated time to return to work at intermediate and long-term follow-up, but did not found any difference between treatment groups.[26] There is therefore conflicting evidence for effectiveness of supervised exercises at short-term follow-up in reducing the time to return to work and limited evidence of no effectiveness at intermediate and long-term follow-up.

Return to sport

Three studies, all with high risk of bias, included time to return to sport as an outcome measure.[21, 26, 27] All studies included a more active population, e.g. athletes and soldiers, who were more likely to sustain an ankle sprain. Conventional treatment was similar in the three studies. All used a more reserved policy in the first week of rehabilitation by prescribing cryotherapy, compression bandage or aircast brace, and minimal weight bearing (with or without crutches).

At short-term follow-up, Karlsson et al. reported that patients who received functional treatment, range of motion, and proprioceptive training returned earlier to sports activity than patients who received conventional treatment.[21] We could not calculate effect sizes for short term follow-up from the study of Reinhardt et al. because of incomplete data.[27] There is therefore limited evidence for the effectiveness of additional supervised exercises at short term follow-up in reducing the time to return to sport. Though the study by Oostendorp found a significant difference between treatment groups at 12 weeks'

Follow-up (intermediate), it failed to show differences at 6 weeks and 24 weeks.[26] There is therefore conflicting evidence for the effectiveness at intermediate term follow-up and limited evidence for no effectiveness at long-term follow-up.

DISCUSSION

In this systematic review of treatment of patients who sustained an acute lateral ligament ankle sprain we found only moderate or limited evidence in favour of adding supervised exercises to conventional treatment compared with conventional treatment alone, according to the outcome measures of recovery and return to sport at short-term follow-up. There was no strong evidence of additional supervised exercises for any of the outcome measures.

The evidence for effectiveness of additional supervised exercises is based on a limited number of studies (n=11), with a maximum of five studies per outcome measure. In these studies conventional treatment was defined as no treatment, ice application, partial or complete immobilisation, home exercise program, early ankle mobilization instructions, or a combination of these treatments. As the effectiveness of additional supervised exercises could depend on the type conventional treatment, we planned to present the results classified by type. We were unable to do this, however, because of the limited number of studies included and the different types of conventional treatment.

The supervised treatment in the included studies was quite similar and consisted of visits to the physical therapy department, during which rehabilitation focused on strength, mobility and balance exercises, with or without the use of a balance board. The number of visits and the duration of treatment follow-up differed between studies, and included a maximum of nine half hour sessions within 3 months, a 12 week training program, a 6 week training program with 3 sessions a week, a maximum of 10 sessions of 45 minutes, and a 3 phase training program in 14 days.

In addition, studies were heterogeneous regarding the study populations, outcome assessment and follow-up time. Most of the studies, except one, were assessed as having high risk of bias. We therefore refrained from undertaking statistical pooling of the results of the individual studies and conducted a best-evidence synthesis.

Risk of bias

The assessment of risk of bias resulted in ten of the eleven studies (91%) being assessed as having high risk of bias. The threshold to differentiate between low and high risk of bias studies was based on a methodological study of van Tulder et al.,[31] in which they assessed the validity of the cochrane collaboration's tool for assessing risk of bias in trials of interventions for back pain. A threshold of 50% or less was associated with bias, therefore we considered studies with six or more points were regarded as studies having a low risk of bias.

Critical items in the risk of bias assessment were the items on blinding (items 3, 4 and 5), allocation concealment (item 2) and similarity of treatment groups at baseline (item 8).

None of the studies scored positively on the items of blinding, probably because of the difficulty of blinding of patients or care providers in physical therapy. Also, in all studies the patient was the outcome assessor so that when patients were not blinded for the intervention, the item on blinding of outcome assessor so that was automatically scored as negative. Of the 11 studies, 10 were classed as unclear on the items concerning allocation concealment and 9 on similarity of treatment groups at baseline. These studies are therefore more susceptible to selection bias, and, as a consequence, this will affect the generalisability of our results. A critical note concerning the risk of bias assessment is that disagreements were resolved in a consensus meeting between the assessors. For more transparency and objectivity it might have been better to consult a third reviewer.

Limitations

Although we considered only significant differences in the individual studies for the evaluation of the evidence for the effectiveness of additional supervised exercises, there were non-significant differences in favour of the supervised treatment. In these studies, significant differences could be easily missed because of low power (small number of patients); 10 studies did not provide a power analysis. For example, the study of Wester et al.[29], which included only 48 patients and found no difference between treatment groups concerning the number of reported re-sprains. This resulted in a relative risk of 0.46 with a 95% confidence interval of 0.21 to 1.01, implying that there is an effect in favour of additional supervised exercises that could become significant if this study was conducted with enough power in a larger population. To confirm such an effect the sample size should be almost doubled. Furthermore, van Rijn and colleagues performed a subgroup analysis of a randomised trial, distinguishing between patients with a mild and a severe sprain based on the ankle function score.[16, 20] In patients with severe injuries, they found significant differences in favour of the group who received supervised exercises additional to usual care. This subgroup analysis, however, was explorative and not predefined. Also, because of the classification into mild and severe injuries the groups became relatively small, resulting in low power.

The limited evidence found for the effectiveness of additional supervised exercises in our review corresponds with findings in studies comparing functional treatment with surgery or immobilisation, or both. In 1965, Freeman showed that external protection combined with mobilisation resulted in a shorter mean time to resolution of symptoms compared with immobilisation and surgery after rupture of the lateral ligament of the ankle.[32] Recently, Bleakley and colleagues showed that early therapeutic exercises during the first week after an ankle sprain improved ankle function compared with the current best treatment available (applying ice and compression).[33] Kannus et al.[2] concluded that functional treatment, including protection by tape, bandage or brace, early weight-bearing, range of motion exercises and neuromuscular training, resulted

in the quickest recovery to full range of motion and faster return to work and physical activity after a grade III ankle sprain compared with surgery or immobilisation. They found no differences for outcome measures like instability, pain and swelling. In a more recent review Kerkhoffs et al.[10] showed that functional treatment, which includes elastic bandage, softcast, tape or orthosis with associated coordination training, resulted in improved outcomes compared with immobilisation alone. However, they did not differentiate between supervised and non-supervised treatment as in our present review.

The effectiveness of additional supervised exercises in a more specific population was restricted to moderate or limited evidence concerning the outcomes of return to work and return to sport only. There were indications from the individual studies included that more specific patient groups might benefit to a greater extent from participation in an additional supervised exercise program. Oostendorp reported significantly less pain at 6 weeks follow-up in favour of the supervised exercise group in participants who sustained their ankle sprain during volleyball, basketball, handball or soccer.[26] In the study by Holme and colleagues, patients who sustained their ankle sprain during sports and receiving supervised treatment reported significant fewer re-sprains at 12 months follow-up compared with the conventional treatment group.[24] Furthermore, in the study of van Rijn and colleagues, patients with a severe injury who received additional supervised exercises showed significant less instability at 8 weeks follow-up compared with the conventional treatment group.[20] More high quality randomised controlled trials are needed to evaluate the effectiveness of additional supervised exercises in more defined subgroups such as athletes and patients with severe injuries.

CONCLUSIONS

In conclusion, we found moderate or limited evidence of effectiveness in favour of additional supervised exercises compared with conventional treatment alone, according to the outcome measures of recovery, and return to sport at short-term follow-up. We did not find strong evidence for any of the outcome measures. In a more specific population, athletes and soldiers, there was limited to moderate evidence that supervised treatment leads to an earlier return to work and return to sports. Furthermore, there was limited evidence for the effectiveness of supervised treatment additional to conventional treatment in patients with severe injuries. There were, however, only a few studies, most were assessed as having high risk of bias, and most were lacking power. High quality randomised controlled trials, concentrating on the effectiveness of additional supervised treatment in specific study populations such as athletes and patients with severe injuries, are inquired. In order to improve complete and transparent reporting of RCTs, future trials should comply with the CONSORT statement.[34]

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APPENDIX 1. SEARCH STRATEGY

Studies	((randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized controlled trials [mh] OR random allocation [mh] OR double-blind method [mh] OR single-blind method [mh] OR clinical trial [pt] OR clinical trials [mh] OR ("clinical trial" [tw]) OR ((singl* [tw] OR doubl* [tw] OR trebl* [tw] OR tripl* [tw]) AND (mask* [tw] OR blind* [tw])) OR ("latin square" [tw]) OR placebos [mh] OR placebo* [tw] OR random* [tw] OR research design [mh:noexp] OR comparative study[pt] OR evaluation studies[pt] OR follow-up studies [mh] OR prospective studies [mh] OR cross-over studies [mh] OR control* [tw] OR control[tw] OR controlled[tw] OR controled[tw] OR controls[tw] OR prospectiv* [tw] OR volunteer* [tw]) NOT (animal [mh] NOT human [mh]))
Location	(ankle OR talocrural OR (anterior AND talofibular AND ligament) OR (posterior AND talofibular AND ligament) OR (calcaneofibular AND ligament) OR (lateral AND ligament AND complex))
Injury	(ankle OR talocrural OR (anterior AND talofibular AND ligament) OR (posterior AND talofibular AND ligament) OR (calcaneofibular AND ligament) OR (lateral AND ligament AND complex)) AND (inversion OR sprain OR strain OR rupture OR injur* OR distortion)
Treatment	(training OR therapy OR treatment OR rehabilitation OR exercise OR physiotherapy OR (early AND mobilisation))

APPENDIX 2.

Sources of risk of bias

Item	Judgment
A) Sequence generation	
1. Was the method of randomization adequate?	Yes / No / Unsure
B) Allocation concealment	
2. Was the treatment allocation concealed?	Yes / No / Unsure
C) Blinding of participants, personnel and outcome	
Was knowledge of the allocated interventions adequately prevented during the study?	
3. Was the patient blinded to the intervention?	Yes / No / Unsure
4. Was the care provider blinded to the intervention?	Yes / No / Unsure
5. Was the outcome assessor blinded to the intervention?	Yes / No / Unsure
D) Incomplete outcome data	
Were incomplete outcome data adequately addressed?	
6. Was the drop-out rate described and acceptable?	Yes / No / Unsure
7. Were all randomized participants analysed in the group to which they were allocated?	Yes / No / Unsure
E) Other sources of potential bias	
8. Were the groups similar at baseline regarding the most important prognostic indicators?	Yes / No / Unsure
9. Were co-interventions avoided or similar?	Yes / No / Unsure
10. Was the compliance acceptable in all groups?	Yes / No / Unsure
11. Was the timing of the outcome assessment similar in all groups?	Yes / No / Unsure

Criteria for a judgment of "yes" for the sources of risk of bias

1. Was the method of randomization adequate?
A random (unpredictable) assignment sequence. Examples of adequate methods are coin toss (for studies with two groups), rolling a dice (for studies with two or more groups), drawing of balls of different colours, drawing of ballots with the study group labels from a dark bag, computer-generated random sequence, pre-ordered sealed envelopes, sequentially-ordered vials, telephone call to a central office, and pre-ordered list of treatment assignments.

Examples of inadequate methods are: alternation, birth date, social insurance/security number, date in which they are invited to participate in the study, and hospital registration number.

2. Was the treatment allocation concealed?
Assignment generated by an independent person not responsible for determining the eligibility of the patients. This person has no information about the persons included in the trial and has no influence on the assignment sequence or on the decision about eligibility of the patient.

Was knowledge of the allocated interventions adequately prevented during the study?

3. Was the patient blinded to the intervention?
This item should be scored "yes" if the index and control groups are indistinguishable for the patients or if the success of blinding was tested among the patients and it was successful.

4. Was the care provider blinded to the intervention?
This item should be scored "yes" if the index and control groups are indistinguishable for the care providers or if the success of blinding was tested among the care providers and it was successful.

5. Was the outcome assessor blinded to the intervention?
Adequacy of blinding should be assessed for the primary outcomes. This item should be scored "yes" if the success of blinding was tested among the outcome assessors and it was successful or:

for patient-reported outcomes in which the patient is the outcome assessor (e.g., pain, disability): the blinding procedure is adequate for outcome assessors if participant blinding is scored "yes" for outcome criteria assessed during scheduled visit and that

supposes a contact between participants and outcome assessors (e.g., clinical examination): the blinding procedure is adequate if patients are blinded, and the treatment or adverse effects of the treatment cannot be noticed during clinical examination for outcome criteria that do not suppose a contact with participants (e.g., radiography, magnetic resonance imaging): the blinding procedure is adequate if the treatment or adverse effects of the treatment cannot be noticed when assessing the main outcome for outcome criteria that are clinical or therapeutic events that will be determined by the interaction between patients and care providers (e.g., co-interventions, hospitalization length, treatment failure), in which the care provider is the outcome assessor: the blinding procedure is adequate for outcome assessors if item "E" is scored "yes" for outcome criteria that are assessed from data of the medical forms: the blinding procedure is adequate if the treatment or adverse effects of the treatment cannot be noticed on the extracted data.

Were incomplete outcome data adequately addressed?

6. Was the drop-out rate described and acceptable?
The number of participants who were included in the study but did not complete the observation period or were not included in the analysis must be described and reasons given. If the percentage of withdrawals and drop-outs does not exceed 20% for during follow-up and does not lead to substantial bias a "yes" is scored. (N.B. these percentages are arbitrary, not supported by literature).

7. Were all randomized participants analysed in the group to which they were allocated?
All randomized patients are reported/analyzed in the group they were allocated to by randomization for the most important moments of effect measurement (minus missing values) irrespective of non-compliance and co-interventions.

Other sources of potential bias:

8. Were the groups similar at baseline regarding the most important prognostic indicators?
In order to receive a "yes", groups have to be similar at baseline regarding demographic factors, severity of complaints, and value of main outcome measure(s).

9. Were co-interventions avoided or similar?
This item should be scored "yes" if there were no co-interventions or they were similar between the index and control groups.

10. Was the compliance acceptable in all groups?

The reviewer determines if the compliance with the interventions is acceptable, based on the reported intensity, duration, number and frequency of sessions for both the index intervention and control intervention(s). For example, physiotherapy treatment is usually administered over several sessions; therefore it is necessary to assess how many sessions each patient attended. For single-session interventions (for ex: surgery), this item is irrelevant.

11. Was the timing of the outcome assessment similar in all groups?

Timing of outcome assessment should be identical for all intervention groups and for all important outcome assessments.

Note: These instructions are adapted from van Tulder 2003, Boutron et al, 2005 (CLEAR NPT) and the Cochrane Handbook of Systematic Reviews of Interventions.

Chapter 3

Chronic complaints after ankle sprains: a systematic review on effectiveness of treatments

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ABSTRACT

Objective: To determine the effectiveness of treatments for patients with chronic complaints after ankle sprain.

Design: Systematic review.

Background: Though most people recover completely after a lateral inversion ankle injury, a considerable percentage have persistent complaints. Currently it is still unclear which treatment options are best for these patients.

Methods: Major databases, including Pubmed, Embase, Cinahl and PEDro were searched for randomized controlled trials and controlled clinical trials conducted from 1966 to October 2012. Due to clinical heterogeneity, the data were analysed using a best-evidence synthesis.

Results: A total of 20 randomized controlled trials and 1 controlled clinical trial were included in the analysis. The included studies compared different treatments (training programs, physiotherapy, chiropractic/manual therapy, surgery, postoperative training and functional treatment). For pain and function outcomes, limited to moderate evidence was found for effectiveness of a training program compared to conservative treatment. Two studies found a decrease of recurrences after a proprioceptive training program. Four studies showed good results for different surgical methods, but did not include a non-surgical control group for comparison. Limited evidence was found for the effectiveness of an early mobilization program after surgery.

Conclusions: In chronic ankle complaints after an ankle sprain, a training program gives better results for pain and function, and a decrease of recurrent ankle sprains, than a 'wait and see' policy. There was insufficient evidence to determine the most effective surgical treatment, but limited evidence suggests that postoperative, early mobilization is more effective than plaster cast.

Key Words: ankle injury; instability; training program

INTRODUCTION

Ankle sprain is a common musculoskeletal injury that frequently occurs in sports activity. In most cases, the injury involves an inversion trauma of the ankle, with damage to the lateral ligament, and in particular, rupture of the anterior talofibular ligament. In some cases there is more damage, often involving a rupture of the calcaneofibular ligament. In the Netherlands about 600.000 people sustain an ankle sprain each year; of these, general practitioners see about 125.000 patients (8 per 1000 patients per year).[1] In the USA and the UK about 23.000 and 5.000 injuries of the ankle, respectively, occur each day.[2]

Initial treatment for a lateral ankle sprain is mostly conservative and consists of functional interventions that include early mobilization with instruction for rest, ice, time period and way of walking, continued weight bearing, and sometimes physiotherapy, together with external support for the ankle (tape, bandage or brace).[2] In 36-85% of patients, conservative treatment leads to a full recovery.[3] However, for severe acute ankle sprains, surgical interventions may yield slightly better outcomes for function and instability compared with conservative treatment.[4,5] Nevertheless, it remains unclear whether this slight benefit compensates for the higher costs and higher risk of complications post-surgery.

In different studies, it has been reported that 3% to 34% of patients with lateral ankle sprain experience persistent complaints of pain, swelling, re-sprain, a 'giving way' sensation or limitations in activities and sports participation; and 10% to 20% of patients have persistent complaints of instability of the injured ankle.[6] When these complaints persist for more than 6 months, the term 'chronic (lateral) ankle complaints' or 'functional ankle instability' is often used.[6]

While most patients recover completely after a lateral inversion ankle injury, a considerable percentage have persistent complaints. Currently, it is still unclear which treatment options are best for these patients. Although many types of treatments are available, there is lack of evidence for the effectiveness of these treatments in case of chronic ankle complaints.

Therefore, the aim of this study was to systematically review the effectiveness of the different types of interventions used for chronic ankle complaints after a lateral ankle sprain, including different conservative treatments (i.e. training programs, postoperative training programs, manual and chiropractic therapy), as well as various surgical procedures.

METHODS

Criteria for the inclusion of studies

Selected articles had to fulfil the following criteria:

(1) A sample of persons over 18 years of age who had suffered a lateral ankle sprain or had a re-sprain and had persistent complaints (at least 6 months after the ankle sprain occurred) of pain, swelling, instability or giving way.
(2) The study design had to be a randomized controlled trial (RCT) or controlled clinical trial (CCT).
(3) Publication in English, French, German or Swedish language.
(4) Any one of the following outcome measures described at follow-up: pain, function, swelling, proprioception, balance, and recurrences.
(5) Interventions that included functional treatment, training programs (neuromuscular, strength, balance training), physiotherapy, manual therapy, chiropractic therapy or surgery, or a combination of these.

Literature search

A primary search was conducted in the databases of Pubmed (Medline), from 1966 to October 2012, Embase, Cinahl and PEDro from 1984 to October 2012, and the Cochrane Central Register of Controlled Trials. The terms location, injury treatment and design of the studies were linked by the Boolean operator AND. For each of the terms, one or more synonyms were used (see Appendix 1 for details).

Starting this review we identified all references included in three earlier reviews (van Rijn et al.[3], van Os et al. [7] and de Vries et al.[8]).

Study selection

Two reviewers (DM and JvO) independently screened the titles and abstracts to identify potentially relevant studies for full review. Abstracts for which full articles were not available or not published were not included in this study. After reading the full text of the identified articles, the same two reviewers (independently of each other) selected the studies to be included in this review. Additionally, references from these studies were screened for potential relevant articles. Any disagreement between the reviewers regarding inclusion was resolved by consensus.

Risk of Bias assessment

Two reviewers (MvM and JvO) independently from each other, conducted the risk of bias assessment of the included studies using the Risk of Bias tool, as advised by the Cochrane Collaboration, which consists of 12 items (Table 1; appendix 2).

Each criterion was scored as positive, unclear, or negative. Criteria scored as positive received 1 point, and those scored as negative/unclear received no points. Disagreements in assessment were solved by discussion. The risk of bias score for each study was calculated by summing the total number of positive criteria. A low risk of bias was defined as fulfilling 6 or more of the internal validity criteria.

Data extraction

Relevant data from the included articles were extracted by one reviewer (JvO), including the names of the authors, year of publication, study design (RCT or CCT), type of interventions, outcome measures, outcomes expressed in scores (e.g. mean, median, standard deviation, percentage and confidence interval), study results/conclusions, and additional relevant comments (Appendix 3).

The included outcome measures were categorized as followed: function, including function measures (self-perceived functional ability, functional limitations and participation expressed in Foot and Ankle Disability Index (FADI), FADI-sports, Sefton, Tegner score and Karlsson score) and objective measures of function (range of Motion, eversion torque and peak Torque); or combined subjective and objective measures, such as the Zwipp score, balance center of pressure, static postural control, postural sway, and Star Excursion Balance Test (SEBT), proprioception (defined as joint position sense, change in muscle reaction time, or onset latency), pain (visual analogue scale (VAS)), numbering rating scale (NRS), McGill Pain Questionnaire, and part of Zwipp and Sefton scores, swelling (part of Sefton), recovery (expressed in subjective scoring scales) and recurrences (expressed in number of re-sprains).

When possible, the mean differences (MD) or odds ratios (OR), with 95% confidence interval (95% CIs) were extracted or calculated from the original studies.

The included outcome measures were categorized as followed: function, including function measures (self-perceived functional ability, functional limitations and participation expressed in Foot and Ankle Disability Index (FADI), FADI-sports, Sefton, Tegner score and Karlsson score) and objective measures of function (range of Motion, eversion torque, and peak Torque); or combined subjective and objective measures, such as the Zwipp score, balance (center of pressure, static postural control, postural sway, and Star Excursion Balance Test (SEBT)), proprioception (defined as joint position sense, change in muscle reaction time, or onset latency), pain (visual analogue scale (VAS), numbering rating scale (NRS), McGill Pain Qustionnaire, and part of Zwipp and Sefton scores), swelling (part of Sefton), recovery (expressed in subjective scoring scales), and recurrences (expressed in number of re-sprains).

When possible, the mean differences (MD) or odds ratios (OR), with 95% confidence interval (95% CIs) were extracted or calculated from the original studies.

Table 1. Overview risk of bias for the included studies in this systematic review

Study		1	2	3	4	5	6	7	8	9	10	11	12	Total
Bernier	1998	U	U	N	N	Y	Y	U	U	U	U	U	Y	3
Clark	2005	U	U	N	N	N	U	U	U	Y	U	U	Y	2
Dinesha	2011	U	U	N	N	N	N	U	U	U	U	U	U	0
Eils	2001	N	N	N	N	N	U	U	U	Y	U	U	Y	2
Hale	2007	U	U	N	N	U	Y	U	U	U	U	U	Y	2
Han	2009	U	U	N	N	U	Y	U	U	U	U	U	Y	2
Hennrikus	1996	Y	U	U	N	U	N	U	U	U	U	Y	N	2
Hoch	2010	Y	Y	N	N	Y	Y	U	U	U	U	Y	Y	6
Hoines	2003	Y	N	N	N	U	Y	U	U	Y	U	Y	Y	5
Hupperets	2009	U	Y	N	N	N	Y	Y	Y	Y	U	N	Y	6
Kaminski	2002	U	U	N	N	U	U	U	U	U	U	U	Y	1
Karlsson	1995	U	U	N	N	Y	Y	U	U	U	U	U	Y	3
Karlsson	1997	Y	N	N	N	U	Y	U	U	U	U	Y	N	3
Karlsson	1999	U	U	N	N	Y	U	U	U	U	U	U	Y	2
Kidgell	2007	U	U	N	N	U	U	U	U	U	U	U	Y	1
Knop	1999	Y	U	N	N	N	Y	U	U	U	U	U	U	2
Larsen	1988	Y	U	N	N	N	U	N	U	U	U	N	Y	2
McKeon	2008	U	Y	N	N	N	U	U	U	Y	U	U	Y	3
Mohammadi	2007	U	U	N	N	N	U	U	U	Y	U	U	Y	2
Pellow	1999	Y	U	N	N	N	U	U	U	U	U	U	Y	2
Rosenbaum	1999	U	U	N	N	N	U	U	U	U	U	Y	N	1

Y= yes; N= no; U= unknown/uncertain

1) Was the method of randomization adequate ?
2) Was the treatment allocation concealed ?
3) Was the patient blinded to the intervention ?
4) Was the care provider blinded to the intervention ?
5) Was the outcome assessor blinded to the intervention ?
6) Was the drop-out rate described and acceptable ?
7) Were all randomized participants analysed in the group to which they were allocated?
8) Are reports of the study free of suggestion of selective outcome reporting ?
9) Were the groups similar at baseline regarding the important prognostic indicators?
10) Were co-interventions avoided or similar ?
11) Was the compliance acceptable in all groups ?
12) Was the timing of the outcome assessment similar in all groups ?

ANALYSIS

Treatments reported in studies were combined into four main clusters: I = training programs, II = manual therapy and chiropractic treatment, III = surgery and IV = postoperative training programs. If trials reported outcomes only as graphs, where possible, the mean score and standard deviation (SD) were estimated from these graphs. Results of

continuous data were presented as MD with 95% CI. For dichotomous data, the OR was calculated. (Table 3)

Statistical pooling was performed when studies were clinically homogeneous concerning population, intervention(s) used for treatment, and outcome measures. In the case of clinical or measured heterogeneity in outcome, data were analysed using a best-evidence synthesis based on a rating system with four levels of evidence to express the quality of the studies:

1) strong evidence (scientific proof in multiple RCTs with a low risk of bias)
2) moderate evidence (high level of proof in one RCT with a low risk of bias, and one or more RCTs with a high risk of bias, or by generally consistent findings in multiple RCTs assessed as having a high risk of bias)
3) limited evidence (only one RCT assessed as having either a low or high risk of bias)
4) conflicting evidence (conflicting findings in the RCTs, less than 75% of the studies report consistent findings)
5) no available evidence-based evidence (no RCTs available).

Outcomes measured up to 3 months after baseline were considered to be short-term outcomes and those measured 12 months or more after baseline were considered to be long-term outcomes.

RESULTS

Description of studies

The database search yielded 3272 potentially relevant articles. After screening titles and abstracts, 56 articles were extracted for full-text review. Finally, 21 studies fulfilled the criteria for inclusion in this review. (Figure 1) The included studies investigated: training programs (n=12),[9-20] surgery (n=4),[21-24] post-operative training programs (n=3)[22, 25, 26] and chiropractic or manual treatment (n=2)[27, 28] and used different outcome measures. (Table 2) The different training programs consisted of multiple components, including strength training, balance exercises, proprioceptive exercises and a combination of these. Table 3 shows the results of effectiveness of interventions for the different outcome measures for patients with chronic ankle complaints.

RISK OF BIAS

Table 1 presents the overall assessment of the risk of bias in the included studies. Of the 21 studies, most had 2-3 positive items and only three studies had a score of 5-6 points[14, 19, 27]. Therefore, only two studies were defined as having a low risk of bias.[19, 27]

The patient, care provider and outcome assessor were not blinded in 95% of the included studies. Moreover, in most studies it was unclear or not stated (n=20) whether the randomized participants were analysed in their allocated groups, whether the reports of the studies were free of selective outcome reporting, and whether or not co-interventions were avoided.

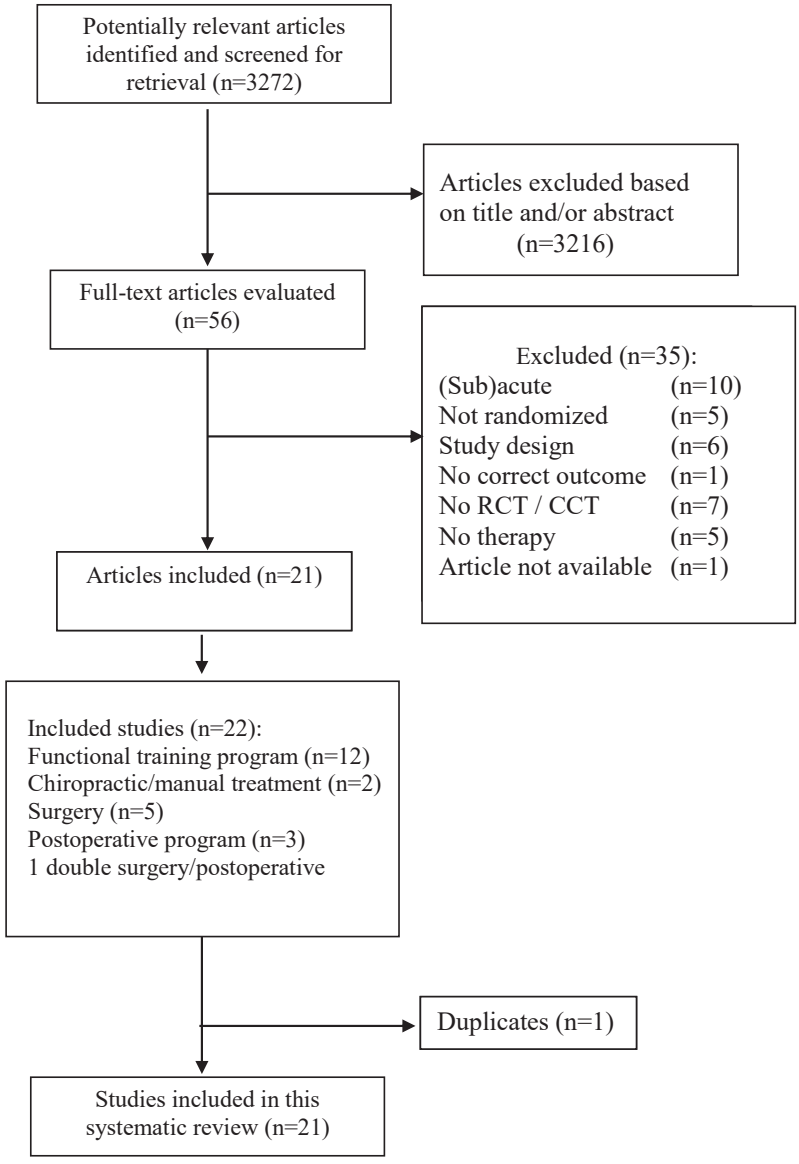

Figure 1. Flow diagram of studies included in this systematic review. Abbreviations: CCT, controlled critical trial; RCT, randomized controlled trial

EFFECTIVENESS OF INTERVENTIONS

I a. Training programs versus controls ('wait and see')

- Short term

Nine studies (one CCT) compared a training program with a control group, with a follow-up of 4-6 weeks.[9-17] All of these studies had a high risk of bias and reported outcomes of balance (expressed in postural stability by sway index, SEBT and centre of pressure), both self-perceived as well as objectively measured function (expressed in FADI and eversion torque) and proprioception (passive/active position sense, muscle reaction time and onset latency).

Of the nine studies, eight measured balance as an outcome measure. In three of these eight studies, no differences were found in effectiveness of the training program compared with controls on the outcome of balance. [9, 11, 13] In six studies, balance was expressed in centre of pressure, postural sway and the SEBT[9, 11-14, 16] and significant effects were found in favour of the intervention group compared with controls in four of these studies. In two of these studies[12, 17] there was a significantly better effect in the intervention group compared with controls, measured mainly with the SEBT.

Therefore, in patients with chronic ankle complaints, there is conflicting evidence for the effectiveness of balance training in the invention group compared with the control group.

Proprioception was measured as an outcome in three studies.[9-11] Two studies [10, 11] found a significantly better effect in the training group compared with the control group, with outcomes expressed as onset latency and muscle reaction time. The Mean Difference (MD) for onset latency time ranged from 1.29 to 1.20 milliseconds (effect size -9.5 and -3.4, respectively). One study compared a balance and coordination training program with sham electric-stimulation and with a control group. The outcome of active and passive joint position sense showed no significant difference between the three study groups. [9]

Therefore, for the outcome proprioception, there was conflicting evidence for the effectiveness of the training group compared with a control group.

Ankle function was assessed in four studies.[12, 14, 15, 17] Of these, three found a significant effect on both self-perceived function as well as objectively measured function after a training program compared with controls at short-term follow-up, expressed in FADI, FADI sports, Karlsson score, average torque and peak torque.

Therefore, for the outcome of function, there was moderate evidence for the effectiveness of a training program compared to controls at 4-6 week follow-up.

Only one study investigated pain as outcome (expressed in a visual analogue scale) in which a significantly better effect of the training group was seen compared with controls.[14]

Therefore, for the outcome pain, there is limited evidence for the effectiveness of a training program compared with controls.

- Long term

Two studies with a follow-up of 12 months compared a group that received proprioceptive training using a wobble board and an ankle disc with a control group, with the incidence of recurrences as a clinical outcome.[18, 19] In both studies, the training program, significantly reduced the incidence of recurrences in the intervention group compared with controls (reduction of recurrence ranged from 33% to 22%).

Therefore, long-term follow-up of incidence of recurrences provided moderate evidence for the effectiveness of proprioceptive training compared with no intervention in patients with chronic ankle instability.

I b. Comparison of a 2 and 4 week training program

One study with a high risk of bias compared two exercise training groups (identical program with a wobble board) with different time schedules.[20] The first intervention group did exercises for 2 weeks and the second group for 4 weeks. For the outcomes of function and balance, the 4-week exercise program showed significantly greater effect sizes in function measured with the ankle joint function assessment tool (AJFAT) compared with the 2-week program.

Therefore, there is limited evidence for the effectiveness of a training program with a wobble board for 4 weeks compared with the same program for 2 weeks.

II Chiropractic or manual therapy versus control

One study with a high risk of bias compared chiropractic therapy with a 'wait and see' approach for the clinical outcome measures of pain and function (range of motion).[28] Significant differences were found in favour of the chiropractic therapy group for the outcome pain at the last treatment session and at 1-month follow-up. Also, significantly better results in function (expressed as dorsiflexion range of motion and overall ankle functioning) were found in the intervention group compared with the control group. Another study (with a low risk of bias) compared an intervention group that received a single joint mobilization treatment with a control group. [27] A significant difference in favour of the mobilization treatment on the outcome function (expressed as a larger range of motion) was found.

Therefore, for the outcomes of pain and function on short-term follow-up, there was moderate evidence that chiropractic therapy and/or manual therapy may be effective in patients with chronic ankle complaints.

III Comparisons of Surgical treatments

Four studies[21, 23, 24, 29] compared two different kinds of surgical interventions in subjects with chronic ankle instability. In all studies the outcome measures included a general outcome score (excellent to poor, measured with the Sefton or Karlsson score), physical examination (range of motion; ROM) and radiographic results [anterior talar tilt (ATT), expressing anterior drawing and talar tilt (TT)], all with a follow-up of 10 to 29 months. All studies showed excellent to good result, ranging from 80% to 95% success in the surgical treatment groups. In three studies there were almost no significant differences in the postoperative outcomes.[21, 24, 29] In one study, there was a significantly better outcome on the subjective scoring scale after static repair treatment compared to the dynamic repair treatment.[23] In one other study significantly better findings on radiographs (decreased talar tilt) were found in the Evans group compared to the Periost group.[29]

In one study there were more side-effects after the Chrisman-Snook procedure compared with the Modified-Broström procedure. In three of the four studies, no comparison was made between a surgical intervention group and a non-surgical control group (e.g. a functional treatment group).

Therefore, among surgical interventions, there is insufficient evidence to identify a superior surgical treatment .

III b Surgical Treatment versus Conservative Functional Therapy

One study[22] compared surgical treatment with a functional treatment (training program) in patients with second-stage rupture of the lateral ankle ligament. Function was measured by the Zwipp score, consisting of a scoring list (range -30 to +30), physical examination (-20 to +20) and radiographic findings (-20 to +20). The mean difference between the intervention groups was a Zwipp score of 10.6, mainly caused by the differences on radiographic findings.

Table 2. Studies on therapy for chronic ankle complaints

Treatment	Intervention		Control		Outcome
Training program					
Bernier et al 1988	2) Sham treatment with electrical stimulation n. peroneus 3) 6 weeks balance and coordination training	N = 14 N = 17	1) No participation in strength or stability activity	N = 14	Passive and active joint position sense Postural stability by Sway Index
Clark et al 2005	4-week wobble board training	N = 10	No interventions	N = 9	Results in a questionnaire The onset latency, s-EMG from the m. tib. ant. and m. peroneus longus
Dinesha et al 2011	2-week wobble board training	N = 15	4-week wobble board training	N = 15	AJFAT : Ankle Joint Functional Assessment tool Questionnaire Muscle onset latency in TA and PL
Eils et al 2001	Exercise group : A 6-week physiotherapeutic exercise group	N = 20 31 CAI	No specific interventions	N = 10 17 CAI	Joint Position Sense Postural Sway Muscle Reaction time
Hale et al 2007	1) Rehabilitation group 4-week training (CAI group) 2) Healthy group	N = 16 N = 19	3) Control Group (CAI control)	N = 13	Self-reported questionnaire FADI FADI sports COPV SEBT
Han et al 2009	A 4-week exercise program on balance using elastic : CAI group Healthy group	 N = 10 N = 10	Control group: CAI group Healthy group	 N = 10 N = 10	Change in balance, measured by TTD (total travel distance) of the CoP
Hoines et al 2003	Test group: using a bi-directional bicycle pedal	N = 10	Control group : using an uni-directional pedal	N = 9	Figure-of-eight running; subjects using a Visual Analog Scale from 0-100 Postural sway Eversion Torque Single Leg Stance Test Modified Karlsson Functional Score

Table 2. Studies on therapy for chronic ankle complaints (continued)

Treatment	Intervention		Control		Outcome
Hupperets et al 2009	Treatment according to usual care and an additional 8 weeks home-based proprioceptive training program	N=256	Received treatment according to usual care	N=266	Incidence density of ankle sprain per 1000 hours of exposure Recurrences reported in a web-based questionnaire Health care costs
Kaminski et al 2002	1) Strength training group (S) using a Thera Band 2) Propriocepsis training (P) involved "T-band kicks" 3) Combination of S+P (B)		Control (C) : No specific training		Isokinetic strength Isokinetic dynamometer Range of Motion involving 40gr Average torque E/I ratio Peak torque E/I ratio
Kidgell et al 2007	1) Dura Disc training (DT) 2) Mini-trampoline training (MT)	N = 7 N = 6	3) Control no specific training	N = 7	Postural sway (a single leg stance) Centre of pressure
McKeon et al 2008	1) 4-wk Balance Training group	N = 16	2) Control group	N = 15	Self-reported disability on FADI and FADI sports Static postural control (TTB) Center of Pressure with eyes open and eyes closed Dynamic balance in PM and PL reach
Mohammadi et al 2007	1) Proprioceptive Training group 2) Strength Training group 3) Orthosis group	N = 20 N = 20 N = 20	4) Control group No intervention	N = 20	Incidence of ankle sprain (recurrence)
Chiropractic and Manual Therapy					
Pellow et al 1999	1) The adjustment or experimental group	N = 15	2) The control or placebo group (detuned ultrasound therapy)	N = 15	Short-form McGill Pain Questionnaire Numerical Pain rating Scale Functional Evaluation Scoring Scale Ankle dorsiflexion ROM

Table 2. Studies on therapy for chronic ankle complaints (continued)

Treatment	Intervention		Control		Outcome
Hoch et al 2010	1) Joint mobilization group in two sessions	N = 10	2) Control group in two sessions	N = 10	Weight bearing lunge test (DF ROM) Arthrometry (talar disp. and stiffness) Dynamic postural Control (SEBT) Static postural Control (COP)
Surgical Treatment	**Surgery**		**Surgery / conservative**		
Hennrikus et al 1996	Surgical treatment for CAI: Christmas-Snook procedure	N = 20	Surgical treatment for CAI: Modified Brostrom procedure	N = 20	Standardized questionnaire Physical examination X-Ray
Karlsson et al 1997	1) Reconstruction of the ligaments described by Karlsson et al.	N =30 N = 30	2) Modification of the Brostrom procedure described by Gould et al.	N = 30	Subjective Scoring Scale using the Tegner Scale Mechanical Stability : ATT and TT
Knop (1) et al 1999	Operated after the first ankle sprain : B) Second-stage rupture: Operative functional D) Re-rupture : Operative functional	 N = 25 N = 24	Conservative functionally treated: A) Second-stage rupture: Conservative functional C) Re-rupture: Conservative functional	 N = 25 N = 26	Subjective Scoring Scale Clinical examination (scale) Stress radiography (ATT and TT)
Larsen et al 1988	Static repair group (S) An operative procedure	N = 56	Dynamic repair group (D) An operative procedure	N = 26	Subjective Scoring Scale Functional balance test Radiographic: TT and AD
Rosenbaum et al 1999	1) Evans group : A modified Evans tenodesis	N = 10 N = 10	2) Periost group : A fibular periostal flap repair	N = 10	Physical examination Radiographic stress diagnostics (ATT and TT) Dynamic Pedobarography Single pressure measurements
Postoperative Program					

Table 2. Studies on therapy for chronic ankle complaints (continued)

Treatment	Intervention		Control		Outcome
Karlsson et al 1995	1) Immobilization in a plaster cast for 6 weeks after ankle ligament construction	N = 20	2) Early range of motion training with a Walker boot after ankle ligament construction	N = 20	Scoring scale Range of Motion Standardized stress radiographs (ATT and TT)
Karlsson et al 1999	1) Postoperative immobilized in a below-knee plaster cast	N = 15	2) Early immobilization using an Air-Cast ankle brace	N = 15	Subjective scoring scale (8 items) Torque measurements Mechanical stability: ATT and TT by radiographs
Knop (2) et al 1999	C) Re-rupture and therapy : Operative functional	N = 24	D) Re-rupture and therapy : Conservative functional		Subjective Scoring Scale Clinical examination Stress radiography (ATT and TT)

The total Zwipp score for the surgical group was significantly higher compared with the functional treatment group.

Therefore, there is limited evidence in favour of surgery over a training program on function at long-term follow-up in patients with second-stage ankle instability after ankle sprains.

IV Postoperative treatment programs compared

Three studies investigated the effectiveness of postoperative treatments.[22, 25, 26] Outcomes measured were recovery (a subjective scoring scale on clinical complaints), function (physical examination; range of motion) and radiographic results (ATT and TT). Early mobilization with a Walker boot after surgery gave a significantly better effect on both outcomes compared with treatment with a plaster cast. In contrast, in subjects with a re-rupture after an ankle sprain there was a significantly better effect after a second surgical treatment compared with conservative functional treatment.[22] In one study, there was no difference in outcome after surgery between patients who had treatment with an ankle brace or a plaster cast.[26]

Therefore, there is limited evidence for the effectiveness of early mobilization with a Walker boot and a training program after surgery in patients with ankle instability. Also, there is limited evidence for the effectiveness of a second operative procedure after re-rupture of the lateral ligament compared to a conservative training program on the outcome function.

DISCUSSION

This systematic review summarizes the effectiveness of different treatments for patients with chronic ankle complaints, mainly involving persistent ankle instability and function loss. Training programs for chronic ankle complaints gave overall better results in subjectively/objectively measured outcomes and preventive effects on recurrence in the intervention group compared with controls (receiving conservative or functional treatment). However, the clinical evidence for this effect was of a limited to moderate level.

Surgery had good results in patients with recurrent ankle sprains, as expressed in subjective scoring scales (high percentage of good to excellent results); however, the evidence for effectiveness is insufficient due to the lack of comparing to a non-surgical control group.

In one study a second operative procedure after re-rupture of the lateral ligament showed a better effect than a conservative training program for the outcome function and balance.

Quality of evidence

Our database search yielded 21 studies for the present review (RCTs and 1 CCT), the majority of which had a high risk of bias. Compared to previous reviews, more studies of better quality with different treatment options were identified and could be included in this review, so that the selected studies could consequently be divided into subgroups: i.e. training and postoperative training group, chiropractic and manual therapy and surgical treatment.

For the training group, no significant differences in the outcome measures, as tested in joint position sense, postural sway, centre of pressure and eversion peak torque were found in four of the studies in which these tests were applied.[9, 11, 13, 14] In seven studies there were significant effects on the outcome function using FADI and FADI sports, balance using the SEBT as balance test and decrease of recurrences. One study showed a significant difference in onset latency, between the training group and a control group.[10]

For the balance tests, we found that most of the applied tests were unable to demonstrate significant differences between the groups, whilst these differences have been seen on other functional outcome measures. However, in three studies we found a significant effect on the outcome balance using the postural sway and the SEBT, resulting in conflicting evidence.[12, 16, 17]. The lack of effect of the applied tests might be due to the test characteristics, or the fact that functional training does not have much influence on balance.

Positive effects on clinical outcomes, measured with the FADI and Karlsson score, were found in the short term functional training group in three studies [12, 14] . Strength

and proprioception gave better results in another study.[15] In two long-term studies [18, 19] there was a significant positive effect in decreasing recurrences after a training program. Therefore, clinical assessment of the effectiveness of training programs in patients with chronic ankle complaints with a standardized questionnaire and physical examination to assess function and recurrence is recommended. To measure proprioception and balance, it would seem best to use a selection of standardized tests measuring different outcomes. However, balance and proprioception are two outcomes that are hard to differentiate from each other, because an improvement in proprioception will consequently lead to better balance. Proprioception often refers to a sense of joint position, measured by a change in onset latency or muscle reaction time. Based on the studies in this review, we found a positive effect in onset latency for proprioception, postural sway and the SEBT balance test (both balance), when comparing intervention groups to control groups. Further studies should give more evidence for the value of the different tests.

Surgery is often considered to be an effective treatment for patients with chronic ankle instability. A good to excellent effect on clinical outcome was found in most of the selected studies. Both Static Repair[23] and the Modified Broström[24] procedure were good surgical treatments for subjects with chronic ankle instability. However, in four of the studies, no comparison was made with a control or usual care group. Therefore, it remains unknown whether surgery gives a better outcome compared to functional training or usual care in patients with chronic ankle complaints. One study, however, did show a reduction in recurrences of sprains after a secondary re-operation compared to functional training.[22] It is important to note that most of the included patients in these studies were recruited from a secondary care setting, in contrast to the training studies, which might have influenced the outcomes.

Comparison with other studies or reviews

An earlier systematic review [8] published in 2011 included 10 RCTs investigating the effectiveness of both conservative and surgical interventions for treating chronic ankle instability. De Vries et al. reported insufficient evidence to support any specific surgical treatment for chronic ankle instability. In addition it was concluded that neuromuscular training alone was effective at the short term for chronic ankle instability compared to no training.[8] Given the lack of consensus on the definition of ankle instability as chronic complaint, we selected all studies describing any type of chronic complaints after a lateral ankle sprain.[30] This resulted in 11 additional studies and, consequently, in a more complete overview on the current literature, including two studies on chiropractic/manual therapy treatment. Therefore, the present systematic review provides a comprehensive overview of different treatments currently applied in patients with chronic ankle complaints. Like de Vries et al. we found that training programs were effective at

short term follow-up: however, we also found long-term beneficial effects in the current review.

Another systematic review assessed the effectiveness of additional supervised exercises compared with conventional treatment alone in patients with acute lateral ankle sprains[31] and found no strong evidence for the effectiveness of supervised exercise therapy on the different outcome measures. In patients with chronic ankle complaints, we found conflicting evidence on the outcomes balance and proprioception but moderate evidence for the effectiveness of a stabilizing training program on function and re-sprains.

In summary, evidence indicating the best treatment for subjects with chronic ankle complaints remains scant. There is limited to moderate evidence that a training program yields a better effect on function and pain compared to no training program. In most of the studies, although many different outcome measures were used to express function, no differences were found between the intervention groups. Therefore, for future studies it is recommended that the outcome measure of function be standardized.

Balance was the most frequently reported outcome measure, and in many studies this was also one of the inclusion criteria. However, a recent review on persistent complaints showed that both pain and function are also mentioned as frequent complaints after a lateral ankle sprain.[6] Moreover, our review showed that within the different dimensions of persistent complaints (e.g. pain, instability, swelling and re-sprain incidence) different outcome measures are used.

For clinical practice standardized training programs may provide effective treatment of chronic ankle instability and prevent recurrence after a lateral ankle sprain. Persistent ankle instability and recurrence can be treated by surgery, though with consideration that there are no studies comparing surgery to training program or controls. Further studies to support these findings are necessary.

Strength and limitations

A strength of this review is that the literature search was performed according to the Cochrane criteria and only RCTs and a CCT were included (dating from 1966 to 2012). The search included all interventions used for patients with chronic ankle complaints, without any restriction on clinical outcomes types.

The present review we included studies of chronic ankle instability without differentiating between mechanical instability, perceived instability or recurrent sprain, which might have influenced the outcomes.[32]

Due to the heterogeneity of the trials, it was not possible to perform statistical pooling. The main cause of heterogeneity was the use of different outcome measures, meaning that we had to perform a best-evidence synthesis rather than pool the results. In addition, the setting in which the studies took place might also have influenced the

outcomes and therefore indirectly might have caused heterogeneity between the studies. It is recommended future studies use standardized tests for outcome measures to enable the pooling of results. Based on this systematic review we suggest that the FADI and FADI-sport be used to assess function; the postural sway and SEBT be used to evaluate balance, and to consider muscle reaction time to be used to assess proprioception. The usefulness of the muscle reaction time as an outcome is however debatable since a recent review demonstrated that muscle reaction time (mostly delayed) is not a feature of people with chronic ankle sprains. In this systematic review, studies were scored by a rating system that also evaluates the quality of the evidence, which found that, overall, the quality of the evidence in the included studies was limited to moderate. Many of the included studies that compared training with a control treatment had very low power, due to the small study population. For higher-quality evidence on the effect of training programs among patients with chronic ankle instability, more RCTs with sufficient power and a longer period of follow-up are required.

Relevance to Sports Medicine

For treatment of chronic ankle complaints many procedures are mentioned, mostly functional training or surgery. Until now, there has been no clear evidence for the effectiveness of any specific surgical or conservative intervention in the treatment of chronic ankle complaints after an ankle sprain. Compared to previous reviews, the present review found more studies that compared training programs with a control group and had longer follow-ups, which resulted in a higher level of evidence. In addition, there were two studies on chiropractic/manual therapy treatment, both of which suggested a better effect of these treatments compared with a 'wait and see' approach. We found limited to moderate evidence for the effectiveness of training programs compared with control groups, mostly functional treatment, in patients with chronic ankle complaints, for the outcomes of function and pain. Recurrence of ankle sprains might be prevented by a proprioceptive training program.

CONCLUSIONS

This review found limited to moderate evidence for the effectiveness of a training program compared with control groups in patients with chronic ankle complaints for the outcomes of function and pain. Recurrence of ankle sprains may be prevented by a functional training program. For patients who have surgery for chronic ankle complaints, a postoperative early mobilization training program can be advised.

Implications for future research

More evidence on the effectiveness of different interventions in individuals with chronic ankle complaints (often expressed in instability, pain and functional loss) compared to controls is needed from RCTs with higher statistical power, adequate randomization, and longer follow-up periods. In addition, more studies should compare surgery with training programs in patients with persistent instability complaints after an ankle sprain.

Also, when comparing studies, standardized, less ambiguous outcome measures are needed to determine the most important dimensions of the chronic character of the complaints, that is, not only outcomes for instability and imbalance but for also pain, function and re-sprains. This will allow an evaluation of how to obtain better effects from specific treatment. Such a core set of outcome measures should be standardized and have worldwide consensus so that the results of future trials can be summarized and the best possible treatment can be provided for patients with persistent complaints after a lateral ankle ligament sprain.

Key Points

Findings: There is limited to moderate evidence for the effectiveness of a functional training program compared to control groups in patients with chronic ankle complaints on the outcomes of function and pain.

Implications: Functional training programs, often supervised by physiotherapists, seem to be beneficial for patients with chronic ankle complaints, and recurrences might be prevented by such functional training programs.

Caution: Many of the included studies comparing training with a control treatment had very low power, due to a small study population and short time of follow up.

Table 3. Effectiveness of interventions for the different outcome measures for patients with chronic ankle complaints.

Author	*Outcome*	*Follow-up*	*Intervention*		*Control*		*Mean difference or Odds Ratio*
			Mean (SD)	N	Mean (SD)	N	
I. Training programs versus controls ('wait and see')							
Function							
Short term							
Hale, 2007	Function (FADI (%))	4 weeks		16		13	
	Involved		95.79 ± 11.38		90.96 ± 5.82		7.30 (2.47,12.13)
	Uninvolved		99.65 ± 1.90		98.54 ± 3.18		0.46 (-0.45,1.37)
	Function (FADI – sports (%))	4 weeks		16		19	
	Involved		91.41 ± 12.87		79.40 ± 13.20		11.10 (6.35,15.86)
	Uninvolved		99.21 ± 3.47		97.46 ± 4.88		1.11 (-2.03,4.52)
Hoines , 2003	Karlsson score (0-85)	6 weeks		10		9	
	Eversion peak torque+ ROM (in Nm)	6 weeks		10		9	
	Unstable ankles 60º		25.50		22.11		3.39
	Unstable ankles 180º		15.20		13.33		1.87
Kaminski, 2002	Average torque E/I ratio	6 weeks		38-*		38-*	
	Peak torque E/I ratio	6 weeks		38-*		38-*	
	Strength 30º/s		1.07 (0.44)		1.06 (0.29)		0.01 (-0.16;0.18)
	120º/s		0.63 (0.13)		0.81 (0.20)		-0.18 (-0.26;-0.10)
			76.9		66.3		10.6
	Function (FADI sport (%))						
			85.0 ± 14.4		66.3 ± 11.8		18.7 (8.99;28.41)

Table 3. Effectiveness of interventions for the different outcome measures for patients with chronic ankle complaints. (continued)

Author	*Outcome*	*Follow-up*	*Intervention*		*Control*		*Mean difference or Odds Ratio*
			Mean (SD)	N	Mean (SD)	N	
Kaminski, 2002	Peak torque E/I ratio	6 weeks		38-*		38-*	
	Strength 30º/s		1.07 (0.44)		1.06 (0.29)		0.01 (-0.16;0.18)
	120º/s		0.63 (0.13)		0.81 (0.20)		-0.18 (-0.26;-0.10)
			76.9		66.3		10.6
McKeon 2008	FADI (%)	4 weeks		16		15	
			93.7± 7.4		81.40± 18.1		12.3(2.26;22.34)
	FADI-sport (%)						
			85.0± 14.4		66.3± 11.8		18.7(8.99;28.41)
Proprioception							
Bernier, 1998	A+P Joint position sense (in degrees)	6 weeks		17		14	
	Active inversion		5.26 (3.70)		7.28 (6.26)		-2.02 (-5.72;1.68)
	Passive inversion		5.85 (4.35)		4.46 (3.12)		1.39 (-1.45;4.23)
	Active neutral		5.76 (3.94)		4.00 (3.32)		1.76 (-0.95;4.47)
	Passive neutral		3.62 (2.13)		4.89 (2.80)		-1.27 (-3.08;0,54)
	Active eversion		5.56 (3.58)		5.85 (3.46)		-0.29 (-2.89;2.31)
	Passive eversion		3.79 (3.04)		5.50 (3.96)		-1.71 (-4.28;0.86)
	Active 25/ inversion		5.24 (4.61)		7.61 (3.96)		-2,37 (-5,57;0,83)
	Passive 25/ inversion		4.44 (4.35)		4.29 (3.51)		0.15 (-2.80;3,10)
	Active 25/ neutral		4.76 (2.81)		5.14 (2.82)		-0.38 (-2.46;1.70)
	Passive 25/ neutral		5.74 (3.95)		5.32 (4.40)		0.42 (-2.65;3.49)
	Active 25/ eversion		6.18 (3.70)		5.61 (3.96)		0.57 (-2.25;3.39)
	Passive 25/ eversion		4.74 (2.87)		5.11 (2.87)		-0.37 (-2.49;1.75)
	Active 25/ max. inversion		7.24 (5.95)		7.54 (5.78)		-0.3 (-4.64;4.04)
	Passive 25/ max. inversion		4.29 (2.76)		4.64 (3.81)		-0.35 (-2.77;2.07)

Table 3. Effectiveness of interventions for the different outcome measures for patients with chronic ankle complaints. (continued)

Author	*Outcome*	*Follow-up*	*Intervention*		*Control*		*Mean difference or Odds Ratio*
			Mean (SD)	N	Mean (SD)	N	
Clark, 2005	Onset latency, s-EMG (TA+PL)	4 weeks		10		9	
	Tibialis anterior (TA)		- 29.9% (6.3)		+ 0.13 % (2.5)		-30.3
	Peroneus longus (PL)		- 31.2% (4.8)		- 1.9 % (0.4)		-33.1
Eils, 2001	Joint position sense (in degrees)	6 weeks		20		10	
	10º dorsiflexion		1.3 ± 0.6		1.3 ± 0.6		0 (-0.48;0.48)
	20º dorsiflexion		1.2 ± 0.4		1.2 ± 0.4		0 (-0.32;0.32)
	15º plantarflexion		1.5 ± 0.6		1.4 ± 0.5		0.1 (-0.35;0.55)
	30º plantarflexion		1.8 ± 0.7		2.0 ± 0.8		-0.2 (-0.78;0.38)
	Mean error (in degrees)		1.5 ± 0.4		1.4 ± 0.3		0.1 (-0.19;0.39)
Eils, 2001	Muscle reaction time (in msec)	6 weeks		20		10	
	Reaction time peroneus longus		64.8 ± 6.2		65.4 ± 5.4		-0.6 (-5.32;4.12)
	Reaction time peroneus brevis		70.4 ± 6.0		72.6 ± 3.4		-2.2 (-6.41;2.01)
	Reaction time tibialis anterior		72.6 ± 6.7		74.6 ± 5.5		-2 (-7.03; 3.03)
	IEMG peroneus longus		13.0 ± 5.2		11.6 ± 4.7		1.4 (-2.60;5.40)
	IEMG peroneus brevis		7.5 ± 4.1		8.4 ± 2.5		-0.9 (-3.81;2.01)
	IEMG tibialis anterior		4.8 ± 3.5		5.6 ± 3.4		-0.8 (-3.55;1.95)
Balance							
Bernier, 1998	Postural sway (sway index (in cm)	6 weeks		17		14	
	Stable / eyes open		0.60 (.12)		0.63 (.11)		-0.03 (-0.12;0.06)
	Stable/ eyes closed		1.68 (.42)		1.77 (.33)		-0.09 (-0.37;0.19)
	Dynamic / eyes open		0.75 (.20)		0.80 (.20)		-0.05 (-0.20;0.10)
	Dynamic / eyes closed		2.32 (.42)		2.27 (.38)		0.05 (-0.25;0.35)

Table 3. Effectiveness of interventions for the different outcome measures for patients with chronic ankle complaints. (continued)

Author	*Outcome*	*Follow-up*	*Intervention*		*Control*		*Mean difference or Odds Ratio*
			Mean (SD)	N	Mean (SD)	N	
Eils, 2001	Postural sway (in mm)	6 weeks		20		10	
	SD medio-lateral		4.3 ± 0.7		4.4 ± 1.1		-0.1 (-0.77;0.57)
	SD antero-posterior		6.1 ± 1.5		5.9 ± 1.6		-0.2 (-1.02;1.42)
	Max. sway medio-lateral		20.4 ± 2.8		20.7 ± 4.1		-0.3 (-2.90;2.30)
	Max. sway antero-posterior		28.4 ± 6.2		27.8 ± 7.8		0.6 (-4.76;5.96)
	Total sway distance		438.8 ± 103.0		406.2 ± 77.2		32.6
Hale, 2007	COPV (center of pressure) (in seconds)	4 weeks		16		13	
	Involved / eyes open		3.79 ± 1.30		3.61 ± 1.31		-0.38 (-0.97,0.21)
	Uninvolved / eyes open		3.53 ± 0.63		3.18 ± 0.94		-0.11 (-0.40,0.18)
	Involved / eyes open		9.12 ± 3.81		9.04 ± 3.81		-1.09 (-2.99,0.81)
	Uninvolved / eyes closed		8.33 ± 2.94		8.21± 2.68		-1.07 (-2.64,0.50)
	SEBT (Star Excursion Balance Test in cm)	4 weeks		16		13	
	Involved / anterior reach		0.74 ± 0.08		0.69 ± 0.12		0.03 (-0.01,0.07)
	Uninvolved / anterior reach		0.74 ± 0.06		0.71 ± 0.11		0.01 (-0.02,0.04)
	Involved / anteromedial reach		0.79 ± 0.08		0.74 ± 0.11		0.04 (-0.01,0.08)
	Uninvolved anteromedial reach		0.78 ± 0.05		0.77 ± 0.09		0.00 (-0.02,0.02)
	Involved / medial reach		0.86 ± 0.07		0.82 ± 0.14		0.04 (-0.01,0.09)
	Uninvolved / medial reach		0.87 ± 0.07		0.85 ± 0.11		0.02 (0.00,0.04)
	Involved / posteromedial reach		0.87 ± 0.09		0.80 ± 0.16		0.07 (0.02,0.12)
	Uninvolved posteromed. reach		0.88 ± 0.10		0.82 ± 0.13		0.03 (-0.01,0.07)
	Involved / posterior reach		0.81 ± 0.11		0.74 ± 0.13		0.05 ((-0.02,0.12)
	Uninvolved posterior reach		0.82 ± 0.13		0.76 ± 0.15		0.03 (-0.04,0.10)
	Involved / posterolateral reach		0.86 ± 0.10		0.73 ± 0.11		0.12 (0.06,0.18)
	Uninvolved / posterolat. reach		0.82 ± 0.08		0.77 ± 0.13		0.04 (0.00,0.08)
	Involved / lateral reach		0.74 ± 0.07		0.66 ± 0.13		0.09 (0.04,0.14)

Table 3. Effectiveness of interventions for the different outcome measures for patients with chronic ankle complaints. (continued)

Author	*Outcome*	*Follow-up*	*Intervention*		*Control*		*Mean difference or Odds Ratio*
			Mean (SD)	N	Mean (SD)	N	
	Uninvolved / lateral reach		0.74 ± 0.10		0.70 ± 0.11		0.04 (-0.01,0.09)
	Involved / anterolateral reach		0.68 ± 0.07		0.62 ± 0.11		0.02 (-0.03,0.07)
	Uninvolved / anterolateral reach		0.71 ± 0.07		0.65 ± 0.12		0.03 (-0.01,0.07)
	Involved / mean reach		0.80 ± 0.07		0.73 ± 0.12		0.06 (0.02,0.10)
	Uninvolved / mean reach		0.80 ± 0.07		0.75 ± 0.10		0.03 (-0.01,0.05)
Han, 2009	TTD (total travel distance) / CoP (in seconds)	8 weeks		10		10	
	Exercise / control		97.9 (4.4)		91.7 (4.4)		-11.8 (2.8)
	CAI / healthy		99.5 (4.3)		90.2 (4.4)		- 4.3 (2.8)
Hoines , 2003	Postural sway (figure of eight) (in seconds)	6 weeks		10		9	
Kaminski, 2002	Average torque E/I ratio						
	Proprioception 30°/s		0.96 (0.33)		1.08 (0.27)		-0.12 (-0.26;0.02)
	120°/s		0.80 (0.27)		0.92 (0.25)		-0.12 (-0.24;0.00)
	S + P 30°/s		1.07 (0.21)		1.08 (0.27)		-0.01 (-0.12;0.10)
	120°/s		0.84 (0.19)		0.92 (0.25)		-0.08 (-0.18;0.02)
Kaminski, 2002	Peak torque E/I ratio						
	Proprioception 30°/s		0.92 (0.28)		1.06 (0.29)		-0.14 (-0.27;-0.01)
	120°/s		0.70 (0.21)		0.81 (0.20)		-0.11 (-0.20;-0.02)
	S + P 30°/s		1.06 (0.30)		1.06 (0.29)		0.00 (-0.13;0.13)
	120°/s		0.75 (0.15)		0.81 (0.20)		0.06 (-0.14;0.02)

Table 3. Effectiveness of interventions for the different outcome measures for patients with chronic ankle complaints. (continued)

Author	*Outcome*		*Follow-up*	*Intervention*		*Control*		*Mean difference or Odds Ratio*
				Mean (SD)	N	Mean (SD)	N	
Kidgell, 2007	Postural sway / CoP (in mm)		6 weeks		7		7	
	Dura disc			27.2 ± 4.8		36.7 ± 8.2		-9.5 (-1.68)
	Mini-trampoline			33.3 ± 8.5		36.7 ± 8.2		-3.4 (6.33)
McKeon, 2008	Static postural control (Time-To-Boundery in seconds)							
	In different directions	Eyes open	4 weeks		16		15	
	Abs. Min. TTBML	medial / lateral		1.36 ± 0.53		1.23 ± 0.26		0.13 (-0.18;0.44)
	Abs. Min. TTBAP	anterior/ posterior		4.13 ± 0.95		4.22 ± 0.79		-0.09 (-0.73;0.55)
	Mean Min. TTBML			5.09 ± 2.38		4.53 ± 1.13		0.56 (-0.82;1.94)
	Mean Min. TTBAP			13.90 ± 4.01		13.20 ± 1.9		0.70 (-1.63;3.03)
	SD Min. TTBML			4.48 ± 2.98		3.62 ± 1.27		0.86 (-0.84;2.56)
	SD Min. TTBAP			8.43 ± 3.26		7.93 ± 1.67		0.50 (-1.42;2.42)
		Eyes closed						
	Abs. Min. TTBML			0.56 ± 0.11		0.50 ± 0.10		0.06 (-0.02;0.14)
	Abs. Min. TTBAP			1.74 ± 0.61		1.50 ± 0.47		0.24 (-0.16;0.64)
	Mean Min. TTBML			2.15 ± 0.61		1.89 ± 0.48		0.26 (-0.15;0.67)
	Mean Min. TTBAP			6.04 ± 1.88		4.81 ± 1.23		1.23 (0.05;2.41)
	SD Min. TTBML			2.05 ± 0.99		1.69 ± 0.70		0.36 (-0.27;0.99)
	SD Min. TTBAP			3.91 ± 1.20		2.97 ± 0.79		0.94 (0.19;1.69)
	CoP (center of pressure)/(in seconds)							
		Eyes open	4 weeks		16		15	
	COPML SD			0.18 ± 0.05		0.18 ± 0.03		0.00 (-0.03;0.03)
	COPAP SD			0.26 ± 0.06		0.26 ± 0.05		0.00 (-0.04;0.04)
	Range of COPML			0.85 ± 0.23		0.87 ± 0.12		- 0.02 (-0.16;0.12)

Table 3. Effectiveness of interventions for the different outcome measures for patients with chronic ankle complaints. (continued)

Author	*Outcome*	*Follow-up*	*Intervention*		*Control*		*Mean difference or Odds Ratio*
			Mean (SD)	N	Mean (SD)	N	
	Range of COPAP		1.22 ± 0.27		1.15 ± 0.14		0.07 (-0.09;0.23)
	Velocity of COPML		0.89 ± 0.34		0.86 ± 0.15		0.03 (-0.17;0.23)
	Velocity of COPAP		0.74 ± 0.26		0.71 ± 0.08		0.03 (-0.11;0.17)
	COP area		5.34 ± 2.54		5.52 ± 1.20		-0.18 (-1.66;1.30)
	Eyes closed						
	COPML SD		0.40 ± 0.07		0.42 ± 0.06		-0.02 (-0.07;0.03)
	COPAP SD		0.50 ± 0.15		0.51 ± 0.13		-0.01 (-0.09;0.07)
	Range of COPML		2.38 ± 0.75		2.63 ± 0.71		-0.25 (-0.09;0.07)
	Range of COPAP		1.95 ± 0.53		2.09 ± 0.54		-0.14 (-0.53;0.25)
	Velocity of COPML		1.93 ± 0.55		2.11 ± 0.43		-0.18 (-0.54;0.18)
	Velocity of COPAP		1.82 ± 0.76		2.04 ± 0.54		-0.22 (-0.71;0.27)
	COP area		23.8 ± 12.3		27.1 ± 9.0		-3.30 (7.15;0.55)
	Dynamic postural control (SEBT) (in cm)	4 weeks		16		15	
	Anterior reach Anterior		0.67 ± 0.08		0.67 ± 0.05		0.00 (-0.04;0.04)
	PM reach Posteromedial		0.91 ± 0.13		0.80 ± 0.06		0.11 (0.03;0.19)
	PL reach Posterolateral		0.87 ± 0.13		0.76 ± 0.08		0.11 (0.03;0.19)

Table 3. Effectiveness of interventions for the different outcome measures for patients with chronic ankle complaints. (continued)

Author	*Outcome*	*Follow-up*	*Intervention*		*Control*		*Mean difference or Odds Ratio*
			Mean (SD)	N	Mean (SD)	N	
Long term							OR
Recurrences							
Hupperets , 2009	Recurrence of ankle sprains	12 months	56 (22%)	256	89 (33%)	266	0.53 (0.35;0.78)
	Incidence of injury		1.86		2.90		- 0.63
Mohammadi , 2007	Recurrence of ankle sprains	12 months		20		20	
	Proprioception training		1 (5%)		8 (40%)		-7 (-3.20)
	Strength training		4 (20%)		8 (40%)		-4 (-4.59;-3.40)
Functional training versus functional training							
Short term							
Function							
Dinesha, 2011		2 weeks		15	4 weeks	15	
	AJFAT (Ankle Joint Functional Assessment tool Questionnaire)		9.20±3.29		15.80±3.45		1.88 (<0.001) VL
Proprioception							
	Muscle onset latency	2 weeks		15	4 weeks	15	
	PL (peroneus longus)		15.73± 6.01		30.20±6.44		2.26 (<0.001) VL
	TA (tibialis anterior)		21.13±11.47		30.53±8.48		0.91 (<0.016) L

Table 3. Effectiveness of interventions for the different outcome measures for patients with chronic ankle complaints. (continued)

Author		*Outcome*	*Follow-up*	*Intervention*		*Control*		*Mean difference or Odds Ratio*
				Mean (SD)	N	Mean (SD)	N	
Chiropractic or Manual therapy versus control								
Short term								
Function								
Pellow ,	**1999**	Dorsiflexion Range of motion (degrees)	4 weeks		15		15	
		Goniometer		13.20		80.00		-66.80
		Algometer		4.18		3.86		0.32
		Functional		96.67		82.33		14.34
Hoch	**2010**		Post-treatment		10		10	
		Dorsiflexion Range of motion (cm)		12.62±2.79		12.20±3.01		0.34
		Posterior talar displacement (mm)		7.22±2.35		6.31±2.46		1.26
		Posterior stiffness (N/mm)		20.36±6.42		22.49±7.65		5.69
Balance								
Hoch	**2010**	Dynamic postural Control in SEBT (%)	Post-treatment		10		10	
		Anterior SEBT reach		79.44±4.73		78.91±5.51		1.81
		Posteromedial SEBT reach		94.06±8.15		93.30±8.48		3.16
		Posterolateral SEBT reach		87.48±10.55		86.89±11.02		5.25
		Static Postural Control in TTB (seconds) / eyes open						
		Mean min. TTB AP		5.93±1.40		4.95±1.05		0.58
		Mean min. TTB ML		2.17±0.71		1.89±0.63		0.36
		SD min. TTB AP		3.85±1.03		3.04±0.86		0.76
		SD min. TTB ML		1.64±0.70		1.42±0.58		0.43
		eyes closed						

Table 3. Effectiveness of interventions for the different outcome measures for patients with chronic ankle complaints. (continued)

Author	*Outcome*	*Follow-up*	*Intervention*		*Control*		*Mean difference or Odds Ratio*
			Mean (SD)	N	Mean (SD)	N	
	Mean min. TTB AP		1.96±0.60		1.95±0.45		0.46
	Mean min.TTB. ML		0.77±0.18		0.78±0.19		0.19
	SD min. TTB AP		1.20±0.37		1.23±0.33		0.38
	SD min. TTB ML		0.72±0.31		0.72±0.22		0.23
Pain							
Pellow , 1999		4 weeks		15		15	
	Shortform Mc.Gill questionnaire (0-100)		0.03		0.12		-0.09
	NRS (0-10)		8.33		16.87		-8.54
Surgical Treatments compared							
Long term			**CSP**		**MBP**		
Recovery							
Hennrikus , 1996		29 months	N (%)	19	N (%)	21	OR
	General outcome (Exc./ Good)		16 (84.2%)		17 (80.9%)		1.25 (0.24;6.50)
Larsen , 1988	General outcome scoring scale (0-12pt)	25 months		56		26	OR
	Exc./ Good		54 (%)		18 %		12.0 (2.33;61.78)

Table 3. Effectiveness of interventions for the different outcome measures for patients with chronic ankle complaints. (continued)

Author	*Outcome*	*Follow-up*	*Intervention*		*Control*		*Mean difference or Odds Ratio*
			Mean (SD)	N	Mean (SD)	N	
Function							
Hennrikus , 1996	Physical examination	29 months		19		21	
	Ant. Drawer sign+		1 (5%)		0 (0%)		1(5%)
	Wound complications		5 (26%).		0 (0%)		5(26%)
	Sensory loss		11 (58%)		2 (10%)		13.06 (2.34;72.82)
	X-Ray	29 months		19		21	
	TT > 8°		All+		All+		0
			RL Karlsson		**MBP**		
Karlsson , 1997		24 months	N (%)	30	N (%)	30	OR
	Karlsson Scoring scale (0-100, Exc.(91-100) / Good (81-90))		27 (90)		25 (83)		1.80 (0.39;8.32)
	Tegner score		5.8		6.1		-0.3
Larsen , 1988	X-Ray (AD and TT), difference in degrees from baseline		-1.0° and 0,5°		0° and 0°		-1.0 and 0.5
Rosenbaum , 1999	Mobility in degrees (phys. Examination) ; Inversion		-4.9 ± 6.3		-3.7 ± 5.8		-1.20 (-6.89;4.49)
	Mobility in degrees (phys. Examination) ; Eversion		0.4 ± 7.3		-1.7 ± 3.6		2.10 (-3.31;7.51)
	Mobility in degrees (phys. Examination) ; Dorsiflexion		-0.6 ± 8.1		-0.3 ± 4.6		-0.30 (-6.49;5.89)
	Mobility in degrees (phys. Examination) ; Plantarflexion		- 2.0 ± 8.7		-3.1 ± 8.5		1.1 (-6.98;9.18)
	X-Ray (degrees) ; Decrease TT		-7.3 ± 6.3		-2.0 ± 3.3		-5.30 (-10.02;-0.58)
	X-Ray (degrees) : Decrease ATT		-0.5 ± 3.6		0.2 ± 2.1		-0.70 (-3.47;2.07)

Table 3. Effectiveness of interventions for the different outcome measures for patients with chronic ankle complaints. (continued)

Author		*Outcome*			*Follow-up*	*Intervention*		*Control*		*Mean difference or Odds Ratio*
						Mean (SD)	N	Mean (SD)	N	
Balance										
Karlsson ,	**1997**	Mechanical stability:	ATT			5.8 (3-8)		5.9 (3-8)		-0.1
				Exc.						
				Good		5.9 (3-8)		6.2 (4-9)		-0.3
				Fair/poor		6.0 (3-9)		10.7 (9-14)		-4.7
			TT			4.6 (0-7)		4.0 (1-7)		0.6
				Exc.						
				Good		4.9 (0-7)		3.8 (0-6)		1.1
				Fair/poor		6.0 (3-8)		6.0 (4-8)		0.0

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APPENDIX 1

Terms used for the database search in Pubmed, Medline and Cinahl

Location	Ankle[tw] AND (inversi*[tw] OR sprain*[tw] OR strain*[tw] OR rupture* OR injur*[tw] OR distor*[tw] AND (therapeutic[mesh] OR therapy[sh] OR treat[tw]
Treatment	OR treated[tw] OR treatment*[tw] OR intervent*[tw] OR therapy[tw] OR therapies[tw] OT therapeut*[tw] OR rehabil*[tw] OR revalid*[tw] AND
Injury	biomechanic*[tw] OR recurrent*[tw] chronic[tw] OR complaint*[tw] OR instabil*[tw] ORre-injur*[tw] OR reinjur*[tw] OR risk*[tw] OR recov*[tw]
Studies	AND (randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized clinical trials[mesh] OR random allocation[mesh] OR double-blind method[mesh] OR single-blind method[mesh] OR clinical trial*[pt] OR clinical trials[mesh] OR clinical trial[tw] OR ((singl*[tw] OR doubl*[tw] OR trebl*[tw] OR tripl*[tw] AND (mask*[tw] OR blind*[tw] OR latin square[tw] OR placebos [mesh] OR placebo*[tw] OR random*[tw] OR research design[mesh: noexp] OR comparative study[pt] OR evaluation study OR evaluation studies[pt] OR follow-up studies[mesh] OR prospective studies[mesh] OR cross-over studies[mesh] OR control group*[tw] OR controlled[tw] OR controlled[tw] OR controls[tw] OR prospective*[tw] OR volunteer*[tw] NOT (animals[mesh] NOT humans[mesh]

APPENDIX 2

Risk of Bias table (as advised by the Cochrane Collaboration)
Criteria used for quality assessment for including the articles in the review:

1) Was the method randomization adequate ?
2) Was the treatment allocation concealed ?
3) Was the patient to the intervention ?
4) Was the care provider blinded to the intervention ?
5) Was the outcome assessor blinded to the intervention ?
6) Was the drop-out rate described and acceptable ?
7) Were all randomized participants analysed in the group to which they were allocated ?
8) Are reports of the study free of suggestion of selective outcome reporting ?
9) Were the groups similar at baseline regarding the most important prognostic indicators?
10) Were co-interventions avoided or similar ?
11) Was the compliance acceptable in all groups ?
12) Was the timing of the outcome assessment similar in all groups ?

APPENDIX 3

Characteristics of the included studies.

Author, year	**Julie N. Bernier 1998** "Effect of Coordination Training on Propriocepsis of the Functionally Unstable Ankle"
Study design	RCT
Participants	N= 45 Patients who reported a history of chronic ankle functional instability FAI : one ankle inversion sprain, unable to bear weight, followed by repeated injury and/or a feeling of instability and giving way Duration of complaints: 2 episodes 12 months before testing All subjects pain free at moment of testing Age: 18-32 years; 22.53 ± 3.95 (SD), gender (% males/females) Setting: secondary care; research laboratory Country: USA
Interventions	Intervention: 3 groups; randomly assigned Group 1 control n=14; no participation in strength or stability activity Group 2 sham n=14; sham treatment with electrical stimulation peroneus l+b Group 3 training n=17; experimental, participating in 6 weeks of balance and coordination; single leg exercises on floor and on a tilt board, with eyes open and eyes closed
Outcome measures	Results were measured in a pre- and a post test (after 6 weeks)\ 2 persons from the control group and 1 from the sham group did not return for the post test; of 48 subjects, 45 completed the study Measures: on behalf of propriocepsis and balance Active and passive Joint Position Sense Postural sway: anterior and posterior sway Medial and lateral sway
Outcomes	Passive and active joint position sense (see Table 2) All groups: No main effect or interaction involving groups A main effect for test F (1,42) = 5.46, p=0.024, with the post test better than the pretest Also for mode, F (1,42) = 15.75, p<0.001 with active position sense (X = 5.21 ± 3.56) A significant interaction for mode by position, F (6.252) = 3.52, p = 0.002, Passive position sense was significantly better than active position in the maximum inversion position (p <0.05) Postural stability Sway Index. The means for sway index are presented in Table 3 The ANOVA for sway index revealed no differences between groups. Modified equilibrium score. The mean modified equilibrium scores for anterior/posterior and medial/lateral are presented in Table 4. ANOVA anterior/posterior revealed main effects for test , F(1,42) = 6.63,p=0.014; condition, F(1,42) = 56.64, p<0.001; and eyes, F(1,42) = 1118.18;p<0.001 ANOVA medial/lateral main effect for test, F(1,42) = 7.59, p=0.009; condition, F(1,42) = 89.2, p<0.001; and eyes, F(1,42) = 1212.81, p<0.001;

Authors results/ conclusions	6 weeks of coordination and balance training had a significant effect on the modified equilibrium scores of balance in both the anterior/posterior and medial/lateral direction. There was no effect on sway index or position sense of the ankle. Results suggest that balance and coordination training can improve some measures of postural sway with persons with chronic unstable ankles.
Notes	No clinical outcomes The posttest scores for joint position sense were significantly improved compared with the pretest scores for all 3 groups. Passive position sense was significantly better than active position sense for all 3 groups
Author, year	**Victoria M. Clark 2005** A 4-week wobble board exercise program improved muscle onset latency and perceived stability in individuals with a functionally unstable ankle
Study design	RCT
Participants	N=19, participants with a subjective complaint of a weak ankle and a history of at least 3 ankle sprains of the lateral complex over the past 2 years Randomly assigned into 2 groups; no injury last 3 months Duration of complaints: minimally 2 years Age: 29.7 years (SD 4.9), gender (100% males) Setting: Department of Exercise and Sports Science Manchester Metropolitan University Country: United Kingdom
Interventions	Intervention: n=10, exercise: 4 weeks wobble board training (3/week,10 min) Control: n=9, no interventions All participants completed a questionnaire on functional stability Using surface–EMG on the onset time of TA and PL Pre- and posttests for all participants
Outcome measures	Outcome measures: the onset latency ,s-EMG, from the m.tibialis anterior (TA) and the m. peroneus longus (PL) Measurements as pretest after 2 weeks training and posttest after 4 weeks
Outcomes	No significant difference in the pre-exercise scores between the 2 groups. In the exercise group there was a significant difference between pre and post results ($p<0.01$), not for the control group; mean (SD) percentage was 28.4% (13.8%) in the exercise group and 0.6% (11.1%) in the control group. A significant difference during wobble board training program: TA, ($F1.3,22.0= 8.74, p<0.05$) PL, ($F1.4,24.3=8.07, p<0.01$)) and a significant interaction for both muscles: (TA, $F1.3,22.0=8.92, p<0.05$) (PL, $F1.4,24,3=6.20, p<0.05$) Within exercise group a significant difference exists in onset latency for the TA ($F2.20=10.07, p<0.05$) and PL ($F2.20=9.052, p<0.05$) Differences occur for both muscles between pre-mid and pre-post periods Effect sizes for the pre-post period in the exercise group were 1.29 and 1.20 for the TA and PL, respectively, which resulted in a power of 0.94

Authors results/ conclusions	Post training, the exercise group, 4 weeks of wobble board training, showed a significant decrease in muscle onset latency ($p<0.05$) and a significant improvement in perception of their functional stability ($p<0.01$) Wobble board training exercise reduces the likelihood of further sprains in individuals with functionally unstable ankles, even after a short period
Notes	No clinical outcome
Author, Year	**AS Dinesha 2011** Effect of 2-week and 4-week wobble board exercise program for improving the muscle onset latency and perceived stability in basketball players with recurrent ankle sprain
Study design	RCT (a randomized clinical pre- to post design)
Participants	N = 30 (15;15); 27 men ; 3 female Participants included were subjects, playing basketball between 20-30 years with at least 2 ankle sprains of lateral complex over the last year; and a negative anterior drawer test . Exclusion: TA rupture, fracture, dislocation in foot or ankle At random subjects were selected for 2 or 4-week balance training program Setting: Institute of Physiotherapy Bangalore Country : India
Interventions	2 intervention groups with different time of a balance training program Group 1) 15 subjects who had an exercise wobble board training program for 2 weeks Group 2) 15 subjects who did an exercise wobble board training program for 4 weeks In both programs there were 4 standardized balance exercises on the board Post tests were done after 2 weeks in group 1 and 4 weeks in group 2
Outcome measures	The testing procedures before and after the training programs were compared Used were a wobble board, surface EMG, customized platform Functional scale: AJFAT = Ankle Joint Functional Assessment Tool Questionnaire Muscle onset latency in tibialis anterior (TA) and peroneus longus (PL) using a goniometer
Outcome	Functional outcome: in AJFAT questionnaire Results : Group 1) 9.20±3.29 and group 2) 15.80±; Effect size: 1.88(<0.001)VL Muscle onset latency of peroneus longus and tibialis anterior using ENMG(ms) Results : PL 1) 15.73±6.01 and in 2) 30.20±6.44; Effect size: 2.26(<0.001) VL TA 1) 21.13±11.47 and in 2) 30.53±8.48; Effect size 0.91(<0.016) L Significant differences in reaction time TA and PL muscle; shows a decrease after 4-week wobble board training compared with 2-weeks training; TA 33.36% and PL 33.95% reduction
Author results/ conclusions	Results demonstrated that the 4-weeks wobble board exercise program significantly decreased muscle onset latency of the TA and PL in response to a sudden 20º ankle inversion as compared to a 2 weeks wobble board exercise program and in this way perceived stability in ankle sprains
Notes	In this study a comparison was made between two groups with the same wobble board training program;1 group with 2-weeks training and group 2 with a 4-weeks training program. Study with a high risk of bias

Author,Year	**Eric Eils 2001** A multi-station proprioceptive exercise program in patients with ankle instability
Study design	CCT
Participants	N = 30, 18 female / 12 male All subjects with chronic ankle instability, were included : Repeated ankle inversion sprains and a self-reported subjective feeling of instability or giving way Not used : talar tilt anterior drawer sign (because of the lack between mechanical and functional instability) Subjects were free of pain and divided in 2 groups : The exercise group (EG, N = 20) , participated in a 6-wk physiotherapeutic exercise group and a control group (CG; N = 10) , which only participated in the test procedures before and after the 6-wk period. The data revealed no significant differences between groups. 55% of the participants revealed a bilateral instability. so 48 feet were evaluated in the study (EG, N = 31; CG, N = 17) Age : EG 27.0 ± 7.7 ; CG 26.4+4.9 years Setting : Functionsbereich Bewegungsanalytik Klinik Allgemeine Orthopedie Country Germany , Munster
Interventions	Intervention : EG, N = 20 (31 CAI) and CG, N = 10 (17 CAI) Exercise Group, which participated in a 6-wk physiotherapeutic exercise program. This program consisted of 12 different exercises The control group had no certain intervention, was only tested All participants were tested at the beginning and after 6 weeks
Outcome measures	Three testing procedures before and afterward were compared : Joint position sense (JPS), on a footplate with a Penny and Giles goniometer Postural sway (PS); on a Kristler force plate, a single – limb stance Muscle reaction times; on a customized trapdoor with a 30gr tilting angle in the frontal plane

Outcomes	Joint position sense : improvement was found for all testing conditions Except from 10gr dorsiflexion all improvements were significant Most specific in 15 and 30gr plantarflexion The control group showed only slight improved values, not significant Postural sway: improvement for all parameters in the exercise group and the control group In medio-lateral direction a significant improvement in the exercise group Antero-posterior significant improvement in the control group (P< 0.05) The overall sway distance of the center of gravidity (CoG) was reduced in both exercise (P<0.01) and the control group (P<0.01) Muscle reaction times were prolonged between pre- an posttest in both groups for all muscles . For peroneus longus and brevis the difference of 3ms was significant (P<0.001). No significant differences could be detected for tibialis anterior and for all the muscles in the control group A slight muscular response in the peroneal muscles and tibialis anterior in the exercise group. In the control group peroneus brevis decreased 90% of the subjects in the exercise group returned the questionnaire 1 year after training. Evaluation showed a significantly reduced frequency of ankle inversion after the exercise program of almost 60% (from 27.6 to 11.2 times per year (P<0.001). no patients reported an increased frequency of ankle sprains and had a better feeling of stability and safety 10% reported to perform proprioceptive exercises at home and had no ankle sprains after exercise program
Author results conclusions	Based on the present results, a multi-station proprioceptive exercise program can be recommended for prevention and rehabilitation of recurrent ankle inversion injury
Notes	
Author, Year	**Sheri A. Hale 2007** Effect of a 4-Week Comprehensive Rehabilitation on Postural Control and Lower Extremity Function in Individuals With Chronic Ankle Instability
Study design	RCT
Participants	N = 48, 29 subjects with chronic ankle instability: history of at least 1 unilateral ankle sprain, CAI and giving way of the involved ankle the last 6 months 19 healthy subjects 28 females and 20 males; mean SD age 21.4 ± 3.5 years All recreationally active individuals from the university community Pennsylvania Country : USA
Interventions	Intervention: CAI n = 16 rehabilitation (CAI-rehab); 4-week training (ltf n= 3) n = 13 control (CAI-control) (ltf n= 1) Without CAI n = 19 healthy group (ltf n = 2) Subjects with CAI were randomly assigned. Exercises consisted of stretches, strengthening, single limb stance, box hop, Carioca, figure of eight

Outcome measures	Outcome measures were Range of motion, muscle performance and neuromuscular control. They were selected to identify both impairments (postural control) and functional limitations (Food and Ankle Disability Index (FADI),FADI-sport subscale (FADI-sport) and Star Excursion Balance Test (SEBT) Postural control : using AMTI Accusway force plate Three-dimensional ground reactions were measured in Center of Pressure excursion velocity (COPV)
Outcomes	All subjects completed a self-reported questionnaire Data were analyzed for 42 subjects; 6 did not complete the study COPV : no difference between CAI-rehab and control group (table 2) Results the same for subjects with CAI and healthy group SEBT : no difference between subjects with and without CAI Significant difference between involved and uninvolved limbs for the subjects with CAI. Post hoc test CAI-rehab group had more improvement than the CAI-control group and the healthy group No difference between the CAI-control group and healthy group FADI : at baseline more ability in the healthy group than the CAI group Post hoc the CAI-rehab group showed more improvement than the CAI-control group and the healthy group FADI-sports : comparable results as the FADI (table 3) The follow-up testing included the same measurements as on baseline The CAI-rehab group came for measurements 6 times in 4 weeks (begin, 2 weeks 2/w and in week 3 and 4 1/w; all groups at baseline and after 4 weeks
Author results/ conclusions	Subjects with CAI demonstrated deficits in postural control and functional limitations. Rehabilitation appears to improve these functional limitations There is evidence to suggest the SEBT may be a good measure to monitor change after rehabilitation for CAI
Notes	This was combined study: (relatively small power) CAI-rehab group and control group CAI groups and a group of healthy subjects
Author, year	**Kyungmo Han 2009** Effects of a 4-Week Exercise Program on Balance Using Elastic Tubing as a Pertubation. Force for Individuals With a History of Ankle Sprains
Study design	RCT
Participants	N= 40 subjects ; 20 males and 20 females ; age 21.3 ± 3.9 (table 1) 20 persons with chronic ankle instability (CAI) 20 healthy persons 10 subjects from CAI-group and the healthy-group (5M;5F both groups) were randomly assigned to the exercise and the control group (total 4) CAI-group : 1 or more ankle sprains the last 12 months and at least 2 or more ankle sprains within the last 36 months Country: USA

Interventions	Intervention group :10 subjects from CAI-group and 10 from the healthy group Became a 4-week exercise program on balance using elastic tubing, front and back pull, crossover and reverse Control group : 10 subjects from CAI-group and 10 from the healthy group
Outcome measures	The dependent variable was standing balance as measured by the total travel distance (TTD)of the center of pressure (CoP) using a force platform
Outcomes	Healthy normal subjects demonstrated a better balance prior to training compared to the subjects with CAI. No difference in the pretest values for balance between the exercise and control group. Female subjects had significantly better balance than female subjects. The exercise program caused a significant improvement in balance for the exercise group when compared to the control group (t =-5.51; P<.001) and in the CAI group versus healthy group (t = -2.76; P<.01). See table 2 Subjects with and without history of ankle sprains in the exercise group improved balance as measured by a decrease of the TTD of the CoP by 11.1cm Subjects in the nonexercise control group (CAI+healthy) showed no change in balance, shown in TTD Individuals with ankle sprains improved their balance, as measured by decrease of the TTD of the CoP by 8.2cm, whereas healthy normal subjects only decreased TTD by 2.4cm There was a pretest, test at 4 weeks and 8 week follow up for all groups On the 4 week follow-up there was no difference in the results
Author results/ conclusions	Balance was improved after 4-weeks of elastic resistance exercise in subjects with and without a history of lateral ankle sprains. Balance improvements persisted 4-weeks following the treatment cessation
Notes	CAI group and healthy group were divided in intervention and control group
Author, year	**William L. Hennrikus 1996** Outcomes of the Chrismas-Snook and Modified-Brostrom Procedures for Chronic Lateral Ankle Instability
Study design	RCT
Participants	N = 40 (42 ankles) ; randomly assigned by numbered envelopes Patients with isolated chronic lateral ankle instability, with giving way at least 6 months Age mean 25 year in Chrismas- Snook group (20 men) and 26 year in the modified-Brostrom group (16 men and 4 females) Department of Orthopaedic Surgery in San Diego Country : USA
Interventions	Two different interventions : Surgical treatment for CAI 20 (all men) : Chrismas- Snook procedure 20 16 men and 4 female) : Modified – Brostrom procedure

Outcome measures	Clinical outcomes : Interview by a standardized questionnaire, physical examination and X-ray Following criteria of Sefton :excellent, good, fair and poor (pain, swelling and instability) Follow-up averaged 29 (range, 6-49) months
Outcomes	20 patients only filled in a standardized questionnaire 9 patients with Chrismas-Snook procedure and 10 with the Modified- Brostrom Procedure were available for examination and radiographic follow up. Both surgical procedures resulted mean in excellent or good results (80%) The Sefton scores for the 2 treatments showed were better in the Modified- Brostrom group (P = 0.043) Significantly there were more complications in the Chrismas – Snook group, like wound complications (infections) and sensory complaints
Authors results conclusions	The Chrismas – Snook procedure and the Modified – Brostrom procedure are 2 surgical interventions with a good to excellent result in the treatment of chronic ankle instability. Overall the Modified – Brostrom procedure resulted in higher Sefton scores than the Snook – Chrismas procedure and gave lesser postoperative complications. The Modified – Brostrom anatomic ligament reconstruction was in this study superior for chronic lateral ankle instability.
Notes	Comparison of two operation procedures
Author, year	**Matthew Hoch 2010** Joint Mobilization Improves Spatiotemporal Postural Control and Range of Motion in those with Chronic Ankle Instability
Study design	Randomized, cross-over design
Participants	N = 20 (9M;11F); randomly assigned with concealed envelopes prepared by an independent investigator Inclusion : Patients with a history of at least 1 ankle sprain in the past and at least 2 episodes of giving way within the last 3 months Age = mean 23.4±5.4 years; height 174.6±7.8; weight 76.9±14.8 10 subjects in a joint mobilization group in session 1 and in 2 control 10 subjects in control treatment in session 1and joint mobilization in session 2 Division of Athletic Training, University of Kentucky Country : USA
Interventions	10 subjects received a joint mobilization treatment in session 1 and a control treatment in session 2 10 subjects received the opposite sequence: first control treatment in session 1 and joint mobilization treatment in session 2. 2-min. sets of Maitland grade 3 anterior-to-posterior talocrural mobilization Testing sessions were separated by >24h for a sufficient wash-out period between treatments. All subjects completed both sessions The investigators measuring all dependent variables were blinded to treatment sequences

Outcome measures	Weight-bearing lunge test for measuring Dorsiflexion Range of Motion Instrumented Arthrometry (3 trials) for posterior talar displacement and posterior stiffness based on a previous protocol (in mm) Dynamic Postural Control in using SEBT in anterior, PM and PL position Static Postural Control (1 practice trial and 3 analysis trials) on a forceplate, expressed in Center of pressure AP and ML, analyzed as TTB variables
Outcomes	All patients did both sessions A significant increase in DF ROM was detected for the joint mobilization treatment (p=0.01) No significant differences were found with posterior talar displacement (p=0.08) or stiffness (p=0.27) No significant in the reach distances were found in the SEBT (p=0.98) PM reach direction was significantly higher compared to the PL (p=0.0001) and anterior (p=0.0001).PL significantly higher than anterior (p=0.0001) TTB eyes open values were significantly higher than with eyes closed (p=0.0001). TTB AP with eyes open were significantly higher for joint mobilization treatment (p<0.0001). Post hoc no significant difference was found in the TTB ML with eyes open (p=0.07). Eyes closed no differences.
Authors results/ conclusions	This study indicates that a single joint mobilization treatment has mechanical and functional benefits for addressing impairments in sensorimotor function and arthrokinematic restrictions commonly experienced by individuals with Chronic Ankle Instability
Notes	Single joint mobilization was used in both groups (intervention and control) in 2 sessions with an interval of 6-7 weeks
Author,year	**Per Hoines 2003** High-intensity training with a bi-directional bicycle pedal improves performance in mechanically unstable ankles, prospective randomized study of 19 subjects
Study design	RCT
Participants	N = 19, 11 female and 8 male Age : 25.3 years (range 20-33, SD ± 4.1) 26.2+ 4.4 Control group ; 24.5 ± 3.9 Test group Inclusion : recurrent ankle sprain, no fracture, unilateral recurrent ankle sprain > 6months, no recent injury Ipsilateral mechanical instability of the talocrural joint found on clinical examination and stress X-ray films randomization by closed mixed envelopes
Interventions	Two comparising groups : A test group (N = 10) and a control group (N = 9) Test group : using a bi-directional bicycle pedal Control group : using an uni-directional pedal

Outcome measures	Figure-of-eight running; subjects using a Visual Analog Scale from 0-100 for pain Postural sway : before an after training; on one foot on a moving platform for 25s and tried to keep balance when the platform tilted Eversion peak torque and Range of motion (ROM) :by a Cybex Norm Isokinetic dynamometer Testing with the subjects in the supine position with a seatbelt round the pelvis Recording with one slow (60gr s-1) and one fast (180gr s-1) angular velocity
Outcomes	The subjects underwent a pre-trial on the cycle ergometer, max. oxygen uptake (VO2 max),the work rate in Watts (W) at the end of the test and max. heart rate (HRmax) were measured. Lactate test was done at baseline. The subjects exercised 3 times a week on the cycle ergometer for 45 min. All tests were done before and after the 6-week period of HI training No significant difference in testing was found between the groups at baseline Figure-of-eight : Subjects in the test group ran faster after the trial than in avance and comparing to the control group VAS during running TG 1.9-1.4 and CG 6.4-2.4 Eversion torque : Increased in the TG 11.4% at 60grs-1 (P = 0.037) and 14.2% at 180grs-1 (P =0.020) Not significant in the control group (1.6 and 1.7% at 60 and 180grs-1 Single leg stance test : Both groups better after completion of the training Subjects test group performed to the max. level of 80% after training from a mean 72.5% (SD+ 10.7) before training (P = 0.005) and in the control group from 56.1% (SD+32.0) To 67.8% (SD± 25.6). (P = 0.018,CI 2.3-21.0) The modified Karlsson functional score increased significantly in the test group from 71.8 before training to 76.9 after training (P = 0.005,CI 2.0-8.2) Slight increase in the control group was not significant
Authors result/ conclusions	This study indicates that short-term high-intensity training with a bi-directional pedal improves ankle performance and may be an option in the treatment of recurrent ankle sprains
Notes	Small power
Author, year	**Maarten D.W. Hupperets 2009** Effect of unsupervised home-based proprioceptive training on recurrences of ankle sprain: randomized controlled trial
Study design	RCT
Participants	N = 522 Age : 12-70 years 28.6 (11.8) in Intervention group and 28.0 (11.6) in control group Randomized to intervention or control, with stratification for sex, type of enrolment, and usual care of ankle sprain Athletes were recruited through 11 ERs,5 general practices and 4 physical therapy offices and through adverts in newspaper or sports magazine Inclusion : active sports participants and an ankle sprain up to 2 months before Country : The Netherlands

Interventions	**Intervention** n= 256, athletes received treatment according to usual care and additionally an eight weeks home-based proprioceptive training program; balance board training **Control**: n= 266, athletes received treatment according to usual care
Outcome measures	The outcome was the incidence density of ankle sprain and its 95% confidence interval, expressed as incident ankle sprains per 1000 hours of exposure. There was differentiated self- reported sudden inversions of the same ankle according to severity: recurrences leading to loss of sports time and recurrences resulting in health care costs or lost productivity costs or both. There was 1 year follow-up in both groups, athletes reported recurrences on a monthly basis recurrences were reported in a web-based questionnaire and also registered the health care costs and costs due to loss of productivity Athletes from the intervention group self-rated the compliance after four and eight weeks of training
Outcomes	Results during one-year follow-up Athletes that reported a recurrent ankle sprain : total 145 (28%) Intervention group 56 (22%) Control group 89 (33%) Overall incidence of ankle sprain per 1000 hours of sports was 1.86 (95% confidence interval 1.37 to 2.34) in the intervention group and 2.90 (2.30 to 3.50) in the control group (table 2). The risk of self-reported recurrences of ankle sprain was significantly lower in the intervention group than in the control group (relative risk 0.63, 95% confidence interval 0.45 to 0.88, table 2) For time loss (0.53, 0,32 to 0.88) and costs (0.25, 0.12 to 0.50) The results show that 9 athletes need to be treated to prevent 1 ankle sprain recurrence. The program led to a 35% relative risk reduction in the intervention group. Subgroup analysis carried out for ankle sprains that included medical treatment during usual care at time of inclusion showed an intervention effect only for recurrences leading to costs (0.24,0.08 to 0.72) (table 3).There was no difference for self-reported recurrences (0.89,0.54 to 1.45) and recurrences leading to loss of sports time (0.62,0.30 to 1.30). The intervention group had a significantly lower risk of recurrence than controls. 58(23%) in the intervention group fully complied the training program
Authors results/ conclusions	The use of a proprioceptive training program after usual care of an ankle sprain is effective for the prevention of self-reported recurrences
Notes	Ankle sprain in the preceding two months (subacute?)
Author,year	**T. W. Kaminski 2002** Effect of strength and proprioception training on eversion to inversion strength ratios in subjects with unilateral functional ankle instability
Study design	RCT

Participants	N = 38 (22 men and16 women) Age : 21.6 (2.9) years All participants were compared to a questionnaire, in which strictly criteria were used on behalf of Functional Ankle instability (figure 1) Setting : Department of health, HP Laboratory Delaware New Ark Country : USA
Interventions	All subjects were randomly assigned to one of four treatment groups : Strength training (S): 6 weeks of plantar flexion, dorsiflexion, inversion and eversion strength training using Thera-Band Proprioception training (P) : training which involved "T-band kicks" Strength + Proprioception training (B) : Combination of S + P Control (C) : No specific training The training protocols were for 6 weeks, 3 times a week; only training of the affected ankle
Outcome measures	Isokinetic strength was tested using a Kin Com125 automatic positioning isokinetic dynamometer before and after training Subtalar joint eversion and inversion motions were tested both concentrically and eccentrically through a range of motion involving 40gr Average torque E/I ratio Peak torque E/I ratio Normalized for body mass Taking the concentric eversion value and combining it with the eccentric inversion value
Outcomes	Average torque E/I ratio : Ranged from 0.46 - 2.54 Analysis of the results detected no significant differences after the training for one of the four groups (30 and 120gr/s) Peak torque E/I ratio 0.35 – 2.38 Analysis of variance did not detect any significant differences after training for any of the four groups (30 and 120gr/s) Post hoc power and effect size analysis was performed after the indication of "non-significant findings" Before and after training Data were analysed using a mixed model analysis of variance with repeated measures on the test factor
Authors results/ conclusions	Six weeks of strength and proprioception training (either alone or combined) had no effect on isokinetic measures of strength in subjects with self-reported unilateral functional ankle instability
Notes	Four groups with small power
Author, year	**J. Karlsson 1995** Early range of motion training after ligament reconstruction of the ankle joint
Study design	RCT

Participants	N = 40 , 22 men and 18 women Age : 24 (17-35) years Patients were randomized and blinded with an unbiased observer Functional instability was defined as repeated giving way Setting :Department of Orthopedics Ostra hospital Goteborg Country : Sweden
Interventions	40 patients were operated on with anatomic reconstruction of the lateral ankle ligament, i.e. shortening, imbrication and reinsertion They were randomly postoperative divided in 2 groups : 1) Immobilisation in a plaster cast for 6 weeks 2) Early range of motion training in a Walker-Boot. Both groups underwent an identical rehabilitation program with peroneal strengthening and co-ordination training after 6 weeks
Outcome measures	The functional results were assessed using a scoring scale Range of ankle motion The mechanical stability was measured with standardized stress radiographs (Anterior talar tilt :ATT and talar tilt : TT)
Outcomes	Functional results in scoring scale : Group 1 excellent / good 80% (16); fair/poor 20% (4) Group 2 excellent / good 95% (19): fair/poor 5% (1) Statistically significant difference in dorsal extension and plantar flexion 6wks ROM same before and after operation (table 3) In each group 1 complained of functional instability after operation 3 in group 1 had complaints of stiffness and pain The mean time of sick-leave was shorter in group 2 (6.5 ±1.6wk to 8.5±1.8wk) Return to sports shorter in group 2 (9.5±2.2 to 12.5±2.6) At follow-up return to sports 1): 18; 2) 19 Mechanical stability: both groups decrease in ATT and TT comparable
Author results/ conclusions	Early range of motion training is recommended after ligament reconstruction of the ankle, as will enable earlier return to sports activity, shorter sick leave and preserved mechanical stability
Notes	Operation and 2 ways to revalidate
Author, year	**J. Karlsson 1997** Comparison of Two Anatomic Reconstructions for Chronic Lateral Instability of the ankle joint
Study design	RCT

Participants	N = 60 ; 42 men and 18 female Age: 24 (range 17-36) years Proven objective instability more than 6 months in patients with repeated giving way sensation, pain and swelling There was no difference between the groups in preoperative functional score Before operation all patients had undergone a supervised rehabilitation program with success: peroneal strengthening and proprioceptive training Standardized radiographic examination (AP+Lat) and stress radiography , expressed in ATT and TT was performed Setting : Operation and follow up in Ostra Hospital in Goteborg Country : Sweden
Interventions	After followed a supervised rehabilitation program patients for operation were randomized divided in to 2 groups by choosing a closed envelope Group 1): Reconstruction of the ligaments as described by Karlsson et al. N = 30 Group 2): Modification of the Brostrom procedure described by Gould et al. N = 30 The mean duration of surgery was significantly longer in group 2 than in 1 Follow-up for 2 years (group 1: 3.1yrs and group 2: 3.3yrs)
Outcome measures	A scoring scale validated by Karlsson and Peterson was used Mechanical stability with standardized stress radiographics Minimal follow-up for 2 years
Outcomes	Subjective scoring scale : Group 1 :Excellent / good 90% (27); fair / poor 10% (3) Group 2 :Excellent / good 83% (25); fair / poor 17% (5) No difference between men and women The pre-injury activity level and also in follow up was assessed using the Tegner scale gave no influence of the functional results Patients with poor result had complaints of residual instability Mechanical stability : ATT : group 1: 7.1 (4-10) at follow-up; was preoperative 10.1 (8-15) group 2: 6.7 (3- 9) at follow-up; was preoperative 10.3 (7-15) TT : group 1: 4.9 (0- 8) at follow-up; was preoperative 7.9 group 2: 4.4 (0- 8) at follow-up; was preoperative 7.8 No significant statistically differences between the 2 treatment groups Surgical complications in 6 patients:2 wounds and 4 nerve problems (gr.2)
Author result/ conclusions	In the present study, there was no significant difference in functional outcome Or mechanical stability between the 2 surgical treatment groups. Both surgical methods gave excellent or good functional results in the majority of patients
Notes	2 different operative treatments for chronic ankle instability were compared
Author, year	**J. Karlsson 1999** Early mobilization versus immobilization after ankle ligament stabilization
Study design	Prospective and randomized; RCT

Participants	N = 30 ; 12 female and 18 male Age : 27 (18-36) years Inclusion : all patients with functional and/or mechanical instability of the ankle for at least 6 months Clinical patients Department of Orthopaedics Gotheborg Country : Sweden
Interventions	Postoperative two groups after surgical reconstruction of the lateral ankle ligament ; before operation all patients had undergone a well-supervised rehabilitation program, but without regaining functional ankle stability Group A : (n=15) were postoperative immobilized in a below-knee plaster cast for 6 weeks group B : (n=15) were treated with early mobilization using an Air-Cast ankle brace, after an initial period of 7-10 days in plaster
Outcome measures	Subjective assessments using a scoring scale with 8 different items Pain, swelling, stability, stiffness, stairclimbing, running and ankle support, Work, sports activity and daily living Torque measurements, during concentric/eccentric plantair flexion/dorsiflexion Mechanical stability by radiography : ATT and TT
Outcomes	Scoring scale : preoperative A :45 (34-72) and B 42 (32-75) Functional results : excellent good 12/15 in group A and in B 14/15 No significant ROM between the groups pre- and postoperative Mechanical stability after 2 years better: decrease ATT and TT in both groups No significant difference between the 2 groups by follow up After 2 years tegner activity level was 6 (2-9) in group A and 7 (4-10) in B The peak Torque conc/ecc plantair flexion of the ankle joint at 60% was significant higher after 3 months in group B regarding to A Follow up after 6 weeks, 3 months, 6 months and 2 year
Author results/ conclusions	After the construction of chronic lateral ligament instability of the ankle were the functional and stability results equally good with early postoperative mobilization as with an 6-week immobilization in a plaster cast Using early mobilization plantair flexion strength was regained earlier than with cast immobilization, without any risk of complications (like instability) They recommend early mobilization after anatomical reconstruction of the lateral ankle ligament
Notes	Small power
Author, year	**Dawson J. Kidgell 2007** Effect of Six weeks of Dura Disc and Mini-Trampoline Balance Training on Postural Sway in Athletes With Functional Ankle Instability
Study design	RCT
Participants	N = 20 ; 11 men and 9 female Inclusion subjects who had sustained an ankle inversion injury the last 2 years Mean age : 25.4 ± 4.2 years ; University population, local sports clubs, police School of Exercise and nutrition Sciences, Deakin University Country : Australia

Interventions	3 randomly allocated groups : Dura disc training (DT; n=7 ; 3 men and 4 women) Mini-trampoline training (MT; n=6; 4 men and 2 women) Control (C; n=7; 4 men and 3 women; no specific training Subjects completed a 6-weeks balance training program
Outcome measures	Postural sway performing a single leg stance on a force plate The disbursement of the Centre of Pressure (CoP) was obtained from the force plate in the medial-lateral and anterior-posterior sway path was used for pre- and posttest analysis There was a test at beginning and after 6-weeks of training
Outcomes	Data from the disbursement of CoP in the m-1 did not vary between pre- and posttest conditions for the control group Pre- and posttest disbursement of the CoP was significantly ($p = 0.003$) different between testing conditions for the MT and DT group There was no treatment effect, indicating that there was no significant ($p = 0.193$) difference between training group (MT and DT) and postural sway A trend in the data demonstrated that there was a difference between the MT and DT groups, indicating that the mini-trampoline provided a greater improvement in static balance than the dura disc This is supported by the positive percentage changes from pretest to posttest of 32 and 25.6%, for the MT and DT groups
Author results/ conclusions	There was no significant ($p>0.05$) difference detected for improvements between the MT and DT groups. The mini-trampoline and de dura disc are an effective tool for improving balance after lateral ankle sprain (LAS)
Notes	Small power; Comparing study in revalidation patients with CAI between Mini-trampoline and dura disc
Author, year	**Christian Knop 1999** Die behandlung des Rezidivs einer Fibularen bandruptur Ergebnisse einer prospektiv - randomierten Studie
Study design	RCT / prospective randomized study
Participants	N = 100 (start 109);57 male / 43 female Age : 24 years (range 11-49) Inclusion : recidivating lateral ankle ligament rupture 88% 1e recidive; 12% 2e recidive; 71% sportsrelated 50 patients of 1^{e} injury were conservative treated, 42 with external support (bandage 21, plaster 18,2 ortheses and 2 tape) became a second-stage-rupture Groups A and B) The other 50 : 1^{e} rupture was operated : re-rupture (group C and D) Setting : Surgical ER- department Klinik Hannover Country : Germany

Interventions	First dividing into 2 groups after first ankle sprain: Conservative functionally treated Operated after the first ankle joint ligament rupture Both groups were divided after re-sprain in an operation and functional treated group. So after re-N =rupture there were 4 groups A) Second-stage rupture and therapy : operative functional n = 25 B) Second-stage rupture and therapy : conservative functional n = 25 C) Re-rupture and therapy : operative functional n = 24 D) Re-rupture and therapy : conservative functional n = 26
Outcome measures	Subjective outcome in assessment scale (points scale -30 / +30) : giving way, walking instability, fear for sprain, loss of sports, uncertain feeling, pain with activity, opinion patient Clinical examination : scale -20 / +20; talar tilt and laxity ankle (UEJ and LAJ) Stress radiography : scale -20 / +20 : TT and ATT, signs of arthrosis
Outcomes	In operating groups (A and C ; n = 50) were both 1 wound infection Second-stage rupture : group A significant better result than group B Subjective scale 43.2% to 32.6 % ($p<0.05$);88% (22) Exc/good ; 80% (20) Radiological outcome : Group A 11.9 and group B 2.6 significant difference Re-rupture : Group C significant better than group D Subjective scale : C 40.3; exc/good (83%) and D exc/good 29.4 (62%) Radiological outcome more stability in C than in D (9.6 to 5.7 points)
Author results/ conclusions	Based on the results presented in this study, the authors recommend the surgical repair of ankle joint ligaments in cases of second-stage or re-rupture
Notes	In this study they made a split after the first ankle rupture in surgical and conservative functional treatment and these 2 groups were after re-sprain again divided in an operating and a functionally treated group
Author, year	**Eilif Larsen 1988** Static or dynamic Repair of Chronic Lateral Ankle Instability
Study design	A prospective randomized study
Participants	N = 82 (with 89 chronic lateral unstable ankles) Group S : 60 ankles in 56 patients (30 men and 26 women) Age : men 26 years (17-45) and women 22 years (17-45) Group D : 29 ankles in 26 patients (16 men and 10 women) Age : men 24 years (17-49) and women 21 years (17-45) Time between ankle injury and operation in S 23 months and D 29 months In group S 30 patients (%$%) and in group D 12 patients (46%) had also sprained their other ankle; with 14 (25%) and 6 (23%) ankles being rontgenographically unstable From 82 was instability in 51 patients left and 31 in right ankles 20 ankles (33%) in group S and 13 ankles (44%) in group D had increased subtalar mobility All patients complained of recurring giving way of the ankle without improvement after conservative treatment , on manual examination the ankles were unstable and radiographically all had a pathological TT and AD Setting : Orthopaedic Department of the University Hospital in Copenhagen Country : Denmark

Interventions	To their choice through sealed envelopes patients were divided in 2 groups: Static repair (group S) n = 56 Dynamic repair (group D) n = 26 (were 43) Because of too thin tendons 17 patients from group D were excluded Both ways of an operative treatment in case of ankle instability
Outcome measures	All patients had standardized clinical and rontgenographic examination pre-operatively, at 9 and at 25 months after operation Subjective results in a score system table, with score for pain in activity, degree of instability and decrease in strength (table 1) Functional balance was evaluated by the ability to stand on 1 forefoot for at least 10 seconds. 40 rontgenograms were blindly measured twice for TT and AD, standard deviation were respectively 0.26gr and 5.85. Operating 2 ankles the first ankle came in the analysis; level <0.05 was used
Outcomes	Median sick leave after operation was in group S 6 weeks and 7 in group D After operation the results were significantly better in group S (p = 0.0017) Postoperatively 3 patients had ceased sports activities (in S 1 woman because of low back pain and in D 2 women because of giving way symptoms and pain). All others returned to the required level of activity median at 14wks In group S and 13wks in group D After operation cumulated reduction in ankle and subtalar mobility was a median of 10degr (0-30) in group S and 30degr (20-50) in patients with increased subtalar mobility In group D were 5degr. (0-20) and 10degr (0-25), respectively The difference between S and D was significant (p=0.0236 and p<0.05) Rontgenographic results : In group S AD and TT were significantly reduced at 9 and 25-week follow up Group D AD and TT showed similar values The AD was most pronounced in group S comparing to D after 25 weeks Before operation in group S 44 ankles (73% were swollen and 20 in D (70%), after 2 patients in S. The difference in imbalance in both groups was not significant (p = 0.49). Postural balance improved in both groups after 25 weeks follow-up Postoperative complications were 2 in group S .In D 1 women had an revision Operation because of an osteophyte and dysaesthesy
Author results/ conclusions	In this study, the clinical results were best in the static group, and this was also the case in patients with accompanying increased subtalar mobility Advances of static repair are the location of the malleolar tendon insertions in accordance with the original ligaments, the tendon graft is hidden in the bone, and the end of the tendon graft can be positioned depending on the type of instability.
Notes	2 kind of operative procedures were compared in patients with chronic ankle instability
Author, year	**Patrick O. McKeon 2008** Balance Training improves Function and postural Control in those with chronic Ankle Instability
Study design	RCT

Participants	N = 31 (12M ; 19F) Age : Training group (6M : 10F) 22.2±4.5 Control group (6M ; 9F) 19.5±1.2 Inclusion : Subjects with self-reported CAI; Introduction criteria : A history of more than 1 ankle sprain and residual symptoms, Including subsequent episodes of the ankle giving a quantified by 4 or more "yes" responses on the Ankle Instability Instruments (8) Also symptoms of ankle disability due to ankle sprains with a score 90% or less on the FADI and the FADI sports surveys No sprains the last 6 weeks Setting : Science department of the University of Kentucky Country: USA
Interventions	Randomly patients were divided, concealed by a independent investigator, in a training group (n=16), which group had a 4-week balance training program and a control group (n=15), which had no special program, just usual care Balance training program: single-limb hops, hops for stabilization and reach, unanticipated hops to stabilization, single-limb stance activities There was a pretest and a posttest after 4 weeks
Outcome measures	Results in both groups were measured in a pre- and a posttest after 4 weeks A self-reported function scale measured in FADI and FADI sports survey Static postural control with the Accusway Plus forceps plate Dynamic postural control, measured by the SEBT TTB measures were described in data reduction CoP- based measures
Outcome	Self-reported function : Effect sizes for FADI and FADI sports are in table 1). In the balance training group the effects were significantly greater than in the pretest and also than the control group in the posttest Static postural control : TTB measures. The eyes-open trials showed no effects. For the eyes-closed TTB measures there was a significant increase in posttest comparing pretest in the balance training group, in the ML and the PL directions (table 3) Traditional CoP-based measures : With eyes-open there was no difference in groups. Significant time main effect for CoP velocity in the AP direction (P = 0.04). Both groups had significant decreases in AP velocity in the balance training group, there were no changes in the control group Dynamic balance : Balance training reached further in the PM and PL reach in the posttest than the subjects in the control group
Author results/ conclusions	Four weeks of balance training significantly improved self-reported function, static postural control as detected by TTB measures and dynamic postural control as assessed with the SEBT. TTB measures were more sensitive at detecting improvements in static postural control compared with summary CoP-based measures
Notes	No clinical outcome

Author, year	**Farshid Mohammadi 2007** Comparison of 3 Preventive Methods to Reduce the recurrence of Ankle Inversion Sprains in male Soccer Players
Study design	RCT (level of evidence 1)
Participants	N = 80 (all men) ; selected from a population of 120 people Age : 24.6±2.36 years Inclusion : previous right or left ankle inversion sprain (which caused the player to miss a match or practice session) Follow up for 1 soccer season after the previous sprain Ankle sprain recurrence was a sprain during a scheduled match or training Setting : 80 soccer players in the first division of men's league in Iran Faculty of Rehabilitation University of medical Sciences Teheran Country : Iran
Interventions	The subjects were divided into 4 groups : Proprioceptive training group ; n = 20 Using the ankle disc to train Strength training group ; n = 20 Evertor muscle training (weights and bands) Orthosis group ; n = 20 Using a sport stirrup orthosis Control group ; n = 20 ; This had no intervention
Outcome measures	One-way analysis of variance (overall ankle sprain recurrence among the groups) Differences between groups were tested using the Fisher exact test (alpha 0.05) (See table 2)
Outcome	No difference in characteristics between the groups There were no significant differences among groups in exposure The incidence of ankle sprains in the proprioception training was significantly lower than the control group (RR, 0.13;95% CI,0.003-0.93;p = 0.02) The findings in the strength and orthosis group were not significant better than in the control group (RR, 0.5 ;95%CI,0.11-1.87; P = 0.27 for strength and RR, 0.25;95%CI, 0.03-1.25; p =0.06 for the orthosis group)
Authors results/ conclusions	Proprioceptive training, compared with no intervention, was an effective strategy to reduce the rate of ankle sprains among male soccer players who suffered ankle sprain
Notes	Inclusion criteria were not so clear and the target group ware only male soccer players . The study aimed at a preventive effect for recurrence
Author, year	**Justin Edward Pellow 1999** The Efficacy of Adjusting the Ankle in the Treatment of Subacute and chronic Grade 1 and Grade 2 Ankle Inversion Sprains
Study design	A single-blind, comparative, controlled pilot study

Participants	N = 30 Age : mean 24.9 years ; male 63%/ female 37% (15-50 years) Inclusion : Patients with a subacute or chronic grade 1 and 2 ankle sprain according to the criteria set out to determine ankle sprain severity (See table 1) Diagnosis was based on the history of the most recent sprain Recruiting patients found place through advertisements in local papers an notice boards around the campus and sports clubs Setting : Chiropractic department of Durban Country : South Africa
Interventions	2 treatment groups : Group 1) The adjustment or experimental group ; n = 15 Intervention: Mortise separation adjustment Group 2) The placebo / control group ; n = 15
Outcome measures	Subjective data using : the short-form McGill Pain Questionnaire (ratio) the Numerical Pain Rating Scale (%) A functional evaluation scoring scale was also used Objective data : ankle dorsiflexion range of motion (with goniometer) Algometer measuring pain threshold over ant.talofibular lig. Localized lateral ligament tenderness measurements Follow up at the beginning, the final treatment and after 1 month
Outcomes	Significant differences were found in favor of the adjustment group in terms of pain experienced at the final treatment and at the 1-month follow-up A significant difference was found in favor of the adjustment group in ankle dorsiflexion ROM at the 1-month follow-up, also was this detected in terms of overall ankle functioning at the final treatment and the 1-month follow up Adjusting the ankle was superior to placebo treatment in subjective, objective and functional terms when the groups were compared Statistical analysis within group 1 (table 10) showed significantly improvement In term of pain (quality and intensity) in all stages of follow-up The placebo group did not show statistically changes (after power analysis) within the group in terms of subjective, objective and functional findings
Authors result conclusions	This study appears to indicate that the mortise separation adjustment may be superior to detuned ultrasound therapy in the management of subacute and chronic grade 1 and grade 2 inversion ankle sprains
Notes	This study made a comparison between an chiropractic treatment (adjustment) and a placebo treatment
Author, year	**Dieter Rosenbaum 1999** Clinical and Functional Outcome After Anatomic and Nonanatomic Ankle Ligament Reconstruction: Evans Tenodesis versus Periosteal Flap
Study design	RCT

Participants	N =20 (all men) Age : Evans group 25.0+5.5 ; Periost group 25.1±6.7 years Inclusion : surgery was indicated when the patients reported recurrent inversion injuries and pain in the ankle joint Radiological stress examination : TT > 10gr or ATT > 10mm Setting : Department of Surgery Military hospital Ulm Country : Germany
Interventions	Randomized assignment into two groups for operation : 1) Evans group :a modified Evans tenodesis ; n = 10 2) Periost group : a fibular periostal flap repair ; n = 10
Outcome measures	The two groups did not differ significantly in their anthropometric characteristics (table1) Patients were examined 1 day before 10 days and 10 months after surgery Physical examination : manual evaluation of joint mobility Radiographic stress diagnostics : TT and ATT A dynamic pedobarography (a capacitive pressure platform) Single pressure measurements, maximal pressure picture, gait line and the vertical ground reaction force
Outcomes	10 patients in the Evans group and 9 in the Periost group reported that ankle stability was subjectively improved 3 patients in EG and 1 in the PG complained about remaining occasional pain and swelling during exercise The radiographic results : reduced TT, more in EG (61%;$p<0.05$), less in PG (29%; not significant) ATT < than 5% reduction (table 2) Manually tested motion showed a decrease in inversion (EG 14% ; PG 13%) Plantarflexion was reduced by 5% in both groups (not significant) Gait parameters, total impulse and ground contact time remained constant Peak pressures in the forefoot region increased with 20% in both groups
Authors results/ conclusions	The results in this study indicate that both methods of ankle ligament reconstruction in patients with chronic ankle instability achieve a comparable clinical and functional outcome within one year after surgery
Notes	In this study the effects of two different surgical procedures for the treatment of chronic ankle instability were investigated

Chapter 4

Structural abnormalities and persistent complaints after an ankle sprain are not associated: An observational case control study in primary care

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ABSTRACT

Background: Persistent complaints are very common after a lateral ankle sprain.

Aim: To investigate possible associations between structural abnormalities on radiography and MRI, and persistent complaints after a lateral ankle sprain.

Design: Observational case-control study on primary care patients in general practice.

Methods: Patients were selected who had visited their general practitioner with an ankle sprain 6-12 months before the study; all received a standardized questionnaire, underwent a physical examination, and radiography and MRI of the ankle. Patients with and without persistent complaints were compared regarding structural abnormalities found on radiography and MRI; analyses were adjusted for age, gender and body mass index.

Results: Of the 206 included patients, 98 had persistent complaints and 108 did not. No significant differences were found in structural abnormalities between patients with and without persistent complaints. In both groups, however, many structural abnormalities were found on radiography in the talocrural joint (47.2% osteophytes and 45.1% osteoarthritis) and the talonavicular joint (36.5% sclerosis). On MRI, a high prevalence was found of bone edema (33.8%) and osteophytes (39.5%) in the talocrural joint; osteophytes (54.4%), sclerosis (47.2%) and osteoarthritis (54.4%; Kellgren & Lawrence grade >1) in the talonavicular joint, as well as ligament damage (16.4% in the anterior talofibular ligament).

Conclusion: The prevalence of structural abnormalities is high on radiography and MRI in patients presenting in general practice with a previous ankle sprain. There is no difference in structural abnormalities, however, between patients with and without persistent complaints.

Using imaging only will not lead to diagnosis of the explicit reason for the persistent complaint.

Keywords: ankle - abnormalities – general practice – imaging- sprain

INTRODUCTION

Ankle sprains are one of the most commonly occurring musculoskeletal injuries. In the Netherlands, about 16.000 athletes visit an emergency department each year [1] and about 300.000 patients are seen each year in general practice.[2] The incidence of sprains is higher in males than in females, and higher in young people.[2] The incidence of a fracture after an ankle sprain is 5% in general practice and up to 20% in the emergency departments of hospitals.[2]

More than 75% of the injuries are caused by an inversion sprain, in which the lateral collateral ligament complex generally gets strained or ruptured.[2] Most commonly, the anterior talofibular ligament (ATFL) is the first ligament to be injured.[3] Other structures that may be injured during a lateral ankle sprain are the calcaneofibular and posterior talofibular ligaments, the peroneal tendons, joint capsule, and the proprioceptive nerve endings found within the surrounding soft tissues.[3]

Despite the many treatment options available, such as early mobilisation, cooling, instruction for weight bearing, taping and exercises many patients have persistent complaints after an acute ankle sprain. [4-7] Up to 33% still experience pain after one year and re-sprains occur in up to 34% of all patients.[8] When complaints last for at least 6 months, the terms chronic or functional ankle instability are used.[9] In the Netherlands, annual sport-related ankle sprain costs are estimated to be € 187 million and persisting complaints are expected to lead to more costs as a result of productivity loss and health care costs.[10]

It is not known whether these persistent complaints are associated with structural changes or abnormalities in the ankle caused by the trauma. Identification of structural abnormalities possibly associated with persistent complaints could provide help in prognosis and treatment for patients with persistent complaints after a lateral ankle sprain in general practice. Radiography is generally regarded as a reliable method for the detection of fractures, sclerosis or osteophytes, but is not suitable for assessment of soft tissue, bone marrow oedema, lesions of cartilage and ligaments.[11] These can be assessed more directly and accurately using magnetic resonance imaging (MRI). [12]

The purpose of this study, therefore, was to investigate the association between persistent complaints after a lateral ankle sprain and possible structural abnormalities found on radiography and MRI.

METHODS

Patients

The present study is an observational case-control study on primary care patients after a lateral ankle injury. Patients were selected from the medical records of 84 participating general practitioners (GPs) using the diagnostic International Classification of Primary Care (ICPC) code (L77) 'ankle sprain' and with the search terms: ankle, distortion and sprain. Patients were eligible if they had presented themselves 6-12 months before the start of the study at the GP with an inversion trauma of the ankle and were aged 16-65 years. Patients with known fractures, other osseous damage, a reported history of former operations of the ankle, and known systemic diseases with impact on functioning of the musculoskeletal system (e.g. amyotrophic lateral sclerosis, multiple sclerosis, or rheumatoid arthritis) were excluded, as were patients with insufficient knowledge of the Dutch language.

Procedure

Selected patients received a letter with a response card for participation on behalf of their GP. Interested patients were subsequently approached by telephone by the research assistant and inclusion criteria were checked. Additionally, the presence of persistent complaints was checked using a 7-point Likert scale (1=completely recovered, 7=worse than ever). Based on this score, patients were divided into two study groups: patients without persistent complaints [score 1-2 (completely recovered or strongly improved)], defined as control subjects, and patients with persistent complaints [score 3-7 (slightly improved to worse than ever)], defined as cases.

After providing written informed consent, patients were included, asked to fill in an online questionnaire, and were invited for a physical and radiological examination, consisting of radiography and MRI of the injured ankle. Findings from the physical examination were not used for the purpose of the current study.

Measurements

The standardized questionnaire contained questions on patient characteristics [age, sex, body mass index (BMI) and education level], the initial ankle sprain (side, history of previous injuries, and activity that caused the sprain), local symptoms such as swelling (place and severity), and current complaints including pain severity [nummeric rating scale (NRS-11)], subjective feeling of instability (yes/no) and function (Ankle Function Score, 0 representing the worst possible and 100 representing the best possible function).[13]

The radiological examination consisted of a standard anterior-posterior and lateral (non-weight bearing) radiograph of the injured ankle followed by a routine ankle MRI (1.5 Tesla) of the injured ankle.

All X-rays and MRIs were scored by one musculoskeletal radiologist (NP), using a standardized scoring form. A random subsample of 32 X-rays and MRIs was scored by a second musculoskeletal radiologist (EO) to determine the inter-observer reliability. The inter-observer reliability was calculated using Cohen's kappa (range 0.653-1.00) between the different items. The percentage agreement was 99.1% (1681 of the 1696 scored items) and 98.8% (5883 of 5952) for the radiography and MRI items, respectively. Both radiologists were blinded for the clinical scores and group status.

On radiography and MRI the following osseous structures were examined: medial and lateral malleolus, surface of the tibia at the tibiotalar joint, talus at the talocrural joint, subtalar joint, and os naviculare at the talonavicular joint.

Structural abnormalities scored from the radiography included fractures, osteophytes, subchondral cysts, sclerosis, osteochondral lesions (only in the talocrural joint), cartilage loss (only scored in the talocrural joint), joint space narrowing, hydrops, the presence of a loose body, and soft tissue swelling.

MRIs were scored for the same items, as well as for the presence of bone marrow edema, cartilage loss and osteochondral lesions for all joints round the ankle. Furthermore, the presence of synovitis and anterolateral impingement was examined on MRI. Muscles, peroneal tendons and the anterior/posterior tibiofibular and talofibular ligaments, calcaneofibular ligament, deltoid ligament and the plantar calcaneonavicular (spring) ligament were assessed.

On both radiography and MRI, the presence of soft tissue calcification was assessed in the region of the medial malleolus, lateral malleolus, talus and navicular bone. All possible structural abnormalities on radiography and MRI were scored from 0-2: 0=absent, 1=possibly present and 2=evidently present. The talocrural joint, subtalar joint and talonavicular joint were scored for signs of osteoarthritis using the 0-4 point Kellgren and Lawrence (KL) score (0=absent, 1=doubtful, 2=mild, 4=severe)[14] and bone marrow edema was scored as absent, subchondral present, and bone bruise volume < 25%, 25-50%, 50-75% and >75%. Tendons (peroneus longus and brevis tendon) and ligaments were scored as normal, thickened, partial tear, total tear and (in case of the peroneus brevis tendon) split tendon. The large numbers of radiography and MRI item scores were reduced by clustering the osseous structures into talocrural joint, subtalar joint, talonavicular joint and talus.

Statistics

To compare characteristics of patients with and without persistent complaints, differences between both groups were tested with an independent sample *t*-test for continuous variables and a chi-square test for dichotomous variables.

Logistic regression was applied to determine the association between radiography and MRI findings and persistent complaints. All analyses were adjusted for potential confounders age, gender and BMI.

All data were analysed using SPSS (version 20.0, SPSS Inc, Chicago, IL, USA). For all analyses, a p-value <0.05 was defined as statistically significant.

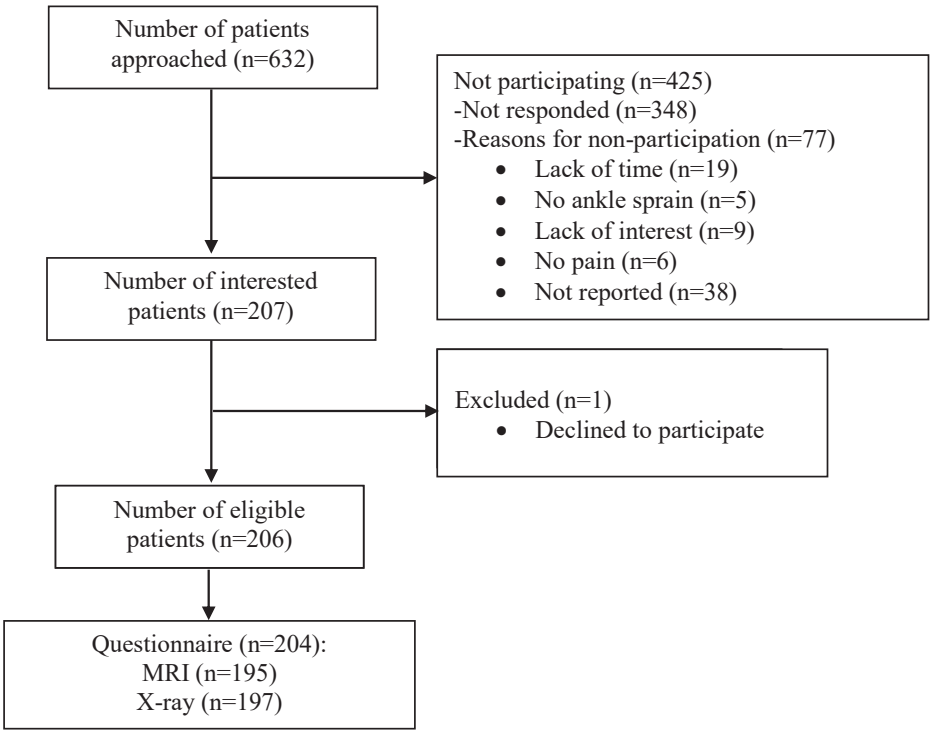

Figure 1. Flowchart of the study

RESULTS

A total of 632 patients were selected from the medical files of 84 GPs; these patients were approached and asked to participate in the study. Finally, 206 patients were included in the study: 98 patients reported persistent complaints and 108 patients reported no persistent complaints (Figure 1). From this total, 204 patients completed the questionnaire, a radiography was performed in 197 patients and a MRI was performed in 195 patients

(Figure 1). The time between inclusion and the physical examination, radiography and MRI ranged from 2-77 (median 7) days.

Baseline characteristics

The mean age of the total study population was 37 (SD 14.7) years and consisted of 87 males (42.2%) (Table 1). The right ankle was the most frequently injured ankle (55.8%). Of the participants, 6% had a previous ankle sprain in former history but with no significant difference between the two groups. Patients with persistent complaints had a significantly higher BMI (26.9 kg/m^2) than the control group (24.9kg/m^2).

Patients with persistent complaints had higher pain scores both in rest and during exercise (1.9 and 3.6, respectively) and the Ankle Function Score was significantly lower ($p<0.001$) compared with patients without complaints (0.4 and 1.25, respectively).

Table 1. Patient characteristics (n (%), unless otherwise stated)

	Total (n = 206)	**Persistent symptoms (n = 98)**	**No symptoms (n = 108)**	***P* value**
Age (years)*	37.33 (14.67)	36.14 (14.51)	38.41 (14.80)	0.270
Gender (male)	87 (42.2%)	36 (36.7%)	51 (47.2%)	0.128
BMI (kg/m^2)*	25.77 (4.80)	26.92 (5.51)	24.94 (4.04)	**0.006**
Education level				0.056
Lower	124 (60.2%)	65 (66.3%)	59 (54.6%)	
Higher	80 (38.8%)	31 (31.6%)	49 (45.4%)	
Sport participation (yes)	119 (57.8%)	35 (35.7%)	84 (77.8%)	
Side of ankle sprain (right)	115 (55.8%)	59 (60.2%)	56 (51.9%)	0.228
Previous ankle sprain	96 (46.6%)	49 (50.0%)	47 (43.5%)	0.277
Ankle sprain during:				0.926
Sport	75 (36.4%)	36 (36.7%)	39 (36.1%)	
Work	26 (12.6%)	13 (13.3%)	13 (12.0%)	
Hobby	14 (6.8%)	5 (5.1%)	9 (8.3%)	
Task around the house	10 (4.9%)	4 (4.1%)	6 (5.6%)	
Traffic participation	21 (10.2%)	9 (9.2%)	12 (11.1%)	
Other	56 (27.2%)	28 (28.6%)	28 (25.9%)	
Ankle swollen after sprain				0.373
No	13 (6.3%)	7 (7.1%)	6 (5.6%)	
Slight	47 (22.8%)	18 (18.4%)	29 (26.9%)	
Serious	142 (68.9%)	70 (71.4%)	72 (66.7%)	
Unknown	4 (1.9%)	3 (3.1%)	1 (0.9%)	

Table 1. Patient characteristics (n (%), unless otherwise stated) (continued)

	Total (n = 206)	Persistent symptoms (n = 98)	No symptoms (n = 108)	*P* value
Place swelling after sprain				0.080
Medial side	20 (9.7%)	13 (13.3%)	7 (6.5%)	
Lateral side	169 (82%)	75 (76.5%)	94 (87.0%)	
Other place	17 (8.3%)	10 (10.2%)	7 (6.5%)	
Most pain after sprain				0.113
Medial side	25 (12.1%)	12 (12.2%)	13 (12.0%)	
Lateral side	109 (52.9%)	42 (42.9%)	67 (62.0%)	
Frontal side	14 (6.8%)	9 (9.2%)	5 (4.6%)	
Caudal side	7 (3.4%)	5 (5.1%)	2 (1.9%)	
Other place	51 (24.8%)	30 (30.6%)	21 (19.4%)	
Instability after sprain				**0.020**
yes	170 (82.5%)	86 (87.8%)	84 (77.8%)	
Pain score at baseline*				
In rest (VAS 0-10)	1.11 (1.83)	1.87 (2.20)	0.44 (1.03)	**<0.001**
During exercise (VAS 0-10)	2.37 (2.46)	3.62 (2.62)	1.25 (1.64)	**<0.001**
Ankle Function Score at baseline* (AFS 0-100)*	73.45 (20.50)	62.47 (20.24)	82.90 (15.44)	**<0.001**
Baseline recovery score				n.a.
Completely recovered	36 (17.5%)	-	36 (33.3%)	
Greatly improved	72 (35.0%)	-	72 (66.7%)	
Slightly improved	52 (25.2%)	52 (53.1%)	-	
The same	17 (8.3%)	17 (17.3%)	-	
Slightly deteriorated	21 (10.2%)	21 (21.4%)	-	
Sharply deteriorated	6 (2.9%)	6 (6.1%)	-	
Worse than ever	2 (1.0%)	2 (2.0%)	-	

*Expressed mean (SD); n.a. = not applicable; statistically significant differences in bold

Radiological findings

Radiography

In the talocrural joint, possibly and evidently osteophytes were seen in 47.9% of the patients with persistent complaints compared with 46.6% in the control group. Moreover, 44.7% of the patients with persistent complaints and 45.7% of the patients without persistent complaints had a KL grade ≥1 with no significant difference between the groups (Table 2).

At the talonavicular joint, a prevalence of possibly and evidently osteophytes of 41.5% and 46.6%, respectively, was found in patients with and without persistent complaints

and 39.4% and 46.6% of the patients, respectively, had a KL grade ≥1. In addition, 30.9% of the cases and 41.7% of the control subjects had sclerosis.

Adjusted for age, gender and BMI no significant differences were found for any of the radiographic scores between the patients with and without persistent complaints.

Table 2. Prevalence of abnormalities on radiography in patients with and without persistent symptoms

		Total (n = 197)		Persistent symptoms (n = 94)		No symptoms (n = 103)		*P* value#
		n	%	n	%	n	%	
Talocrural joint								
*Fracture**:	- Present	6	3.0	3	3.2	3	2.9	0.98
*Osteophyte**:	- Possibly	63	32.0	33	35.1	30	29.1	0.73
	- Evident	30	15.2	12	12.8	18	17.5	
*Subchondral cyst**:	- Present	1	0.5	1	1.1	0	0.0	0.98
*Sclerosis**:	- Present	3	1.5	2	2.1	1	1.0	0.54
*Osteochondral lesion**:	- Present	3	1.5	1	1.1	2	1.9	0.98
*Cartilage loss**:	- Present	2	1.0	2	2.1	0	0.0	0.97
*Joint space narrowing***:	- Present	17	8.6	8	8.5	9	8.7	0.89
*Kellgren and Lawrence score**:	- Normal	106	53.8	51	54.3	55	53.4	0.82
	- Grade 1	70	35.5	31	33.0	39	37.9	
	- ≥ Grade 2	19	9.6	11	11.7	8	7.8	
Subtalar joint								
*Fracture***:	- Present	0	0.0	0	0.0	0	0.0	0.81
*Osteophyte***:	- Possibly	3	1.5	0	0.0	3	2.9	0.99
	- Evident	3	1.5	0	0.0	3	2.9	
*Subchondral cyst***:	- Present	0	0.0	0	0.0	0	0.0	0.81
*Sclerosis***:	- Present	11	5.6	4	4.3	7	6.8	0.96
*Joint space narrowing***:	- Present	1	0.5	0	0.0	1	1.0	0.97
*Kellgren and Lawrence score***:	- Normal	188	95.4	93	98.9	95	92.2	0.96
	- Grade 1	6	3.0	0	0.0	6	5.8	
Talonavicular joint								
*Fracture****:	- Present	0	0.0	0	0.0	0	0.0	0.31
*Osteophyte****:	- Possibly	67	34.0	30	31.9	37	35.9	0.72
	- Evident	20	10.2	9	9.6	11	10.7	
*Subchondral cyst****:	- Present	0	0.0	0	0.0	0	0.0	0.31
*Sclerosis****:	- Present	72	36.5	29	30.9	43	41.7	0.35
*Joint space narrowing****	- Present	17	8.6	8	8.5	9	8.7	0.58
*Kellgren and Lawrence score****:	- Normal	107	54.3	56	59.6	51	49.5	0.56
	- Grade 1	74	37.6	33	35.1	41	39.8	
	- ≥ Grade 2	11	5.6	4	4.3	7	6.8	

Table 2. Prevalence of abnormalities on radiography in patients with and without persistent symptoms (continued)

		Total (n = 197)		Persistent symptoms (n = 94)		No symptoms (n = 103)		*P* value#
		n	%	n	%	n	%	
Calcification								
*Medial malleolus**:	- Present	14	7.1	6	6.4	8	7.8	0.98
*Lateral malleolus**:	- Present	24	12.2	9	9.6	15	14.6	0.65
*Talus***:	- Present	10	5.1	3	3.2	7	6.8	0.56
*Navicular bone***:	- Present	19	9.6	7	7.4	12	11.7	0.50
Other								
*Joint effusion***:	- Present	5	2.5	0	0.0	5	4.9	0.96
*Loose body***:	- Present	6	3.0	2	2.1	4	3.9	0.93
*Soft tissue swelling**:	- Present	2	1.0	1	1.1	1	1.0	0.93

analyses adjusted for age, gender and BMI;)

*Missing data: Total/Persistent symptoms/Without persistent symptoms = 2 (1,0%)/1 (1,1%)/1 (1,0%)

**Missing data: Total/Persistent symptoms/Without persistent symptoms = 3 (1,5%)/1 (1,1%)/2 (1,9%)

*** Missing data: Total/Persistent symptoms/Without persistent symptoms = 5 (2,5%)/1 (1,1%)/4 (3,9%)

MRI

Bone edema was most frequently seen in both the talocrural and subtalar joint in patients with and without persistent complaints (18.1% vs. 31.7% and 22.3% vs. 26.7%, respectively) (Table 3). Osteophytes were most frequently seen in the talonavicular joint in patients with and without persistent complaints (48.9% and 59.4%, respectively).

A KL grade ≥ 1 was present most frequently in the talocrural and talonavicular joint in patients with and without persistent complaints (40.4% vs. 42.5% and 49% vs. 61.3%, respectively). In the talocrural joint, 13.8% of the subjects with persistent complaints and 5.9% of the subjects without persistent complaints had a KL grade ≥ 2. Nearly half of the patients (44.7% of cases and 49.7% of controls) had sclerosis in the talonaviculair joint on MRI. In both groups, the two ligaments most often affected were the ATFL ligament and the calcaneofibular ligament.

Adjusted for age, gender and BMI, no significant differences were found in any of the MRI items between the patients with and without persistent complaints.

Table 3. Prevalence of abnormalities on MRI in patients with and without persistent symptoms

		Total (n=195)		Persistent symptoms (n=94)		No symptoms (n=101)		p-value#
		n	%	n	%	n	%	
Talocrural joint								
Fracture:	- Present	8		4		4		0.46
Bone edema:	- Subchondral	17	8.7	8	8.5	9	8.9	0.25
	- <25%	33	16.9	11	11.7	22	21.8	
	- > 25	16	8.2	6	6.4	10	9.9	
Osteochondral lesion:	- Present	11	5.6	6	6.4	5	5.0	0.61
Osteophyte:	- Slightly	57	29.2	24	25.5	33	32.7	0.37
	- Evident	20	10.3	11	11.7	9	8.9	
Subchondral cyst:	- Present	4	2.1	3	3.2	1	1.0	0.16
Cartilage loss:	- Present	20	10.3	8	8.5	12	11.9	0.60
Sclerosis:	- Present	4	2.1	1	1.1	3	3.0	0.48
Kellgren and Lawrence score:	- Normal	114	58.5	56	59.6	58	57.4	0.16
	- Grade 1	62	31.8	25	26.6	37	36.6	
	- ≥ Grade 2	19	9.7	13	13.8	6	5.9	
Subtalar joint								
Fracture:	- Present	0	0.0	0	0.0	0	0.0	0.15
Bone edema:	- Subchondral	11	5.6	6	6.4	5	5.0	0.83
	- <25%	39	20.0	18	19.1	21	20.8	
	- > 25	9	4.6	3	3.2	6	5.9	
Osteochondral lesion:	- Present	1	0.5	1	1.1	0	0.0	1.00
Osteophyte:	- Slightly	12	6.2	3	3.2	9	8.9	0.18
	- Evident	5	2.6	1	1.1	4	4.0	
Subchondral cyst :	- Present	5	2.6	3	3.2	2	2.0	0.29
Cartilage loss:	- Present	5	2.6	1	1.1	4	4.0	0.35
Sclerosis:	- Present	15	7.7	3	3.2	12	11.9	0.05
Kellgren and Lawrence score:	- Normal	178	91.3	90	95.7	88	87.1	0.67
	- Grade 1	17	8.7	4	4.3	13	12.9	
Talonavicular joint								
Fracture:	- Present	2	1.0	2	2.1	0	0.0	1.00
Bone edema:	- Subchondral	3	1.5	2	2.1	1	1.0	0.76
	- <25%	15	7.7	8	8.5	7	6.9	
	- > 25	8	4.1	5	5.3	3	3.0	
Osteochondral lesion:	- Present	0	0.0	0	0.0	0	0.0	0.15
Osteophyte:	- Slightly	84	43.1	36	38.3	48	47.5	0.59
	- Evident	22	11.3	10	10.6	12	11.9	
Subchondral cyst:	- Present	1	0.5	0	0.0	1	1.0	1.00

Table 3. Prevalence of abnormalities on MRI in patients with and without persistent symptoms (continued)

		Total (n=195)		Persistent symptoms (n=94)		No symptoms (n=101)		p-value#
		n	**%**	**n**	**%**	**n**	**%**	
Cartilage loss:	- Present	39	20.0	17	18.1	22	21.8	0.59
Sclerosis:	- Present	92	47.2	42	44.7	50	49.5	0.39
Kellgren and Lawrence score:	- Normal	87	44.6	48	51.1	39	38.6	0.45
	- Grade 1	80	41.0	34	36.2	46	45.5	
	- ≥ Grade 2	28	14.4	12	12.8	16	15.8	
Calcification								
Medial malleolus:	- Present	12	6.2	5	5.3	7	6.9	0.77
Lateral malleolus:	- Present	21	10.8	7	7.4	14	13.9	0.33
Talus:	- Present	9	4.6	2	2.1	7	6.9	0.14
Os naviculaire:	- Present	19	9.7	8	8.5	11	10.9	0.61
		n	**%**	**n**	**%**	**n**	**%**	**p-value#**
Other								
Hydrops:	- Present	68	34.9	33	35.1	35	34.7	0.99
Anterolateraal impingement	- Present	22	11.3	10	10.6	12	11.9	0.73
	- Missing	2	1.0	1	1.1	1	1.0	
Synovitis:	- Present	1	0.5	0	0.0	1	1.0	1.00
Corpus liberum:	- Present	2	1.0	1	1.1	1	1.0	0.83
Soft tissue swelling:	- Present	20	10.3	8	8.5	12	11.9	0.57
	- *Missing*	5	2.6	3	3.2	2	2.0	
Tendons muscles								
*Peroneus longus**:	- Affected	1	0.5	0	0.0	1	1.0	1.00
*Peroneus brevis**:	- Affected	2	1.0	1	1.1	1	1.0	1.00
Ligaments								
Anterior Tibiofibular **:	- Normal	170	87.2	83	88.3	87	86.1	0.97
	- Thickened	20	10.3	9	9.6	11	10.9	
	- Partial tear	1	0.5	0	0.0	1	1.0	
	- Total tear	1	0.5	1	1.1	0	0.0	
	- Edema	0	0.0	0	0.0	0	0.0	
Posterior Tibiofibular **:	- Normal	187	95.9	89	94.7	98	97.0	0.80
	- Thickened	4	2.1	3	3.2	1	1.0	
	- Partial tear	0	0.0	0	0.0	0	0.0	
	- Total tear	1	0.5	1	1.1	0	0.0	
	- Edema	0	0.0	0	0.0	0	0.0	
Anterior Talofibular ***:	- Normal	85	43.6	43	45.7	42	41.6	0.44

Table 3. Prevalence of abnormalities on MRI in patients with and without persistent symptoms (continued)

		Total (n=195)		Persistent symptoms (n=94)		No symptoms (n=101)		p-value#
		n	%	n	%	n	%	
	- Thickened	77	39.5	37	39.4	40	39.6	
	- Partial tear	22	11.3	11	11.7	11	10.9	
	- Total tear	10	5.1	3	3.2	7	6.9	
	- Edema	0	0.0	0	0.0	0	0.0	
Posterior Talofibular ***:	- Normal	193	99.0	94	100.0	99	98.0	1.00
	- Thickened	1	0.5	0	0.0	1	1.0	
	- Partial tear	0	0.0	0	0.0	0	0.0	
	- Total tear	0	0.0	0	0.0	0	0.0	
	- Edema	0	0.0	0	0.0	0	0.0	
*Calcaneofibular****:	- Normal	121	62.1	59	62.8	62	61.4	0.97
	- Thickened	72	36.9	35	37.2	37	36.6	
	- Partial tear	1	0.5	0	0.0	1	1.0	
	- Total tear	0	0.0	0	0.0	0	0.0	
	- Edema	0	0.0	0	0.0	0	0.0	
*Deltoid****:	- Normal	173	88.7	85	90.4	88	87.1	0.94
	- Thickened	19	9.7	8	8.5	11	10.9	
	- Partial tear	2	1.0	1	1.1	1	1.0	
	- Total tear	0	0.0	0	0.0	0	0.0	
	- Edema	0	0.0	0	0.0	0	0.0	
Calc. nav. Plantar (Spring):	- Normal	195	100.0	94	100.0	101	100.0	n.a.
	- Thickened	0	0.0	0	0.0	0	0.0	
	- Partial tear	0	0.0	0	0.0	0	0.0	
	- Total tear	0	0.0	0	0.0	0	0.0	
	- Edema	0	0.0	0	0.0	0	0.0	

analyses adjusted for age, gender and BMI;); n.a. = not applicable

* Missing data: Total/ Persistent symptoms/ Without persistent symptoms = 2 (1,0%)/0 (0,0%)/2 (2,0%)

** Missing data: Total/ Persistent symptoms/ Without persistent symptoms = 3 (1,5%)/1 (1,1%)/2 (2,0%)

*** Missing data: Total/ Persistent symptoms/ Without persistent symptoms = 1 (0,5%)/0 (0,0%)/1 (1,0%)

DISCUSSION

Overall, on radiography as well as on MRI, a large percentage of structural abnormalities were found in patients both with and without persistent complaints after a sustained ankle sprain. These structural abnormalities were predominantly present in the talocru-

ral and talonavicular joint. However, no differences were found between patients with and without persistent complaints in the prevalence of structural abnormalities.

Strength and limitations

This is the first study in general practice, including patients with and without complaints after a lateral ankle sprain, to compare associations with structural abnormalities on radiography and MRI. Unfortunately, we could not make a comparison with a control group without a history of a lateral ankle sprain.

Based on the literature, we expected to find a 1:3 ratio of patients with and without persistent complaints.[8] However, since 47.5% of our study population consisted of patients with persistent complaints this suggests a possible selection bias. This may be caused by the willingness of patients with persistent complaints to participate in a study. However, despite the possible selection bias, we managed to include a representative control group from general practice without persistent complaints and the study was sufficiently powered to demonstrate potential differences between the two study groups.

Although the chosen definition for persistent complaints based on the outcome measure 'recovery' is debatable, it is frequently applied in other studies.[15, 16] Consequently, 47.5% were defined as patients with persistent complaints; however, only half of these were completed recovered according to the Likert scale.

Comparison with existing literature

To our knowledge this is the first study to compare patients from primary care, with and without complaints persisting ≥ 6 months after an ankle injury, regarding structural abnormalities on MRI and radiography. Therefore, it is difficult to compare our outcomes with previous reports.

In both our study groups a relatively high prevalence of structural abnormalities was found. Several studies in secondary care investigated pathologies in patients with persistent complaints after an ankle sprain.[17] Based on arthroscopic findings of patients undergoing lateral ankle stabilization surgery, synovitis (100%), osteochondral defects (7%), loose bodies (11%), anterolateral impingement (14%) and anterior tibial osteophytosis (14%) were frequently reported. [17, 18] Other studies found intra-articular lesions on arthroscopy in 90-97% of the patients seen in secondary care.[19, 20] The percentages of abnormalities found in these latter studies are much higher compared with ours. Although this difference might be attributed to the techniques applied, it is most likely due to the different study populations.[20]

In addition to the frequent abnormalities we found in the ligaments, structural damage was also frequently seen in the bone and cartilage. Most apparent are the findings in the talocrural and talonavicular joint. Early signs of osteoarthritis, manifested as

osteophytes, cartilage loss and a KL grade of ≥ 1 were frequently seen in this relatively young and healthy patient population. This might imply that an injury in primary care, often regarded as self-limiting, can result in significant structural damage; however, is unknown whether such damage can lead to serious problems at a later age.

In the present study we used a 7-point Likert scale to classify patients into the two study groups. Van Rijn et al. (2011) investigated the explanatory variables for reported recovery according to this scale in patients with acute ankle sprains and found an association between differences in pain intensity and a feeling of 'giving way' during high ankle load activities and reported recovery.[21] Therefore, we replicated our analyses according to a classification based on pain (NRS ≤2) and instability (yes or no) outcomes (data not presented). These analyses showed similar findings: no differences were found between patients with or without pain, and with or without instability, regarding the structural abnormalities. This might be related to the relatively large percentage of patients with combined persistent complaints expressed in pain, function and instability. When we compared the classifications of persistent complaints and pain, 75% of our patients with persistent complaints reported to have pain. Comparing patients on the classification of persistent complaints and instability showed that 65% of the patients without persistent complaints still reported instability; however, 80% of the patients with persistent complaints also reported complaints of instability. This indicates the variety of persistent complaints in patients after a lateral ankle sprain and suggests that the terminology often applied for persistent complaints, i.e. chronic instability, may not be appropriate for this total group.

Clinical implications

Persistent complaints are frequently seen after a lateral ankle sprain. However, when patients consult their GP, further examination with imaging will not assist in diagnosing the explicit reason for the persistent complaints. It is doubtful whether structural abnormalities seen on radiography or MRI are associated with the persisting complaints for which the patient consults the GP.

CONCLUSION

Structural abnormalities on radiography and MRI are very common after a lateral ankle sprain in patients presenting in general practice within 6-12 months after an ankle sprain. However, these structural abnormalities are not associated with persistent complaints. These findings are important for clinical practice, as the current concept of an ankle sprain is that it is associated with a greater risk of structural damage in the ankle.

We need to investigate other potential associations with persistent complaints in our aim for better diagnosis and treatment of lateral ankle sprains.

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Chapter 5

Magnetic resonance imaging abnormalities after lateral ankle trauma in injured and contralateral ankles

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ABSTRACT

Purpose: To compare the prevalence of abnormal MRI findings associated with lateral ankle trauma in injured and contralateral ankles to identify lesions that may be pre-existent.

Material and methods: The study was approved by the institutional review board and informed consent was obtained from all subjects. 195 Patients (mean age 37,5 ± 14,7 years; 43% male) who visited their general practitioner 6-12 months earlier with an ankle sprain were selected. All patients completed a standardized questionnaire and underwent MRI (1.5T) of both ankles. Structural MRI abnormalities in the injured and contralateral ankle were compared using the McNemar test (for paired samples).

Results: Bone marrow edema was frequently seen in the injured and contralateral ankle at the talocrural joint (25.1% versus 14.8%) and subtalar joint (24.6% versus 8.7%), but significantly more frequently in the injured ankle**.** Anterior talofibular ligament (ATFL) and calcaneofibular ligament (CFL) lesions were frequently found in both ankles, in 55.9% and 37.4% of injured ankles respectively and in 17.9% and 5.6% of contralateral ankles respectively. Fractures, anterior and posterior tibiofibular ligament lesions, deltoid ligament lesions and signs of talonavicular osteoarthritis were almost exclusively found in injured ankles. Peroneal tendon lesions were not frequently found in both ankles.

Conclusions: The prevalence of structural MRI abnormalities in patients presenting with a previous ankle sprain in primary care is very high. However, especially bone marrow oedema and lateral ligament lesions can also be found in a substantial percentage of contralateral ankles and may be either pre-existent or due to increased stress on the contralateral ankle after an ankle injury. Correlation with clinical findings is essential.

Keywords: ankle; abnormalities; general practice; imaging; sprain

INTRODUCTION

Acute ankle sprains are one of the most common musculoskeletal injuries[1-4]. In the Netherlands, an estimated 600.000 people sustain an ankle injury each year.[5] Approximately half of these patients present for medical care, either at their general practitioner or a hospital emergency department.[5] The majority of these injuries involve the lateral ankle ligament complex[6;7]as inversion injuries are the most common trauma mechanism. Several treatment options for lateral ankle injuries have been published.[8-10] Although non-operative treatment is successful in most patients, residual symptoms do occur and may lead to chronic ankle instability when complaints last for at least 6 months. A systematic review showed that at 1-year follow-up after conservative treatment, 5% to 33% of the patients still experience pain and instability, 34% of patients reported at least one recurrent sprain and 15% to 64% reported incomplete recovery from their initial injury.[11] 20 to 40% of patients with chronic ankle instability have associated injuries, including osteochondral lesions, peroneal tendon tears or intra-articular loose bodies, which may be an important cause of long term problems.[12, 13] Additional MR imaging could be of value in patients with chronic ankle instability to guide appropriate treatment. Given the frequency of ankle sprains, the prevalence of structural abnormalities in patients with persistent complaints has been well documented.[12-15] van Ochten et al recently reported that structural abnormalities on radiography and MRI after lateral ankle sprain in patients consulting their GP are not associated with persistent complaints.[16] Data on the prevalence of structural abnormalities in contralateral (asymptomatic) ankles are scarce; however they are essential for clinical decision making to avoid over interpreting the significance of injuries not causing the patient's actual symptoms. Only two studies reported data on structural MRI abnormalities in asymptomatic ankles [17, 18], but in both studies patients were not truly asymptomatic and underwent MRI examination for "non-lateral ankle pain" in a secondary or tertiary care setting. The purpose of this study was to determine the prevalence of abnormal MRI findings associated with lateral ankle trauma in a primary care setting and compare these to MRI findings in the contralateral ankle to identify lesion types that may be preexistent.

METHODS

The study was approved by the Institutional Review Board of the hospital and written informed consent was obtained from each patient.

Patients

We used data from patients included in an observational case-control study on persistent symptoms after lateral ankle trauma presenting in Dutch general practice.[16] Patients were selected from the files of 84 participating general practitioners (GP) using the diagnostic code 'ankle sprain' according to the International Classification of Primary Care (ICPC) and with the search terms: 'ankle', 'distortion', and 'sprain'. Patients aged 16 to 65 years were considered eligible if they had presented themselves at their GP with an inversion trauma of the ankle 6 to 12 months before start of the study. Patients with known systemic diseases that affect the functioning of the musculoskeletal system (i.e. amyotrophic lateral sclerosis, multiple sclerosis; auto-immune disorders such as rheumatoid arthritis and psoriatic arthritis etc.) as well as patients with insufficient knowledge of the Dutch language were excluded. Potentially eligible patients received a letter with a response card for participation on behalf of their GP. Interested patients forwarded their contact details to the researchers. On the response card, several questions were asked regarding general patient characteristics and persistent symptoms. Researchers contacted the patients to further inform them of the study and to verify whether the inclusion criteria were met. After signing informed consent, patients were included and asked to fill in an online questionnaire and were invited for a standardized physical examination of both ankles (data not used for present study) and radiological examination, consisting of radiography of the injured ankle and MRI of both ankles. The self-administered questionnaire contained questions on patient characteristics (age, gender, body mass index (BMI) and education level), the initial ankle sprain (side, history of previous injuries and activity causing the sprain), local symptoms and current complaints. Pain severity was assessed using the Numeric Rating Scale (NRS-11), an 11–point scale for patients self-reported pain.[19] The mean ankle function score was determined based on five categories: pain, stability, weight bearing, swelling, and gait pattern. All categories were summed to a total score (range 0-100, with 0 representing the worst possible and 100 representing the best possible function.[20] 195 Patients have been previously reported.[16] This prior article dealt with the associations between structural abnormalities on radiography and MRI and persistent complaints after lateral ankle trauma. The data of the contralateral ankle were not reported in this study.

Magnetic Resonance Imaging (MRI)

MRI of both ankles was performed on a 1.5 Tesla MRI scanner (Magnetom Essenza, Siemens Healthcare, Erlangen, Germany) with a head-neck coil. The ankles were placed in neutral position. In Table 1 the MRI acquisition protocol for the injured ankle is shown. A field of view of 20 cm for most sequences and a slice thickness of 3 mm were used for all sequences. The total acquisition time was approximately 20-30 minutes. For feasibility

reasons, in the contralateral ankle only the coronal and axial sequences were obtained, using the same scan parameters.

Table 1. MRI protocol for the injured ankle.

MRI Sequence	Orientation	TR (ms)	TE (ms)	Flip Angle (degrees)	TI (ms)	FOV (mm)	Matrix	NEX/ Average
T1 SE	Sagittal	550	16	90		384	288 x 384	1
T1 TIRM	Sagittal	3500	33	150	170	200	205 x 256	2
T1 FLASH	Sagittal	785	7,1	60		200	224 x 320	1
PD/T2 dual TSE	Coronal	4200	33/76	150		200	256 x 256	1
T1 TIRM	Coronal	5330	33	150	170	200	205 x 256	2
T1 FLASH	Coronal	785	7,1	60		200	224 x 320	1
PD/T2 dual TSE	Axial	3500	33/76	150		200	256 x 256	1

Ms = millisecond; mm = millimeter; TR = repetition time; TE = echo time; TI = inversion time; FOV = field of view; SE = Spin echo; TIRM = Turbo inversion recovery magnitude; FLASH = 2D fast low angle shot; TSE = turbo spin echo;

MRI: assessment and definitions

MR images of the injured and contralateral ankle were evaluated by one radiologist (3 years of experience in musculoskeletal MR imaging) using a standardized scoring form. A random sample of 35 MRIs was also scored by a second musculoskeletal radiologist (6 years of experience in musculoskeletal MR imaging) to assess interobserver reliability. The interobserver reliability was calculated for the different MRI items scored using Cohen's kappa and in case of variables with > 2 categories using the intraclass correlation coefficient (ICC) resulting in a range of 0.653 to 1. The percentage agreement was 98,8% (5883 of 5952 items). Because of high agreement, the remainder of the MRIs was primarily scored by one observer, but difficult cases were interpreted together and decision was based on consensus. Both readers were blinded to the patients' characteristics and clinical data. Osseous structures were scored for the presence or absence of the following abnormalities: fractures, bone marrow edema, osteochondral lesions, osteophytes, subchondral cysts, cartilage loss (diffuse and/ or focal) and sclerosis. These items were scored separately for the medial and lateral malleolus, inferior articular surface of the tibia at the tibiotalar joint, medial and lateral talus, the talus and calcaneus at the subtalar joint, and the talus and navicular bone at the talonavicular joint. Bone marrow edema was dichotomized as absent or subchondral versus present (including < 25%, 25-50%, 50-75% and > 75% bone marrow edema).

Table 2. Patients characteristics (n=195) at inclusion expressed as n (%) or mean (SD)

General patient characteristics	**Mean (SD)**
Age (years)	37,5 (14,7)
Gender (male)	84 (43,1%)
Height (cm)	176,1 (10,7)
Weight (cm)	78,9 (16,8)
BMI (kg/m^2)	25,7 (4,8)
Education level	
Lower	116 (59,5%)
Higher	77 (39,5%)
Clinical characteristics (injured ankle)	
Side of ankle sprain (right)	108 (55,4%)
Previous ankle sprain	91 (46,7%)
Mean pain score (NRS)	
In rest	1,15 (1,86)
During exercise	2,40 (2,47)
Mean Ankle Function Score (AFS)	72,7 (20,5)
Persistent symptoms (Likert scale)	
Completely recovered	30 (15,4%)
Greatly improved	71 (36,4%)
Slightly improved	50 (25,6%)
The same	17 (8,7%)
Slightly deteriorated	20 (10,3%)
Sharply detoriated	5 (2,6%)
Worse than ever	2 (1,0%)

Presence of osteophytes was dichotomized as absent or small versus definite. Osteoarthritis of the ankle was evaluated using an adapted Kellgren and Lawrence scale.[21] This scale was originally developed for conventional radiography. Because no MRI specific scale for osteoarthritis exists for the ankle, we adapted and dichotomized this scale into grade ≥ 1 indicating minimal signs of osteoarthritis versus grade 0 and grade ≥ 2 indicating definite osteoarthritis versus grade < 2. Both thresholds were used in the analyses. For the purpose of the analyses, the large numbers of items scored were clustered for the talocrural joint, subtalar joint and talonavicular joint. Tendons (in particular peroneus longus and brevis tendon) and ligaments, including the anterior and posterior tibiofibular ligaments, anterior and posterior talofibular ligaments, calcaneofibular ligament, deltoid ligament and the spring ligament complex, were scored for signs of post-traumatic injury and classified as normal, old lesion/ thickened, partial tear, complete tear and (in case of the peroneus brevis tendon) split tendon. For the analyses, we dichotomized the MRI appearance of tendons and ligaments into normal versus abnormal. The presence of joint effusion, soft tissue edema, and loose bodies was

assessed for the talocrural joint. Synovitis was also scored for the talocrural joint and was present when nodular/ thickened synovium was seen (there was no administration of contrast agent in this study). We also recorded peri-articular calcifications as well as the presence or absence of anterolateral impingement, indicated by a proliferative synovitis and fibrotic scar tissue at the lateral gutter.

Statistical analyses

The prevalence of MRI abnormalities was determined for the injured and contralateral ankles. Descriptive statistics were calculated. To test the differences in imaging findings between the injured ankle and contralateral ankle the McNemar test (for paired samples) was used. When lesions were seen almost exclusively in the injured ankle, we considered it reasonable to attribute these lesions to recent trauma. When lesions were seen in both the injured and contralateral ankles, we assumed that they may be pre-existent. All data were analysed using SPSS for Windows (version 18.0, SPSS Inc, Chicago, Ill, USA). For all analyses, a p-value of $< 0,05$ was indicative for statistical significance.

RESULTS

Figure 1 shows an overview of recruitment and inclusion of the patients. Of the 207 interested patients, 195 patients completed the questionnaire and underwent MRI of both injured and contralateral ankle and are therefore included in the analysis for the current study purpose. Baseline characteristics are shown in Table 2. Approximately half of the patients (48,2%) experienced persistent symptoms after lateral ankle injury (7-point Likert scale category ≥ 2). Pain scores ranged from 1,2 and 2,4 in rest and during exercise respectively. Most ankle injuries were sustained during sports (36,9%) and work (12,3%) related activities. 46,7% of patients sustained one or more previous ankle sprains in the injured ankle. The frequency distributions of structural abnormalities on MRI of osseous/ cartilaginous lesions and tendons/ ligaments are shown in Tables 3 and 4, respectively.

Osseous and cartilaginous abnormalities

Eight fractures (either consolidated or not) in the injured ankle were detected around the talocrural joint with seven fractures of the lateral malleolus and 1 distal crural fracture. (Table 3) Five of these patients had undergone operative fixation of the fracture. Two fractures of the navicular bone were detected in the injured ankles. No fractures were found in the contralateral ankle. In two patients operative fixation material was visible in the ankle due to a previous injury unrelated to the current trauma for which they had been included in the present study (1 injured and 1 contralateral ankle). Bone marrow edema was frequently seen in both the injured and contralateral ankle at the talocrural

joint and subtalar joint, but significantly more frequently in the injured ankle (Table 3). There was a trend towards more osteochondral lesions in the injured ankle at the talocrural joint. Minimal and definite signs of osteoarthritis (Kellgren and Lawrence score $\geq$ 1 and $\geq$ 2 respectively) of the talocrural joint were found significantly more in injured compared to contralateral ankles. In the subtalar joint hardly any signs of osteoarthritis were found in both injured and contralateral ankles. Minimal signs of talonavicular osteoarthritis were almost exclusively found in the injured ankles with a Kellgren and Lawrence score $\geq$ 1 in 55.4% of the injured ankles and in 4.6% of the contralateral ankles ($p<0.001$). Periarticular calcifications, soft tissue edema and signs of anterolateral impingement were found in both injured and contralateral ankles, although significantly more frequently on the injured side (Tables 3 and 4).

Tendon and ligament abnormalities

Peroneal tendon lesions were not frequently seen in both injured and contralateral ankles. In four injured and 2 contralateral ankles a peroneus brevis split syndrome was diagnosed. In the injured ankles one patient had a partial tear and one patient thickening of the peroneus brevis tendon. (Figure 3)

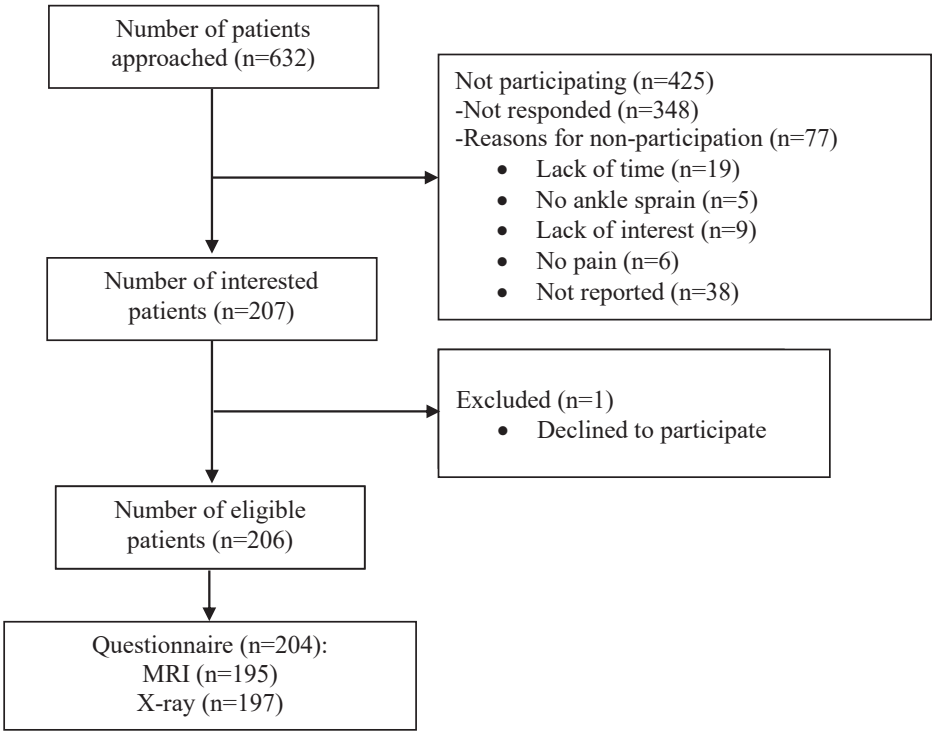

Figure 1. Flowchart of the study

Anterior and posterior tibiofibular and deltoid ligament abnormalities were almost exclusively found in injured ankles. Posterior talofibular ligament lesions were only detected in 1 injured and 1 contralateral ankle. Anterior talofibular ligament (ATFL) injury was common in both injured and contralateral ankle, although significantly more frequently in injured ankles (55,9% and 17,9% respectively, p<0,001). (Figure 2) Of those patients with an abnormal ATFL (n=109) at the injured ankle, 82% showed a normal ATFL at the contralateral ankle and 18% showed an abnormal ATFL at the contralateral ankle. Of the 84 patients without ATFL lesions on the injured side, 17% had an abnormal ATFL on the contralateral side. Calcaneofibular ligament (CFL) was found significantly more frequent in the injured ankle compared to the contralateral ankle. Of the patients with an abnormal CFL (n=74) at the injured ankle, 90% showed a normal CFL at the contralateral ankle and 10% showed an abnormal CFL on the contralateral ankle. Of the 120 patients without CFL lesions on the injured side, 98% of patients had a normal CFL on the contralateral side and only 2% of patients and abnormal CFL on the contralateral side. In the majority of the patients (64.2%) with ATFL lesions in the injured ankle, the CFL was also injured. 35.8% of patients had an isolated injury of the ATFL in the injured ankle. Only three patients had an isolated lesion of the CFL in the injured ankle.

Table 3. Number of MRI abnormalities in the injured and contralateral ankles of 195 patients with lateral ankle trauma: osseous and cartilaginous structures

	Injured ankle		**Contralateral ankle**		**P-value**
	n	*%*	*n*	*%*	
Talocrural joint					
Fracture	8	4,1	0	0,0	0,008
Bone marrow edema					0,003*
Subchondral	17	8,7	15	7,7	
<25%	33	16,9	18	9,2	
>25%	16	8,2	11	5,6	
Osteochondral lesion (present)	11	5,6	3	1,5	0,057
Osteophyte					<0,001**
Small	57	29,2	20	10,3	
Evident	20	10,3	3	1,5	
Subchondral cyst (present)	4	2,1	3	1,5	1,000
Cartilage loss (present)	20	10,3	3	1,5	<0,001
Sclerosis (present)	4	2,1	0	0,0	0,125
Kellgren and Lawrence score					0,001/ <0,001***
Normal	114	58,5	171	87,7	
Grade 1	62	31,8	19	9,7	
≥ Grade 2	19	9,7	4	2,1	

Table 3. Number of MRI abnormalities in the injured and contralateral ankles of 195 patients with lateral ankle trauma: osseous and cartilaginous structures (continued)

	Injured ankle		**Contralateral ankle**		**P-value**
	n	%	*n*	%	
Subtalar joint					
Fracture	0	0	1	0,5	1,000
Bone marrow edema					<0,001#
Subchondral	11	5,6	5	2,6	
<25%	39	20	15	7,7	
>25%	9	4,6	2	1,0	
Osteochondral lesion (present)	1	0,5	0	0,0	1,000
Osteophyte					0,063**
Small	12	6,2	0	0,0	
Evident	5	2,6	0	0,0	
Subchondral cyst (present)	5	2,6	2	1,0	0,375
Cartilage loss (present)	5	2,6	0	0,0	0,063
Sclerosis (present)	15	7,7	0	0,0	<0,001
Kellgren and Lawrence score					<0.001/ 1,000***
Normal	178	91,3	194	100,0	
Grade 1	17	8,7	0	0,0	
≥ Grade 2	0	0	0	0,0	
Talonavicular joint					
Fracture	2	1	0	0,0	0,500
Bone marrow edema					0,027*
Subchondral	3	1,5	3	1,5	
<25%	15	7,7	7	3,6	
>25%	8	4,1	5	2,6	
Osteochondral lesion (present)	0	0	0	0,0	1,000
Osteophyte					<0,001**
Small	84	43,1	5	2,6	
Evident	22	11,3	3	1,5	
Subchondral cyst (present)	1	0,5	2	1,0	1,000
Cartilage loss (present)	39	20	4	2,1	<0,001
Sclerosis (present)	92	47,2	3	1,5	<0,001
Kellgren and Lawrence score					<0,001/ <0,001***
Normal	87	44,6	185	94,9	
Grade 1	80	41	6	3,1	
≥ Grade 2	28	14,4	3	1,5	

Table 3. Number of MRI abnormalities in the injured and contralateral ankles of 195 patients with lateral ankle trauma: osseous and cartilaginous structures (continued)

	Injured ankle		Contralateral ankle		P-value
	n	%	*n*	%	
Soft tissue calcification					
Medial malleolus (present)	12	6,2	2	1,0	0,013
Lateral malleolus (present)	21	10,8	6	3,1	0,007
Talus (present)	9	4,6	4	2,1	0,227
Os naviculare (present)	19	9,7	0	0,0	<0,001

* Absent and subchondral bone marrow edema versus ≥25% bone marrow edema

** Absent/ small osteophytes versus definite osteophytes

*** Minimal signs of osteoarthritis(Kellgren and Lawrence score grade ≥1) versus no osteoarthritis/ Definite signs of osteoarthritis (Kellgren and Lawrence score ≥ 2) versus no osteoarthritis

DISCUSSION

This is the first study to report on structural MRI abnormalities in both injured and contralateral (asymptomatic) ankles in the general population after lateral ankle trauma. We found that the prevalence of structural MRI abnormalities is significantly higher in injured compared to contralateral ankles. This study also shows that a substantial number of MRI abnormalities can be found in the contralateral ankle suggesting that some lesions may be pre-existent. In particular bone marrow edema and ATFL lesions were often found at the contralateral side; 1 out of 7 patients had bone marrow edema at the talocrural joint and 1 out of 5 patients had an abnormal ATFL in the contralateral ankle. This emphasizes the danger of making clinical decisions based on MRI alone without clinical information, especially in view of the increasingly widespread use of MRI. Some of the contralateral MRI abnormalities could also be the result of increased stress on the contralateral ankle after an ankle injury. Acute ankle sprains are one of the most common musculoskeletal injuries with injuries to the lateral collateral ligaments being responsible for the majority of ankle sprains.[2, 4] The predictable pattern of injury first involves the ATFL, followed by the CFL, and ultimately the PTFL.[2, 4] Broström reported surgical data on the frequency of chronic ligament injury after ankle sprains.[15] In 66% of cases isolated injury of the ATFL was found, in 20% of cases a combination of ATFL and CFL tear was reported. Isolated CFL injury was found to be very rare and the PTFL was seldom injured. In a study on accuracy of MRI findings in 48 patients with clinically suspected chronic ligament injury 40 ATFL injuries (83%) and 16 CFL injuries (33%) were diagnosed on MRI.[12] Lee and colleagues recently reported a frequency of 188 ATFL lesions (82%) and 84 CFL lesions (37%) on MRI in 229 patients with recurrent ankle sprain or subjective signs of ankle instability.[22] Our data for the injured ankle partially support these findings with a somewhat lower prevalence of ATFL lesions in the injured ankles,

but a substantially higher prevalence (64.2%) of combined injury of the ATFL and CFL. In only three patients an isolated CFL injury was found in the injured ankle and only one patient had a PTFL injury, which is in agreement with the findings of Broström et al. In contrast to our findings several authors reported a frequent association between chronic lateral ankle instability and (partial) peroneal tendon tears with percentages ranging from 17-44% diagnosed on MRI.[23-25] Especially peroneal split syndrome due to subluxation of the tendon has been described.[25] We only found peroneal tendon injuries in 4% of the injured ankles. The differences in prevalence of ankle lesions in the injured ankles are most likely attributable to the difference in study population: primary care patients after lateral ankle trauma in our study versus symptomatic patients with chronic lateral ankle instability in secondary or tertiary care centers for all previous studies.

The prevalence of abnormal MRI findings in asymptomatic patients has been reported for several joints, including the knee, wrist and hip.[26-28] Only two (retrospective) studies reported data on abnormal MRI findings in asymptomatic lateral ankles, in which ATFL and CFL lesions were frequently found; Saxena et al reported 29% ATFL lesions and 11% CFL lesions[17] compared to 62% ATFL lesions and 39% CFL lesions in the study of Galli et al.[18] Both studies reported 30% peroneal tendon lesions. There was a high prevalence of other lesions found in these patients, including medial ligament lesions (31%)[18], Achilles tendinopathy (40%)[17] and tibial tendon dysfunction (26%).[17] These percentages are substantially higher than in our study. However, patients in both studies were not truly asymptomatic but underwent MRI examination in a secondary/ tertiary care center for "non-lateral ankle pain". This very likely explains the high prevalence of lesions in the two studies and in our view does not accurately represent the true prevalence of lesions in asymptomatic ankles in the general population. It could be argued that our population does not represent a truly asymptomatic population. The injuries found in the contralateral ankle may be the result of overloading the contralateral asymptomatic ankle after an ankle injury or influenced by the chance that a patient who injures one ankle is more likely to have injured the other ankle in the past. Performing a study in normal asymptomatic volunteers could unravel this more accurately. Data on osteoarthritis in the ankle in general and more specifically after ankle trauma are sparse. The prevalence of primary ankle osteoarthritis is much lower than for the knee and hip, but the number of patients diagnosed with secondary osteoarthritis due to a posttraumatic etiology is much higher.[29-30] In our study, signs of talocrural and especially talonavicular osteoarthritis were found significantly more frequently in injured compared to contralateral ankles. It could be speculated that in these patients osteoarthritis develops secondary to the ankle sprain due to the occurrence of acute osteochondral lesions/ fractures or chronic changes in ankle biomechanics (e.g. due to ligamentous instability) leading to repetitive cartilage stress and subsequent degeneration, or a combination of these two processes.[29] Although osteoarthritis features were more commonly found in the injured ankle, we cannot be completely sure if all osteoarthritis findings were attributable

to the injury. Because of the relatively short time interval between trauma and MR imaging, some osteoarthritis findings could have been pre-existent. We believe however that this percentage was not very high because of the relatively young age of the study group.

Our study had limitations. There was a difference in the number of images/ MRI sequences between the injured and contralateral ankle. Radiologists were therefore not completely blinded to information on the injured and contralateral side. Although a large number of items on MRI were scored primarily by one radiologist with three years of experience in musculoskeletal MRI, we feel that interpretation errors will likely be minimal, since all difficult cases were reviewed in consensus with a more experienced musculoskeletal radiologist and a very high level of interobserver agreement was demonstrated for the subset of patients scored by both radiologists. Information on history of previous ankle injury was only available for the injured ankle.

Table 4. Number of MRI abnormalities in the injured and contralateral ankles of 195 patients with lateral ankle trauma: tendons, ligaments and other abnormalities

	Injured Ankle		**Contralateral Ankle**		**P-value**
	n	*%*	*n*	*%*	
Tendons					
Peroneus longus tendon (affected)	1	0,5	1	0,5	1,000
Peroneus brevis tendon (affected)	6	3,1	2	1,0	0,219
Ligaments					
Anterior talofibular ligament					<0,001
Normal	85	43,6	159	81,5	
Partial rupture	22	11,3	6	3,1	
Total rupture	10	5,1	7	3,6	
Old lesion/ thickened	77	39,5	22	11,3	
Posterior talofibular ligament					1,000
Normal	193	99	191	97,9	
Partial rupture	0	0	0	0,0	
Total rupture	0	0	0	0,0	
Old lesion/ thickened	1	0,5	1	0,5	
Calcaneofibular ligament					<0,001
Normal	121	62,1	183	93,8	
Partial rupture	1	0,5	0	0,0	
Total rupture	0	0,0	0	0,0	
Old lesion/ thickened	72	36,9	11	5,6	
Anterior tibiofibular ligament					<0,001
Normal	170	87,2	192	98,5	

Table 4. Number of MRI abnormalities in the injured and contralateral ankles of 195 patients with lateral ankle trauma: tendons, ligaments and other abnormalities (continued)

	Injured Ankle		Contralateral Ankle		P-value
	n	%	*n*	%	
Partial rupture	1	0,5	0	0,0	
Total rupture	1	0,5	0	0	
Old lesion/ thickened	20	10,3	2	1,0	
Posterior tibiofibular ligament					0,219
Normal	187	95,9	193	99,0	
Partial rupture	0	0	0	0,0	
Total rupture	1	0,5	0	0,0	
Old lesion/ thickened	4	2,1	1	0,5	
Deltoid ligament					<0,001
Normal	173	88,7	192	98,5	
Partial rupture	2	1	1	0,5	
Total rupture	0	0	0	0,0	
Old lesion/ thickened	19	9,7	1	0,5	
Spring ligament					1,000
Normal	195	100	194	99,5	
Partial rupture	0	0	0	0,0	
Total rupture	0	0	0	0,0	
Old lesion/ thickened	0	0	0	0,0	
Other					
Joint effusion (present)	68	34,9	35	17,9	<0,001
Anterolateral impingement (present)	22	11,3	7	3,6	0,003
Synovitis (present)	1	0,5	1	0,5	1,000
Loose body (present)	2	1	0	0,0	0,500
Soft tissue edema (present)	20	10,3	10	5,1	0,031

CONCLUSION

We conclude that the prevalence of structural MRI abnormalities in patients presenting in general practice with a previous ankle sprain is very high. However, especially bone marrow edema and lateral ligament lesions can also be found in a substantial percentage of contralateral ankles suggesting that they may be pre-existent or the result of increased stress on the contralateral ankle after an ankle injury. Correlation with clinical findings is essential for clinical decision making.

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Chapter 6

Association between patient history and physical examination and early signs of osteoarthritis in patients after a lateral ankle sprain: a cross-sectional study

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Submitted

ABSTRACT

Study design: Cross-sectional study in general practice.

Objective: To determine the association between patient history, physical examination and early signs of osteoarthritis on MRI in patients with persistent complaints after a previous ankle sprain.

Background: Structural abnormalities on MRI are frequently found after a lateral ankle sprain and may lead to osteoarthritis.

Method: 98 patients with an ankle sprain 6-12 months prior to inclusion and reporting persistent complaints were included in the study. Patient history taking and standard physical examination were applied and all patients had an MRI. Both univariate and multivariable analyses were used to test the association between patient history and physical examination and features of early stage osteoarthritis (OA).

Results: Overall, features of early stage OA in the talocrural joint (TCJ) were seen in 40% of the subjects and in 49% in the talonavicular joint (TNJ). The multivariable model showed a significant positive association between swelling (OR 3.57, 95%CI 1.13;11.4), a difference in ROM of passive plantar flexion (OR 1.09, 95%CI 1.01;1.18) and the presence of bone edema in the TCJ. A difference in ROM of passive plantar flexion (OR 1.07, 95%CI 1.00;1.15) and pain at the end range of dorsiflexion and/or plantar flexion (OR 5.23, 95%CI 1.88;14.58) were positively associated with the presence of osteophytes in the TNJ.

Conclusion: Pain at the end of dorsiflexion and/or plantar flexion, a difference in ROM of passive plantar flexion and swelling performing physical examination seem to be associated with the presence of features of early stage OA in both the TCJ and TNJ. Our findings may guide physicians and physical therapists to predict structural joint abnormalities as signs of early stage osteoarthritis.

Keywords: ankle injury examination radiographic abnormalities

INTRODUCTION

Ankle sprains are one of the most common musculoskeletal injuries.[1] The incidence rates range from 2.2 sprained ankles per 1000 person-years in the USA to 5.3-7.0 per 1000 person-years in Europe. [2 3] About half of these acute injuries occur during sport. In the Netherlands, nearly 20% of all ankle sprains are seen by physicians in primary care, while a reasonable amount of patients visit the physical therapist (PT) by direct access or are referred by a general practitioner (GP).[4] The majority of ankle sprains involve the lateral ligament complex of the ankle joint. [5]

Treatment consisting of early mobilization, often combined with additional external support (tape, brace or bandage), is the most frequently applied and most evidence-based treatment for an acute ankle sprain.[6-8] After treatment most patients with an ankle sprain recover within 3 months. However, approximately 30% of the patients will suffer from persistent complaints, including pain, functional loss or instability.[9]

Earlier studies have shown that trauma, fractures and sprains are the most common causes of degenerative changes in the ankle joint.[10, 11] It has even been suggested that a single ankle sprain may eventually result in degenerative cartilage lesions.[10, 12, 13] In a recent study performed in general practice cartilage loss, osteophytes and bone marrow edema on MRI were frequently found in patients 6-12 months after an ankle sprain. These abnormalities were seen in patients both with and without persistent complaints, indicating that persistence of complaints is not automatically associated with the presence of structural abnormalities in the ankle joint.[14] These abnormalities were however more often seen in the injured ankle than in the contralateral ankle.[15] Such structural abnormalities are in general regarded as signs of (early stage) osteoarthritis (OA).[16 17] These abnormalities include bone marrow edema, cartilage loss and osteophytes.[16-18] Thereby, OA in the ankle can also have a significant impact on daily life and may lead to high healthcare costs and reduced quality of life.[19]

Patients with persistent complaints after an ankle sprain are often seen in primary care, but their access to MRI facilities is limited and thereby it is often difficult to screen for early OA features if appropriate. However, particularly for patients with persistent complaints it could be important to identify those individuals at higher risk for developing OA and to improve early detection of signs of OA in primary care by using patient history and physical examination. Early detection might improve the prognosis of patients and minimize the costs due to unnecessary diagnostics and later functional loss.

Since no earlier studies have investigated the contribution of patient history together with clinical examination findings in identifying signs of early stage OA, the present study aims to evaluate the association between characteristics from patient history and physical examination and features of early stage OA, assessed on MRI in patients with persistent complaints after a previous lateral ankle sprain.

METHODS

Design and participants

This cross-sectional study was performed with approval of the Medical Ethical Committee of Erasmus MC Rotterdam (NL30644507810).[14] Patients aged 16-65 years who visited the general practitioner for a lateral ankle sprain 6-12 months prior to start of the study were selected from the medical records of 84 participating general practitioners using the diagnostic International Classification of Primary Care (ICPC) code (L77) 'ankle sprain' and the search terms: ankle, distortion, and sprain.

Patients were excluded if they had known systemic illnesses (e.g. neurological diseases: amyotrophic lateral sclerosis, multiple sclerosis, autoimmune disease: rheumatoid arthritis, psoriatic arthritis), known fractures, other osseous damage, a reported history of previous operations of the ankle or no knowledge of the spoken/written Dutch language. Any contraindication for MRI was also an exclusion criterion.

Procedures

All selected patients received a letter from their own general practitioner with adequate study information and a response card for participation; patients willing to participate were contacted by telephone. Inclusion- and exclusion criteria were checked and patients were included in the study after providing informed consent.

After inclusion, patients completed an online questionnaire for patient history taking and were invited for a physical examination, radiography and MRI of the ankle. Extensive details on these items are already published.[14]

For the present study, all participants were included who reported persistent complaints (defined as a score of 3-7 points on a 7-point Likert scale (1=completely recovered, 7=worse than ever, score 3-7 = slightly improved to worse than ever) at inclusion, 6 to 12 months after they visited the GP with a lateral ankle sprain.

Measurements

The questionnaire included questions on patient characteristics (age, gender, body mass index (BMI) and education level), history of ankle symptoms directly after the injury (preferred leg, side, swelling, instability, previous sprain) and current complaints (pain in rest and during exercise, measured on a numerical rating scale (NRS 0-10, where 10 represents worst pain), the Ankle Function Score (AFS, 0-100 points where 100 represents highest function), feeling of instability (subscale of the AFS) [20], swelling and occurrence of re-sprains.

A standard physical examination was performed by a trained research assistant and consisted of inspection of both ankles for swelling (dichotomized and expressed in no/ yes (slight or severe)) and position of the hind foot (varus, valgus or normal).[21] Passive range of motion (ROM) of plantar and/or dorsiflexion of both ankles was determined using a goni-

ometer (in degrees) [22] together with the presence of pain at the end of ROM. To determine instability, the anterior drawer test (dichotomized in positive/doubtful or negative) [23] and the talar tilt test (dichotomized in positive/negative) were carried out in both ankles.[23]

The difference in ROM in passive dorsiflexion and/or plantar flexion was calculated between the injured and the uninjured ankle. The position of the hind foot, expressed in varus and valgus, was dichotomized in 'no difference between the symptomatic and the asymptomatic foot' and 'a difference between symptomatic and asymptomatic foot'. An MRI (1.5 Tesla) was taken of the injured ankle and outcome measurements were scored by one radiologist (NP) specialized in musculoskeletal complaints, using a standardized scoring form. A random subsample of 32 MRIs from the original study (n=206) were scored by a second radiologist (EO) to determine the inter-observer reliability. In the original study sample (n=206) the inter observer reliability was calculated using Cohen's kappa (range 0.653-1.00) between the different items. The percentage agreement was 98.8% (5883 of the 5952 scored items) for the MRI items. Both radiologists were blinded for the clinical scores.

Structural abnormalities seen on MRI were scored from 0-2 (0 = absent, 1 = possibly present, and 2 = evidently present). Bone marrow edema was scored as absent, only subchondral or, when present more extensively, expressed in affected percentage (< 25%, 25-50%, 50-75% and > 75%) of the volumes of the evaluated regions. Scores were clustered for the findings in osseous structures and percentage of osteochondral lesions in the talocrural joint (TCJ) and the talonavicular joint (TNJ). The scores of bone marrow edema were dichotomized as present or absent. Cartilage loss in the TNJ, scored as diffuse or focal, possible, moderate or severe was dichotomized in present (possible, moderate or severe) or absent. The presence of osteophytes were scored from 0-2 and dichotomized into 'no osteophytes' (score 0) and possible or evident osteophytes (score 1-2). These scores were chosen because an overall grading system for OA severity on MRI for ankle joints is lacking, only individual features are presented.[24]

Statistical analysis

Descriptive statistics were used to describe patient characteristics. The association between the presence of early stage OA features on MRI (i.e. bone marrow edema, osteochondral lesions, cartilage loss and osteophytes) and the factors from patient history (re-sprain) and physical examination (swelling, differences in ROM in passive dorsiflexion and/or plantar flexion between injured and non-injured ankle, pain at end range dorsiflexion and/or plantar flexion and function, measured in the anterior drawer test, the talar tilt test and the position of the hind foot) were examined using univariate logistic regression models, with adjustment for age. Secondly, multivariable analyses [ENTER models] were performed on the features that were present in more than 10% of the subjects, including all factors from patient history taking and physical examination, adjusted for age. Results of the regression analyses were presented in odds ratios

(OR) with 95% confidence intervals (CI). We additionally presented Nagelkerke R^2 for the multivariable models. Data were analyzed using the SPSS (version 21.0). For all analyses, $p<0.05$ was defined as being statistically significant.

RESULTS

In total, 98 patients of the 206 included participants had persistent complaints and were therefore selected for the current study purpose; of this latter group 94 patients underwent physical examination and MRI (Figure 1).

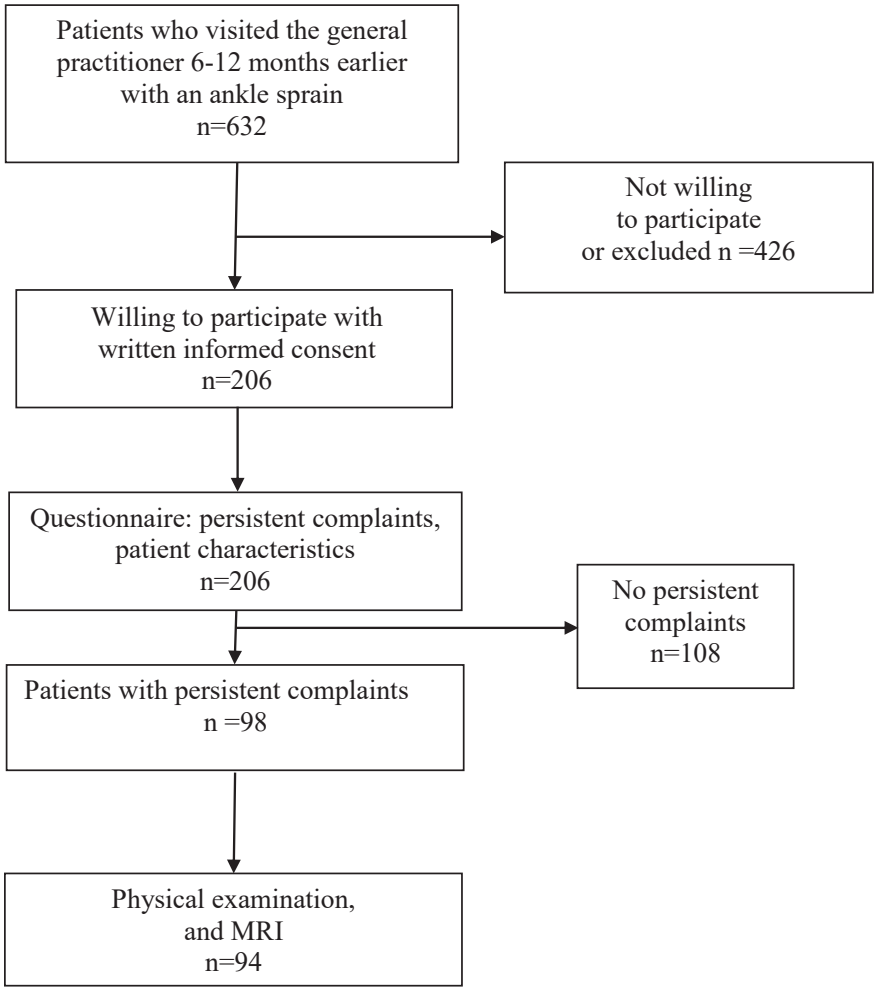

Figure 1. Flowchart showing inclusion of the study participants

Table 1 presents the patient characteristics of the study population. The mean age was 36.1 (SD 14.5) years, 65.4% of the population was aged younger than 46 years, 36.7% were male and more than 49% had a BMI over 25 kg/ m2. Directly after the injury 71.4% of the patients noticed serious swelling of the ankle, 87.8% had instability feelings and 50% reported this injury as a re-sprain.

Table 1: Baseline characteristics of the study participants

PATIENT CHARACTERISTICS		(N =98)
Age (years)		36.1 (14.5)
16-25 (n, %)		32 (32.7%)
26-45 (n, %)		32 (32.7%)
46-60 (n, %)		28 (28.6%)
>60 (n, %)		6 (6.1%)
Male gender (n, %)		36 (36.7%)
BMI (kg/m^2)		26.9 (5.5)
Complaints directly after injury		
Swelling (n, %)	no	7 (7.1%)
	slightly	18 (18.4%)
	severe	70 (71.4%)
Instability (n, %)		86 (87.8%)
Complaints on inclusion		
Pain during exercise (NRS, 0-10)		3.6 (2.6)
Instability (item Ankle Function Score), (n, %)		
no instability		17 (17.3%)
sometimes during sports		38 (38.8%)
frequently during sports		3 (3.1%)
sometimes during ADL		23 (23.5%)
frequently during ADL		9 (9.2%)
with every step		2 (2.0%)
Swelling (item Ankle Function Score)	none (n, %)	59 (60.2%)
	light	22 (22.4%)
	mild	10 (10.2%)
	severe	1 (1.0%)
Ankle Function Score (0-100 points)		62.5 (20.2)
Re-sprain (n. %)		49 (50%)
Physical examination on inclusion		
Difference in range of motion passive dorsal flexion symptomatic versus asymptomatic ankle (degrees)		-2.0 (4.9)
Difference in range of motion passive plantar flexion symptomatic versus asymptomatic ankle (degrees)		4.7 (7.1)
Pain end range dorsal flexion and/or plantar flexion (symptomatic side) (n, %)		24 (24.5%)
Anterior drawer test positive on symptomatic side (n, %)		33 (33.7%)
Talar tilt test positive on symptomatic side (n, %)		43 (43.9%)
Position of hind foot symptomatic different from asymptomatic varus/valgus/ normal (n, %)		21 (21.4%)
Swelling (yes) (n, %)	none	65 (66.3%)
	slightly	25 (25.5%)
	severe	4 (4.1%)

Data are presented as means (SD), unless stated otherwise

Of all patients with persistent complaints 6-12 months after the ankle sprain, 34 (34.7%) still had instability feelings during normal daily activities and 41.9% during sports activities. The mean ankle function score was 62.5 (SD 20.2) and pain severity experienced during activity was 3.6 (SD 2.6).

When performing the physical examination, pain at the end range of dorsiflexion and/or plantar flexion at the affected side was present in 24.5% of the patients. A positive talar tilt test was found in 43.9% of the patients and the anterior drawer test was positive in 33.7%. Severe subjective swelling at study inclusion was rarely seen (4.1%).

MRI showed that 6.4% of the participants had osteochondral lesions in the talocrural joint, whereas no osteochondral damage was found in the talonavicular joint (Table 2).

Table 2 MRI findings as an indication of osteoarthritis in the talocrural and talonavicular joint

MRI features	N=94
Talocrural joint	
Osteochondral lesion	6 (6.4%)
Cartilage loss	8 (8.5%)
Bone marrow edema	25 (26.6%)
Osteophytes	35 (37.2%)
Early stage OA (KL_{mri} score >=1)	38 (40.4%)
Talonavicular joint	
Osteochondral lesion	0 (0%)
Cartilage loss	17 (18.1%)
Bone marrow edema	14 (15.1%)
Osteophytes	46 (48.9%)
Early stage OA (KL_{mri} score >=1)	46 (48.9%)

Data are presented as numbers (%)

Cartilage loss was more frequently seen in the talonavicular joint compared to the talocrural joint (18.1% versus 8.5% respectively) whereas bone marrow edema was especially present in the talocrural joint compared to the talonavicular joint (26.6% versus 15.1% respectively). Osteophytes were most frequently (48.9%) seen in the talonavicular joint.

Table 3 presents the univariate associations between early stage OA features on MRI and factors from patient history and physical examination. The univariate analyses showed a positive significant association between pain at the end range of dorsiflexion and/or plantar flexion and the presence of osteophytes in the talonavicular joint (OR 2.97, 95%CI 1.26;6.97). None of the other associations tested were significant.

Table 3 Univariate associations between variables from anamnesis and physical examination and features of early OA in the TCJ and TNJ on MRI (n=94)

	Talocrural joint				Talonavicular joint		
	Osteochondral lesion	**Cartilage loss**	**Bone edema**	**Osteophytes**	**Cartilage loss**	**Bone edema**	**Osteophytes**
	(n=6)	**(n=8)**	**(n=25)**	**(n=35)**	**(n=17)**	**(n=14)**	**(n=46)**
Resprain (> 1 sprain)	p=0.623	p=0.444	p=0.612	p=0.763	p=0.454	p=0.374	p=0.607
Swelling present at physical examination in ankle	1.04 (0.17;6.39) p=0.966)	0.66 (0.12;3.61) p=0.662	2.20 (0.84;5,73) p=0.107)	1.03 (0.42;2.55) p=0.95	1.70 (0.57;5.07) p=0.339	0.34 (0.07;1.63) p=1.77	0.76 (0.32;1.85) p=0.55
Difference ROM S/AS passive dorsal flexion (degrees)	0.94 (0.81;1.09) p=0.394	0.97 (0.85;1.11) p=0.636	1.02 (0.93;1.12) p=0.667	1.02 (0.93;1.11) p=0.741	1.07 (0.96;1.20) p=0.246	0.98 (0.88;1.10) p=0.767	1.04 (0.95;1.13) p=0.393
Difference ROM S/AS passive plantar flexion (degrees)	1.00 (0.88;1.14) p=0.998	0.99 (0.86;1.10) p=0.830	1.07 (0.99;1.14) p=0.053	1.03 (0.97;1.09) p=0.407	1.06 (0.99;1.14) p=0.102	1.05 (0.97;1.13) p=0.254	1.05 (0.99;1.11) p=0.123
Pain at end range dorsiflexion and/ or plantar flexion symptomatic ankle	0.82 (0.13;5.16) p=0.836	1.62 (0.36;7.36) p=0.534	0.52 (0.20;1.36) p=0.182	0.48 (0.19;1.08) p=0.072	1.65 (0.57;4.77) p=0.360	1.39 (0.45;4.36) p=0.568	**2.97 (1.26;6.97) p=0.013**
Anterior drawer test positive symptomatic ankle	2.41 (0.42;13.75) p=0.324	0.65 (0.12;3.54) p=0.619	1.08 (0.41;2.81) p=0.883	0.96 (0.40;2.32) p=0.927	1.94 (0.66;5.70) p=0.227	0.44 (0.11;1.72) p=0.239	1.00 (0.43;2.35) p=0.996
Talar tilt test Positive symptomatic ankle	0.26 (0.03;2.43) p=0.238	0.40 (0.07;2.18) p=0.291	0.46 (0.18;1.21) p=0.116	0.70 (0.30;1.63) p=0.402	1.10 (0.38;3.16) p=0.865	0.27 (0.07;1.02) p=0.054	0.60 (0.26;1.36) p=0.222
Difference hind foot position S/AS side; varus/valgus	0 (0-∞) p=0.998	0.66 (0.07;6.06) p=0.713	0.40 (0.10;1.50) p=0.172	1.09 (0.40;3.02) p=0.863	0.44 (0.09;2.12) p=0.304	0.22 (0.03;1.81) p=0.159	0.46 (0.16;1.28) p=0.137

Data are presented as OR (95% CI) with accompanying p-values. TCJ =talocrural joint, TNJ=talonavicular joint; S=Symptomatic, AS=Asymptomatic; OD TNJ not included because no structural abnormalities were found; Analysis adjusted for age; significant associations (p<0.05) presented in bold.

The multivariable analysis showed a significant association between a difference in ROM of passive plantar flexion and both bone edema (OR 1.09, 95%CI 1.01;1.18) in the TCJ and osteophytes (OR 1.07, 95%CI 0.95;1.17) in the TNJ (Table 4). Swelling in the ankle was positively associated with the presence of bone edema (OR 3.58, 95%CI 1.13;11.4) in the TCJ. Additionally, a significant positive association was found between pain at the end range of dorsiflexion and/or plantar flexion and osteophytes (OR 5.23, 95%CI 1.88;14.58) in the TNJ.

Table 4 Multivariable associations between factors from physical examination and anamnesis and features of early stage osteoarthritis in the TCJ and TNJ on MRI.

	Talocrural joint		**Talonavicular joint**		
	Bone edema (n=25)	**Osteophytes (n=35)**	**Cartilage loss (n=17)**	**Bone edema (n=14)**	**Osteophytes (n=46)**
Resprain (> 1 sprain)	0.69 (0.21;1.89)	0.94 (0.63;2.43)	1.36 (0.40;4.60)	2.77 (0.70;10.89)	1.56 (0.57;4.26)
Swelling in ankle at physical examination	3.58 (1.13;11.4)**	1.08 (0.40;2.91)	2.39 (0.69;8.23)	0.47 (0.08;2.57)	1.01 (0.36;2.84)
Difference in ROM passive plantar flexion(degrees)	1.09 (1.01;1.18)**	1.03 (0.96;1.09)	1.08 (0.99;1.17)*	1.08 (0.98;1.18)	1.07 (1.00;1.15)**
Difference in ROM passive dorsal flexion (degrees)	1.02 (0.92;1.14)	1.00 (0.91;1.10)	1.11 (0.96;1.27)	0.97 (0.85;1.11)	1.05 (0.95;1.17)
Pain end range dorsal and/or plantar flexion	0.63 (0.21;1.87)	0.45 (0.18;1.12)	2.71 (0.76;9.59)	2.27 (0.56;9.23)	5.23 (1.88;14.58)**
Anterior drawer test positive	1.54 (0.44;5.47)	1.30 (0.46;3.72)	2.37 (0.64;8.80)	0.46 (0.08;2.63)	1.53 (0.50;4.68)
Talar tilt test positive	0.33 (0.10;1.15)*	0.59 (0.21;1.64)	0.66 (0.18;2.41)	0.23 (0.05;1.21)*	0.34 (0.11;1.05)*
Different hind foot position (varus/valgus) symptomatic / asymptomatic side	0.48 (0.11;2.19)	1.43 (0.47;4.36)	0.34 (0.06;1.97)	0.35 (0.04;3.31)	0.48 (0.14;1.62)
R^2	0.231	0.079	0.192	0.147	0.263

Data are presented as OR (95% CI).TCJ=talocrural joint; TNJ=talonavicular joint;
Analyses adjusted for age; ** P<0.05; * P<0.1

DISCUSSION

In our study, features of early stage OA were frequently seen on MRI. Some of the variables from patient history and physical examination seem to be associated with features of early stage OA. The strongest association was between the presence of pain at the end range of dorsiflexion and/or plantar flexion and the presence of osteophytes in the TNJ.

Aim of the present study was to identify signs or symptoms from patient history and physical examination associated with early degenerative signs of OA in patients with persistent complaints after a lateral ankle sprain. For the present study we selected patients from general practice who had a previous ankle sprain 6-12 months before. A previous study from our group showed that early signs of OA seen on MRI were also frequently seen in patients without persistent complaints after a lateral ankle sprain. Therefore, in an explorative way, we also examined the associations between signs of early stage OA on MRI and features from patient history and physical examination in the total study population (n=206), which included both patients with and without persistent complaints. Overall, these analyses yielded similar results indicating that the associations are not dependent of having persistent complaints. Although several studies have evaluated the diagnostic value between items from patient history and physical examination and MRI findings of the musculoskeletal system, to our knowledge none has evaluated these items in the ankle joint after a lateral ankle sprain. Most studies focused on the knee, in which the explained variance ranged from 23% to 28% for the presence of specific knee abnormalities.[25, 26] These percentages are comparable to the explained variance found in the present study for the presence of bone edema in the TCJ and osteophytes in the TNJ.

Since early signs of OA were not prevalent in all patients, it might be important to distinguish between patients with early degenerative changes and patients without these structural abnormalities on MRI, in order to decide which management and treatment should be followed. However, we do not know whether the early signs of OA will lead to severe OA and currently there is no specific treatment to 'cure' OA. In contrast to the often slowly developing OA in joints due to ageing, it is known that joint trauma, i.e. an ankle sprain can cause development of OA on a relative young age.[10] This was also seen in our study population, i.e. participants were (on average) 36.1 (14.5) years old and had a high level of sport participation The acute onset enables clinicians to perform a proper follow-up and apply diagnostic and therapeutic interventions when needed. Treatments, such as disease-modifying drugs, may become available in future and can then be applied in an early stage of the disease when it may still be reversible. [27, 28]

In the present study the relatively large amount of structural abnormalities seen on MRI in general practice is consistent with other reports in which also serious abnormali-

ties were seen on MRI after repeated (or even a single) ankle sprain.[10, 12] However, these other studies were performed in secondary and tertiary settings, whereas ours was performed in primary care. Moreover, we clearly showed in our earlier published paper that structural abnormalities, indicating early signs of OA, are more frequently present in the injured ankle compared to the non-injured ankle.[15] Therefore, even among primary care patients in whom less serious lesions and symptoms are expected, early signs of OA are visible on MRI in the injured ankle. This emphasizes the potential impact of an ankle sprain. Although, such a sprain is often regarded as a self-limiting disorder, it seems to lead to signs of early stage OA in a substantial number of patients. These early signs might be a strong predictor for the presence of OA in later life.[12, 17]

Strengths and limitations

A strength of our study is that it is the first study in primary care to examine the association between clinical findings and MRI abnormalities in patients with persistent complaints after an ankle sprain. Most other studies on MRI findings were conducted in secondary or tertiary care settings.[10-12]

In contrast to other lower extremity joints, there is no consensus yet on the definition of OA in the ankle using radiography or MRI.[17, 29] We therefore based our outcomes on a recent consensus paper published by Hunter et al. (2011) in which a Delphi procedure was applied to define knee, hip and/or hand OA on MRI.[17] The MRI definition of knee OA included the following items: osteophytes, cartilage loss and bone marrow lesions. We have therefore presented these items as separate outcomes in our study. Additionally, the radiologists gave an overall score for the presence of OA on MRI in the different joints of the ankle, using an for MRI adapted Kellgren and Lawrence system.[24] Analyses on these outcomes showed similar results with a strong and significant association between pain at the end range of dorsiflexion and/or plantar flexion (OR 5.23, 95%CI 1.88;14.58) and early OA in the TNJ. Though, the absence of consensus on the definition of ankle OA using both X-ray and MRI does highlight the need for this.

We used a combined score to determine pain at the end range of dorsiflexion and/or plantarflexion at physical examination. This outcome appeared to be important in the association with early stage OA of the TNJ. As a consequence of this combined score we are not able to determine the usefulness of separate dorsiflexion and plantarflexion measures. Therefore, future research should investigate the specific predictive value of pain at the end range of plantar and dorsiflexion in association with abnormalities in the TCJ and TNJ.

The original aim of the data collection was to detect differences between patients with persistent complaints and those with non-persistent complaints, after an ankle sprain. For the present research question we selected relevant variables from both patient history and physical examination. However, although morning stiffness and joint

line tenderness are regarded as early signs of OA in hand and knee[30], these variables were not included in our questionnaire or physical examination; this can be considered a limitation of our study.

Since we applied a cross-sectional design with measurements 6 to 12 months after the patients visit to a GP with an ankle sprain, no information is available on the severity of the sprain in the acute phase. It is however questionable whether the severity of the injury will impact the long-term outcome. [31]

CONCLUSION

This study aimed to find variables from patient history and physical examination associated with the presence of structural abnormalities on MRI indicating a potential disabling disorder (OA) of the ankle. Pain at the end of dorsiflexion and/or plantar flexion, a difference in ROM of passive plantar flexion and swelling during physical examination seem to be associated with the presence of features of early stage OA in both the TCJ and TNJ. Our findings may serve as guidance for clinicians to predict the presence of structural abnormalities on MRI as an early sign of OA after a lateral ankle sprain using patient history and physical examination. Future studies need to further elucidate whether this early prediction of structural changes, relates to future further structural and symptomatic deterioration of the ankle joint after a sprain.

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Chapter 7

Impact of a lateral ankle sprain in general practice: comparison between patients with and without persistent complaints after 6-12 months

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Submitted

ABSTRACT

Background: Although ankle sprains are common and often lead to persistent complaints, their impact on functioning and related costs remains unclear.

Objective: To investigate the impact of a lateral ankle sprain on functioning and health care utilization at 6-12 months follow-up.

Design: Cross-sectional study

Setting: General practice

Patients: Of the 204 included patients from general practice after a lateral ankle sprain 6-12 months previously, 96 reported persistent complaints and 108 reported no persistent complaints. Patients were divided using a 7 "point" Likert scale (respectively 3-7 and 1-2 points).

Assessment of Risk factors: A standardized questionnaire included the 7 "point" Likert scale to measure recovery.

Main outcome measures: A standardized questionnaire assessing history, pain and function.

Results: A significantly higher BMI (26.9 and 24.9 kg/m^2) , higher pain scores at rest (1.87 vs. 0.44) and during exercise (3.62 vs. 1.25) and a lower Ankle Function Score (72.47 vs. 82.90) were reported in the group with persistent complaints, while a higher percentage of patients in the group without persistent complaints participated in sports (77.8% vs. 36.4%). Limitations in functioning due to ankle sprain and a high medical consumption (76.5% visiting the GP, 20.1% a specialist and 45.6% a physiotherapist) and radiographic imaging (35.3%) were reported in both study groups.

Conclusions: A lateral ankle sprain has a high impact on functioning and physical health, especially in those with persistent complaints. In patients with and without persistent complaints, considerable use of health care resources was found 6-12 months after the initial visit to the general practitioner.

Keywords: ankle sprain impact health care

INTRODUCTION

Ankle sprains are one of the most commonly occurring musculoskeletal injuries. In The Netherlands, of the 600.000 people who yearly sustain an acute ankle injury, 50% are seen in general practice or visit (on their own initiative) emergency departments of hospitals.[1]

In Dutch general practice there is an incidence of 12.8 per 1000 patients per year and the incidence is higher in younger people, and in men compared to women. In ≥ 75% of the patients, damage to the lateral ligament complex occurred due to an inversion sprain of the ankle.[1]

Conventional treatment consisting of early mobilization combined with the use of an external support (tape, bandage or brace) is the preferred initial treatment for acute ankle sprains.[2-4] In daily practice, although physiotherapy is often used as an additional treatment, there is no evidence that physiotherapy is effective for the treatment of acute ankle sprains.[5] Also, in patients from primary care, a supervised training program combined with conventional treatment provided no better results compared with conventional treatment alone.[6]

A systematic review revealed that one year after a lateral ankle sprain, a high percentage of patients still experienced persistent complaints like pain, functional loss and instability. Many patients (range 36-85%) reported full recovery after 3 years, while a third of the patients with an acute ankle sprain reported at least one re-sprain.[7] One study found that nearly 50% of patients with chronic ankle disorders reported persistent complaints for ≥ 10 years and the majority of those patients were limited in their physical activities.[8] Consequently, healthcare costs, and costs due to productivity loss, are certainly expected.[9] However, the exact impact on daily functioning and the use of medical care after a lateral ankle sprain is unknown.

Therefore, this study assesses the impact on functioning and medical consumption of a lateral ankle sprain at 6-12 months follow-up. We also compared these aspects for patients with and without persistent complaints 6-12 months after their initial visit to the general practitioner (GP).

MATERIALS & METHODS

Design

Data of a cross-sectional study on patients with a previous lateral ankle sprain were used to study the impact on functioning and medical consumption.

Participants

Patients were selected from the medical records of 84 general practices in the Netherlands. To select patients, the International Classification of Primary Care (ICPC) code 'ankle sprain' (L77) was used in combination with the text search terms 'ankle', 'distortion' and 'sprain'. Eligible for the study were patients aged 16-65 years who were registered at the GP's practice 6-12 months before the start of this study with a new ankle sprain.[10] Patients with structural damage like fractures, other osseous abnormalities, former ankle operations or known systematic diseases involving the ankle with an impact on functioning (e.g. multiple sclerosis, rheumatoid arthritis) were excluded, as were patients with insufficient knowledge of the Dutch language.

Procedures

Eligible patients from general practice received a letter from their own GP with study information and a response card. Responding patients were subsequently approached by telephone and the inclusion criteria were checked. Additionally, the presence of complaints was reported using a 7 "point" Likert scale (1=completely recovered to 7=worse than ever). Based on this score included patients were divided into two groups: those without persistent complaints after an ankle sprain [score 1-2 on the Likert scale ('completely recovered' or 'strongly improved')] and those with persistent complaints after an ankle sprain [score 3-7 ('slightly improved' to 'worse than ever')].

Patients were included after they had provided informed consent and were subsequently asked to fill in a standardized questionnaire. In addition, all participants were invited for a physical and a radiological examination (although these findings are not used for the present study).

Measurements

All included patients received a standardized questionnaire with questions on patient characteristics [age, gender, body mass index (BMI) and education level] and history of the ankle sprain, i.e. the side of the injury, preferred leg, previous sprains, the cause of sprain, and related change in) activity. Measurement of the current symptoms included: pain at rest and during exercise [rated on a numeric rating scale (NRS) 0-10], function measured with the Ankle Function Score (AFS; 0-100)[11] and the Tegner score (11-point activity level score)[12], feeling of instability (expressed in a subscale of the AFS), as well as symptoms, pain and functioning during physical sport [Foot and Ankle Disability Index (FADI) on a 0-34 point scale ranging from 'no difficulty' to 'unable to do'].[13] The current impact on work and physical activity was measured using a question on ability, participation and bothersomeness, expressing limitation in activity. Ability was measured using a single question with three response categories: 'not able to do due to ankle complaints'; 'not able due to other reasons'; 'able to do'. Current bothersomeness in work and

physical activities was measured using a 0-10 NRS scale. Details of sports participation in terms of competing, intensity and complaints were asked in separate questions. All impact measures were registered by the patients as perceived at the moment of filling in the questionnaire. Perception of general health at the time of filling in the questionnaire was measured using the EQ-5D subscale, ranging from bad to excellent. Medical consumption was asked for the complete follow-up period, by means of total number of visits to the GP, medical specialist and/or physiotherapist. Any diagnostic imaging performed during follow-up was registered (radiograph, MRI). In addition, the applied physiotherapeutic treatment protocols and any additional support items were reported.

Statistical analysis

Descriptive statistics were used to analyze patient characteristics, impact on functioning, and medical consumption of participants with and without persistent complaints. Differences between the groups were tested using an independent sample t-test for continuous variables and a chi-square test for dichotomous variables. Data were analyzed using SPSS (version 20.0, SPSS Inc. Chicago, IL, USA). For all analyses, a p-value < 0.05 was assigned as statistically significant.

RESULTS

A total of 632 patients were found in the electronic medical records of 84 general practices, of whom 206 were willing to participate in the study.[10] Finally, 204 patients completed the online questionnaire and are included in the present study. Based on the 7 "point" Likert scale, two groups were formed based on the current presence of complaints: 96 patients had persistent complaints and 108 patients reported no persistent complaints.

Table 1. Patient characteristics (n (%), unless otherwise stated)

	Total (n = 204)	Persistent symptoms (n = 96)	Without symptoms (n = 108)	*P* value
Age (years)*	37. 53 (14.6)	36.55 (14.38)	38.41 (14.80)	0.37
Gender (male)	85 (41.7%)	34 (35.4%)	51 (47.2%)	0.128
BMI (kg/m^2)*	25.77 (4.80)	26.92 (5.51)	24.94 (4.04)	**0.006**
Education level				0.056
Lower	124 (60.8%)	65 (67.7%)	59 (54.6%)	
Higher	80 (39.2%)	31 (32.3%)	49 (45.4%)	
Sport participant (yes)	119 (58.3%)	35 (36.4%)	84 (77.8%)	0.477
Preferred leg (right)	167 (81.9%)	81 (84.4%)	86 (79.6%)	0.359
Side of ankle sprain (right)	114 (55.9%)	58 (61.4%)	56 (51.9%)	0.219
Previous ankle sprain	96 (47.0%)	49 (51.0%)	47 (43.5%)	0.277
Diagnosis made by				0.316
General practitioner	120 (58.8%)	52 (54.2%)	68 (63.0%)	
Physiotherapist	14 (6.9%)	6 (6.2%)	8 (7.4%)	
Orthopedic surgeon	22 (10.8%)	14 (14.6%)	8 (7.4%)	
Self	6 (2.9%)	2 (2.1%)	4 (3.7%)	
Unknown	42 (20.6%)	22 (25.0%)	20 (18.5%)	
Complaints directly after the ankle sprain (retrospectively reported)				
Reported cause ankle sprain				0.854
Distortion	96 (47.0%)	44 (45.8%)	52 (48.1%)	
Out of balance	19 (9.3%)	9 (9.4%)	10 (9.3%)	
Hit against ankle	9 (4.4%)	5 (5.2%)	4 (3.7%)	
Unknown	80 (39.2%)	38 (39.6%)	42 (38.9%)	
Ankle sprain occurred during				0.926
Sport	75 (36.8%)	36 (37.5%)	39 (36.1%)	
Work	26 (12.7%)	13 (13.5%)	13 (12.0%)	
Hobby	14 (6.9%)	5 (5.2%)	9 (8.3%)	
Task around the house	10 (4.9%)	4 (4.2%)	6 (5.6%)	
Traffic participation	21 (10.3%)	9 (9.4%)	12 (11.1%)	
Other	56 (27.4%)	28 (29.2%)	28 (25.9%)	
Ankle swollen after sprain				0.373
No	13 (6.4%)	7 (7.3%)	6 (5.6%)	
Slight	47 (23.0%)	18 (18.7%)	29 (26.9%)	
Serious	142 (69.6%)	70 (72.9%)	72 (66.7%)	
Unknown	2 (1.0%)	1 (1.0%)	1 (0.9%)	
Place swelling after sprain				0.080
Medial side	20 (9.8%)	13 (13.5%)	7 (6.5%)	
Lateral side	169 (82.8%)	75 (78.1%)	94 (87.0%)	
Other place	15 (7.4%)	8 (8.3%)	7 (6.5%)	

Table 1. Patient characteristics (n (%), unless otherwise stated) (continued)

	Total (n = 204)	Persistent symptoms (n = 96)	Without symptoms (n = 108)	*P* value
Most pain after sprain				0.113
Medial side	25 (12.2%)	12 (12.5%)	13 (12.0%)	
Lateral side	109 (53.4%)	42 (43.7%)	67 (62.0%)	
Frontal side	14 (6.9%)	9 (9.4%)	5 (4.6%)	
Caudal side	7 (3.4%)	5 (5.2%)	2 (1.9%)	
Other place	49 (24.0%)	28 (29.2%)	21 (19.4%)	
Instability after sprain (yes)				**0.020**
yes	170 (83.3%)	86 (89.6%)	84 (77.8%)	

*Expressed mean (SD); statistically significant differences in bold

Baseline characteristics

Table 1 presents the baseline characteristics of the included patients**:** mean age was 37 (SD 14.7) years and 42.6% was male. In 56.4% the right ankle was injured and almost 50% had an previous ankle sprain in their medical history, with no significant difference between the two groups. The BMI was significantly higher in the group with persistent complaints compared to those without persistent symptoms (26.9 and 24.9 kg/m^2, respectively). A higher percentage of patients in the group without persistent complaints participated in sport at the time of study inclusion (77.8% vs. 36.4%). Directly after the ankle sprain, in 82% of the patients swelling was present and in 53.4% pain was localized at the lateral side of the ankle, but with no significant differences between the two groups.

Effects on functioning 6-12 months after a sprain

Overall, significantly higher pain scores at rest (1.87 vs. 0.44) and during exercise (3.62 vs. 1.25), and a lower function expressed in AFS (72.47 vs. 82.90) and FADI sport (0.80 vs. 0.90), were seen in patients with persistent complaints compared to patients without persistent complaints (Table 2). A high percentage of patients reported a feeling of instability, with a significantly higher percentage in the group with persistent complaints (78% vs. 64.8%); ≥ 10% of patients with persistent complaints maintained a feeling of instability with every step, or in normal daily activities. During follow-up, no significant differences were seen in work activity and physical activity between the two groups. Overall, 4.4% of the patients were unable to work due to ankle complaints. In addition, in patients both with and without persistent complaints, 22.9% and 15.7%, respectively, reported the impossibility to participate in physical activity due to their ankle complaints. Significantly higher bothersomeness scores both during work (2.4) and physical

activities (4.8) were reported in patients with persistent symptoms. No differences were found between the two groups in general health status.

Medical consumption after an ankle sprain

A high level of medical consumption was found in both groups (Table 3). Most patients (76.5%) had visited the GP, while the remaining patients entered the study based on the medical records of the GP (i.e. this latter group had visited an emergency department, which was subsequently reported to the GP). In patients with and without persistent complaints, the physiotherapist was visited by 52.1% and 39.8%, respectively. In the total group of patients a medical specialist was consulted by 20.1% of them.

Table 2. Impact on functioning 6-12 months after an ankle sprain

	Total (n = 204)	**Persistent symptoms (n = 96)**	**No symptoms (n = 108)**	***P* value**
Pain score *				
In rest (VAS 0-10)	1.11 (1.83)	1.87 (2.20)	0.44 (1.03)	**<0.001**
During exercise (VAS 0-10)	2.37 (2.46)	3.62 (2.62)	1.25 (1.64)	**<0.001**
Recovery (7-point Likert scale)				n.a.
Completely recovered	36 (17.6%)	-	36 (33.3%)	
Strongly improved	72 (35.3%)	-	72 (66.7%)	
Slightly improved	51 (25.0%)	51 (53.1%)	-	
No change	17 (8.3%)	17 (17.7%)	-	
Slightly worsened	20 (9.8%)	20 (20.8%)	-	
Sharply worsened	6 (2.9%)	6 (6.2%)	-	
Worse than ever	2 (1.0%)	2 (2.1%)	-	
Ankle Function Score (0-100)*	73.45 (20.50)	62.47 (20.24)	82.90 (15.44)	**<0.001**
Instability (subscale of AFS)				**<0.001**
Every step	2 (1%)	2 (2.1%)	0 (0.0%)	
Frequently in normal activity	9 (4.4%)	9 (9.3%)	0 (0.0%)	
Sometimes in normal activity	38 (18.6%)	23 (23.9%)	15 (13.9%)	
Frequent during sports	4 (2.0%)	3 (3.1%)	1 (0.9%)	
Sometimes during sports	92 (45.1%)	38 (39.6%)	54 (50.0%)	
Never	54 (26.5%)	17 (17.7%)	37 (34.3%)	
FADIsport (0-5 points)*	0.86 (0.14)	0.80 (0.15)	0.92 (0.09)	**<0.001**
Tegner (0- 10 levels of activity)	5 (1-9)	5 (1-9)	5 (0-10)	0.22
Work activities				0.67
Not able to work due to ankle complaints	9 (4.4%)	4 (4.2%)	5 (4.6%)	
Not able to work due to other reasons	5 (2.4%)	1 (1.0%)	4 (3.7%)	
Had paid work	150 (73.5%)	72 (75.0%)	78 (72.2%)	

Table 2. Impact on functioning 6-12 months after an ankle sprain (continued)

	Total (n = 204)	**Persistent symptoms (n = 96)**	**No symptoms (n = 108)**	***P* value**
Bothersomeness work (0-10)*	1.73 (2.39)	2.40 (2.48)	1.14 (2.16)	**0.004**
Physical activity (PA)				0.53
No PA due to ankle complaints	39 (19.1%)	22 (22.9%)	17 (15.7%)	
No PA due to other reasons	8 (3.9%)	3 (3.1%)	5 (4.6%)	
Did PA	127 (62.3%)	56 (58.3%)	71 (65.7%)	
Bothersomeness during PA (0-10)*	3.72 (2.93)	4.80 (2.52)	2.78 (2.96)	**<0.001**
Sports participation				
Competition (yes)	46 (22.5%)	19 (19.8%)	27 (25.0%)	0.477
Intensity (hours per year)*	160.74 (207.89)	167.42 (251.93)	154.93 (161.17)	0.673
Ankle complaints during sports	61 (29.9%)	35 (36.5%)	26 (24.1%)	**0.006**
General Health (EQ 5D subscale)				0.097
Excellent	29 (14.2%)	11 (11.5%)	18 (16.7%)	
Very good	57 (27.9%)	22 (22.9%)	35 (32.4%)	
Good	95 (46.6%)	48 (50.0%)	47 (43.5%)	
Moderate	18 (8.8%)	11 (11.5%)	7 (6.5%)	
Poor	3 (1.5%)	3 (3.1%)	0 (0.0%)	
Missing	2 (1.0%)	1 (1.0%)	1 (0.9%)	

*Expressed mean (SD); 3 median, range; n. a. = not applicable; statistically significant differences in bold

Radiographic imaging was applied in 38.5% of the group with persistent complaints and in 32.4% of those without complaints, while a MRI or CT scan was made in 9.4% of patients with persistent complaints and in 4.6% of those without complaints. The most frequently applied additional supports included cold compresses (59.8%), elastic ankle brace (34.8%), braces (30.9%), tape (42.6%), and crutches (37.3%). Finally, when physiotherapy was applied, in most cases this included stability (33.8%) and mobilizing exercises (22.5%).

Table 3. Medical consumption, expressed n (%)

	Total period (n = 204)	Total period Persistent complaints (n = 96)	Total period Without complaints (n = 108)
Visits to medical care			
General practitioner	156 (76. 5%)	72 (75.0%)	84 (77.8%)
Sports physician	3 (0.01%)	2 (2.1%)	1 (0.95%)
Physiotherapist	93 (45.6%)	50 (52.1%)	43 (39.8%)
Medical Specialist	41 (20.1%)	23 (24%)	18 (16.7%)
Doctor at work	10 (4.9%)	5 (5.2%)	5 (4.6%)
MRI / CT-scan	14 (6. 9%)	9 (9.4%)	5 (4.6%)
Radiology	72 (35.3%)	37 (38.5%)	35 (32.4%)
Manual therapist	4 (2.0%)	2 (2.1%)	2 (1.9%)
Usage of additional support			
Cold compress	122 (59.8%)	55 (57.3%)	67 62.0%)
Orthopedic insoles	16 (7.8%)	12 (12. 5%)	4 (3.7%)
Elastic ankle brace	71 (34.8%)	32 (33.3%)	39 (36.1%)
Brace / bandage	63 (30.9%)	32 (33.3%)	31 (28.7%)
Tape	87 (42.6%)	45 (46.9%)	42 (38.9%)
Crutches	76 (37.3%)	35 (36.5%)	41 (38.0%)
Plaster	22 (10.8%)	14 (14.6%)	8 (7.4%)
Physical therapy			
Stability exercises	69 (33.8%)	37 (38.5%)	32 (29.6%)
Strength exercises	39 (19.1%)	20 (20.8%)	19 (17.6%)
Mobilizing exercises	46 (22.5%)	25 (26.0%)	21 (19.4%)
Massage	43 (21.1%)	26 (27.1%)	17 (15.7%)
Walk training	26 (12.7%)	18 (18.8%)	8 (7.4%)
Bicycle training	16 (7.8%)	10 (10.4%)	6 (5.6%)

DISCUSSION

This study, performed in general practice, shows that lateral ankle sprain has a high and prolonged impact on functioning and leads to a considerable use of medical resources, expressed in a high percentage of visits to the GP, physiotherapist and medical specialist, both in patients with and without persistent complaints. In both groups there was considerable use of radiographic imaging. Almost 20% of all participants still had restrictions to their physical activities due to the ankle sprain at 6-12 months follow-up; moreover, 23% reported complaints of persistent instability during daily normal activities and 47% during sports activities. Overall, the impact on function, expressed in

different outcomes related to daily activity and sport activities, was significantly higher in the group with persistent complaints compared to the group without complaints.

In an earlier study using a population-based computer-aided telephone survey of patients in primary care, 20% of the participants reported chronic ankle disorders, mostly due to a previous ankle sprain and 64.6% of these participants reported to have limited (or changed) physical activity.[8] Also, nearly 50% of patients with chronic ankle disorders reported persistent complaints for ≥ 10 years and a decrease in their sports activities.[8] Comparable to our study, most patients visited their GP, and used tape and braces.[8] A systematic review on the economic evaluation of diagnostic tests, treatment and prevention for lateral ankle sprains concluded that there is evidence (although limited) for potential cost-effectiveness of the use of the Ottawa Ankle Rules (OAR) for diagnosing lateral ankle sprains in an emergency setting, the use of NSAIDs and plaster in the acute phase, and use of neuromuscular training in preventing recurrence.[14] In the present study, patients were selected in general practice for which the Dutch Guidelines (the OAR) on ankle complaints are mostly used. However, we found that in more than one third of the patients radiography was applied. In a national study on diseases in general practice in The Netherlands, only 6.2% of the patients with ankle sprains had radiography and 6.6% was referred to a physiotherapist after an ankle sprain.[15] In the present study we found that radiography was performed more often among participants who also visited a medical specialist (83%) than those who had not visited a specialist (5%).[1] This may be due to the severity of the complaints, or to the potential difference in the implementation of the existing decision rules (such as the OAR) in excluding fractures or other osseal abnormalities. In their systematic review, Lin et al. suggested to implement the OAR more frequently in emergency departments to decrease costs.[14] In the present study, more than 40% of the patients received physiotherapy as a consequence of their ankle sprain (in both groups). A balance training program was shown to prevent re-sprains in an athletic population[16] and this is confirmed by a recent review on the treatment of chronic ankle sprain complaints.[17] However, Kerkhoffs et al. [5] found no effect of the use of physiotherapy in acute ankle sprains on the outcome function. Therefore, it is debatable whether all these patients should have received therapy after their ankle sprain. In the present study, MRI was performed in only 6.9% of the patients. In The Netherlands, GPs cannot directly refer patients to an MRI; therefore, all MRIs documented in our study were initiated by a medical specialist. Based on their review, one of the conclusions of Lin et al. was to discourage the use of MRI as a too-often performed diagnostic measure. Additionally, based on the same study population as in the present study, our group earlier demonstrated no direct correlation between MRI findings and persistent complaints after a lateral ankle sprain.[10] Therefore, it does not seem appropriate to initiate MRI for ankle sprains in general practice, and 'free access' to this should not be stimulated.

Many additional support devices (e.g. cold compresses, elastic ankle braces and tape) were used in both study groups. A study on the economic impact of different treatment options for ankle distortions in occupational accidents [18] found a high rate of inappropriate use of cast immobilization and concluded that conventional treatment, consisting of rest, ice, compression and elevation, led to the fastest, full resumption of activities with the lowest medical costs.

Strengths and limitations

Our original aim was to design a case-control study to compare participants with persistent complaints with those without persistent complaints. Based on earlier reports[7] we expected at least twice as many controls as cases and aimed to match controls and cases on age and gender (with 100 persons per group). However, because an equal number of respondents reported persistent and non-persistent complaints we refrained from matching, and evaluated the data as a cross-sectional cohort study. Despite this possible bias induced by recruiting the patients, we found sufficient patients with adequate statistical power to demonstrate differences in impact and medical consumption after a lateral ankle sprain between the two groups. A strength is that we performed our study in general practice, whilst most studies recruited their patients from secondary care (e.g. emergency departments). Ankle sprains are most commonly seen in general practice and (apart from the few studies mentioned above) we are not aware of other studies investigating the impact and medical consumption after a lateral ankle sprain in primary care. A limitation could be that we could not establish whether it was a first ankle injury or the recurrence of a previous ankle sprain, because we had no details of the medical history before the patients filled in the questionnaire. It could be argued that the range of follow-up, i.e. 6-12 months, might have influenced our results. However, because the follow-up time was highly comparable in both study groups (median 44.2 vs. 43.9 weeks) it is unlikely that this variability influenced our study outcomes.

Implications for future research or clinical practice

We found that a lateral ankle sprain has a large impact on functioning, especially in those with persistent complaints. The sprain also results in considerable use of medical consumption, without large differences between patients who do or do not have persistent complaints. Based on the literature, there is considerable doubt as to whether the routine use of radiographic imaging or MRI shortly after a lateral ankle sprain (in both general practice and emergency departments) has any additional value; more research on this is needed. Although physiotherapy is often applied as a treatment option directly after a lateral ankle sprain, its effectiveness seems limited and can lead to high costs. Therefore, more

research on the most efficient type of care, and optimal implementation of efficient decision rules (like the OAR) and proven treatment options for these patients is warranted.

CONCLUSION

A lateral ankle sprain has a high impact on functioning and also leads to considerable use of medical resources 6-12 months after the initial visit to the GP. Also, a high impact on physical health, expressed as a decrease of physical activity and sports participation was found. The considerable use of medical resources was mainly attributed to visits to the GP, physiotherapist and medical specialist, to the use of radiographic imaging, and the use of additional supports like bandage, tape and crutches. This was found in patients both with and without persistent complaints, after a previous ankle sprain.

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Chapter 8

Center Of Pressure during stance and gait in subjects with or without persistent complaints after a lateral ankle sprain

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ABSTRACT

Study Aim: To investigate differences in the Center Of Pressure (COP) during gait and single leg stance between subjects with persistent complaints (PC) and without persistent complaints (NPC) after a lateral ankle sprain.

Methods: 44 Patients who consulted the general practitioner, 6 to 12 months prior to inclusion, with a lateral ankle sprain were included for the current study purpose. Using a 7 "point" Likert scale patients were divided into the PC or NPC group. All subjects filled out an online questionnaire, walked along a walkway and performed a single leg stance, both on the RSscan. Primary outcomes included the COP displacement, range and percentage used in mediolateral and anterio-posterior direction.

Results: There was a trend ($p < 0.05$) towards a more medially COP trajectory during walking at 34-46% and 83-96% and more anteriorly at 21%-31% and 91%-100% of the stance phase in the PC group compared to NPC group. Additionally, the COP was more laterally located in the sprained leg compared to the non-sprained leg in the PC group in the loading response phase ($p < 0.05$). An interaction was found for the percentage of anterior-posterior range used in single leg stance without vision.

Conclusion: The COP trajectory discriminates between patients with PC and NPC. This indicates that roll off during gait might play an important role in the recovery of patients after a lateral ankle sprain and could be used to monitor treatment.

Key words: sprain; ankle; persistent complaints; gait; balance

INTRODUCTION

A lateral ankle sprain is the most common injury in general practice. A substantial percentage of these injuries have their origin in sports. [1-3] Within three years following their first ankle sprain, one third of the patients reports persistent complaints[4]. These persistent complaints (PC) can be pain, subjective instability, recurrent ankle sprain and a combination of these problems. A systematic review by Van Rijn et al. reported an occurrence of re-sprains in 34% of the patients within 96 months after their first sprain and subjective instability in 33%. [4] Numerous studies emphasized one aspect of PC, i.e. chronic instability and have compared characteristics of these patients with a group of healthy subjects [5-18]. Since it is unknown whether these PC are directly associated with instability, it is interesting to study differences between patients who maintain PC and patients who fully recover after a lateral ankle sprain.

Traditionally, the factor to evaluate postural control and stability is the Center Of Pressure (COP). The COP can be interpreted as the application point of ground reaction force. During the stance phase of gait the COP moves mainly in heel-to-toe, anterior-posterior (AP), direction and slightly in medial-lateral (ML) direction. Willems et al. reported a more laterally COP during gait for patients with a lateral ankle sprain [5]. In addition, during running, a more lateral COP trajectory is reported in subjects with chronic ankle instability.[17] Furthermore, it has been suggested that it is possible to discriminate between healthy controls and patients with chronic ankle instability during a single leg stance task.[15] Therefore, the aim of the present study is 1) to investigate the differences in COP during gait between subjects with a previous lateral ankle sprain with self-reported PC and self-reported NPC and 2) to investigate differences in displacement of the COP in subjects with PC in comparison to subjects with NPC during single leg stance with vision and without vision. Because patients with chronic ankle instability show a more lateral trajectory of COP [5, 17], we hypothesized that PC will have a more lateral COP trajectory compared to NPC. For the balance control, more sway for PC patients was expected.

METHODS

Subjects

Data was used from patients included in an observational case-control study on persistent symptoms after a lateral ankle sprain.[19] Subjects were selected by searching the databases of 28 general practitioners (GPs) in the region of Rotterdam, The Netherlands. Subjects, who consulted the GP minimally 6 months and maximally 12 months prior to inclusion, with a lateral ankle sprain and who were aged 16 to 65 years, were asked to

participate. For this particular study, patients were included between May and August 2011 and were eligible for participation for the current study purpose.

Exclusion criteria were known conditions that influence the locomotor system, such as systemic, rheumatic or neurological diseases and no knowledge or understanding of the Dutch language. All subjects provided written informed consent and the Ethical Committee of Erasmus MC University approved the study.

All patients were divided into two study groups by using a 7 "point" Likert-scale to score their recovery. Patients with a 1-2 score (completely recovered or strongly improved) were defined as controls, i.e. patients with NPC and the subjects with a 3-7 score (slightly improved to worse than ever) were defined cases, i.e. patients with PC.

Procedure

After the selection of eligible patients from the GP databases, patients received a letter from the GP and were asked to return a reply card, if interested in the study. Interested patients were contacted by phone and inclusion criteria were re-checked. After inclusion, all patients were asked to complete an online questionnaire and were invited to our research center for the COP measurements.

Measurements

The online questionnaire informed on age, gender, pain intensity (VAS score, 0 = no pain, 10 = worst pain imaginable) during rest and exercise. Function was measured with the Ankle Function Score (AFS) [20, 21]. The AFS consists of five categories: pain, instability, weight bearing, swelling and gait pattern. In each category a maximum of total 100 points (indicating fully recovered) could be scored.

Participants performed three tasks in which the COP was measured; barefoot walking, single leg stance, with and without vision, on the RSscan footscan®. The footscan was positioned in the middle of the consulting room on a 6 meter walkway. During barefoot walking a removable barrier was placed 2,5 meter from the edge of the plate. The subjects walked at a self-selected comfortable speed along the 6 meter walkway starting with their right or left feet depending on the measurement.[22] They were allowed one test trial to familiarize them self with the track. The starting position was modified to ensure placement of the correct foot on the sensor platform with the third step. After striking the plate, the subject continued walking to the end of the walkway. Five valid left and five valid right stance phases were measured with a 30 seconds pause between each trial. A trial was considered to be valid when the following criteria where met: a heel strike pattern and no adjustments in step to aim on the footscan.

During single leg stance, subjects were asked to make an one-leg-stance in the middle of the footscan keeping the foot as still as possible. All subjects performed twelve single leg stance trials of 10 seconds with a 30 seconds pause between them. The single leg

stance included six measurements, all started with the right leg, followed by the left leg; three with vision, eyes open, and three without vision, eyes closed. A trial failed when the subjects touched down with the opposite leg and hopped or re-positioned with their stance leg or could not complete the 10 seconds trial. Every subject was allowed to perform three attempts to pass to the next stance. If the subject failed within these three attempts, no further tests were executed for this particular trial and leg. Only valid attempts were used for data collection.

The width and length of every foot step was acquired with the RSscan International and the mean width or length of every subject's five gait measurements was used.

Equipment

The RSscan INTERNATIONAL footscan® system (Belgium, Olen), with an outline of 0.5 x 0.4 x 0.008m and a maximum measurement frequency of 300Hz, was used for all measurements. COP was calculated through footscan® Gait scientific software and footscan® Balance software.

Outcome measures

The main outcome parameter in the gait analysis was the COP displacement. To describe the COP, the foot was normalized for foot size and foot progression angle.[23] The mean COP trajectory for each subject was normalized for the duration of the stance phase (0–100%). The COP was identified in medial-lateral (ML) and anterior-posterior (AP) direction as a percentage of foot width and length, respectively.[5, 24] The mean COP path of the five trials for each subject was also calculated.

The spatiotemporal gait parameters contact time, foot flat and heel-off were determined.[25] Contact time was defined as the time between heel strike and toe off. Heel strike was defined when the ground reaction force was above 15 N and toe off when the ground reaction force was below 15 N. Foot flat represents the time between the heel strike and the forefoot contacting the ground, which was defined if the force under the forefoot was above 25 N. Heel off specifies the time between heel strike and the instant the force under the heel was smaller than 25 N.

During single leg stance trials with vision and without vision, the percentage of range used in the ML and AP directions (distance between the minimum and maximum COP positions) were calculated as a percentage of foot length and width.

Statistical analysis

Baseline characteristics were described descriptively. Differences on dichotomous variables between study groups were analyzed using a chi-squared test. Continuous variables were analyzed using the Mann-Whitney U test.

Generalized Linear models, with a between factor group (NPC /PC) and a within factor side (sprained/non-sprained) were applied to test differences in contact time, heel off, foot flat and foot progression angle. When a significant interaction effect was found, post hoc analyses were conducted in the subgroups of interest using a student T-test.

To indicate differences in COP, four comparisons were made for each percent of the stance phase in mediolateral ad anteroposterior direction. The NPC and PC group for both feet were compared using a unpaired t-test (comparison 1). Differences between the sprained leg and non-sprained leg for the NPC (comparison 2) and PC group (comparison 3) with a paired T-test. Finally, differences between the sprained leg between the NPC and PC group were tested using a T-test (comparison 4). Differences were considered as relevant when at least 10 subsequent percentages had a p-value ≤ 0.05.

The analyses for postural control were performed for both legs, sprained and non-sprained. The percentage of range used in ML and AP direction of each subject during the three balance trials with and without vision were calculated. Differences between the two groups in the range and the attempts used to complete a balance trial were analyzed with Generalized Linear Models, with a between factor group (NPC /PC) and a within factor side (sprained/non-sprained), and post hoc analyses were conducted when a significant interaction effect was found. A Holm-Bonferroni Sequential Correction was applied for the balance analyses and an adjusted p-value ≤ 0.05 was considered as statistically significant.[26] SPSS software (version 21.0) for Windows was used for all statistical analyses and the alpha level for all testing was set a priori at $p \leq 0.05$.

RESULTS

Characteristics

A total of 44 participants were eligible and included in this study: 30 participants were classified with NPC and 14 participants with PC. No significant differences between both groups were observed for gender, age, height, weight, BMI and shoe size. (Table 1) The VAS score during rest was significantly higher in subjects with PC ($p = 0.029$) and the function score (AFS) was significantly ($p = 0.043$) lower for the subjects with PC compared to the subjects who have NPC.

Gait

All subjects completed all trials and were all included in the analyses. The two way ANOVA revealed no significant between groups effect, no significant side effect nor an interaction effect for the spatiotemporal parameters heel contact, foot flat, heel off and foot progression angle (Table 2).

Table 1. Subject characteristics (mean, SD, unless otherwise stated).

	Total n=44	NPC n=30	PC n=14	P-value
Gender, female (n, %)	21 (47.7%)	16 (53.3%)	5 (35.7%)	0.28^
Age (years)	35.45 (14.0)	37.00 (14.0)	32.14 (14.0)	0.29
Weight (kg)	78.20 (13.5)	76.47 (11.7)	81.93 (16.7)	0.21
Height (m)	1.77 (0.1)	1.77 (0.1)	1.78 (0.1)	0.55
BMI (kg/m^2)	24.81 (3.6)	24.47 (3.7)	25.54 (3.5)	0.24
Shoe size (EU)	41.76 (2.9)	41.55 (2.7)	42.21 (3.3)	0.29
Preferred leg, right (n, %)	33 (75.0%)	22 (73.3%)	11 (78.6%)	0.71^
Sprained leg, right (n, %)	28 (63.6%)	20 (66.4%)	8 (57.1%)	0.54^
Preferred leg is sprained leg (n, %)	29 (65.9%)	18 (60.0%)	11 (78.6%)	0.23^
Self-reported recovery				**<0.001^**
1 – Fully recovered (n, %)	6 (13.6%)	6 (13.6%)		
2 – Strongly improved (n, %)	24 (54.5%)	20 (54.5%)		
3 – Slightly improved (n, %)	9 (20.5%)		9 (20.5%)	
4 – Stayed the same (n, %)	2 (4.5%)		2 (4.5%)	
5 – Slightly worsened (n, %)	1 (2.3%)		1 (2.3%)	
6 – Strongly worsened (n, %)	1 (2.3%)		1 (2.3%)	
7 – Worse than ever (n, %)	1 (2.3%)		1 (2.3%)	
Function (AFS, 0-100)	75.32 (20.6)	79.21 (18.3)	65.92 (23.5)	**0.04**
Pain during rest (VAS, 0-10)	1.07 (1.7)	0.63 (1.2)	2.00 (2.4)	**0.03**
Pain during exercise (VAS, 0-10)	2.30 (2.4)	1.67 (1.7)	3.64 (3.2)	0.07

NPC= no persistent complaints, PC = persistent complaints; significant differences in bold; ^ tested with Chi-square

Table 2. Gait analyses with a between factor (NPC /PC) and a within factor (sprained/non-sprained)

	NPC		PC				
	Sprained	Non-sprained	Sprained	Non-sprained	p-value/F-value		
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Between	Within	Interaction
N (number of subjects)	30		14		-	-	-
Gait speed (m/sec)	1.12 (0.15)		1.04 (0.20)		0.30	-	-
Contact time (sec)	0.73 (0.08)	0.73 (0.07)	0.79 (0.13)	0.79 (0.13)	0.05/3.96	0.58/0.31	0.62/0.25
Heel-off (sec)	0.07 (0.01)	0.07 (0.02)	0.08 (0.02)	0.08 (0.03)	0.19/1.79	0.37/0.84	0.17/1.99
Foot-flat (sec)	0.41 (0.08)	0.40 (0.08)	0.45 (0.17)	0.45 (0.16)	0.17/1.95	0.64/0.23	0.63/0.24
Percentage Heel-off'	0.10 (0.02)	0.10 (0.03)	0.10 (0.02)	0.10 (0.03)	0.99/0.01	0.56/0.35	0.28/1.21
Percentage foot-flat	0.55 (0.07)	0.55 (0.08)	0.56 (0.12)	0.56 (0.11)	0.79/0.07	0.70/0.15	0.66/0.20
Foot progression angle (degrees)	8.0 (4.2)	8.3 (4.5)	9.6 (4.6)	9.4 (3.8)	0.28/1.18	0.87/0.03	0.72/0.13

NPC= no persistent complaints, PC = persistent complaints; significant differences in bold

Figure 1 presents the mean COP trajectories of sprained and non-sprained leg of the two groups and the displacement relative to the mean COP trajectory as percentage of foot width and length. A more medially/anteriorly located COP for the PC compared to the NPC group was found at 34-46% and 83-96% of the stance phase in mediolateral direction and at 21-31% and 91-100% in anterior-posterior direction. The comparison between sprained and non-sprained leg revealed a more laterally located COP. The differences in COP between NPC and PC in ML at 92-93% and in AP at 96-98% had a p-value < 0.005. The comparison between sprained and non-sprained leg revealed a more laterally located COP for the sprained leg in PC group at 4-18% ($p < 0.05$). Plantar pressure pattern for the different groups are shown in Figure 2. No differences in plantar pressure were found between the NPC and PC group and also not between the sprained and non-sprained leg.

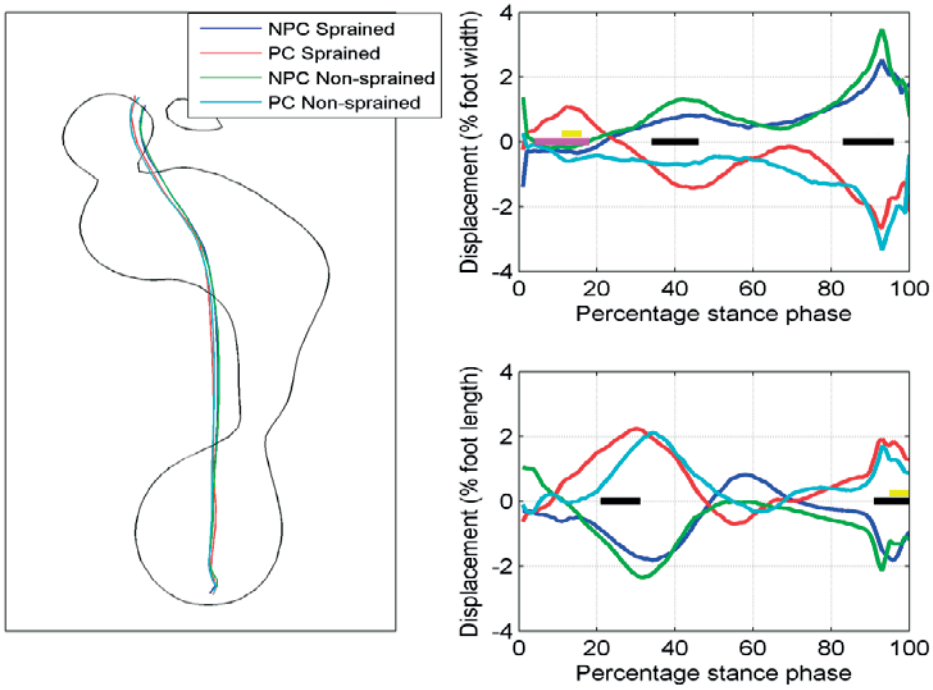

Figure 1. COP trajectory NPC Sprained, NPC Non-sprained, PC Sprained and PC Non-sprained
Left panel: COP trajectory of sprained and non-sprained leg of the NPC and PC group. Right panels: COP trajectory of sprained and non-sprained leg of the NPC and PC group relative to the mean COP trajectory in mediolateral (upper) and anteroposterior (lower) directions as percentage of foot width and length. Positive value indicates more laterally/posteriorly located COP.
Black line indicates significant difference between NPC and PC group. Magenta line indicates significant difference between sprained and non-sprained leg of PC group. Yellow line indicates significant difference between the sprained leg of the NPC and PC group.

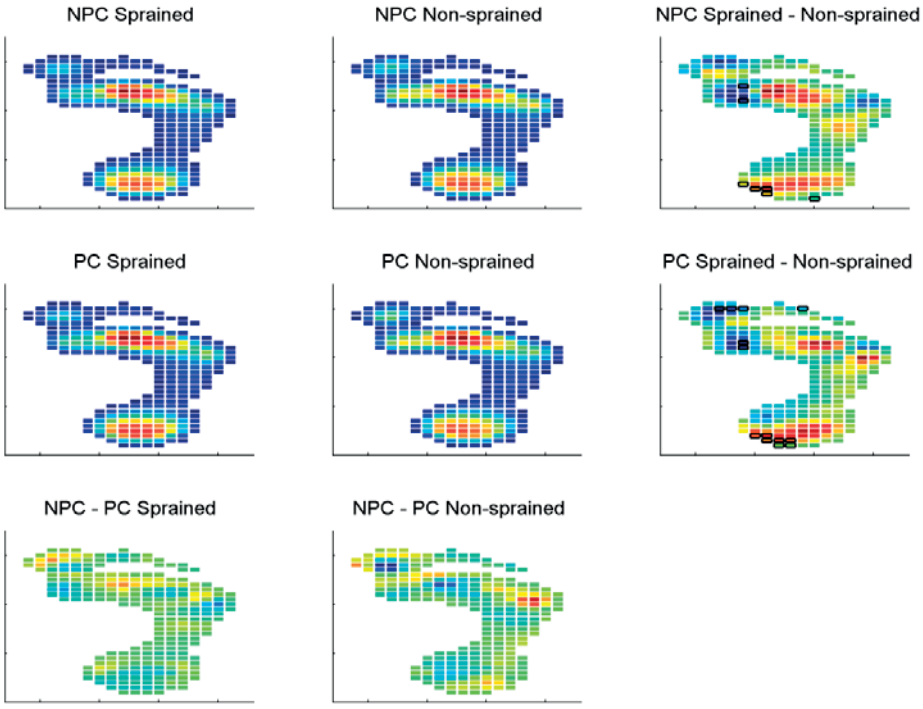

Figure 2. Pressure per sensor (Mean pressure pattern for the sprained leg for the PC and NPC group. A box indicates a significant difference between the sprained leg of the NPC and PC group

Balance

In total two participants (4.5 %, 1 NPC; 1 PC) were unable to finish all three trials with vision and 17 subjects (38.6 %, 11 NPC; 6 PC) without their vision while standing on their non-sprained leg. These subjects were therefore excluded from the analysis (Table 3). A positive trend for an interaction was found for the percentage of range used in AP direction ($p = 0.02$, adjusted p-value 0.12) for standing without vision. Post hoc analyses revealed no statistical significant differences.

Table 3. Postural control (mean, SD, unless otherwise stated) during single leg stance balance task. Statistical results are the result of a two-way ANOVA with a between factor (NPC /PC) and a within factor (Sprained/ Non-sprained).

		No persistent complaints		**Persistent complaints**		**Significance**		
	#NPC / #PC	Sprained	Non-sprained	PC Sprained	Non-sprained	p-value / F-value		
		Mean (SD)	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Between**	**Within**	**Interaction**
% ML range used WV	28 / 13	22.23 (6.41)	21.77 (5.86)	24.81 (7.90)	26.08 (10.84)	0.11/ 2.64	0.75/ 1.05	0.49/ 0.49
% AP range used WV	28 / 13	11.88 (3.75)	11.31 (3.63)	12.29 (5.15)	14.53 (7.25)	0.18/1.89	0.32/0.99	0.10/ 2.84
% ML range used WOV	18 / 8	43.04 (9.93)	42.90 (7.55)	41.35 (5.73)	46.05 (10.96)	0.81/0.06	0.30/1.13	0.27/ 1.26
% AP range used WOV	18 / 8	25.99 (8.72)	22.76 (7.84)	20.18 (3.19)	24.74 (3.87)	0.48/0.53	0.68/0.18	0.02/ 6.16
Attempts WV	29 / 13	1.02 (0.09)	1.05 (0.15)	1.03 (0.09)	1.13 (0.29)	0.24/1.46	0.11/2.73	0.30/ 1.10
Attempts WOV	19 / 8	1.40 (0.50)	1.53 (0.50)	1.38 (0.52)	1.42 (0.61)	0.70/0.15	0.53/0.40	0.76/ 0.10

NPC= no persistent complaints, PC = persistent complaints, WV = with vision, WOV = without vision
3 subjects had an uncompleted trail WV, 17 subjects had an uncompleted trail WOV and 1 subject with a failed data processing.

DISCUSSION

This study compared the COP during stance phases of gait and single leg stance between a group of patients with no persistent complaints after a lateral ankle sprain and a group with persistent complaints. Differences in both mediolateral and anterior-posterior displacement between both study groups were found at early mid-stance and push off and between the sprained and non-sprained leg of PC patients in the loading response phase during gait. In addition, a positive trend was seen for a difference in the anterior-posterior range during single leg stance without vision.

Baseline differences in pain and function were observed between both study groups, likely the result of the classification using the 7 "point" Likert scale to measure self-reported recovery. Van Rijn et al. found an association between self-reported pain severity, a feeling of giving way and self-reported recovery, indicating that both pain and function are aspects of self-reported recovery in ankle sprain patients.[26] The ankle function scores of 66 (SD 23.5) and 79 (SD 18.3) in this particular study correspond to the

results of De Bie et al. in which subjects with PC scored < 75 points in contrast to the NPC group who scored > 75 points.[21]

The COP trajectory during gait was more laterally situated in subjects with PC during early mid-stance and push off. The more lateral trajectory of COP during the last phase of gait was similar to the results of previous reports on patients with chronic ankle instability.[5, 17] Willems et al. found a lateral displaced COP in subjects with exclusively chronic ankle instability in comparison with a healthy population.[5] They suggested that monitoring the gait pattern, and in subjects at risk of a sprain, adjustment of foot biomechanics should be a part of prevention and therapy. The findings in this study support this conclusion. For subjects who fully recovered and reported no persistent complaints, in the COP trajectory there was a significant difference from those with PC. Morrison et al. also suggested a different COP displacement between subjects with and without PC during running.[17] However, they limited their research to subjects who solely self-reported chronic ankle instability in comparison to a healthy group and a group of subjects who only suffered one inversion ankle injury in the past and did not develop chronic symptoms. Therefore, it still remains unclear if the difference found in COP during the end phase of gait is preexisting and could be a discriminating factor between these subjects even before a lateral ankle sprain is present.

A possible explanation for the difference found in COP trajectory between the PC and NPC groups could be a more cautious roll off during gait. The more posterior COP trajectory in the PC group suggest a lower ankle joint moment and less loading of the ankle. Although not statistically significant, a longer contact time was seen in the group with PC. The more posterior and lateral COP trajectory could be the result of pain experienced during activities, which was significantly higher in the PC group and it could therefore be hypothesized that patients with PC use a compensatory mechanism during walking to avoid their pain. It is however unknown what the impact of modification of the COP trajectory would be on experienced pain and instability.

The absence of a difference in single leg postural sway with eyes open was consistent with previous literature in which no significant differences were found between subjects with chronic or functional ankle instability compared to healthy controls with eyes open on a stable surface.[6, 9, 27] As suggested in these studies, we added a more challenging test for postural stability by removing the vision. Without vision, we found a positive trend towards an interaction effect in anterior-posterior range used. However, post-hoc analyses revealed no differences in the separate subgroups. Surprisingly, although not statistically significant, a positive trend was found for an increase of mean range and mean attempts in the standing task for the non-sprained leg compared to the sprained leg (p=0.11, adjusted p-value 0.66). This could be the result of the combination between the non-sprained leg and non-dominant leg in a large part of our population, resulting in a lack of stability to complete the 10 second-trial. Another possibility is the poten-

tial larger amount of exercises that might be performed during rehabilitation for the sprained leg compared to the non-sprained leg. Unfortunately there is no data available to confirm this hypothesis.

Strengths and limitations

This is the first study comparing subjects with and without persistent complaints after a lateral ankle sprain regarding COP measurements during gait and balance. Subjects were selected from primary care and are a representative group of patients. We used a 7"point" Likert scale to divide patients in a recovered and non-recovered group. We were unfortunately not able to use the CAI criteria based on a consensus statement by Gribble et al. [28] Though our criteria seem to cover all items (i.e. instability, pain and function) as discussed in the consensus statement, though perhaps not as specifically as suggested.

We were only able to include 44 patients for the present study that was conducted within a larger cross-sectional study with the aim to get more insight into persistent complaints after a lateral ankle sprain, As a consequence some power problems may have occurred. However, we have been cautious on our conclusions and findings, using the conservative Holm-Bonferroni method for the balance outcomes. For the gait outcomes, we considered differences as relevant when at least 10 subsequent percentages had a p-value ≤ 0.05. Furthermore, the differences in COP between NPC and PC in ML at 90-94% and in AP at 93-100% had a p-value below 0.005. We therefore think that the chances on a type I error were very small.

CONCLUSION AND IMPLICATIONS

A difference was seen in the COP trajectory between recovered and non-recovered patients after a lateral ankle sprain indicating that the roll off during gait might play an important role in the recovery trajectory of patients. For treatment and secondary prevention, COP measurements could be used to monitor treatment, and gait analysis and training might be integrated in the rehabilitation of subjects who suffered a lateral ankle sprain.

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Chapter 9

General discussion

The aim of the work in this thesis was to provide insight into the course of chronic ankle complaints that were caused by a previous ankle sprain in primary care. This chapter discusses the main findings emerging from our investigations. The results are interpreted in light of the existing literature, various methodological issues are addressed, implications for the general practitioner (GP) are discussed, and recommendations are made for further research.

MAIN FINDINGS

In key sentences:

- Although many structural abnormalities are found on MRI after an ankle sprain, imaging will not lead to diagnosing the exact reason for persistent complaints.
- The prevalence of structural abnormalities seen on MRI is high in both the injured and contralateral ankle 6-12 months after a sprain, but bone marrow edema and lateral ligament lesions are more frequently seen in the injured ankle.
- Pain at the end of dorsiflexion and/or plantar flexion, a difference in ROM of passive plantar flexion and swelling measured with physical examination seem to be associated with the presence of features of early stage osteoarthritis in both the TCJ and TNJ on MRI after a sprain.
- A lateral ankle sprain has considerable impact on functioning and physical health, especially in patients with persistent complaints.
- A lateral ankle sprain leads to substantial medical consumption and use of healthcare resources in patients both with and without persistent complaints.
- Differences are seen in both gait and balance tasks (reflected in the center of pressure), between patients with and without persistent complaints at 6-12 months after a lateral ankle sprain
- For patients with chronic complaints after a lateral ankle sprain, a training program is more effective than a wait-and-see policy on the outcomes pain, function, and recurrences.
- After an acute ankle sprain, additional supervised exercises provide some benefit regarding recovery and return to sports compared with conventional treatment alone.

Discussion of main findings

Although ankle sprains are the most common musculoskeletal injury seen in general practice in the Netherlands [1], many details on the course, impact and effective treatment options remain unclear. Therefore, the aim of the studies in thesis was to gain more insight into the reasons for persistent complaints, the value of radiography (X-ray and

MRI) in the diagnosis of these persistent complaints, and the most appropriate options for the treatment of both acute and chronic complaints after an ankle sprain.

Diagnosis

For the GP, patients' history taking and physical examination are the main tools applied when diagnosing and treating a lateral ankle sprain. In the Dutch guidelines, the Ottawa Ankle Rules (OAR) are used to exclude a fracture or other osseous abnormalities in the acute ankle sprain.[2] The prevalence of a such a fracture in general practice is 5% and in the emergency department of a hospital the incidence rises to 20%.[3] After excluding a possible fracture based on the OAR, the next aim is to establish the etiology of the injury, pain, function loss, swelling and previous sprains, in order to gain a complete overview regarding the severity of the sprain.[2] In performing a physical examination, swelling, pain at palpation, and the anterior drawer test are the main issues. The presence of a hematoma still present 5 days after the trauma, pain at palpation, and/or a positive anterior drawer test predict the presence of a rupture of the anterior talofibular ligament; conversely, the absence of these factors strongly predicts the absence of a rupture.[4] However, for the diagnosis of persistent complaints after ankle sprains, no specific guidelines for physical examination and history taking are available.

Function scores

Apart from the usual examination in clinical practice, no patient-related outcome measures or function scores to assess severity or to be used as a diagnostic tool so far have been recommended in the Dutch national guideline, or in any international clinical guideline. Generally, such scores are primarily aimed to monitor patients with ankle injury but, secondarily, they also aim to distinguish the more severe ankle injury with a ligament rupture from the less severe distortion. A function tool such as the FADI[5] or the Karlsson AFS[6] score provide insight into function loss, as does the Ankle Function Score (AFS) which is based on patient-rated function loss and symptoms.[6] The Foot and Ankle Ability Measure (FAAM) is reported to be a reliable diagnostic tool to measure function and instability after a sprain.[5,7] However, the diagnostic performance of these scores with respect to distinguishing severe from less severe injury, thereby predicting fast recovery, are poor for the AFS[8], or unknown for the Karlsson, FADI or FAAM score. In addition, the diagnostic ability of these scores in persisting complaints have not yet been assessed. In our study, the AFS was 62.5 (SD 20.2) in patients with persistent complaints compared to 82.9 (SD 15.4) in those without persistent complaints. These scores correspond to the study of De Bie et al., in which patients with persistent complaints scored < 75 points on the AFS compared with the > 75 points scored by those with no persistent complaints.[6]

Imaging

For our study purpose, all participating patients with or without persistent complaints received an MRI of both the injured ankle and the contra-lateral ankle. Many structural abnormalities related to osteoarthritis (OA), such as bone marrow edema, cartilage loss and osteophytes, were mainly found in the talocrural and talonavicular joints; however, all the abnormalities scored were almost equally distributed in the two groups, i.e. patients with and without persistent complaints. This implies that assessing structural abnormalities on MRI was not related to the existence of persistent complaints findings and, therefore, cannot be used as a diagnostic tool to differentiate between patients with and without persistent complaints.

Anterior talofibular ligament

In our study, the MRI showed injury of the anterior talofibular ligament (ATFL) (partial/total rupture or thickened) in both the persistent complaints group (54.3%) and in the group without persistent complaints (57.4%), with no significant difference between both groups (Chapter 4). However, when comparing the injured ankle to the contralateral non-injured ankle in the total study population 6-12 months after a sprain, we found 55.9% ligament damage in the injured ankle compared to 18% in the contralateral ankle. In addition, ligament tears were found in 16.4% in the injured ankle compared to 6.7% in the contralateral ankle (Chapter 5). Thus, these results indicate that the ATFL injuries are most probably related to the recent injury.

A few studies have investigated the prevalence of MRI findings in the ankle.[9, 10] These studies also show joint abnormalities in asymptomatic ankles, with 66% and 100% of the included participants, respectively, without an ankle sprain in their history, where ATFL lesions were frequently seen. In a study investigating the accuracy of MRI in patients with clinically suspected ligament lesions, 83% had a ligament lesion of the ATFL[11], whereas another study reported an injury of the ATFL in patients with recurrent or chronic ankle instability in 82% of the patients.[9] However, all three studies were performed in a secondary care setting.[9-11]

In summary, based on MRI findings after an ankle sprain, although the ATFL is most often injured, many other structural abnormalities in the ankle joint are also found. These findings are not associated with the presence of persistent complaints. Moreover, structural abnormalities are also seen on MRI in the asymptomatic ankle.

Talonavicular joint

It was remarkable that a high percentage of osteochondral damage was found on MRI in the talonavicular joint 6-12 months after the ankle injury. Generally, the talonavicular joint is not involved in a lateral ankle sprain.[12] It can be speculated that, after an ankle sprain, patients show more signs of OA (cartilage loss, bone marrow edema) second-

ary to the ankle sprain. We found a relatively high percentage of early signs of OA in the talonavicular joint, such as marrow bone edema (14.9%) and cartilage loss (18.1%). These structural abnormalities in the talonavicular joint were seen significantly more frequently in the injured ankle than in the contra-lateral ankle. This is in contrast to the talocrural joint where these abnormalities were seen in both ankles, suggesting that these abnormalities may be pre-existent in this joint.

Physical examination

Chapter 6 examines whether patient history taking and performing a physical examination helps the GP to identify early stage OA in the ankle joint after a recent ankle sprain. We found an association between pain at the end range of dorsiflexion and/or plantar flexion and a difference in ROM of plantar flexion the presence of osteophytes in the talonavicular joint. To our knowledge, no comparable studies are available on the association between physical findings and early signs of OA in the ankle joint. In most studies on arthroscopic treatments for chronic complaints after an ankle sprain, many osteochondral defects, osteophytes and other intra-articular lesions are found; however, all these studies were performed in a secondary setting.[13-16] Since pain at the end range of dorsiflexion and/or plantar flexion during physical examination and a difference in ROM in passive plantar flexion seem to be associated with the presence of features of early stage OA in the talocrural and talonavicular joint, this may guide clinicians to predict the presence of structural abnormalities on MRI using patient history and physical examination in patients with persistent complaints after a lateral ankle sprain. When ankle sprains often occur in a population of young people (e.g. in our study mean age is 37.3 years), identification of a high-risk group for early OA might be important, as identifying these individuals may help to prevent further deterioration of the ankle joint after an ankle sprain.

Gait and balance

Chapter 8 investigates whether gait pattern is able to distinguish between patients with and without persistent complaints after a lateral ankle sprain. A subsample of patients included in our cross-sectional study walked over a RSscan and also performed a single-leg test. There was a trend towards a more medially located center of pressure (COP) trajectory during walking and a more anterior COP in the stance phase in patients with persisting complaints compared to those without complaints. In the loading phase, in the group with persistent complaints the COP was more laterally located in the sprained ankle compared to the non-sprained ankle. A positive trend for an interaction was found for the percentage of anterior/posterior range used in single-leg stance without vision.[17] In addition to subjective complaints, the gait pattern may have the potential to be an objective outcome and, perhaps, to be used in the follow-up of patients after an ankle sprain.

Impact

In Chapter 7 we showed that an ankle sprain has a considerable impact on functioning and is related to high use of medical consumption, e.g. physiotherapy, specialists and additional supports. In this study, half of the respondents reported persistent complaints 6-12 months after the injury; moreover, even in those with no persistent complaints 64% reported a feeling of instability. Additionally, high medical consumption was observed in patients with and without persistent complaints after their ankle sprain. In an open population study, 19.6% reported chronic musculoskeletal ankle disorders, of which 42% were caused by a sprain.[18] In these patients, sport activities were limited in 17.7%, 16.1% visited a GP, and 12.9% a physiotherapist.[18] Thus, patients with an ankle sprain often suffer persistent complaints with a high impact, also in terms of medical care.

In this study, it was notable that a large percentage of patients reported the impossibility to participate in physical activity due to their ankle complaints. In a recent animal study, a significant decrease in physical activity during life span (up to 18-21 months) was seen in the artificially sprained mice group compared to a sham control group.[19] These findings strengthen our outcomes by indicating that a single ankle sprain can lead to a significant impact on physical functioning. Therefore, it can be speculated that these ankle sprains may cause long-term health risks if not treated properly.[20, 21]

In our study the incidence of the use of radiography during follow-up was much higher than expected. In a Dutch national study using registries of general practice, 6.2% of the patients with an ankle sprain received radiography compared to 35.3% in our study.[3, 22] This high percentage of radiography might be explained by the selected patient population recruited for our study, as well as by the follow-up time since the injury. We do not know whether this imaging was performed in the acute phase or during later follow-up; neither do we know whether the GP referred for X-ray examination, or a specialist in secondary care. In The Netherlands, GPs do not have open access to MRI for the ankle, limiting its use in primary care. An MRI was performed in only 7% of our patients and all of them by a specialist.

Treatment

In The Netherlands, GPs use the guideline of the Dutch College of General Practitioners when diagnosing and treating an acute lateral ankle sprain.[2] In this guideline, a conventional treatment strategy is recommended consisting of rest, ice, compression and elevation (RICE) together with early mobilizing, with or without external support (tape or brace). A second Dutch multidisciplinary guideline (CBO; published by 11 medical specialties) recommends the same treatment after an acute lateral ankle sprain, including RICE and external support (tape, elastic bandage or semi-rigid brace).[23] In addition, this CBO guideline concludes that there is no evidence for the effectiveness of the use

of training exercises on functioning as an outcome after an ankle sprain after a longer follow-up period.[24]

However, while in 36-85% of patients who suffer an ankle sprain conservative treatment leads to full recovery, up to 33% of the patients experience persisting complaints, and 34% report one or more re-sprains after 1-year follow-up.

According to the findings of our review on the treatment of acute ankle sprains, we found limited to moderate evidence for the effectiveness of supervised exercises; these exercises could lead to a better subjective feeling of stability and a quicker recovery and return to sports after a lateral ankle sprain (Chapter 1). Although this review was published in 2010, to our knowledge no later studies have been published that can add to the evidence.

Hupperets et al. investigated the effectiveness of a proprioceptive training program after usual care for an ankle sprain and found this program to be more effective in the prevention of self-reported recurrences than usual care alone.[25] Therefore, our group are currently investigating the effect of a proprioceptive training program after an acute ankle sprain guided by an App (trAPP-study) on the outcomes pain, function and recurrences, compared to a group with usual care in general practice.

For the treatment of chronic ankle complaints (Chapter 3), limited to moderate evidence was found that training programs for chronic complaints after an ankle sprain lead to less pain and function loss, together with a decrease of recurrence of ankle sprains, compared to conservative treatment alone. We realize that three of the included studies on training programs in the review on chronic complaints consisted of a small group of participants and the studies had a relatively short follow-up.[26-28] However, two studies performed in a large group of participants, using a proprioceptive training program with a 12-month follow-up, found a significant decrease in recurrences compared to a control group.[25, 29] This implies that recurrences of ankle sprains can be decreased using a neuromuscular training program.

Regarding the treatment options, we also found that ankle mobilization gave a significant better outcome on pain and function with a larger ROM and better total functioning in the intervention group in patients with chronic ankle complaints.[30, 31] These findings, together with the findings from our study (Chapter 3) suggest that limitations in ROM, especially in dorsiflexion and/or plantar flexion, in the ankle should be examined. Patients with these limitations might potentially (and specifically) benefit from treatment of these limitations.[30, 31]

Methodological considerations

Our observational study had a retrospective design. Patients were included 6-12 months after they had visited the GP with an acute lateral ankle sprain. Because we asked patients about their symptoms directly after the sprain, as well as their medical consumption in the period after the sprain, recall bias might have influenced the outcomes of this study.

Patients were included by searches in the medical records of the GPs, for which we used the ICPC code 'ankle sprain'. All potentially eligible patients received an invitation letter from the GP and were asked if they would like to participate. Thereafter, they were screened by telephone by a research assistant. As a consequence, the clinical symptoms of the 'ankle sprain' were mostly the subjective self-reported items of the patients. Therefore, we asked patients to thoroughly report their complaints and symptoms in the questionnaire. However, by using the ICPC codes from the medical files together with the telephone screening, it is highly unlikely that patients were misdiagnosed and incorrectly included in our study.

For this study, we selected patients that we had asked whether they still had persistent ankle complaints. Based on the literature, we expected to find a 1:3 ratio of patients with and without persistent complaints.[32] However, because almost half of our study population consisted of patients with persistent complaints, this suggests a possible selection bias. This can be caused by the willingness of patients with persistent complaints to participate in the study. However, despite the possible selection bias, a representative control group was included from general practice without persistent complaints, and the study was sufficiently powered to demonstrate potential differences between the two study groups.

A 7" point" Likert scale, (1=completely recovered to 7=worse than ever) was used to divide the patients into two study groups: patients without persistent complaints (score 1-2, completely recovered or strongly improved) defined as control participants; and patients with persistent complaints (score 3-7, slightly improved to worse than ever), defined as cases. The use of this outcome measure to define the cases and control subjects was chosen from a clinical perspective. This implied that 'persistent complaints' was based on the degree of perceived pain, functional limitations and/or instability. It even implied that some patients with non-persistent complaints reported instability. In the literature, the presence of complaints after an ankle sprain is often defined by Chronic Ankle Instability (CAI). In 2014 an international consensus was published as to which criteria of CAI to use in controlled research.[33] This consensus statement presented the following criteria:

1. A history of at least one significant ankle sprain (initial sprain at least 12 months prior to study enrolment, sprain was associated with inflammatory symptoms, created at least one interrupted day of desired physical activity and most recent injury must have occurred more than 3 months prior to study enrolment).
2. A history of the previously injured ankle joint 'giving way' and/or recurrent sprain and/or 'feelings of instability'.
3. A general self-reported foot and ankle function questionnaire (the FAAM and FAOS) is recommended to describe the level of disability.

Because this statement was published after we started our study, we did not apply these criteria. However, since one of the main aims of our study was to gain more insight into

persistent complaints, we decided not to focus on instability alone; in fact, we covered all the items of the consort statement, although perhaps not as specifically as suggested.

One of the strengths of our case-control study was that the radiologists were blinded for the patient's status, in contrast to the research assistant performing the patient's physical examination. As a consequence, the scores of the radiography (both X-ray and MRI) are objective findings and not influenced by patient status, nor were they influenced by the findings from either the X-ray or MRI.

In two studies we did not use the total patient group. For the study in Chapter 5 we selected patients with persistent complaints to study the associations between factors from patient history and physical examination, and signs of OA. The study in Chapter 8 included 44 patients, 14 with persistent complaints and 30 without complaints, to examine differences in the COP between these population. Therefore, both these latter analyses are less powered and additional associations might not be identified due to this decrease of power.

IMPLICATIONS FOR DAILY PRACTICE

Acute treatment

An ankle sprain is the most common of musculoskeletal injuries. It is clear that the impact of a lateral ankle sprain is substantial: i.e. decrease in functioning in daily life and sports activities, high medical consumption, use of many additional supports, and a high percentage of persisting complaints and recurrence. Moreover, ankle sprain can cause structural abnormalities in the ankle joint and can lead to early signs of OA on MRI. Together, all these factors can lead to high medical costs.

For a GP it is not always clear how severe the ankle sprain is in patients visiting their general practice. Severity is generally expressed as mild (grade I), moderate (grade II) or severe (grade III).[34] The Dutch guidelines recommend similar conventional treatment and additional support of a sprain (independent of severity); this is also reported in the review of van Rijn et al., that gave no indication that the severity of an acute sprain influenced the clinical course of recovery after injury.[32] Based on that same review, in acute ankle sprain it is still advised to treat with RICE (rest, ice, compression and elevation) and additional support in the form of tape or brace, without differentiating between the severity of the ankle sprain. However, a supervised training program is recommended to enhance an earlier return to daily activities or sports participation.

Our department recently started a study using an App with a stabilizing training program after an acute ankle sprain; when completed, the results should provide more data on the effect of such a training program.

X-ray in acute and sub-acute ankle sprains

In the GP guideline, it is recommended to use the Ottawa Ankle Rules (OAR) to decide whether an X-ray is required; appropriate use of the OAR will prevent unnecessary radiography. The impact of an ankle sprain is high, leading to pain at rest/during exercise, a decrease in function and can lead to structural abnormalities in the ankle joint, as seen on radiography and MRI (Chapter 7). Regarding the high percentage of patients in our study groups who underwent radiography, it is debatable whether the OAR is always used in an appropriate way in general practice and/or in emergency departments. There is certainly room for improvement (reduction) in the numbers of X-rays performed in both settings.

Function scores

In general practice no short questionnaire or easy-to-use function score list is available for a GP in case of an ankle sprain. Currently, many different function score lists are used, including: the AFS, the Karlsson score list, the FADI and FADI sports, the FAAM, and the FAOS. However, most of these lists are too large or not practical for use in daily practice. Regarding the literature, the AFS might be a helpful tool to monitor patients in the revalidation period or during the training program after an ankle sprain. The availability of an easy-to-use tool for general practice, that provides information on the severity of the injury and function loss, would be very helpful in diagnosing and treating patients with an ankle sprain.

Treatment in persistent ankle sprain complaints

In mild cases of complaints after an ankle sprain, the GP can give (besides advice for RICE) training exercises at home by letter or by means of an App.

The treatment strategy for patients presenting in general practice with more severe or chronic ankle complaints (including pain, fear, function loss, instability or recurrence) should consist of the following elements:

- treatment with RICE additional support in forms of tape or brace in the acute phase
- a standardized training program for a longer period (at least 3 months) and/or
- treatment by a physiotherapist to mobilize the foot/ankle in case of a disturbed ROM, mainly found in dorsiflexion and plantar flexion, in case of persisting pain, fear of moving, or persisting feelings of instability.
- coaching following a stabilizing training program

If this treatment does not result in adequate success, patients can be referred to an orthopedic surgeon in case of persisting pain or complaints of instability. The medical specialist can decide whether further additional examination (radiography or MRI) is needed. Based on these results, the orthopedic surgeon can advise which treatment is necessary (conservative treatment, arthroscopic or open surgery). However, no placebo-controlled studies have investigated surgical treatments for chronic ankle stability, only

comparisons have been made between the various surgical treatments.[35-37] In the available (but limited) literature, the effect of surgical treatment appears to be good.

Use of radiography (X-ray or MRI) in persistent ankle complaints

In general practice, according to the practical guideline, the Ottawa Ankle Rules should be used to decide whether or not a fracture could be involved. The study in Chapter 4 found that the persistence of complaints after an ankle sprain is not associated with any structural abnormalities on MRI or X-ray. Therefore, GPs are advised not to routinely refer to radiography or MRI, as this will lead to over-diagnosing and unnecessary use of these diagnostic tools without giving additional useful information.

IMPLICATIONS FOR FUTURE RESEARCH

Exercises and mobilizing

Patients with chronic ankle complaints after a lateral ankle sprain have better scores on pain, function and recurrence after a training program than with a wait-and-see policy. However, because most of the studies included in the review had a low power and a short follow-up, the evidence is rather thin. Another interesting finding was the association between a disturbed ROM (dorsiflexion and plantar flexion) and early osteoarthritis features in people with persistent complaints. This is especially interesting since two studies in our review found an improvement of ROM following manual therapy treatment. To acquire additional proof for the best treatment options for chronic ankle complaints after an ankle sprain, studies with sufficient power, adequate randomization and a longer follow-up are needed. Specific interventions of interest are: mobilizing treatment of the ankle in case of a disturbed ROM, and/or a standardized balance and stabilizing training program compared to a control group.

Function outcomes in studies

Comparison of the studies included in the review, shows that many different outcomes were measured using many different measurement tools. According to our findings, the Food & Ankle Disability Index score (FADI), the Ankle Function Score (AFS) and the Food and Ankle Ability Measure (FAAM) are often used for function outcome. For balance, the Star Excursion Balance Test (SEBT), the single-leg test and postural sway (Chapter 2) are often used. In a recent study, the Foot and Ankle Outcome Score (FAOS) showed to be a good measurement tool for the functioning of ankle and foot.[38]

A recent consensus paper on chronic ankle instability recommends to describe the level of disability by the FAAM or the FAOS in the enrollment of patients with chronic ankle instability.[33] However, it is important that a standardized core list of the most use-

ful outcomes with the best measurement tool properties (such as responsiveness and reliability) should be measured and reported in all studies that include patients with ankle complaints.

Surgery as treatment option

Considering the substantial number of patients with persistent complaints, studies on additional treatment options, including surgical treatment, are needed. Until now, no studies are available on the additional value of surgery. Studies on surgical treatment, in which different surgical interventions are compared with a control patient group without surgery (i.e. surgical care versus usual care) can express the effect and value of surgical treatment, and help establish for which cases surgery is the best option.

Prevention of osteoarthritis

Persistent complaints after an ankle sprain are not associated with structural abnormalities found on MRI. However, in the sprained ankle with persistent complaints, we found an association between pain at the end range of dorsiflexion/plantar flexion, a difference in ROM of passive plantar flexion and swelling performing physical examination and the presence of features of early signs of OA in both the TCJ and the TNJ. It is useful to identify other features from patient history and physical examination that relate to early OA features, enabling early treatment and prevention of clinical symptoms of OA. Options in preventing the development of OA could be: to lose or prevent increase of bodyweight, stabilizing the ankle joint to prevent recurrence, mobilizing the joint when the ROM is limited compared to the other ankle, and choosing other types of sports activities.

To date it remains unclear whether the structural abnormalities on MRI after the ankle sprain will lead to more complaints or a more severe grade of OA. Therefore, a long-term follow-up study of a cohort of patients who sustained an ankle sprain should be set up in general practice to investigate these potential associations, as well as clinical prognostic indicators from patient history taking and physical examination. Hopefully, these measures will help in our aim to prevent chronic complaints after an ankle sprain and the development of OA in vulnerable patients.

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Chapter 10

Summary

SUMMARY

Ankle sprains are often seen in daily practice of the general practitioner and are the most common injury of the musculoskeletal system. The injury is often due to sport participation and is frequently seen in relatively young people. Notwithstanding the high number of sprains, the injury is often still seen as an innocent lesion, despite the sometimes long duration of complaints and the associated costs. In The Netherlands, an ankle sprain occurs in 680.000 people yearly, mostly on the lateral side. The prevalence of ankle sprains in general practice is 130.000 a year, while the physical therapist sees about 87.000 subjects a year. Treatment is, according to the guidelines for general practitioners, conservative consisting of RICE and early mobilization, often with additional support of a tape or brace. Despite of applied treatments almost one third of the injured subjects keep persistent complaints as pain, function loss and re-sprains. The practical guidelines for general practitioners identified a lack of diagnosis and treatment options for persistent complaints after an ankle injury. This thesis, therefore, aimed to study systematically, the effectiveness of the different types of interventions used for persistent ankle complaints after an ankle sprain. Additionally we aimed to investigate the association between persistent complaints after an ankle sprain and possible structural abnormalities found on radiography and MRI and whether these are associated with characteristics from anamnesis and physical examination.

Chapter 2 describes the results of a systematic review regarding the current evidence of the effectiveness of additional supervised exercises compared to conventional treatment alone in patients with an acute ankle sprain. For inclusion eleven randomized controlled trials, quasi- randomized controlled trials and clinical trials were selected. Most of the included studies had a high risk of bias, with few having adequate statistical power to detect clinically relevant differences. Because of clinical heterogeneity data were analyzed using a best evidence synthesis. There was limited to moderate evidence that the addition of supervised exercises to conventional treatments leads to faster and better recovery and a faster return to sport at short term follow-up than conventional treatment alone. There was no strong evidence for the effectiveness for any of the outcome measures. In specific populations as athletes and soldiers, the evidence was restricted to a faster return to work and sports only. Because most of the included studies had a high risk of bias and lack of power, high quality randomized controlled trials investigating the effect of additional supervised exercise treatment compared to conventional treatment is necessary to draw further conclusions.

In **chapter 3** we performed a systematic review of the literature to determine the effectiveness of different treatments for chronic complaints after a lateral ankle sprain. A total of 20 randomized controlled trials and 1 controlled clinical trial of high quality were included in the analysis. Only two studies had a low risk of bias, while the other

included studies had a high risk of bias and most studies had a short follow-up. The treatments in the studies were reported in four main clusters: (1) training programs, (2) manual therapy and chiropractic treatment, (3) surgery and (4) postoperative training programs. Limited to moderate evidence was found for the effectiveness of a training program for pain and function outcomes compared to conservative treatment. Two studies found a decrease of recurrences after a proprioceptive training program and in two other studies there was a good effect on function after chiropractic treatment and manual therapy. Four studies showed good results for different surgical methods but did not include a nonsurgical control group for comparison. Limited evidence was found for the effectiveness of an early mobilization program after surgery compared to use of a plaster cast.

Chapter 4 presents the results of an observational case control study on patients selected in general practice who sustained an ankle sprain 6-12 months before inclusion. Purpose of the study was to find the possible associations between structural abnormalities on radiography and MRI and the persistence of ankle complaints after a previous lateral ankle sprain. From the medical files of GPs patients were included in the study 6-12 months after their ankle sprain. 206 Patients filled in a standardized questionnaire, underwent a physical examination and received radiography and a MRI. Using a 7 "point" Likert scale, patients were divided in a group patients with persistent complaints (n=98) and a group without complaints (n=108). In both groups, however, many structural abnormalities were found on radiography in the talocrural joint (47.2% osteophytes and 45.1% osteoarthritis) and the talonavicular joint (36.5% sclerosis). On MRI, a high prevalence of bone edema (33.8%) and osteophytes (39.5%) in the talocrural joint was found; osteophytes (54.4%), sclerosis (47.2%) and early stage osteoarthritis (55.4%, Kellgren and Lawrence grade>1) in the talonavicular joint, as well as ligament damage (16.4%) in the anterior talofibular ligament. Despite the high prevalence of structural abnormalities on radiography and MRI in patients presenting in general practice with a previous ankle sprain, we found no differences between patients with and without persistent complaints. Using imaging only will not lead to diagnosis of the explicit reason for the persistent complaints.

Purpose of **chapter 5** was to compare the prevalence of abnormal MRI findings associated with a lateral ankle trauma in the injured and contralateral ankle to identify lesions that may be pre-existent. 195 patients (mean age 37.5 + 14.7 years; 43% male) who visited their general practitioner 6–12 months earlier with an ankle sprain were selected. All patients complete a standardized questionnaire and underwent MRI of both ankles. MRI abnormalities in the injured and contralateral ankle were compared using the McNemar test (for paired samples). Bone marrow edema was frequently seen in the injured and contralateral ankle at the talocrural joint (25.1% versus 14.8%) and subtalar joint (24.6% versus 8,7%), but significantly more frequently in the injured ankle.

In both ankles, ligament lesions in the anterior talofibular ligament (ATFL; 55.9%) and calcaneofibular ligament (CFL; 37.4%) in the injured ankle were found compared to the contralateral ankle (ATFL 17.9% and CFL 5.6%). Other lesions like fractures, anterior / posterior tibiofibular and deltoid ligament lesions were almost exclusively found in the injured ankles. In patients in primary care with a previous ankle sprain the prevalence of structural MRI abnormalities is high. However, especially bone marrow edema and lateral ligament lesions can also be found in a substantial percentage of contralateral ankles and may be either be pre-existent or due to increased stress on the contralateral ankle after an ankle injury. Correlation with clinical findings is essential.

The objective in **chapter 6** was to determine the association between patient history and physical examination and early signs of osteoarthritis on MRI in patients with persistent complaints after a previous lateral ankle sprain. A total of 98 patients with an ankle sprain 6-12 months prior to inclusion and reporting persistent complaints were included in the study. Patient history taking and standard physical examination were applied and all patients had an MRI. Both univariate and multivariable analyses were used to test the association between patients' history and physical examination and features of early stage osteoarthritis (OA). Overall, features of early stage OA in the talocrural joint (TCJ) were seen in 40% of the subjects and in 49% in the talonavicular joint (TNJ). The multivariable model showed a significant positive association between swelling (OR 3.57, 95%CI 1.13;11.4), a difference in ROM of passive plantar flexion (OR 1.09, 95%CI 1.01;1.18) and the presence of bone edema in the TCJ. A difference in ROM of passive plantar flexion (OR 1.07, 95%CI 1.00;1.15) and pain at the end range of dorsiflexion and/ or plantar flexion (OR 5.23, 95%CI 1.88;14.58) were positively associated with the presence of osteophytes in the TNJ. Based on this study, we can conclude that pain at the end of plantar and/or dorsiflexion, a difference in ROM of passive plantar flexion and swelling performing physical examination seem to be associated with the presence of features of early stage OA in both the TCJ and the TNJ. Our findings may guide general practitioners and physical therapists to predict structural joint abnormalities as signs of early stage osteoarthritis.

The impact of a lateral ankle sprain in general practice was studied in **chapter 7**. We made a comparison of the impact on functioning and the use of health care resources between patients with and without persistent complaints after previous ankle sprain 6-12 months before. In a cross-sectional study we included 204 patients who visited the general practitioner with a lateral ankle sprain 6-12 months before inclusion and divided patients in a group with persistent complaints (n=96) and a group without persistent complaints. Therefore we used the 7 "point" Likert scale (respectively 3-7 and 1-2 points) to measure recovery, while all included patients filled in a standardized questionnaire. In the group with persistent complaints, we found a significantly higher BMI, higher pain scores at rest and during exercise, together with a lower Ankle Function Score (AFS). In

the group without complaints we found much higher number of patients participating in sports. In both groups we found limitations in functioning due to the ankle sprain and a high medical consumption, especially in visiting the GP, physical therapist, specialist and the use of radiographic imaging (X-ray and MRI). We can conclude that a lateral ankle sprain has a high impact on functioning and physical health, mostly in those patients with persistent complaints after a lateral ankle sprain. In as well the group with as the group without persistent complaints, considerable use of health care resources was found 6-12 months after the initial visit for the ankle injury to the GP.

In **chapter 8** we aimed to investigate the differences in the center of pressure (COP) during gait and single leg test between a group of patients with persistent and a group of patients without persistent complaints. 44 Patients who consulted the general practitioner, 6 to 12 months prior to inclusion, with a lateral ankle sprain were included for the current study purpose. Using a 7 "point" Likert scale patients were divided into the a persistent complaints (PC) and non-persistent complaints (NPC) group. All subjects filled out an online questionnaire, walked along a walkway and performed a single leg stance, both on the RSscan. Primary outcomes included the COP displacement, range and percentage used in mediolateral and anteroposterior direction. There was a trend ($p< 0.05$) towards a more medially COP trajectory during walking at 34-46% and 83-96% and more anteriorly at 21%-31% and 91%-100% of the stance phase in the PC group compared to NPC group. Additionally, the COP was more laterally located in the sprained leg compared to the non-sprained leg in the PC group in the loading response phase ($p< 0.05$). An interaction was found for the percentage of anterior-posterior range used in single leg stance without vision. The COP trajectory discriminates between patients with and without persistent complaints. This indicates that roll off during gait might play an important role in the recovery of patients after a lateral ankle sprain and could be useful to monitor treatment and recovery.

Chapter 9 summarizes the main findings of this thesis and reflects in a discussion on the course of chronic ankle complaints caused by a previous ankle sprain in general practice. The results were interpreted regarding existing literature and methodological issues are discussed. This to give direction to further research and give implications for the clinical practice of the general practitioner.

Chapter 11

Nederlandse samenvatting

SAMENVATTING

Een enkelverstuiking wordt vaak gezien in de dagelijkse praktijk van de huisarts en is het meest voorkomend letsel van het houdings- en bewegingsapparaat. Meestal lopen jonge mensen een verstuiking van de enkel op en is de schade te wijten aan deelname aan sportactiviteiten. Ondanks het grote aantal verstuikingen, wordt deze blessure vaak nog gezien als een onschuldige aandoening, alhoewel het vaak een langere periode van arbeidsongeschiktheid inhoudt en de daarmee gepaard gaande verbonden kosten hoog zijn. Jaarlijkse lopen 680.000 mensen een verstuiking van de enkel op en de meeste letsels betreffen de laterale zijde. De prevalentie van enkelverstuikingen in de huisartspraktijk is 130.000 per jaar, terwijl de fysiotherapeut 87.000 patiënten per jaar ziet.

De behandeling bestaat op dit moment, conform de geldende NHG-richtlijn betreffende enkelklachten voor huisartsen, uit conservatieve behandeling bestaande uit RICE (rust, ijs, compressie en elevatie) met vroege mobilisatie en vaak steun van een tape of brace.

Ondanks deze therapie houdt bijna een derde van de patiënten last van aanhoudende klachten zoals pijn, functieverlies of krijgt een recidief. In de NHG-standaard enkeldistorsie wordt weinig wetenschappelijk bewijs gevonden ten aanzien van het diagnosticeren en behandelen van deze aanhoudende klachten na een doorgemaakt enkeltrauma.

In dit proefschrift is getracht om systematisch wetenschappelijke onderbouwing te vinden voor de effectiviteit van de verschillende behandelingsmethodes, die gebruikt worden bij aanhoudende klachten na een enkelverzwikking. Aangezien er vaak structurele afwijkingen bij radiologisch onderzoek worden gevonden, is ook de associatie tussen aanhoudende klachten na een enkelverzwikking en de mogelijk aanwezigheid van structurele afwijkingen op röntgenfoto of MRI onderzocht.

Hoofdstuk 2 beschrijft de resultaten van een systematische review, waarin onderzocht is wat er aan wetenschappelijk bewijs bekend is over de effectiviteit van een toevoeging van een begeleid oefenprogramma in vergelijking tot conventionele behandeling zonder oefeningen bij patiënten na een acuut enkelbandletsel. Elf gerandomiseerde klinische trials (RCT's), quasi – gerandomiseerde klinische trials en gecontroleerde klinische trials (CCT's) werden geselecteerd. De meeste geïncludeerde studies hadden een hoog bias risico en weinig studies hadden voldoende statistische power om klinisch relevante verschillen te kunnen vinden. Vanwege klinische heterogeniteit werd de data geanalyseerd met behulp van een "best-evidence synthese".

Er was beperkt tot matig bewijs, dat de toevoeging van gecontroleerde oefeningen gecombineerd met conventionele behandeling tot een sneller en beter herstel leidt en tot een snellere terugkeer naar sporthervatting op korte termijn follow-up dan conventionele behandeling alleen. Er was geen sterk bewijs voor de effectiviteit voor elk van

de uitkomstmaten. In specifieke populaties zoals atleten en soldaten bleef het bewijs beperkt tot een snellere terugkeer naar werk en sporthervatting. Omdat de meeste geïncludeerde studies een hoog bias risico en onvoldoende power hadden, zijn studies van hoge kwaliteit, zoals RCT's, die het effect van de toevoeging van gesuperviseerde oefeningen aan de momenteel geldende conservatieve behandeling onderzoeken, noodzakelijk om verdere conclusies te kunnen trekken.

In **hoofdstuk 3** wordt een systematische review van de literatuur beschreven, waarin de effectiviteit van de verschillende behandelingsmethodes van persisterende klachten na een doorgemaakte laterale enkelverzwikking onderzocht werd. In totaal werden 20 gerandomiseerde gecontroleerde trials en een gecontroleerde klinische trial van matig tot hoge kwaliteit geïncludeerd. Slechts twee studies hadden een laag bias-risico, terwijl de andere geïncludeerde studies een hoog bias risico hadden en de meeste studies ook een korte follow-up kenden. De behandelmogelijkheden, genoemd in de geselecteerde studies werden verdeeld in vier belangrijkste clusters: (1) trainingsprogramma's, (2) manuele therapie en chiropractie, (3) chirurgie en (4) postoperatieve trainingsprogramma's. Beperkt tot matig bewijs werd gevonden voor de effectiviteit van een trainingsprogramma voor de uitkomstmaten pijn en functie ten opzichte van conservatieve behandeling. Twee studies vonden een daling van het aantal recidieven na een proprioceptief trainingsprogramma en in twee andere studies werd er een positief effect op de uitkomstmaat functie na chiropractische behandeling en manuele therapie gevonden. Vier studies toonden goede resultaten voor verschillende chirurgische interventiemethodes, die wel onderling vergeleken werden, maar die geen controlegroep bevatten zonder chirurgische behandeling ter vergelijking. Beperkt bewijs werd er gevonden voor de effectiviteit van een vroeg mobilisatie programma na chirurgische behandeling in vergelijking tot het gebruik van gipsbehandeling.

Hoofdstuk 4 toont de resultaten van een observationele case controle studie, verricht met patiënten uit de huisartspraktijk, die 6 tot 12 maanden daarvoor hun huisarts bezochten in verband met een enkelbandverzwikking. Doel van het onderzoek was de mogelijke associaties tussen structurele afwijkingen op een röntgenfoto en/of MRI en de aanwezigheid van persisterende enkelklachten na een eerder opgelopen laterale enkelbandverstuiking te onderzoeken. Uit de medische dossiers van 84 huisartspraktijken werden patiënten geïncludeerd in de studie, die 6-12 maanden daarvoor op het spreekuur waren geweest in verband met enkelklachten na een verstuiking. Door 206 patiënten werd een gestandaardiseerde vragenlijst ingevuld, werd een lichamelijk onderzoek verricht en een röntgenfoto en MRI van de enkel gemaakt. Met behulp van een 7 "point" Likert-scale werden patiënten verdeeld in een groep patiënten met persisterende klachten (n = 98) en een groep zonder persisterende klachten (n = 108). In beide groepen werden veel structurele afwijkingen gevonden op de röntgenfoto in met name het talocrurale gewricht (in 47.2% osteofyten en in 45,1% tekenen van artrose)

en het talonaviculaire gewricht (36,5% sclerose). Op de MRI werd een hoge prevalentie van bot oedeem (33,8%) en osteofyten (39,5%) in het talocrurale gewricht vastgesteld; daarnaast werden osteofyten (54.4%), sclerose (47.2%) en vroege tekenen van artrose (55.4%), een Kellgren and Lawrence score > 1 in het talonaviculaire gewricht gevonden met eveneens schade aan het ligamentum talofibulare anterius (16.4%). Ondanks het hoge percentage structurele afwijkingen op de röntgenfoto en MRI werden er geen verschillen gevonden tussen de groep met en zonder persisterende klachten. Het alleen gebruik maken van beeldvorming door middel van röntgenfoto of MRI geeft geen uitsluitsel over de specifieke oorzaak van de persisterende klachten.

Doel van het onderzoek in **hoofdstuk 5** was het beschrijven van de prevalentie van afwijkingen op een MRI na een doorgemaakt lateraal enkeltrauma, waarbij de verschillen tussen de aangedane en de contralaterale enkel werden vergeleken. Door 195 patiënten, die werden geselecteerd in de huisartspraktijk en 6-12 maanden tevoren een laterale enkelband verstuiking hadden doorgemaakt en daarvoor het spreekuur hadden bezocht, werd een gestandaardiseerde vragenlijst ingevuld en kregen een MRI van beide enkels. MRI-afwijkingen in de aangedane en contralaterale enkel werden vergeleken met behulp van de McNemar-test (voor gepaarde metingen). Beenmerg oedeem werd vaak gezien, zowel in de aangedane als de contralaterale enkel in het talocrurale gewricht (25,1% versus 14,8%) en het subtalaire gewricht (24,6% versus 8,7%), maar aanzienlijk vaker in de aangedane enkel. In beide enkels werden ligamentaire laesies in het ligamentum talofibulare anterius (ATFL; 55,9%) en het ligamentum calcaneofibulare (CFL; 37,4%) in zowel de aangedane enkel als de contralaterale enkel (ATFL 17,9% en CFL 5,6%) gevonden. Andere letsels zoals fracturen, letsels van het voorste / achterste tibiofibulare ligament, alsmede het ligamentum deltoideus werden bijna alleen maar in de aangedane enkel gevonden. Bij patiënten in de eerste lijn, die een laterale enkelbandverzwikking hebben doorgemaakt, word een hoog percentage aan structurele afwijkingen op de MRI gevonden. Er wordt echter ook in een aanzienlijk percentage beenmerg oedeem en schade aan de laterale ligamenten gevonden in de niet-aangedane enkel. Dit kan ofwel pre-existent aanwezig zijn of te wijten zijn aan een toegenomen overbelasting van de niet-aangedane enkel na een enkeltrauma. Samenhang met klinische bevindingen is hierbij essentieel.

Doelstelling in **hoofdstuk 6** was het bepalen van de associatie tussen anamnese en lichamelijk onderzoek en het vaststellen van vroege tekenen van artrose, zoals die werden gezien op de MRI, bij patiënten met aanhoudende klachten 6-12 maanden na een laterale enkelbandverstuiking. Voor een cross-sectionele studie werden 98 patiënten uit de huisartsenpraktijk geselecteerd, die 6-12 maanden voorafgaand aan de inclusie hun enkel hadden verstuikt. De anamnese werd afgenomen met gebruikmaking van een gestandaardiseerde vragenlijst en werd er een standaard lichamelijk onderzoek verricht waarna alle patiënten een MRI kregen. Kenmerken van een vroeg stadium van artrose

(OA) werd bij 40% van de deelnemende patiënten in het talocrurale gewricht (TCJ) gezien en in 49% in het talonaviculaire gewricht (TNJ). Een multivariabele regressie analyse werd gebruikt om de mogelijke associatie tussen anamnese en lichamelijk onderzoek en vroege tekenen van artrose te onderzoeken. Een significant positieve associatie werd gevonden tussen aanwezigheid van zwelling, een verschil in bewegingsuitslag (ROM) in dorsi- en/of plantairflexie en de aanwezigheid van bot oedeem in het TCJ. Een verschil in ROM van passieve plantairflexie en pijn in de eindstand van dorsi- en/of plantairflexie bleken evident geassocieerd met de aanwezigheid van osteofyten in het TNJ. Op basis van dit onderzoek kunnen we concluderen, dat pijn in de eindstand van plantair- en/of dorsiflexie, een verschil in range of motion van passieve plantairflexie en zwelling, zoals die kunnen worden vastgesteld bij het verrichten van een lichamelijk onderzoek, geassocieerd lijken te zijn met de aanwezigheid van tekenen van een vroeg stadium van artrose in zowel het TCJ en TNJ. Onze bevindingen kunnen een aanzet zijn voor huisartsen en fysiotherapeuten om structurele afwijkingen in het enkelgewricht als teken van een vroege fase van artrose te voorspellen.

In **hoofdstuk 7** werd de impact van een laterale enkelbandverstuiking bij patiënten in de huisartspraktijk bestudeerd. We vergeleken de impact op het totaal functioneren en het gebruik maken van medische voorzieningen tussen een groep patiënten met en zonder persisterende klachten na een 6-12 maanden daarvoor doorgemaakt enkeltrauma, waarvoor de huisarts werd geconsulteerd. Voor een cross-sectionele studie includeerden we 204 patiënten uit de huisartsenpraktijk, die 6-12 maanden daarvoor een laterale enkelbandverstuiking hadden doorgemaakt en waarna de patiënten verdeeld konden worden in een groep met aanhoudende klachten (n = 96) en een groep zonder blijvende klachten. Hiervoor gebruikten we de 7 "point" Likert scale (respectievelijk 3-7 punten: persisterende klachten en 1-2 punten: geen klachten) voor het registreren van de mate van herstel, waarbij alle geselecteerde patiënten een gestandaardiseerde vragenlijst invulden. In de groep met blijvende klachten vonden we een significant hogere BMI, hogere pijn scores in rust en tijdens training, samen met een lagere Ankle Function Score (AFS). In de groep zonder persisterende klachten vonden we een significant hoger aantal patiënten die na het enkeltrauma weer konden sporten. In beide groepen vonden we beperkingen in functioneren ten gevolge van het doorgemaakte enkelletsel en een daarnaast een hoge medische consumptie, met name ten aanzien van het bezoek aan de huisarts, fysiotherapeut, specialist en het gebruik maken van radiologische beeldvorming (röntgen en MRI). We kunnen concluderen dat een verstuiking van de enkel leidt tot een grote impact op het totaal functioneren van de patiënt en het verdere fysiek welbevinden, vooral bij patiënten met aanhoudende klachten na een laterale enkelbandverstuiking. In zowel de groep met persisterende als de groep zonder persisterende klachten, wordt veelvuldig gebruik gemaakt van allerlei

gezondheids- voorzieningen 6-12 maanden na het eerste bezoek aan de huisarts in betrekking tot zijn initiële enkelblessure.

In **hoofdstuk 8** worden de resultaten beschreven van een onderzoek waarin de verschillen in de center of pressure (COP) tijdens het lopen en een "single leg test" werden gemeten tussen een groep van patiënten met aanhoudende en een groep van patiënten zonder blijvende klachten na een laterale enkelbandverstuiking. Patiënten werden geselecteerd uit een grotere onderzoeksgroep, die werden geïncludeerd voor een observationele case controle studie in de huisartspraktijk. Voor dit doel werden 44 patiënten geïncludeerd, die werden verdeeld met behulp van de 7 "point" Likert scale, in een groep met aanhoudende klachten (3-7 punten; N = 14) en een groep zonder aanhoudende klachten (1-2 punten: N = 30). Alle patiënten vulden een online vragenlijst in, liepen over een looppad, dat gemonitord werd middels een RS footscan en waarbij een "one leg standing test" op de RS-scan plaat werd uitgevoerd. Als primaire uitkomstmaten werden de COP-verplaatsing, de mate van verplaatsing, die in mediolaterale en voor en achterwaartse richting tijdens de vroege middenstand- en afzetfase tijdens het lopen gevonden werden, bepaald. Ook de duur van staan op een been (single leg test) en de verschillen tussen de groepen werden gemeten. Potentiële groep specifieke verschillen werden geanalyseerd met behulp van een Mann-Whitney U test. Er was een positieve trend naar een meer mediaal gericht COP traject en een meer naar voren gerichte standsfase tijdens het lopen in de groep met aanhoudende klachten vergeleken met de groepen zonder blijvende klachten. Bovendien bleek de COP meer naar lateraal gelokaliseerd in de aangedane zijde ten opzichte van de niet aangedane zijde in de groep met aanhoudende klachten in de late afzet fase van afwikkeling van de voet bij het lopen en een positieve trend naar een verschil in de anteroposteriore richting tijdens de single leg test met gesloten ogen. Het verschil in het COP-traject laat een onderscheid zien tussen patiënten met aanhoudende en zonder aanhoudende klachten. Dit geeft aan dat veranderingen in het looppatroon mogelijk een rol spelen bij het van het herstel van patiënten na een enkelverstuiking en daardoor van nut kunnen zijn bij het monitoren van behandeling en herstel na zo'n enkelletsel.

Hoofdstuk 9 bevat een overzicht van de belangrijkste bevindingen van dit proefschrift en wordt in een discussie een overzicht gegeven van de behandeling en de gevolgen van chronische enkelklachten, veroorzaakt door een eerdere doorgemaakte enkelverstuiking in de eerstelijnszorg. De gevonden resultaten werden geïnterpreteerd in vergelijking tot de bestaande literatuur over dit thema en methodologisch bediscussieerd. Dit alles met als doel om verdere suggesties voor verder onderzoek te initiëren en implicaties te geven voor de dagelijkse praktijk van de huisarts.

Dankwoord

DANKWOORD

Promoveren doe je maar eenmaal in je leven en vaak wordt je dan ook gevraagd: Waarom doe je dit op deze leeftijd nog met al een drukke baan? Tja, en dan weet je eigenlijk geen goed antwoord te geven (uitdaging?, ambitie?, onbekend gebied?). Ik weet wel, dat ik het alleen nooit gekund had en dat het alleen maar gelukt is met de hulp van velen, die elk op hun eigen manier een bijdrage hebben geleverd. Ik ben uiteraard alle patiënten, die hebben deelgenomen aan de BEL-studie, enorm dankbaar voor hun bijdrage en was ik ook erg blij met de financiële ondersteuning van ZonMW en de praktische hulp van het Diagnostisch Centrum Rotterdam, wat sterk gefaciliteerd heeft met het vervaardigen van de röntgenfoto's en MRI's en mij de mogelijkheid heeft geboden om daar ter plekke bij de deelnemende mensen lichamelijk onderzoek te verrichten.

Een aantal mensen moet ik uiteraard wel apart noemen, daar hun rol voor de totstandkoming van dit proefschrift essentieel is geweest en het zonder hen mij niet gelukt was.

Op de eerste plaats moet ik dan natuurlijk mijn motivator, mijn snelle en slimme wetenschappelijke mentor Marienke van Middelkoop noemen. Marienke: "ik vind het knap, dat je zoveel geduld met me hebt gehad, me bleef motiveren en ook steunde als ik het in het hele proces even moeilijk had en ondanks mijn beperkte wetenschappelijke bagage het gelukt is om tot dit eindproduct te komen. Je was voor mij de belangrijkste steun en toeverlaat"!

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Dank aan mijn kamergenoten Gerrit Jan, Lonny en later Claudia, die enige jaren zijn blootgesteld aan mijn gezucht en gesteun, en toch getracht hebben mij positief te blijven stimuleren om het einddoel te halen. Gerrit Jan: nog dank voor je persoonlijke support. Ook een dankwoord voor Monique, die mij heeft bijgestaan in de uitwerking van dit proefschrift.

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Daarnaast hoop ik nu ook wat meer ruimte te kunnen vinden om aan mijn 2 kleinkinderen Diede en Sepp te besteden.

Curriculum vitae

CURRICULUM VITAE

John van Ochten werd op 4 maart 1955 geboren te Oss. Na behalen van het HBS-B examen in 1972 is hij geneeskunde gaan studeren aan de Katholieke Universiteit te Nijmegen, waar hij ook de 1-jarige opleiding tot huisarts heeft gevolgd. Na het artsexamen en ook na het behalen van het huisartsendiploma heeft hij in totaal 2,5 jaar als chirurgisch assistent in het Canisiusziekenhuis te Nijmegen gewerkt, alwaar hij ook verbonden was als clubarts aan betaald voetbalclub NEC.

Na 1,5 jaar waarneming in Brabant, is hij in 1985 begonnen als vrijgevestigd huisarts met steun te Berkel en Rodenrijs. Daar heeft hij geleidelijk aan een volledige huisartspraktijk opgebouwd. Hij was enige jaren vertegenwoordiger van de lokale huisartsvereniging en het lokale Rode Kruis en heeft jarenlang de intercollegiale patiëntenbesprekingen in het St. Franciscus Gasthuis geleid en georganiseerd. Na werkzaamheden als verloskundig actieve huisarts en consultatiebureau arts, werd hij in 1996 huisartsopleider en in 2001 huisartsgroepsbegeleider op de afdeling huisartsgeneeskunde aan de Erasmus Universiteit te Rotterdam.

Affiniteit met sportgeneeskunde en sportmedische begeleiding is al die tijd gebleven en is hij al jaren clubarts van BVO Excelsior en hoofd van de medische commissie van de marathon te Rotterdam. In 2011 was hij mede 1 van de initiatiefnemers voor de nieuwe kaderopleiding bewegingsapparaat, waarvoor hij verantwoordelijk werd voor de medisch-inhoudelijke kant, op de afdeling huisartsgeneeskunde en ontving hij ook zelf in 2013 het diploma tot kaderarts bewegingsapparaat. Hij is verder EKC-er en SCAS gecertificeerd clubarts betaald voetbal.

Door deelname aan een onderzoek betreffende loopblessures tijdens de marathon van Rotterdam, werd hij geënthousiasmeerd tot het doen van wetenschappelijk onderzoek, tot op dat moment voor hem nog een ondergeschoven kindje. Daarop werd hij mede op verzoek van Sita Bierma-Zeinstra van de onderzoek divisie van de afdeling huisartsgeneeskunde in 2010 gevraagd om deel te nemen aan een onderzoek betreffende chronische enkelklachten in de huisartspraktijk. Eind 2010 werd met de BEL-studie begonnen, welke in april 2016 werd afgerond en heeft geleid tot de nodige publicaties in internationale vaktijdschriften en uiteindelijk tot dit proefschrift.

Momenteel is hij voor 60% werkzaam als praktiserend huisarts, functioneert nog als clubarts betaald voetbal, is nog mede verantwoordelijk voor invulling van de differentiatie en kaderopleiding bewegingsapparaat en heeft in zijn takenpakket het

coördinatorschap voor opleiders op de afdeling huisartsgeneeskunde aan de Erasmus Universiteit te Rotterdam.

Portfolio

PHD PORTFOLIO

John van Ochten, MD
Erasmus MC University

Department of general practice

Phd period: 2010-2016
Supervisor: Sita Bierma –Zeinstra
Patrick Bindels
Co-supervisor: Marienke van Middelkoop

		Year	Workload (ECTS/hours)
Courses / training	SPSS / endnote	2011	1 ECTS
	GP with expertise musculoskeletal system	2011-2013	6 ECTS
Congresses	Experts musculoskeletal system	2013	6 hrs
	Sports congress Quatar	2014	6 hrs
	Experts musculoskeletal system	2015	6 hrs
Oral presentations	Department of general practice	2011	0.35 ECTS
	Department of general practice	2012	0.35 ECTS
	VSG congress	2012	0.7 ECTS
	NHG - wetenschapsdag	2013	0.7 ECTS
Poster presentations	NHG - wetenschapsdag	2015	0.6 ECTS
	NHG - wetenschapsdag	2016	0.6 ECTS
International conference	Dublin: International Ankle Symposium		
	oral presentation	2015	0.7 ECTS
	poster presentation	2015	0.6 ECTS
Teaching	GP with special interest in musculoskeletal system	2011-2013	6 ECTS
		2013-2015	6 ECTS
	Differentiation period for residents in general practice	2013-2016	7 ECTS
	Summer course sports medicine (2 sessions/yr)	2011-2016	4 ECTS

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