CLINICAL RESEARCH STUDY

THE AMERICAN JOURNAL of MEDICINE®

What Is the Clinical Course of Acute Ankle Sprains? A Systematic Literature Review

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ABSTRACT

BACKGROUND: Ankle sprains are one of the most common musculoskeletal injuries. In order to evaluate the effectiveness of therapeutic interventions and to guide management decisions, it is important to have clear insight of the course of recovery after an acute lateral ankle injury and to evaluate potential factors for nonrecovery and re-sprains.

METHODS: A database search was conducted in MEDLINE, CINAHL, PEDro, EMBASE, and the Cochrane Controlled trial register. Included were observational studies and controlled trials with adult subjects who suffered from an acute lateral ankle sprain that was conventionally treated. One of the following outcomes had to be described: pain, re-sprains, instability, or recovery. Two reviewers independently assessed the methodological quality of each included study. One reviewer extracted relevant data.

RESULTS: In total, 31 studies were included, from which 24 studies were of high quality. There was a rapid decrease in pain reporting within the first 2 weeks. Five percent to 33% of patients still experienced pain after 1 year, while 36% to 85% reported full recovery within a period of 3 years. The risk of re-sprains ranged from 3% to 34% of the patients, and re-sprain was registered in periods ranging from 2 weeks to 96 months postinjury. There was a wide variation in subjective instability, ranging from 0% to 33% in the high-quality studies and from 7% to 53% in the low-quality studies. One study described prognostic factors and indicated that training more than 3 times a week is a prognostic factor for residual symptoms.

CONCLUSIONS: After 1 year of follow-up, a high percentage of patients still experienced pain and subjective instability, while within a period of 3 years, as much as 34% of the patients reported at least 1 re-sprain. From 36% up to 85% of the patients reported full recovery within a period of 3 years.

 • *The American Journal of Medicine (2008) 121, 324-331*

KEYWORDS: Ankle; Ankle injury; Ankle sprain; Clinical course; Lateral ligament; Review literature

Ankle sprains are one of the most common musculoskeletal injuries. In the Netherlands, an estimated 600,000 people sustain ankle injuries each year, with an incidence of 12.8 per 1000 patients per year. Roughly half of these patients visit a general practitioner or, on their own initiative, an emergency department.[1] In the United States and the United Kingdom, there are, respectively, 23,000 and 5000 injuries of the ankle each day.[2]

Recent reviews indicate that conventional treatment is the preferable initial treatment strategy.[2-7] Conventional treatment consists of early mobilization with mobilization instructions and early weight-bearing, sometimes combined with the use of an external support (tape, bandage, or brace). In order to evaluate the effectiveness of therapeutic interventions and to guide management decisions, it is important to have clear insight of the course of recovery after an acute lateral ankle injury. Beneficial effects or complications of different treatments may be considered against the background of this clinical course. Besides, identification of relevant subgroups of patients with better or worse prognosis also is important. This may guide management decisions, give directions for future research and is helpful for informing patients about the clinical course of their injury. At present there is, however, no clear overview about the clinical course of acute lateral ankle sprains, and an evalu-

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0002-9343/$ -see front matter
doi:10.1016/j.amjmed.2007.11.018

ation of prognostic factors for incomplete recovery and re-sprains is missing.

Therefore, the purpose of this study was to perform a systematic review of the literature about the clinical course of conventionally treated acute lateral ankle sprains in adults and its prognostic factors.

METHODS

Literature Search

One author (RvR) conducted a database search using MEDLINE (from 1966 to August 2006), CINAHL, PEDro, EMBASE (from 1984 to August 2006) and the Cochrane Controlled Trial Register. The terms "disorder," "location," and "design" were linked by the Boolean operator "AND." For each of the terms, one or more synonyms were used (Table 1).

The selected studies had to fulfill the following criteria for inclusion in the review: the adult subjects had to suffer from an acute lateral ankle sprain; the study design had to be longitudinal, that is, observational (prospective as well as retrospective) or a controlled trial; at least one of the following outcomes at follow-up had to be described: pain, re-sprains, subjective instability (feeling of insecurity, tendency for the foot to "give way") or subjective recovery; and the treatment (or one of the arms in a trial) was conventional treatment. Conventional treatment involves early mobilization, including mobilization instructions and early weight-bearing sometimes combined with the use of an external support (tape, bandage, or brace).

From title and abstracts, 2 reviewers (SB-Z and RvR) independently reviewed the literature searches to identify potentially relevant studies for full review. Unpublished studies and abstracts for which full reports were not available were not included. Based on the full text, 2 reviewers (SB-Z and RvR) independently selected studies for inclusion in this review. Relevant articles in the bibliographies of selected articles also were reviewed. The help of a native speaker was obtained for studies published in languages other than English, German, or Dutch. Disagreements were resolved by consensus.

CLINICAL SIGNIFICANCE

- During the first 2 weeks after an acute lateral ankle sprain, there is a rapid decrease in pain, after which it continues to improve more slowly. After 3 years follow-up, some patients still experience residual symptoms of their initial sprain.
- Information about potential prognostic factors for poor recovery and occurrence of re-sprains is rare.

Methodological Quality Assessment

Methodological quality of the selected studies was assessed by 2 reviewers (PL and RvR) independently, using a set of 7 criteria (Table 2). In case of prognostic factors, the methodological quality assessment was expanded with 4 criteria. Each criterion was rated positive, negative, or inconclusive (insufficient information presented). Disagreements were resolved by consensus. A total score for the methodological quality of each study was calculated by summing the number of positive criteria (range 0-7 or range 0-11). Studies with 5 (8 in the case of prognostic factors) or more positive criteria were considered to be of "high quality."

Table 1 Terms Used for the Database Search

Term	Synonym
Disorder	Inversion OR sprain OR strain OR rupture OR injur* OR distortion
Location	[Ankle OR talocrural OR talofibular OR calcaneofibular] AND ligament
Design	Prognos* OR predict* OR "disease course" OR case-control OR longitudinal OR cohort OR prospective OR retrospective OR follow-up OR randomized controlled trial OR controlled clinical trial OR randomized controlled trials OR random allocation OR double-blind method OR single-blind method

Table 2 Criteria Used for the Quality Assessment

	Criterion
01	Sample definition given (at least 3: age, sex, injury grade, and setting)
02	Baseline characteristics assembled within 2 weeks after injury
03	Participants selected by random selection or as consecutive cases
04	A prospective design used
05	Follow-up available from at least 80% of study population
06	Information on completers versus withdrawals available
07	The study provide raw data, percentages, survival rates, RRs, ORs or ES
08	3 or more of the following prognostic determinants were measured (severity or injury grade, weight, BMI, activity level)
09	Independent assessment of outcome measurement (blinded for prognostic factors)
10	Crude estimates are given or can be calculated
11	Adjusted estimates are given or can be calculated

RR = relative risk; OR = odds ratio; ES = estimate; BMI = body mass index. Items 8, 9, 10, and 11 are supplementary and are used for the quality assessment of prognostic studies.

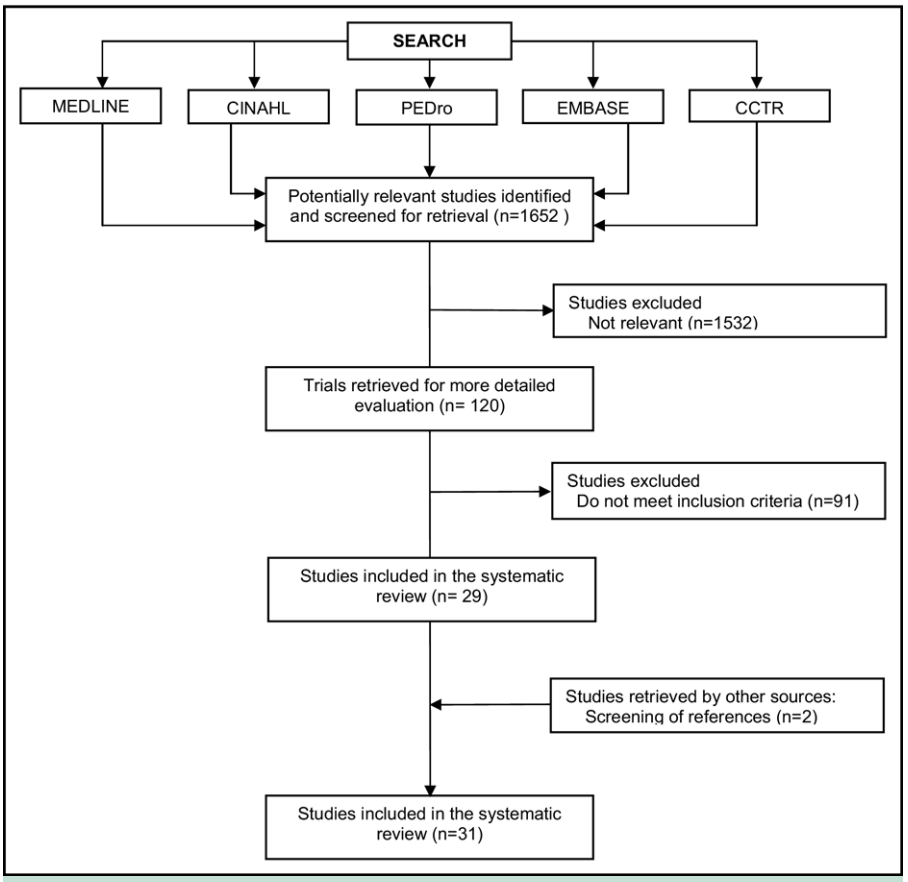

Figure 1 Flow chart of the selected studies.

Data Extraction

One reviewer (RvR) extracted relevant data from the publications. Study characteristics extracted were target population (setting, sex, and age), sample size, duration of follow-up, prognostic factors (severity, weight, length, body mass index, activity level), and outcome measures. Outcome data extracted were pain, subjective instability (feeling of giving way), re-sprain, subjective recovery (restored to preinjury state, free from residual symptoms, cured), swelling (ankle girth), and range of motion.

For the association between prognostic factors and the outcome measures, we extracted odd ratios (OR) or relative risks. When not given and sufficient data were available, for each study the association (OR) with 95% confidence intervals was calculated.

Data Synthesis

The inter-observer reliability of the overall quality assessment was derived by Kappa statistics. Following the suggestions of Fleiss,[8] kappa coefficients >0.75 are considered to represent excellent agreement, values between 0.75 and 0.4 fair agreement, and values <0.4 represent poor agreement.

The study outcomes are statistically pooled if the studies are considered to be homogeneous. However, if the studies are considered to be heterogeneous, we refrain from pooling and only describe the outcomes. When studies do not contain enough information about the association between prognostic factors and outcome, we graphically present the obtained data of the course subdivided by the preassumed prognostic factors.

RESULTS

Characteristics of Identified Studies

Our search strategy resulted in 1652 potentially relevant articles. From title and abstract, we identified 120 relevant articles. Reviewing the full text, 29 publications met our selection criteria. After screening the reference lists, another 2 studies were included, resulting in 31 relevant articles (Figure 1). Information about these 31 studies is presented in Table 3 (available online).

Four studies were retrospective and 27 were prospective. In these studies, the follow-up period ranged from 1 day to 11 years. Patients were recruited in various settings, including hospital emergency departments,[9-33] primary care,[29,34,35] and military health care centers.[36,37]

Five studies evaluated the effect of early mobilization instructions only,[9,13,14,34,36] while in 26 studies, early immobilization instructions were combined with partial immo-

Table 4 Quality Scores of the Included Studies

Authors	1	2	3	4	5	6	7	Score	Quality
Allen and McShane[9]	−	+	+	+	+	+	+	6	High
Anandacoomarasamy and Barnsley[29]	+	−	+	−	+	−	+	4	Low
De Bie et al[11]	+	+	+	+	+	+	+	7	High
Boyce et al[30]	+	+	+	+	−	+	+	6	High
Cetti et al[10]	+	+	+	+	+	−	+	6	High
Chaiwanichsiri et al[36]	+	−	+	+	+	−	+	5	High
Els et al[12]	+	−	−	+	−	−	+	3	Low
Green et al[13]	+	+	+	+	+	+	+	7	High
Grønmark et al[38]	−	−	+	+	+	−	+	4	Low
Holme et al[14]	+	+	+	+	+	+	+	7	High
Kerkhoffs et al[31]	−	+	+	+	+	−	+	5	High
Klein et al[15]	−	+	+	+	+	−	+	5	High
Konradsen et al[16]	+	+	+	−	+	−	+	5	High
Korkala et al[17]	−	−	+	+	−	−	+	3	Low
Leanderson and Wredmark[19]	+	+	+	+	−	−	+	5	High
Leanderson et al[18]	+	+	+	+	−	−	+	5	High
Linde et al[39]	−	+	−	+	+	−	+	4*	Low*
Mazières et al[34]	+	+	+	+	+	+	+	7	High
Moller-Larsen et al[20]	+	+	+	+	+	−	+	6	High
Munk et al[21]	+	+	+	+	−	−	+	5	High
Nilsson[22]	+	+	+	+	+	+	+	7	High
O'Hara et al[35]	+	+	+	+	+	−	+	6	High
Pijnenburg et al[32]	+	+	+	+	+	+	+	7	High
Povacz and Salzburg[23]	+	+	+	+	+	+	+	7	High
Pugia et al[37]	+	+	−	+	+	−	+	5	High
Schaap et al[24]	−	−	−	−	+	+	+	3	Low
Sommer and Arza[26]	+	+	+	+	−	−	+	5	High
Sommer and Arza[25]	+	+	+	+	+	−	+	6	High
Sommer and Schreiber[27]	+	−	−	+	+	+	+	5	High
Wester et al[28]	−	+	+	+	−	−	+	4	Low
Zammit and Herrington[33]	+	+	+	+	−	−	+	5	High

+ Indicates the criterion was clearly satisfied; − indicates that the criterion was not satisfied or it was not clear if it was satisfied.
*Adding the criteria for prognostic factors, the quality score was 6 (low).

bilization.[9,10,12,15-33,35,37,38] In our analysis, we do not differentiate between these differences in conventional treatment.

Two of the included publications did not evaluate pain, subjective instability, re-sprains, or subjective recovery,[13,19] but only reported the range of motion. Only one study reported on prognostic factors.[39]

Quality Assessment

Table 4 presents the results of the methodological quality assessment of the included studies. Of the 31 studies, 24 are deemed to be of high quality (ie, having a score of at least 5 or 8). The following concerns, however, are noteworthy:

In 23% (7 of 31) of the studies, there was a loss to follow-up of 20% or more of the initial study population.

In 68% (21 of 31) of the studies, a comparison of completers versus non-completers at follow-up was missing.

The initial agreement of the 2 reviewers on the total quality assessment of the included trials was 87% (189 of 217 items) and the Kappa value was 0.65, which is considered as a fair agreement. All initial disagreements were solved in a consensus meeting.

Pain

Eighteen studies measured pain. Fourteen studies[9,11,15,16,22-25,27-29,32,35,39] presented pain as the percentage of patients who still experience pain, and 4 studies[30,31,33,34] presented pain by means of the visual analog scale score. Thirteen studies were of high quality and 4 of low quality. Figure 2 shows data on 8 high-quality studies[9,11,15,22,23,25,27,35] with a follow-up period of 3 years or less. Five high-quality studies[11,22,25,31,34] and 2 low-quality studies[28,33] had more than one follow-up moment. In these studies, the number of patients who still experience pain decreased rapidly within the first 2 weeks after injury. This decrease continued after this first phase, although more slowly. Corresponding to this course are the results of the studies with one follow-up moment. Conversely, in 6 studies,[15,16,22,23,32,39] the proportion of patients who reported that they experi-

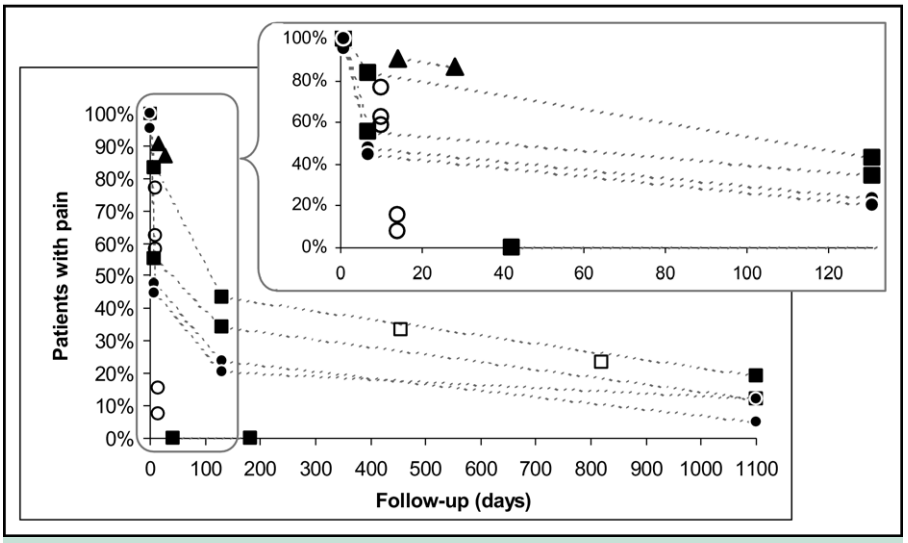

Figure 2 Percentage of patients in high-quality studies who still experienced pain at follow-up. Eight studies (15 treatment groups) with a follow-up ≤3 years are presented. Severity of sprains in studies with 1 follow-up moment: □ = rupture; ○ = no rupture; Δ = mixed or unknown. Severity of sprains in studies with >1 follow-up moment: ■ = rupture; ● = no rupture; ▲ = mixed or unknown.

enced pain after a follow-up period of 1 year or longer still ranged from 5% to 33%. Even after 3 years follow-up, 5% to 25% of patients still experienced pain.[16,22,32]

Re-sprains

Re-sprain was measured in 15 studies.[10-12,14-17,22,23,27-29,32,36,39] Of these, 10 are of high quality and 5 of low quality. Figure 3 shows 8 high-quality studies[10,11,14,15,22,23,27,36] with a follow-up period of 3 years or less. Re-sprains were registered within periods ranging from 2 weeks to 96 months after the injury. The occurrence of a re-sprain ranges from 3% to 34% of the patients. Only Wester et al[28] and Anandacoomarasamy and Barnsley[29] (both low-quality studies) reported a re-sprain in, respectively, 54% and 42% of the patients, after 230 and 882 days follow-up, respectively.

Subjective Instability

Fourteen studies assessed the occurrence of subjective instability,[10,15,17,20-24,26-29,32,39] Of these, 9 are of high quality and 5 of low quality. Figure 4 shows data on 7 high-quality studies[10,15,20,22,23,26,27] with a follow-up period of 3 years or less. There is a large variation in the reported occurrence of

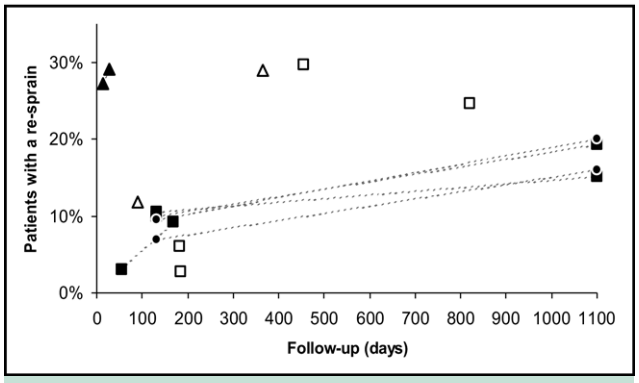

Figure 3 Percentage of patient in high-quality studies who reported at least 1 re-sprain at follow-up. Eight studies (12 treatment groups) with a follow-up ≤3 years are presented. Severity of sprains in studies with 1 follow-up moment: □ = rupture; ○ = no rupture; Δ = mixed or unknown. Severity of sprains in studies with >1 follow-up moment: ■ = rupture; ● = no rupture; ▲ = mixed or unknown.

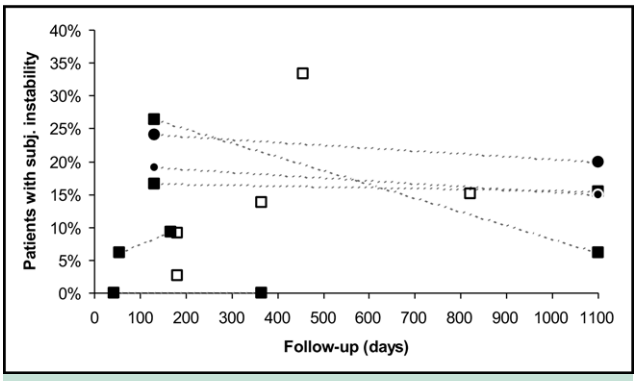

Figure 4 Percentage of patients in high-quality studies who reported instability at follow-up. Seven studies (11 treatment groups) with a follow-up ≤3 years are presented. Severity of sprains in studies with 1 follow-up moment: □ = rupture; ○ = no rupture; Δ = mixed or unknown. Severity of sprains in studies with >1 follow-up moment: ■ = rupture; ● = no rupture; ▲ = mixed or unknown.

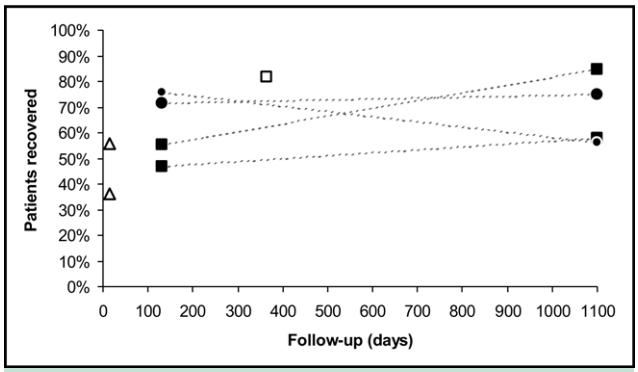

Figure 5 Percentage of patients in high-quality studies who reported full recover at follow-up. Three studies (7 treatment groups) with a follow-up ≤3 years are presented. Severity of sprains in studies with 1 follow-up moment: □ = rupture; ○ = no rupture; Δ = mixed or unknown. Severity of sprains in studies with >1 follow-up moment: ■ = rupture; ● = no rupture; ▲ = mixed or unknown.

subjective instability, ranging from 0% to 33% in the high-quality studies, and from 7% to 53% in the low-quality studies. Nilsson[22] reported a decrease in subjective instability at 36.2 months, compared with 4.3 months after injury in patients with arthrographically verified ruptures, as well as in patients without a rupture. In contrast, Cetti et al[10] reported an increase, from 6% to 9%, in subjective instability after 24 weeks, compared with 8 weeks after spraining an ankle. In general, the occurrence of subjective instability in patients seems higher in studies of low methodological quality[17,24,28,29,39] (Table 3).

Subjective Recovery

Three high-quality studies presented the patients' judgment of full recovery as being restored to preinjury state,[20] completely free from symptoms,[22] and cured on a 6-point scale of improvement.[35] Besides, 1 low-quality study[38] reported full recovery as being free from symptoms. One study[22] had more than one follow-up moment; in 3 of 4 groups that were examined, the percentage of patients who reported full recovery was increased after 36 months compared with 4 months. Ranging from 2 weeks to 36.2 months follow-up, 36% to 85% of all patients reported full recovery (Figure 5).

Prognostic Factors

One study evaluated prognostic factors for incomplete recovery and re-sprains.[39] Sports activity at a high level (training ≥3 times a week) was a significant prognostic factor for residual symptoms compared with sports activity at a low level (training <3 times a week) and no sports activity. However, only percentages and *P*-values were reported. Further, men had an increased risk of residual symptoms compared with women, for which we calculated an OR of 4.78 (95% confidence interval 1.36-16.61), but this difference may be due to the fact that the percentage of athletes among men was greater than among women.

We assessed prognostic factors indirectly according to study population characteristics. The only possible prognostic factor frequently described as a study population characteristic in the included studies was injury grade. When we plotted the outcome of high-quality studies according to this characteristic, we saw no clear difference in recovery rates or re-sprains.

DISCUSSION

This review summarizes the results on the course of pain, re-sprain, subjective instability, and subjective recovery in patients with an acute lateral ankle sprain. Within 2 weeks, a rapid improvement of pain experience was seen in the majority of patients with acute ankle sprains. Further improvement occurred after these 2 weeks, although more slowly. Re-sprains occurred within periods ranging from 2 weeks to 96 months after the initial injury, and ranges from 3% to 34% of the patients. The occurrence of subjective instability ranged from 0% to 33% in the high-quality studies and from 7% to 53% in the low-quality studies. Full recovery was reported by 36% to 85% of the patients at 2 weeks to 36.2 months follow-up. These results seem to be independent of the severity of the initial sprain. After 3 years follow-up, some patients still report residual symptoms (pain, subjective instability) and thus no total recovery. Only one study reports on prognostic factors;[39] the authors found that sports activity at a high level compared with sports activity at a low level and no sports activity is a risk factor for residual symptoms. Furthermore, men had an increased risk of residual symptoms compared with women. Although the authors attributed this latter association to the fact that the percentage of athletes among men was greater than among women, the real association is not clear without multivariable analyses.

The methodological quality, according to our criteria, appeared to be high for most of the studies. The most prevalent methodological shortcoming was no available information on completers versus noncompleters. A potential limitation of the present review might be the literature search, in that our search was limited to indexed journals. Therefore, unpublished studies and studies in nonindexed journals have been missed. However, this is the first time that the course of conventionally treated ankle sprains in adults has been described. Surprisingly, information about potential prognostic factors is rare; future studies on this topic are warranted.

As shown in the included studies, conventional treatment is performed in various ways. Conventional treatment is often combined with partial immobilization, which can be offered by a broad spectrum of devices. In a systematic review, Kerkhoffs et al[5,40] compared the effectiveness of different partial immobilizing devices (semi-rigid ankle support, lace-up ankle support, tape, or elastic bandage) in the treatment for acute lateral ankle ruptures. Their results

show that within 6 weeks follow-up, there might be some difference in persistency of swelling, time to return to work and sport, and subjective instability when using different external supports.

Although the conventional treatments in the included studies are performed in various ways, the small differences, as found by Kerkhoffs et al,[5,40] might explain the large heterogeneity of the outcomes in this review. However, more obvious for the heterogeneity of the results is the difference in how the outcomes are measured and the differences among the study population in the included studies. Linde et al[39] concluded that athletes had an increased risk of residual symptoms and that residual symptoms occurred in 32% of top athletes after 1 year. Because of this, it would have been informative to classify the included studies according to the activity level of their included patient groups; the activity level might have explained some of the heterogeneity of the outcomes of the studies. However, only 8 of the included studies provide some information about the activity level of their study population, and this was insufficient to classify the studies in a reasonable way. Besides, the studies did not report enough data to investigate the influence of age, sex, body weight, and body mass index on the occurrence of pain, re-sprains, subjective instability, and subjective recovery.

As mentioned before, after 3 years follow-up, some patients still have residual symptoms. The factors contributing to persistent complaints are largely unknown. For the time being, injury grade (rupture or no rupture) does not seem to be a strong predictor for the course of lateral ankle sprains. Figures 2-5 show that there are no differences toward the outcome measures. Furthermore, only Linde et al[39] evaluated prognostic factors for residual symptoms. Therefore, more research is needed to evaluate prognostic factors for poor recovery and occurrence of re-sprains. This will make it possible to determine which population is at risk for nonrecovery or for re-sprains. Such a high risk population might especially benefit from a specific treatment added to conventional treatment.

CONCLUSION

In conclusion, this review presents the clinical course of pain, objective and subjective instability, and subjective recovery of adult patients with conventionally treated ankle sprains. During the first 2 weeks there is a rapid decrease in pain, after which it continues to improve more slowly. After 3 years follow-up, some patients still have residual symptoms of their initial sprain. There is a wide variation in reported subjective instability, re-sprains, and subjective recovery among the different studies. A risk factor for residual symptoms might be sports activity at a high level, but more studies evaluating prognostic factors in patients with acute ankle sprains are needed.

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Table 3 Characteristics of the Included Studies

Study	Participants	Injury grade	Treatment	Outcomes	Results	Dropouts (n)
Allen and McShane, 1985[9]	n = 19 ♀: 5 (26%) ♂: 14 (74%) Mean age: 31 yr Mean weight: 73.6 kg	Uncomplicated inversion injuries of the lateral ligament of the ankle joint	Rest with elevation for 24 h, followed by gradually mobilization	At 10 days follow-up: Pain (severe + moderate) ROM (full plantar flexion to full dorsiflexion, % of uninjured ankle)	10 days: Pain: 63% (24%-91%) ROM: 72%	11
	n = 20 ♀: 3 (15%) ♂: 17 (85%) Mean age: 28 yr Mean weight: 69.6 kg		Rest with elevation for 24 h, followed by gradually mobilisation and elastic bandage	At 10 days follow-up: Pain ROM (% of uninjured ankle)	10 days: Pain: 77% (46%-95%) ROM: 75%	7
	n = 18 ♀: 7 (39%) ♂: 11 (61%) Mean age: 32.5 yr Mean weight: 74.8 kg		Rest with elevation for 24 h, followed by gradually mobilisation and taping	At 10 days follow-up: Pain ROM (% of uninjured ankle)	10 days: Pain: 58% (28%-85%) ROM: 78%	6
Anandacoomarasamy and Barnsley, 2005[29]	n = 19 ♀: 7 (37%) ♂: 12 (63%) AL: range from elite level sportsmen and women to recreational athletes	Inversion ankle injury; no fracture with or without dislocation or with or without complete rupture	RICE and early controlled mobilization	At 29 months follow-up: Pain (residual) Subj. instability Re-sprain Swelling	29 months: Pain: 47% Subj. instability: 47% Re-sprain: 42% Swelling: 37%	0
De Bie et al, 1997[11]	n = 35 ♀: 13 (37%) ♂: 22 (63%) Mean age: 28 ± 10 yr	Lateral ankle sprain injury. Patients with fractures, severe injuries demanding operative interventions and patients with open wounds were excluded	Pressure bandage until swelling was reduced or until an ankle dorsiflexion of 90° was possible, followed by tape	At 2, 4 weeks follow-up: Pain (spontaneous) Re-sprain Swelling	2 weeks: Pain: 91% (76%-98%) Re-sprain: 27% (13%-46%) Swelling: 94% 4 weeks: Pain: 87% (70%-96%) Re-sprain: 29% (14%-48%) Swelling: 97%	2
Boyce et al, 2005[30]	n = 25 ♀: 6 (35%) ♂: 11 (65%) Mean age: 35.3 yr	Moderate or severe lateral ligament sprain after an ankle inversion injury	Elastic support bandage with standardised advice of RICE	At 10 days follow-up: Pain (0-10 VAS) Swelling (circumferential measurement of ankle)	10 days: Pain: 2.9 Swelling: 14.4 mm	8
	n = 25 ♀: 11 (44%) ♂: 14 (56%) Mean age: 32.6 yr		Aircast ankle brace with standardized advice of RICE	At 10 days follow-up: Pain (0-10 VAS) Swelling (circumferential measurement of ankle)	10 days: Pain: 1.8 Swelling: 8.5 mm	7
Cetti et al, 1984[10]	n = 65	Acute sprain of the ankle with positive stress radiograms indicating rupture of the fibular ankle ligaments	Semi-rigid ankle support (Mobile Pliton-80 bandage) during 6 weeks	At 8, 24 weeks follow-up: Re-sprain Subj. instability Swelling	8 weeks: Re-sprain: 3% (0%-11%) Subj. instability: 6% (2%-15%) Swelling: 15% 24 weeks: Re-sprain: 9% (3%-19%) Functional instability: 9% (3%-19%) Swelling: 3%	0
Chaiwanichsiri et al, 2005[36]	n = 17 ♂: 17 (100%) Mean age: 16.9 yr Mean weight: 60.0 kg Mean height: 170.7 cm BMI = 20.59 AL: athletes of armed forces academies preparatory school	Grade II ankle sprain	Conventional physical therapy: Superficial heat Ultrasound therapy Range of motion exercise Stretching exercise Strengthening exercise	At 3 months follow-up: Re-sprain	3 months: Re-sprain: 12%	0

Table 3 Characteristics of the Included Studies

Study	Participants	Injury grade	Treatment	Outcomes	Results	Dropouts (n)
Els et al, 1996[12]	n = 133 ♀: 48 (36%) ♂: 85 (64%) Mean age: 28 yr	Injury of the lateral capsulo-ligamentous structures of the ankle	Lace-up ankle support for 6 weeks	At 18 months follow-up: Re-sprain	18 months: Re-sprain: 15%	
Green et al, 2001[13]	n = 19 ♀: 7 (37%) ♂: 12 (63%) Mean age: 24.9 ± 1.6 yr	An acute ankle sprain with sufficient severity to require assisted ambulation	RICE	At 2, 4, 6 days follow-up: ROM (pain free dorsiflexion, Pretreatment→post-treatment)	2 days: ROM: 7.2° →8.1° 4 days: ROM: 13.0° →15.0° 6 days: ROM: 17.5° →16.4°	0
Gronmark et al, 1980[38]	n = 30	Diagnosis of rupture of the lateral ligament	RICE and strapping for 6 weeks	At 17 months follow-up: Subjective recovery	17 months: Subjective recovery: 77%	0
Holme et al, 1999[14]	n = 42 ♀: 15 (36%) ♂: 27 (64%) mean age: 27.4 ± 4.6 yr AL: recreational athletes	Grade I (n = 16), II (n = 22) and III (n = 4) ankle sprains	Standard treatment information regarding early ankle mobilization, including strength, mobility, balance exercises	At 12 months follow-up: Re-sprain	12 months: Re-sprain: 16%	4
Kerkhoffs et al, 2004[31]	n = 721 Age: 16-53 yr Weight: 40-160 kg	Acute lateral ankle sprain, with pain on walking and scored pain as >30 mm on VAS (0-100 mm) and a clinically swollen ankle	10 days placebo and from day 4 until day 14 each patient had a Caligamed brace applied around the ankle	At 4, 7, 14 days follow-up: Pain (0-100 VAS) Swelling (volume of ankle) ROM (sum of dorsal- and plantar flexion)	4 days: Pain: 30 Swelling: 2590 ROM: 40° 7 days: Pain: 12.5 Swelling: 2545 ROM: 45° 14 days: Pain: 2.5 Swelling: 2490 ROM: 52°	47
Klein et al, 1991[15]	n = 27 ♀: 9 (33%) ♂: 18 (67%) Median age: 22 (16-45) yr	Positive stress radiogram (talar tilt ≥7° or anterior drawer test ≥7 mm AND difference between injured and uninjured ankle in: talar tilt ≥5° or anterior drawer test ≥5 mm)	10 days RICE protocol and 6 weeks use of semi-rigid ankle support (Aircast leg brace)	At 15 months (median) follow-up: Re-sprain Pain (extensive load) Subj. instability	15 months Re-sprain: 30% (14%-50%) Pain: 33% (17%-54%) Subj. instability: 33% (17%-54%)	0
Konradsen et al, 2002[16]	n = 648 ♀: 272 (42%) ♂: 376 (58%) Median age:29 (16-67) yr AL: moderate ankle straining work and occasional jogging on uneven terrain.	Swelling and tenderness in the area of the lateral aspect of the ankle following an inversion mechanism injury. No fractures apart from avulsions <5 mm at ligament insertion sites	RICE treatment and written instructions explaining mobilization exercises and early weight-bearing	At 7 yr follow-up: Pain (rest, activity) Swelling (occasional, constant) Re-sprain (3 or more)	7 years: Pain: 16% Swelling: 22% Re-sprain: 19%	0
Korkala et al, 1987[17]	n = 50	The anterior drawer sign exceeded 6 mm and the difference between injured and uninjured ≥ 3 mm. The talar tilt more than 15° and the difference between injured and uninjured ≥10°.	Semi-elastic bandage during 1 week, additional 1-3 weeks elastic bandage. Immediately full weight-bearing	At 2 yr follow-up: Re-sprain Subj. instability	2 years: Re-sprain: 17% (6%-33%) Subj. instability: 53% (25%-53%)	14

Table 3 Characteristics of the Included Studies

Study	Participants	Injury grade	Treatment	Outcomes	Results	Dropouts (n)
Leanderson and Wredmark, 1995[19]	n = 39	Grade II and grade III	Air-Stirrup ankle brace for 3 weeks with instructions to attempt early motion and weight bearing	At 3-5, 2, 4, 10 wk follow-up: ROM (max. dorsal flexion to max. plantar flexion, % of uninjured ankle)	3-5 days: ROM: 65% 2 weeks: ROM: 77% 4 weeks: ROM: 84% 10 weeks: ROM: 95%	15 (whole population)
	n = 34		Compression bandage for 3 weeks with instructions to attempt early motion and weight bearing	At 3-5, 2, 4, 10 wk follow-up: ROM (max. dorsal flexion to max. plantar flexion, % of uninjured ankle)	3-5 days: ROM: 65% 2 weeks: ROM: 77% 4 weeks: ROM: 84% 10 weeks: ROM: 95%	
Leanderson et al, 1999[18]	n = 39	Grade II and III	Air-Stirrup ankle brace for 3 weeks with instructions to attempt early motion and weight bearing	At 3-5 days, 2, 4, 10 wk follow-up: ROM (active eversion and inversion) Pain (Borg scale 0-10)	3-5 days (both groups): ROM: 48° Pain: 1.3	
	n = 34		Compression bandage for 3 weeks with instructions to attempt early motion and weight bearing	At 3-5, 2, 4, 10 wk follow-up: ROM (active e- and inversion) Pain (Borg scale 0-10)	2 weeks (both groups): ROM: 60° Pain: 1.6 4 weeks (both groups): ROM: 66° Pain: 1.1 10 weeks (both groups): ROM: 72° Pain: 0.3	
Linde et al, 1986[39]	n = 137 ♀: 53 (39%) ♂: 84 (81%) Median age: 28 yr AL: 58% athlete, 22% top athlete (training ≥3/week)	Lesion following an inverting injury, with swelling and pain at the lateral ankle joint. No fractures.	Foot elevated during first 24 h, then start doing motion exercise and weight bearing according to ability. No fixation of the ankle	At 1 year follow-up: Pain Re-sprain Subj. instability	1 year: Pain: 14% Re-sprain: 4% Subj. instability: 7%	0
Mazieres et al, 2005[34]	n = 82 ♀: 35 (43%) ♂: 47 (57%) Mean age: 34.4 yr BMI: 24.7	Symptomatic lateral ankle sprain with spontaneous pain ≥50 mm on a 0-100 VAS, benign nature (grade I or II).	A placebo Topical Delivery System (TDS) patch every day for 2 wks	At 3-4, 7, 14 days follow-up: Pain (0-100 VAS) Swelling (circumference of the ankle, injured vs uninjured)	3-4 days: Pain: 40 mm Swelling: 4.0% 7 days: Pain: 28 mm Swelling: 3.5% 14 days: Pain: 20 mm Swelling: 2.2%	0
Moller-Larsen et al, 1988[20]	n = 65 Median age: 23 yr	Acute ankle sprain. Rupture of ATFL, isolated or combined with rupture of the CFL.	Rest with leg elevated for 5 days. Then tape bandage for 4 wks, weight bearing was allowed.	At 1 year follow-up: Subj. instability Swelling (during activity) Subjective recovery	1 year: Subjective instability: 14% Swelling: 14% Subjective recovery: 82%	0

Table 3 Characteristics of the Included Studies

Study	Participants	Injury grade	Treatment	Outcomes	Results	Dropouts (n)
Munk et al, 1995[21]	n = 16 ♀: 5 (31%) ♂: 11 (69%) Mean age: 25	Hematoma and tenderness in the AFTL and/or CFL and severe pain inhibiting walking. No fractures	Elastic bandage until absence of pain and then early mobilization	At 11 years follow-up: Subj. instability ROM (dorsiflexion) ROM (plantar flexion)	11 years: Subj. instability: 6% ROM (dorsiflexion): 12° ROM (plantar flexion): 39°	0
Nilsson, 1983[22]	n = 29 AL: No top athletes	No rupture (arthrographically verified)	Elastic wrapping, 1 day rest followed by weight bearing as much as pain would allow	At 1, 7 d and 4, 36 month follow-up: Pain (constant, when walking) At 1, 7 d follow-up: Swelling (volume) At 4 and 36 months follow-up: Re-sprain Subj. instability Subjective recovery	1 day: Pain: 100% (88%-100%) Swelling: 45 ml 7 days: Pain: 45% (26%-64%) Swelling: 30 ml 4 months: Pain: 21% (8%-40%) Re-sprain: 7% (1%-23%) Subj. instability: 24% (10%-44%) Free from residual symptoms: 76% 36 months: Pain: 12% (3%-31%) Re-sprain: 16% (5%-36%) Subj. instability: 20% (7%-41%) Subjective recovery: 56%	4 (at 36 months)
	n = 30 AL: No top athletes	Arthrographically verified ruptures	Elastic wrapping, 1 day rest followed by weight bearing as much as pain would allow	At 1, 7 d and 4, 36 month follow-up: Pain (constant, when walking) At 1, 7 d follow-up: Swelling (volume) At 4 and 36 months follow-up: Re-sprain Subjective instability Subjective recovery	1 day: Pain: 100% (88%-100%) Swelling: 113 mL 7 days: Pain: 83% Swelling: 75 mL 4 months: Pain: 43% (25%-63%) Re-sprain: 10% (2%-27%) Subj. instability: 17% (6%-35%) Subjective recovery: 47% 36 months: Pain: 19% (7%-39%) Re-sprain: 19% (7%-39%) Subj. instability: 15% (4%-35%) Subjective recovery: 58%	4 (at 36 months)

Table 3 Characteristics of the Included Studies

Study	Participants	Injury grade	Treatment	Outcomes	Results	Dropouts (n)
	n = 21 AL: No top athletes	No rupture (arthrographically verified)	Cold pack was applied for 45 minutes and afterwards replaced by a 2 cm thick foam rubber pad. Compression effect was secured by elastic wrapping	At 1, 7 d and 4, 36 month follow-up: Pain (constant, when walking) At 1, 7 d follow-up: Swelling (volume) At 4 and 36 months follow-up: Re-sprain Subj. instability Subjective recovery	1 day: Pain: 95% Swelling: 53 mL 7 days: Pain: 48% Swelling: 23 mL 4 months: Pain: 24% Re-sprain: 9.5% Subjective instability: 19% Subjective recovery: 71% 36 months: Pain: 5% Re-sprain: 20% Subj. instability: 15% Subjective recovery: 75%	1 (at 36 months)
	n = 38 AL: No top athletes	Arthrographically verified ruptures	Cold pack was applied for 45 minutes and afterwards replaced by a 2cm thick foam rubber pad. Compression effect was secured by elastic wrapping	At 1, 7 d and 4, 36 month follow-up: Pain (constant, when walking) At 1, 7 days follow-up: Swelling (volume) At 4 and 36 months follow-up: Re-sprain Subjective instability Subjective recovery	1 day: Pain: 100% Swelling: 78 mL 7 days: Pain: 55% Swelling: 40 mL 4 months: Pain: 34% Re-sprain: 11% Subjective instability: 26% Subjective recovery: 55% 36 months: Pain: 12% Re-sprain: 15% Subj. instability: 6% Subjective recovery: 85%	5 (at 36 months)
O'Hara et al, 1992[35]	n = 118	Acute ankle injury unassociated with bony injury or major ligamentous damage	Malleotrain ankle support	At 2 weeks follow-up: Pain at rest Pain at night Pain at activity Subjective recovery	2 weeks: Pain at rest: 7.5% Pain at night: 8% Pain at activity: 14% Subjective recovery: 56%	0
	n = 102		Advice on resting the affected joint and a simple support (Tubigrip	At 2 weeks follow-up: Pain at rest Pain at night Pain at activity Subjective recovery	2 weeks: Pain at rest: 16% Pain at night: 14% Pain at activity: 21% Subjective recovery: 36%	

Table 3 Characteristics of the Included Studies

Study	Participants	Injury grade	Treatment	Outcomes	Results	Dropouts (n)
Pijnenburg et al, 2003[32]	n = 189	Painful ankle caused by an indirect supination injury	Functional treatment: wearing a non weight bearing cast for 5 days followed by elastic bandaging or taping for 6 weeks.	At 8 yr (median) follow-up: Pain (residual) Swelling Subj. instability Re-sprain	8 years: Pain: 25% Swelling: 14% Subj. instability: 32% Re-sprain: 34%	31
Povacz et al, 1998[23]	n = 88	Acute injury of the collateral ligaments of the ankle. Arthrographically verified rupture with a talar tilt ≥5°	3-7 days elastic wrapping, ice and elevation. Followed by 6 weeks ankle brace and weight bearing as tolerated and exercise instructions (ROM, proprioceptive, isometric)	At 27 (24-31) month follow-up: Pain (severe, mild) Subj. instability Re-sprain Swelling	27 months: Pain: 23% (14%-35%) Subj. instability: 15% (8%-25%) Re-sprain: 25% (15%-36%) Swelling: 8%	15
Pugia et al, 2001[37]	n = 29 ♀: 9 (31%) ♂: 20 (69%) mean age: 30.88 ±11.37	Acute lateral ankle sprain with tenderness and swelling over the lateral ankle ligaments	RICE	At baseline: Swelling (figure of eight measurement, injured vs. uninjured)	Baseline: Swelling: 1.77 cm	
Schaap et al, 1989[24]	n = 617	Grade I; no demonstrable sign of instability	Compression with bandages	At 9 months follow-up: Pain Subj. instability Swelling	9 months: Pain: 28% Subj. instability: 32% Swelling: 26%	126
	n = 319	Grade II; mild or incomplete instability present	Partial immobilization by means of tape	At 9 months follow-up: Pain Subj. instability Swelling	9 months: Pain: 27% Subj. instability: 28% Swelling: 30%	56
Sommer et al, 1987[25]	n = 40 ♀: 8 (20%) ♂: 32 (80%) mean age: 28.6 ± 7.6	Arthrographically verified rupture: talar tilt ≥10° and leakage of contrast fluid	2 weeks elastic strapping followed by 4-6 weeks tape, weight bearing as tolerated	At 6 wks and 3-8 month follow-up: Pain	6 weeks: Pain: 0% 3-8 months: Pain: 0%	5
Sommer et al, 1989[26]	n = 40 ♀: 8 (20%) ♂: 32 (80%) mean age: 26.1 ± 7.3 AL: No competitive sportsmen	Arthrographically verified rupture: talar tilt ≥10° and leakage of contrast fluid	2 weeks elastic strapping followed by a bandage for a further 6 weeks. Weight bearing as tolerated.	At 6 wks and 1 yr follow-up: ROM Subj. instability	6 weeks: ROM: full movement Subj. instability: 0% 1 year: ROM: full movement Subj. instability: 0%	13
Sommer et al, 1993[27]	n = 40 ♀: 13 (33%) ♂: 27 (67%) Mean age: 24.9 ± 8.6 n = 40 ♀: 15 (38%) ♂: 25 (62%) Mean age: 24.5 ± 5.5	Arthrographically verified rupture: talar tilt ≥10° and leakage of contrast fluid	Immediate mobilization and weight bearing as tolerated, 6 weeks semi-rigid ankle support Immediate mobilization and weight bearing as tolerated, 2 weeks bandage, 4 weeks tape	At 6 months follow-up: Re-sprain Pain Subj. instability At 6 months follow-up: Re-sprain Pain Subj. instability	6 months: Re-sprain: 3% (0%-14%) Pain: n = 0 Subj. instability: 3% (0%-14%) 6 months: Re-sprain: 6% (1%-20%) Pain: n = 0 Subj. instability: 9% (2%-24%)	37

Table 3 Characteristics of the Included Studies

Study	Participants	Injury grade	Treatment	Outcomes	Results	Dropouts (n)
Wester et al, 1996[28]	n = 24 AL: All active in sports for at least 2 h a week	Grade II, without positive anterior drawer sign or talar tilt	2 days elevation and immobilization, 1 week compression bandage, mobilisation based on pain sensations	At 1, 6, 12 weeks follow-up: Pain at sports Pain at rest Pain at walking Swelling (volume, injured vs uninjured) At 230 days follow-up: Re-sprain Subj. instability	1 week: Pain at sports: 96% (79%-100%) Pain at rest: 29% Pain at walking: 83% Swelling: 65 mL 6 weeks: Pain at sports: 75% (53%-90%) Pain at rest: 0% Pain at walking: 21% Swelling: 22 mL 12 weeks: Pain at sports: 29% (13%-51%) Pain at rest: 4% Pain at walking: 4% Swelling: 10 mL 230 days: Re-sprain: 54% (33%-74%) Subj. instability: 25% (10%-47%)	
Zammit and Herrington, 2005[33]	n = 12	Grade I and II injuries	Ice and Tubigrip for 2 weeks and exercises depending on response of the patient	At 1, 8, 15, 22 days follow-up: Pain (VAS 0-10) Swelling (figure 8 measurement) ROM (dorsiflexion and plantarflexion)	1 day: Pain: 4.9 Swelling: 54.8 cm ROM (dorsiflexion): 2.1° ROM (plantarflexion): 41° 8 days: Pain: 2.9 Swelling: 54.5 cm ROM (dorsiflexion): 6.5° ROM (plantarflexion): 45° 15 days: Pain: 1.6 Swelling: 54 cm ROM (dorsiflexion): 8.1° ROM (plantarflexion): 48° 22 days: Pain: 0.7 Swelling: 53.7 cm ROM (dorsiflexion): 7.6 ROM (plantarflexion): 51°	3

OROM = range of motion; AL = activity level; RICE = rest, ice, compression, elevation; VAS = visual analog scale; BMI = body mass index.