

Original article

The relationship between pain and associated characteristics of chronic ankle instability: A retrospective study

Saeed Al Adal^{a,b,*}, Martin Mackey^a, Fereshteh Pourkazemi^a, Claire E. Hiller^a

^a Faculty of Health Sciences, University of Sydney, Sydney, PO Box 170, Lidcombe, NSW 1825, Australia

^b Faculty of Applied Medical Sciences, Najran University, Najran, PO Box 1988, Saudi Arabia

Received 21 February 2019; revised 3 June 2019; accepted 10 June 2019

Available online 25 July 2019

Abstract

Background: Up to 74% of people with a history of ankle sprain develop chronic ankle instability (CAI). One commonly reported residual impairment is ankle pain; however, it has not been included in models or inclusion criteria for CAI. We investigated the prevalence of pain in people with CAI and the association between presence of pain and other CAI characteristics.

Methods: Retrospective data from 1147 participants with CAI (age 26.6 ± 10.7 years, 59% female) were collated from previous studies that used the Cumberland Ankle Instability Tool as an assessment tool. Pain was assessed from Item 1 of the Cumberland Ankle Instability Tool, which asks participants about ankle pain. Responses were divided into 3 categories: pain during daily activities, pain during moderate/vigorous physical activities, and no pain. The presence of pain was analyzed with descriptive statistics, the correlation between pain category and CAI characteristics was analyzed by χ^2 tests and factors associated with each pain category were analyzed by logistic regression.

Results: Among the participants, 60.1% ($n = 689$) reported ankle pain. Of all participants, 12.4% ($n = 142$) reported pain during daily activities, 47.7% ($n = 547$) reported pain during moderate/vigorous physical activities, and 39.9% ($n = 458$) reported no pain. There was a strong association between ankle instability and ankle pain ($\chi^2 = 122.2$, $p < 0.001$, OR = 5.38, 95% confidence interval (CI): 3.84–7.53). Perceived ankle instability, age and unilateral ankle sprains were independently associated with pain (ankle instability: $\chi^2 = 43.29$, $p < 0.001$; age: $\chi^2 = 30.37$, $p < 0.001$; unilateral ankle sprains: $\chi^2 = 6.25$, $p < 0.05$). There was no significant difference in the presence of pain between genders.

Conclusion: The prevalence of pain in people with CAI was high and was related to perceived ankle instability. Number of sprains, age, gender and unilateral or bilateral sprain did not modify this result except for the first pain category (pain during daily activities). There is large gap in current knowledge about the impact of pain in people with CAI, and this topic needs further investigation.

2095-2546/© 2020 Published by Elsevier B.V. on behalf of Shanghai University of Sport. This is an open access article under the CC BY-NC-ND license. (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Keywords: Ankle impairments; Ankle instability; Ankle sprain; CAIT; Pain

1. Introduction

Ankle sprains are among the most common injuries in sports and the general population.^{1–3} A high prevalence of this injury has been reported in school and college athletes^{4–6} and in military populations.⁷ Despite the high incidence and severe debilitating symptoms after a sprain, around 55% of people with acute sprain do not seek medical attention,⁸ and this injury is often thought to be relatively harmless and receives limited treatment.^{9,10}

Acute symptoms of ankle sprain are usually resolved after the initial injury; however, persistent residual symptoms are commonly reported and remain for a long period.^{11,12} These difficulties include recurrent sprains,¹³ episodes of giving way,¹⁴ self-reported disability,¹⁵ diminished physical activities,^{16,17} and pain.¹³ As a result of such persistent impairments, people experience changes in their ability to perform activities of daily living¹³ and occupational activities,^{18,19} and consequently adverse impacts on quality of life usually occur.²⁰

A recent systematic review showed that around 58% of participants with chronic ankle instability (CAI) reported ankle pain.²¹ However, no studies have had pain as the primary outcome or investigated the effects of pain in people with CAI.²¹ A high prevalence of pain and functional limitations has been found in

Peer review under responsibility of Shanghai University of Sport.

* Corresponding author.

E-mail address: sala7451@uni.sydney.edu.au (S.A. Adal).

common musculoskeletal injuries such as groin-area injuries^{22,23} anterior cruciate ligament injuries,²⁴ and foot impairments.²⁵

Despite the fact that pain is one of the major impairments after an ankle sprain, pain is not considered as one of the inclusion criteria in many different models of CAI when identifying participants with CAI.¹⁶ Therefore, the first aim of this study was to investigate the prevalence of pain in people with CAI using a validated self-reported questionnaire. The second aim was to investigate whether the presence of pain was related to other CAI characteristics, such as recurrent sprains or demographic factors such as age and gender. We hypothesized that ankle pain would be prevalent in our sample and that the presence of persistent pain would be associated with increased number of sprains, older age, female gender, and ankle instability.

2. Methods

This study was a retrospective study using data from 26 previous studies on participants with CAI. All studies used the Cumberland Ankle Instability Tool (CAIT) as one of the assessment tools. Data from 1147 participants with CAI (age 26.6 ± 10.7 years (mean \pm SD), range 10–86 years, 59% female) were included. All provided data were de-identified and came from studies that did not exclude the use of data in future research. The study was approved by the Human Research Ethics Committee at the University of Sydney. All the participants had provided written informed consent. Common variables were identified and included age, gender, tested leg, the number of sprains for the tested leg, time since the last sprain, unilateral or bilateral sprains, other injuries in the lower limb, rehabilitation history and CAIT score.

2.1. Inclusion and exclusion criteria

Participants with CAI were included if they met the following inclusion criteria: (1) history of an ankle sprain and (2) either (a) a CAIT score of ≤ 25 or (b) a CAIT score between 26 and 30 with either a recurrent sprain within the past 2 years or giving way or rolling over ≥ 2 times per year. We excluded participants with a recurrent acute ankle sprain within 6 weeks, missing data or a history of lower limb fractures.

2.2. CAIT questionnaire

CAIT is a 9-item questionnaire designed to evaluate the severity of perceived ankle instability.¹⁴ The level of ankle instability is reported in different activities, including running, walking, hopping, and descending stairs. The total CAIT score ranges from 0 to 30 on each side, in which 0 represents severe perceived instability and 30 represents normal stability.

We assessed pain from Item 1 of the CAIT, which asks participants about pain in their ankles. Participants selected 1 of the 6 answers to describe the level of pain in each ankle. Responses were divided into 4 categories: (1) people who reported no pain (CAIT answer = never), (2) people who reported pain during daily activities (CAIT answer = pain when walking on level surfaces, pain when walking on uneven surfaces), (3) people who had pain during moderate/vigorous

physical activities (CAIT answer = pain when running on level surfaces, running on uneven surfaces, during sport), and (4) people who reported pain during any level of physical activities (CAIT answer = all categories of pain).

2.3. Variables

Out of the available data, we were able to identify 5 consistent variables: age, gender, ankle instability, number of sprains on each side, and unilateral or bilateral sprains. These variables were dichotomized for further analysis. Age was divided into younger adults and older adults, with the cutoff point occurring at 30 years. This decision was based on the likelihood that sports participation would have declined to recreational at best by age 30. Ankle instability was scored from the CAIT after eliminating the first Item (pain question) and resulted in a score between 0 and 25. The CAIT score cutoff point was 20; people with a score of < 20 were considered to have ankle instability. The number of sprains was dichotomized at 3, so that a definite repeat sprain pattern was identified. Participants with ≥ 3 ankle sprains were coded as 1 whereas participants with < 3 ankle sprains were coded as 0.

2.4. Data analysis

Age, gender, the presence of pain, ankle instability, unilateral or bilateral ankle sprain involvement, and the number of sprains were analyzed with descriptive statistics. The association between presence or absence of pain and each variable was determined by a χ^2 test. To determine the adjusted odds ratio for each variable and the presence of pain, a logistics regression was performed. In order of the magnitude of the χ^2 association, each variable was added to the regression model one at a time, from largest to smallest. All statistical analyses were performed using SPSS software, Version 22.0 (IBM Corp., Armonk, NY, USA).

3. Results

The total number of participants with CAI was 1147. Of these, 41% were male. The results revealed that 69.9% of the participants were young adults (< 30 years old) and 58.1% of the participants reported bilateral ankle sprains (Table 1).

Table 1
Demographic data.

Variables	Pain during daily activities	Pain during moderate/vigorous PA	No pain
F/M (n)	80/62	336/211	261/197
Age (year)	32.5 ± 14.2	25.6 ± 9.8	26.0 ± 9.8
Instability ^a	10.7 ± 5.3	14.9 ± 4.3	18.8 ± 4.2
Number of sprains	5.2 ± 6.3	5.0 ± 6.0	3.6 ± 3.3
U/B sprain (n)	72/70	231/316	178/280

Note: Data are presented as mean \pm SD or number of participants.

^aCAIT out of 25 (without Item 1).

Abbreviations: B = bilateral; CAIT = Cumberland Ankle Instability Tool; F = female; M = male; PA = physical activity; U = unilateral.

Table 2
Reported categories of pain on CAIT, Item 1.

CAIT question 1	Answers	
	<i>n</i>	%
During sport	219	31.8
Running on uneven surfaces	262	38.0
Running on level surfaces	66	9.6
Walking on uneven surfaces	117	17.0
Walking on level surfaces	25	3.6

Abbreviation: CAIT = Cumberland Ankle Instability Tool.

The prevalence of any pain at the ankle joint was 60.1% (*n* = 689). Of these, 20.6% (*n* = 142) reported ankle pain during daily activities and 79.4% (*n* = 547) reported pain during moderate/vigorous physical activities (Table 1). The highest pain percentage was reported while running on uneven surfaces (38.0%) followed by pain during sports (31.8%) (Table 2). Pain was reported in 58.1% of male participants and 61.4% of female participants. Recurrent sprains (≥3) were reported in 57.3% of participants, 64.0% of whom reported ankle pain. From people who had <3 ankle sprains, 55.1% had pain at their ankle joints. In addition, 58.1% of participants reported bilateral ankle sprains, of which 58.0% had ankle pain. When considering age, 59.1% of younger adult participants (<30 years) reported pain. Of these, 50.1% had pain during moderate/vigorous physical activities and 8.2% had pain during daily activities compared to older adults, where 40.3% had pain during moderate-to-vigorous physical activities and 22.0% had pain during daily activities. Only perceived instability was

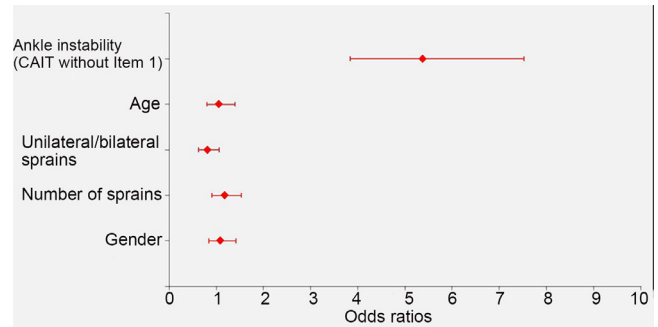


Fig. 1. The association between all variables and any pain.

significantly associated with all pain groups (Fig. 1). In addition, pain during daily activities was associated with having ankle instability, being of older age, and having unilateral ankle sprain (Table 3).

Logistic regression analysis revealed that perceived ankle instability was the only independent factor associated with any pain ($\chi^2 = 122.2, p < 0.001$), odds ratio (OR)=5.38 (95%CI 3.84–7.53) (Tables 3–4). People with unstable ankles were 5.3 times more likely to have any ankle pain (Fig. 1). Perceived ankle instability, age, and unilateral/bilateral ankle sprains were independently associated with pain during daily activities (ankle instability: $\chi^2 = 43.29, p < 0.001$; age: $\chi^2 = 30.37, p < 0.001$; unilateral ankle sprains: $\chi^2 = 6.25, p < 0.05$) (Table 3) (Fig. 2). Adjusted odds ratios showed that people with ankle instability who were >30 years old and had unilateral ankle sprains were 30.4 times (multiplying of adjusted odds ratios 7.48×2.70×1.52) more likely to have ankle pain during daily activities (Table 5).

Table 3
The magnitude of χ^2 for CAI variables in different pain groups.

Variables	Any pain			Pain during daily activities			Pain during moderate/vigorous PA		
	χ^2	<i>df</i>	<i>p</i>	χ^2	<i>df</i>	<i>p</i>	χ^2	<i>df</i>	<i>p</i>
Ankle instability ^a	122.2	1	0.000	43.29	1	0.000	99	1	0.000
Number of sprains	8.8	1	0.226	1.40	1	0.963	9.5	1	0.188
Unilateral/bilateral	2.9	1	0.123	6.25	1	0.049	1.1	1	0.313
Gender	1.3	1	0.518	0.19	1	0.744	2.3	1	0.499
Age	1.0	1	0.710	30.37	1	0.000	1.1	1	0.156

^aCAIT out of 25 (without Item 1).

Abbreviations: CAIT = Cumberland Ankle Instability Tool; PA = physical activity.

Table 4
Binary logistic regression results of odds ratios of all variables vs. presence of any pain, pain during daily activities, and pain during physical activities.

Variables	95%CI for Exp (B)								
	Any pain			Pain during daily activities			Pain during moderate/vigorous PA		
	Exp (B)	Lower	Upper	Exp (B)	Lower	Upper	Exp (B)	Lower	Upper
Ankle instability	5.38	3.84	7.53	7.48	3.65	15.34	5.05	3.54	7.23
Number of sprains	1.18	0.90	1.53	1.01	0.66	1.54	1.20	0.91	1.59
Unilateral/bilateral	0.81	0.63	1.04	1.51	1.00	2.29	0.87	0.66	1.14
Gender	1.09	0.84	1.42	0.93	0.61	1.42	1.10	0.84	1.44
Age	1.05	0.80	1.39	2.69	1.79	4.06	0.80	0.60	1.09

Abbreviations: CI = confidence interval; Exp = exponentiation of the coefficients; PA = physical activity.

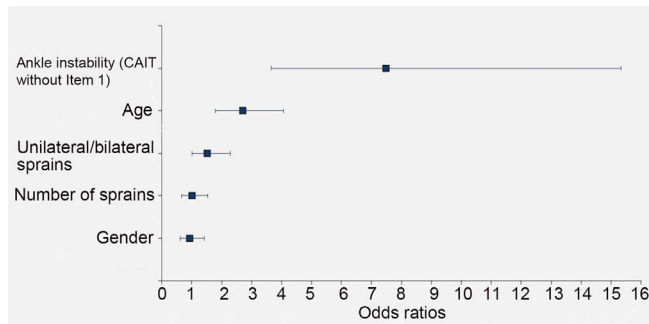


Fig. 2. The association between all variables and pain during daily activities.

4. Discussion

There was a high prevalence of pain in people with CAI, mostly occurring during physical activities and with no difference between genders. Ankle instability was the only independent predictor of all pain categories or pain with physical activities, while ankle instability, age, and unilateral sprain were associated with ankle pain during daily activities.

The occurrence of ankle pain in participants with CAI was 60.1%, which is consistent with the findings of previous studies.^{13,26} In a recent systematic review, pain was presented in 50%–79% of participants with CAI, with the level of pain reported to be 4.9 (out of 10 on the numerical analogue scale) in a few studies.²¹ In the current study, most of the participants with CAI reported pain during moderate/vigorous physical activities rather than as ankle pain during daily activities. This might be due to the majority of participants being younger adults (70%).

Our second finding indicated that people with more severe perceived ankle instability are more likely to report ankle pain. The mean CAIT score for people with pain during moderate/vigorous physical activities and ankle pain during daily activities was low. This could be explained by changes in the biomechanical relationship between the talus and mortis of the ankle.²⁷ As a result of unbalanced loading, people with CAI demonstrated degenerative changes in the articular cartilage over the medial part of the ankle joint.^{28,29}

The positive association between pain and joint instability has been found in other body areas such as the shoulder^{30,31} and patellofemoral joints.³² Gasson et al.³⁰ found that patients with recurrent shoulder instability were likely to have significantly higher levels of continuous pain. They explained this finding by the alterations in central pain mechanisms (central sensitization) when people feel shoulder pain without any nociceptive inputs. In the ankle joint, people with CAI feel

their ankles are unstable, and this is usually associated with the fear of having an acute sprain.¹⁶ In a study by Hass et al.,³³ CAI was found to be associated with negative alternations in supraspinal aspects of motor control, which may explain the neurophysiologic mechanism of CAI. The impact of persistent ankle pain could be an important factor that may play a major role in continuing chronicity of ankle sprain.

We found that age was an additional independent variable for participants with ankle pain during daily activities. Gibson and Farrell³⁴ found that older adults experienced greater pain when pain persisted for longer periods. Age-related changes include changes in the efficacy of the pain inhibitory system reduce the ability of older adults to cope with persistent pain.³⁵ Another explanation for this finding could be the presence of the associated post-traumatic osteoarthritis after ankle sprain, which accounts for >70% of ankle osteoarthritis cases.^{36,37} Older adults may be more likely to report more pain as a result of the biomechanical changes between ankle mortise and talus.²⁹ Although pain is too frequently a companion of elderly people,³⁴ a complete understanding of the impact of age on pain is unclear. It is also important to consider the impact of other factors, such as psychological or social circumstances, that may vary between younger and older adults.³⁸

Unilateral ankle sprain was associated with ankle pain during daily activities. Although, 44% of all participants with CAI who reported any pain (during daily activities or during moderate/vigorous physical activities) were participants with unilateral ankle sprains, they represented 51% of the reported pain only during daily activities. Although the results showed that these 2 variables were statistically associated, it appears that this relationship is weak and may not be clinically significant. Because of missing data on duration of injury, people may have reported the most recent and painful sprain at the time of data collection which could justify this result.

No association was found between gender and ankle pain. Previous studies showed no differences in the severity of pain between males and females in some chronic musculoskeletal conditions.³⁹ Jensen and Petersen⁴⁰ found small differences in nociceptive transmission and neuronal sensitization between males and females, which does not support the hypothesis that females have a higher central pain sensitization. In contrast, other studies have shown that females report higher pain levels. Unruh⁴¹ demonstrated that women reported higher pain intensity, longer duration and more frequent pain than men. In addition, several musculoskeletal pain conditions occur more frequently in women, such as osteoarthritis (after age of 45),

Table 5
Adjusted associations between pain during daily activities and ankle instability, age, and unilateral ankle sprain.

Variables	Participants reported pain during daily activities (%)	Participants reported no pain during daily activities (%)	Adjusted odds ratio (95%CI)	<i>p</i>
Ankle instability	93.6	65.3	7.48 (3.65–15.34)	0.000
Age ≥30 years old	53.5	28.4	2.70 (1.79–4.06)	0.000
Unilateral ankle sprain	50.7	38.9	1.52 (1.00–2.29)	0.049

Abbreviation: CI = confidence interval.

fibromyalgia and carpal tunnel syndrome.^{42,43} The varying results of studies about pain and gender could be a result of differences in tissue damage, biases in pain reporting,⁴³ psychosocial aspects,^{44–46} or genetic differences.⁴⁷

Although the recurrence of ankle sprains is one of the common impairments of CAI, we found no association between pain and the number of sprains. The international ankle consortium endorsed the definition of recurrent ankle sprain as ≥ 2 sprains on the same ankle.¹⁶ In this study the cutoff score for the number of sprains was ≥ 3 sprains. Because of the high mean number of ankle sprains for people who reported pain, we expected that the number of ankle sprains would be associated with pain. However, the results showed that 36.5% of people who had ≥ 3 ankle sprains did not report pain. Because of the lack of data about other characteristics of ankle sprain, it could be that the severity of 1 ankle sprain has a major impact on pain no matter how many sprains people had.

One major limitation of this study was its retrospective design, which did not allow us to investigate the causality relationship between pain and CAI. It is not possible to identify whether participants developed pain secondary to CAI or whether pain is a contributing factor to the development of CAI. Another limitation was the relative youth of our sample. Only 30% of participants were >30 years of age, and this may be reflected in the lack of association of age with pain during moderate or vigorous activities. In addition, there was a lack of data related to some important information, including rehabilitation history, impairments or disability, psychological factors or severity and frequency of ankle pain. Future work should consider all these aspects and their potential associations with pain.

5. Conclusion

The prevalence of pain in people with CAI was high and was related to perceived ankle instability. The number of sprains, age, gender, and unilateral and bilateral sprain did not modify this, except for ankle pain during daily activities. Older age and unilateral ankle sprain were associated factors in people with ankle pain during daily activities. Future work should investigate more detailed profiles of the pain associated with CAI and the effect of other factors such as pathology and biomechanics.

Acknowledgment

Saeed Al Adal is supported by a Ph.D. scholarship from Najran University in Najran, Saudi Arabia.

Authors' contributions

SAA carried out the study design, data collating, data analysis and interpretation, and drafted the manuscript; MM and FP conceived the study, and participated in its design and data interpretation, and helped to draft the manuscript; CEH conceived the study and design, assisted with statistical analysis and data interpretation, and provided a critical review of the manuscript. All authors have read and approved the final

version of the manuscript, and agree with the order of presentation of the authors

Competing interests

The authors declare that they have no competing interests.

References

- Fong DT, Hong Y, Chan LK, Yung PS, Chan KM. A systematic review on ankle injury and ankle sprain in sports. *Sports Med* 2007;**37**:73–94.
- Waterman BR, Owens BD, Davey S, Zacchilli MA, Belmont Jr PJ. The Epidemiology of ankle sprains in the United States. *J Bone Joint Surg Am* 2010;**92**:2279–84.
- Roos KG, Kerr ZY, Mauntel TC, Djoko A, Dompier TP, Wikstrom EA. The epidemiology of lateral ligament complex ankle sprains in National Collegiate Athletic Association Sports. *Am J Sports Med* 2017;**45**:201–9.
- Fernandez WG, Yard EE, Comstock RD. Epidemiology of lower extremity injuries among U.S. high school athletes. *Acad Emerg Med* 2007;**14**:641–5.
- Hootman JM, Dick R, Agel J. Epidemiology of collegiate injuries for 15 sports: summary and recommendations for injury prevention initiatives. *J Athl Train* 2007;**42**:311–9.
- Tanen L, Docherty CL, Van Der Pol B, Simon J, Schrader J. Prevalence of chronic ankle instability in high school and division I athletes. *Foot Ankle Spec* 2014;**7**:37–44.
- Simpson JD, Debusk H, Hill C, Knight A, Chander H. The role of military footwear and workload on ground reaction forces during a simulated lateral ankle sprain mechanism. *Foot (Edinb)* 2018;**34**:53–7.
- McKay GD, Goldie PA, Payne WR, Oakes BW, Watson LF. A prospective study of injuries in basketball: a total profile and comparison by gender and standard of competition. *J Sci Med Sport* 2001;**4**:196–211.
- Birrer RB, Fani-Salek MH, Totten VY, Herman LM, Politi V. Managing ankle injuries in the emergency department. *J Emerg Med* 1999;**17**:651–60.
- Doherty C, Delahunt E, Caulfield B, Hertel J, Ryan J, Bleakley C. The incidence and prevalence of ankle sprain injury: a systematic review and meta-analysis of prospective epidemiological studies. *Sports Med* 2014;**44**:123–40.
- Hertel J. Functional anatomy, pathomechanics, and pathophysiology of lateral ankle instability. *J Athl Train* 2002;**37**:364–75.
- Konradsen L, Bech L, Ehrenbjerg M, Nickelsen T. Seven years follow-up after ankle inversion trauma. *Scand J Med Sci Sports* 2002;**12**:129–35.
- Hiller CE, Nightingale EJ, Raymond J, Kilbreath SL, Burns J, Black DA, et al. Prevalence and impact of chronic musculoskeletal ankle disorders in the community. *Arch Phys Med Rehabil* 2012;**93**:1801–7.
- Hiller CE, Kilbreath SL, Refshauge KM. Chronic ankle instability: evolution of the model. *J Athl Train* 2011;**46**:133–41.
- Harkey M, McLeod MM, Terada M, Gribble PA, Pietrosimone BG. Quadratic association between corticomotor and spinal-reflexive excitability and self-reported disability in participants with chronic ankle instability. *J Sport Rehabil* 2016;**25**:137–45.
- Gribble PA, Delahunt E, Bleakley CM, Caulfield B, Docherty CL, Fong DT, et al. Selection criteria for patients with chronic ankle instability in controlled research: a position statement of the International Ankle Consortium. *J Athl Train* 2014;**49**:121–7.
- Delahunt E, Coughlan GF, Caulfield B, Nightingale EJ, Lin CW, Hiller CE. Inclusion criteria when investigating insufficiencies in chronic ankle instability. *Med Sci Sports Exerc* 2010;**42**:2106–21.
- Verhagen RA, de Keizer G, van Dijk CN. Long-term follow-up of inversion trauma of the ankle. *Arch Orthop Trauma Surg* 1995;**114**:92–6.
- van Rijn RM. What is the clinical course of acute ankle sprains? A systematic literature review. *Am J Med* 2008;**121**:324–31.
- Glazebrook M, Daniels T, Younger A, Foote CJ, Penner M, Wing K, et al. Comparison of health-related quality of life between patients with end-stage ankle and hip arthrosis. *J Bone Joint Surg Am* 2008;**90**:499–505.

21. Al Adal S, Pourkazemi F, Mackey M, Hiller CE. The prevalence of pain in people with chronic ankle instability: a systematic review. *J Athl Train* 2019;**54**:662–70.
22. Lohmander LS, Östenberg A, Englund M, Roos H. High prevalence of knee osteoarthritis, pain, and functional limitations in female soccer players twelve years after anterior cruciate ligament injury. *Arthritis Rheum* 2004;**50**:3145–52.
23. Waldén M, Häggglund M, Ekstrand J. Football injuries during European Championships 2004–2005. *Knee Surg Sports Traumatol Arthrosc* 2007;**15**:1155–62.
24. Falvey EC, Franklyn-Miller A, McCrory PR. The groin triangle: a patho-anatomical approach to the diagnosis of chronic groin pain in athletes. *Br J Sports Med* 2009;**43**:213–20.
25. Feldman DE, Shrier I, Rossignol M, Abenham L. Work is a risk factor for adolescent musculoskeletal pain. *J Occup Environ Med* 2002;**44**:956–61.
26. Braun BL. Effects of ankle sprain in a general clinic population 6 to 18 months after medical evaluation. *Arch Fam Med* 1999;**8**:143–8.
27. Okuda R, Kinoshita M, Morikawa J, Yasuda T, Abe M. Arthroscopic findings in chronic lateral ankle instability: do focal chondral lesions influence the results of ligament reconstruction? *Am J Sports Med* 2005;**33**:35–42.
28. Hintermann B, Boss A, Schäfer D. Arthroscopic findings in patients with chronic ankle instability. *Am J Sports Med* 2002;**30**:402–9.
29. Valderrabano V, Horisberger M, Russell I, Dougall H, Hintermann B. Etiology of ankle osteoarthritis. *Clin Orthop Relat Res* 2009;**467**:1800–6.
30. Gasson A, Jaggi A, Alexander S, Thacker M. Differences in reported severity of pain and the location of pain in patients with recurrent structural and non-structural shoulder instability. *Man Ther* 2016;**25**:e103. doi:10.1016/j.math.2016.05.182.
31. Boileau P, Zumstein M, Balg F, Penington S, Bicknell RT. The unstable painful shoulder (UPS) as a cause of pain from unrecognized anteroinferior instability in the young athlete. *J Shoulder Elbow Surg* 2011;**20**:98–106.
32. Sanchis-Alfonso V. *Anterior knee pain and patellar instability*. London: Springer London; 2011.
33. Hass CJ, Bishop MD, Doidge D, Wikstrom EA. Chronic ankle instability alters central organization of movement. *Am J Sports Med* 2010;**38**:829–34.
34. Gibson SJ, Farrell M. A review of age differences in the neurophysiology of nociception and the perceptual experience of pain. *Clin J Pain* 2004;**20**:227–39.
35. Washington LL, Gibson SJ, Helme RD. Age-related differences in the endogenous analgesic response to repeated cold water immersion in human volunteers. *Pain* 2000;**89**:89–96.
36. Hintermann B, Valderrabano V, Dereymaeker G, Dick W. The HINTEGRA ankle: rationale and short-term results of 122 consecutive ankles. *Clin Orthop Relat Res* 2004;**424**:57–68.
37. Valderrabano V, Hintermann B, Horisberger M, Fung TS. Ligamentous posttraumatic ankle osteoarthritis. *Am J Sports Med* 2006;**34**:612–20.
38. Sluka KA. *ProQuest. Mechanisms and management of pain for the physical therapist*. 2nd ed. Philadelphia, PA: Wolters Kluwer; 2016.
39. George SZ, Bialosky JE, Wittmer VT, Robinson ME. Sex differences in pain drawing area for individuals with chronic musculoskeletal pain. *J Orthop Sports Phys Ther* 2007;**37**:115–21.
40. Jensen MT, Petersen KL. Gender differences in pain and secondary hyperalgesia after heat/capsaicin sensitization in healthy volunteers. *J Pain* 2006;**7**:211–7.
41. Unruh AM. Gender variations in clinical pain experience. *Pain* 1996;**65**:123–67.
42. Bartley EJ, Fillingim RB. Sex differences in pain: a brief review of clinical and experimental findings. *Br J Anaesth* 2013;**111**:52–8.
43. Jeffrey SM. Sex differences in pain and pain inhibition: multiple explanations of a controversial phenomenon. *Nat Rev Neurosci* 2012;**13**:859–66.
44. Keogh E, Eccleston C. Sex differences in adolescent chronic pain and pain-related coping. *Pain* 2006;**123**:275–84.
45. Edwards RR, Dworkin RH, Sullivan MD, Turk DC, Wasan AD. The role of psychosocial processes in the development and maintenance of chronic pain. *J Pain* 2016;**17**(Suppl. 9):S70–92.
46. Elvery N, Jensen MP, Ehde DM, Day MA. Pain catastrophizing, mindfulness, and pain acceptance: what's the difference. *Clin J Pain* 2017;**33**:485–95.
47. Gioiosa L, Chen X, Watkins R, Klanfer N, Bryant CD, Evans CJ, et al. Sex chromosome complement affects nociception in tests of acute and chronic exposure to morphine in mice. *Horm Behav* 2008;**53**:124–30.