

# BMJ Open Risk factors and associated factors for calcaneal apophysitis (Sever's disease): a systematic review

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## ABSTRACT

**Objectives** The aim of this review was to identify the potential intrinsic and extrinsic risk factors (RFs), associated factors (AFs) and consequences of developing calcaneal apophysitis (CA).

**Design** Systematic review.

**Data sources** Cochrane Library, Embase, Medline Ovid, PubMed, Web of Science and Evidence, searched from inception to April 2021.

**Eligibility criteria** We included cohort, case-control and cross-sectional studies that were conducted in patients younger than 18 years who were exposed to RFs or who presented with factors associated with developing CA. Studies in languages other than English or Spanish were excluded.

**Data extraction and synthesis** Two reviewers worked independently to evaluate the risk of bias of included studies. The Newcastle-Ottawa Scale (adapted version) was used.

**Results** A total of 736 studies were identified and 11 observational studies fully met the inclusion criteria, including 1265 participants with a mean age of 10.72 years. Four studies identified extrinsic factors, 10 identified intrinsic factors and three identified both. The extrinsic and intrinsic RFs, AFs and consequences of CA include limitation of ankle dorsiflexion, foot alignment, stiffness and mobility of the midfoot, plantar pressures and ground reaction force, body mass index, age, gender, presence of other osteochondroses and practice of sport. The risk of bias varied, being either moderate or low.

**Conclusions** Regarding the factors and consequences associated with CA (Sever's disease), ankle dorsiflexion limitation is the most frequent intrinsic factor studied, followed by peak plantar pressures and foot malalignment. However, disagreements between the investigators of the included studies were found; in some cases, there is a lack of unanimity between different studies as to which factors are considered to be RFs, AFs and consequences.

**PROSPERO registration number** CRD42021246366.

## INTRODUCTION

Calcaneal apophysitis (CA) or Sever's disease is the most common cause of heel pain in children and young people, showing an incidence of 3.7 per 1000 patients.<sup>1 2</sup> It is a common musculoskeletal disease, representing between 2% and 16% of the consultations in

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This systematic review was registered on PROSPERO and is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses and Meta-analyses Of Observational Studies in Epidemiology reporting guideline checklists.
- ⇒ The Newcastle-Ottawa Scale (adapted version) was used to evaluate the risk of bias of included studies.
- ⇒ The main limitation of the review is the low number of included studies.

sports clinics<sup>3 4</sup> and 5.8%–22.7% of repetitive stress injuries in children.<sup>5–7</sup> The condition is most common in girls between 7 and 12 years of age and in boys between 8 and 15 years of age,<sup>8</sup> showing a peak in both genders between 10 and 12 years of age.<sup>9 10</sup>

CA was described by Dr Sever in 1912, due to sporadic continuous pain in the posterior area of the calcaneus bone in paediatric patients.<sup>11</sup> Histological studies define CA as inflammation or bone oedema due to a stress fracture in the secondary growth centre of the calcaneus, which is not related to necrosis.<sup>8</sup>

The inflammation is due to the traction forces from the triceps surae muscle on the CA, which is composed of hyaline cartilage.<sup>5 6 9</sup> The repetition of these traction forces, combined with the vertical ground reaction force on the calcaneus, generates bending forces on the medial side of the CA. Because the number of chondrocytes is increased in the CA during the development of children, the CA is not able to tolerate these bending forces.<sup>12</sup>

The gender incidence of this condition is controversial. A previous study by Orava and Virtanen<sup>13</sup> concluded that the CA incidence ratio was 10:1, being more common in boys than girls. However, Micheli and Ireland,<sup>14</sup> McKenzie *et al*<sup>5</sup> and Kvist and Heinonem<sup>9</sup> concluded that the ratio was 3:1, 2:1 and 1:1 in their respective studies.



CA is a unilateral condition in most cases,<sup>9 15</sup> which may be related to the dominant leg. However, it has also been described as a bilateral condition in some cases.<sup>5</sup>

The diagnosis of CA is mainly based on its signs and symptoms, but it can also be confirmed with complementary tests, such as X-ray imaging. The pain is mainly located in the posterior and plantar side of the CA<sup>9 16 17</sup> or in the Achilles tendon insertion.<sup>1 5</sup>

Various treatments have been described in the literature and the most frequently used include: stretching and lengthening of the triceps surae muscle, application of ice, restriction or limitation of physical activity, rest, topical non-steroidal anti-inflammatory drugs, taping, and the use of foot orthoses and heel pads.<sup>18–22</sup>

Among the causes of CA, a rapid period of maturation due to accelerated growth that causes muscle–tendon imbalances has been described. Muscle development is slower than bone development, which causes muscular tension.<sup>14 15</sup> Obesity is considered a cause of a valgus deformity of the knees and ankles, which increases the risk of CA.<sup>23 24</sup> The distribution of body weight between the right and left feet in children with CA is higher on the affected lower limb, maintaining the highest peaks of pressure in the feet.<sup>25</sup> Another cause is overuse due to repetitive impacts that generate repetitive micro-traumas, in movements such as jumping or running.<sup>5 9 26</sup> This factor can be worsened by footwear that is inadequate or without cushioning.<sup>1 23</sup> Some sports are associated with the disease, such as athletics, football, basketball, ballet and tennis,<sup>1 14 27</sup> as well as any running activity practised on hard surfaces.<sup>1</sup> The functional limitation of the dorsiflexion movement of the ankle joint, which can be due to a limitation of the triceps surae muscle or the hamstring muscles,<sup>14 25 28</sup> may cause the disease. Furthermore, 95% of children with CA present with biomechanical alterations.<sup>15 25</sup> Some authors have described the flat foot with valgus calcaneus as the most common alteration in children with CA.<sup>1</sup> However, other authors<sup>5</sup> conclude that 50% of the subjects presented a varus calcaneal deviation, which, in dynamic conditions, presents as a pronated foot. The two other main causes of CA that were identified in the literature were clubfoot<sup>1 29</sup> and pes cavus.<sup>29 30</sup>

Knowledge of the risk factors (RFs) related to CA helps to provide important information for the prevention and early treatment of this common pathology in the paediatric population. Therefore, the aim was to conduct a systematic review to identify potentially intrinsic and extrinsic RFs associated with developing CA, as well as the consequences of the condition, as described by the evidence.

## METHODS

The review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.<sup>31</sup> The systematic review protocol was registered at the International Prospective Register of Systematic Reviews (PROSPERO: CRD42021246366).

## Eligibility criteria

The included studies were conducted in accordance with the following PECOS statement (P=population; E=exposure; C=comparator; O=outcome; S=study type), which is based on the P=population; I=intervention; C=comparator; O=outcome statement<sup>32</sup>:

- ▶ P: patients under 18 years with CA.
- ▶ E: exposure to RFs, presenting with the associated factors (AFs) or suffering the consequences of CA.
- ▶ C: non-exposure to RFs presenting with the AFs or suffering the consequences of CA.
- ▶ O: identify the causes of RFs, AFs and consequences of developing CA, without considering the evolution time for exclusion.
- ▶ S: cohort, case–control and cross-sectional studies.

The review was restricted to the following types of studies: case reports, reviews, atlases and guides. No publication status restrictions or publication dates were imposed. Participants were not excluded by weight, height or ethnicity.

Exclusion criteria were as follows:

- ▶ Studies focused on treatments of CA, such as surgery, foot orthoses, stretching exercises, laser treatment, heel pads or kinesiotherapy.
- ▶ Studies focused on animals, fasciitis, ankle instability, Achilles tendinopathy, fractures, rheumatic diseases, cancer or Chopart osteochondrosis.
- ▶ Studies focused on areas other than the foot and ankle.
- ▶ Studies in languages other than English or Spanish.

## Information sources and search strategy

A previous scoping search was carried out in PROSPERO and the Cochrane Library to ensure that this aim had not been addressed by previous studies. JG-C and GG-N designed the search strategy and carried out the search from inception to October 2022 using optimised search strategies using the following databases: Cochrane Library, Embase, Medline Ovid, PubMed, Web of Science and Evidence search. A sensitive search strategy was performed on 21 October 2022 using relevant search terms that were developed from Medical Subject Headings (MeSH), collecting free-text terms (TIAB) and keywords generated from the subject headings (online supplemental appendix): “Osteochondritis”[Mesh], “Osteochondrosis”[Mesh], “Apophysitis” [TIAB], “Sever’s disease” [TIAB], “Calcaneus”(Mesh), “Calcaneus\*“[TIAB], “Humans” [Mesh], “Intrinsic factors”[Mesh], “Extrinsic factors”[Mesh]. Also, a manual search through the reference list of the included articles was performed.

## Selection process

All studies identified by the search strategy were screened using the eligibility criteria. The search was made by two independent reviewers (PN-G and JM-L) to determine whether each item met the requirements for inclusion. The final decision was made by a consensus, or when necessary, a third reviewer evaluated the text and decided

upon its inclusion or otherwise (JG-C). The inclusion and exclusion criteria were applied for selection or rejection. First, duplicates were removed. The second step involved the screening of titles and abstracts by two independent reviewers, and the next step was to perform screening based on the full text.

### Data collection process

The following information was extracted from each study independently by two reviewers: study details (first author, country and year of publication), type of study, sample size, mean age, percentage of boys and girls, and intrinsic and extrinsic factors related to CA. When necessary, the original authors were contacted to obtain further information. Due to the significant heterogeneity of the included studies, it was not possible to combine the studies in a meta-analysis, so the authors have limited themselves to performing a narrative synthesis of the results as a systematic review.

### Risk of bias in individual studies

Two reviewers worked independently to evaluate the risk of bias of included studies. To resolve cases in which the two reviewers' decisions differed, a third reviewer evaluated the text and decided upon its inclusion or otherwise. The Newcastle–Ottawa Scale (NOS) adapted version was used to evaluate observational studies. The modified version of NOS evaluates bias in terms of selection, performance, detection and information. These four domains are composed of seven items and each one is scored from 0 (high risk) to 3 (low risk). Studies with a score of 14–21 are considered to have a low risk of bias, with a score of 7–13 indicating moderate risk of bias and of 0–6 indicating a high risk of bias.<sup>32</sup>

### Patient and public involvement

None.

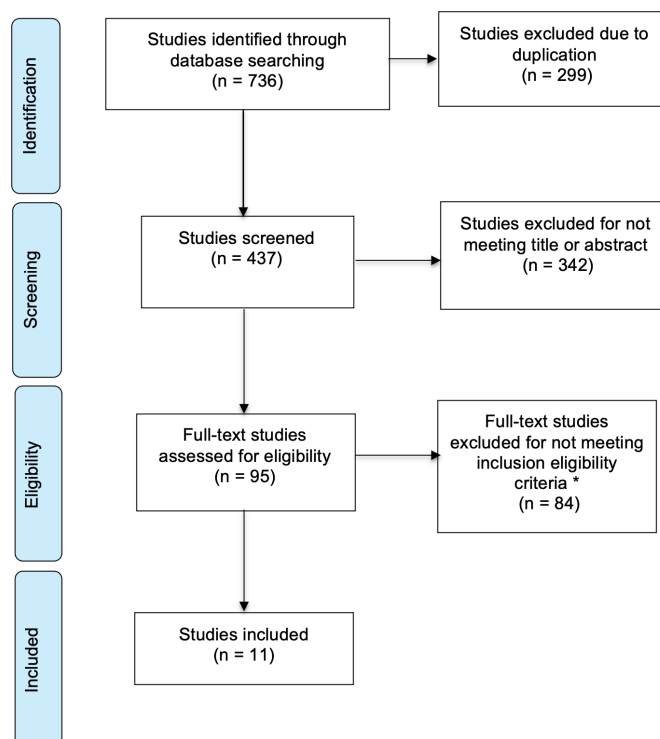
## RESULTS

A total of 736 studies were identified from the electronic databases and reduced to 437 after duplication was removed. These were screened by title and abstract, and 346 were excluded. Therefore, 91 full-text articles were assessed for eligibility. Eleven studies fully met the inclusion criteria and were the basis of our review (figure 1): two cohort studies, four case–control studies and five cross-sectional studies.

### Study characteristics

All selected studies were observational, including cross-sectional studies (n=5),<sup>8 9 15 26 33</sup> cohort studies (n=2)<sup>34 35</sup> and case–control studies (n=4).<sup>7 36–38</sup>

The sample size varied from n=14<sup>8</sup> to n=430<sup>35</sup> with the total sample size being n=1265, of which only 22.25% were female. The mean age of the whole sample was 10.72 years, but one study did not mention the participants' ages.<sup>8</sup>



**Figure 1** Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram. \*Studies focused on treatments of calcaneal apophysitis, such as surgery, foot orthoses, stretching exercises, laser treatment, heel pads or kinesiotherapy; studies focused on animals, fasciitis, ankle instability, Achilles tendinopathy, fractures, rheumatic diseases, cancer or Chopart osteochondrosis; studies focused on areas other than the foot and ankle; and studies in languages other than English or Spanish.

Six studies specified whether the CA was unilateral or bilateral,<sup>7 9 26 33 36 37</sup> being unilateral in the majority of cases.

Four studies<sup>8 9 35 38</sup> identified extrinsic factors, 10 studies identified intrinsic associations and three studies identified both.<sup>9 35 38</sup>

Regarding extrinsic factors, some authors concluded that greater frequency and intensity of activity leads to a higher risk of CA<sup>8 9</sup>; on the other hand, other authors state that the level of activity does not affect the risk,<sup>38</sup> and even low activity levels increase the risk of CA.<sup>35</sup>

Ankle dorsiflexion limitation was the most frequent intrinsic factor studied,<sup>7 15 26 33 37</sup> followed by peak plantar pressures<sup>7 37</sup> and foot malalignment.<sup>26 38</sup> These factors are presented in more detail in online supplemental table 1.

### Risk of bias

The risk of bias of the included studies varied, with 45.45% of the included studies<sup>8 9 15 34 36</sup> showing a moderate risk of bias and 54.54% of the included studies<sup>7 26 33 35 37 38</sup> showing a low risk of bias, as assessed using the NOS adapted version. The study by Scharfbillig *et al*<sup>38</sup> showed the best results using this scale. The risk of bias assessment of all included studies is presented in table 1.

**Table 1** Risk of bias assessment of included studies (Newcastle–Ottawa Scale, adapted version)

Study	Selection bias			Performance bias		Detection bias		Information bias		Total score
	A	B	C	D	E	F	G			
McSweeney <i>et al</i> <sup>36</sup>	1	2	1	2	3	2	2	13		
Martinelli <i>et al</i> <sup>35</sup>	2	3	2	2	3	1	2	15		
McSweeney <i>et al</i> <sup>33</sup>	1	2	1	2	3	3	2	14		
Rodríguez-Sanz <i>et al</i> <sup>37</sup>	2	3	2	2	3	2	2	16		
James <i>et al</i> <sup>26</sup>	2	3	1	1	2	2	3	14		
Becerro-de-Bengoa-Vallejo <i>et al</i> <sup>7</sup>	2	2	2	2	2	2	2	14		
Watanabe <i>et al</i> <sup>34</sup>	1	1	1	1	3	1	2	10		
Scharfbillig <i>et al</i> <sup>38</sup>	2	3	2	2	3	2	3	17		
Ogden <i>et al</i> <sup>8</sup>	1	1	1	0	2	1	2	8		
Alfaro Santafé <i>et al</i> <sup>15</sup>	2	2	1	1	2	2	2	12		
Kvist and Heinonem <sup>9</sup>	1	1	1	1	2	1	1	8		

A=Is the source population appropriate and representative of the population of interest?; B=Is the sample size adequate, and is there sufficient power to detect a meaningful difference in the outcome of interest?; C=Did the study identify and adjust for any variables or confounders that may influence the outcome?; D=Did the study use appropriate statistical analysis methods relative to the outcome of interest?; E=Are there little missing data, and did the study handle them accordingly?; F=Is the methodology of the outcome measurement explicitly stated, and is it appropriate?; G=Is there an objective assessment of the outcome of interest?<sup>46</sup>

## DISCUSSION

The objectives were to conduct a systematic review to identify potentially intrinsic and extrinsic RFs, AFs and consequences of developing CA, and to describe the evidence. The factors identified have generated great controversy in the literature, as since the first description of the disease in 1908,<sup>11</sup> there have been no sufficiently rigorous studies aiming to establish these factors.<sup>39</sup> The data from these studies were obtained through observations or from expert opinions, in terms of the characteristics, causes and treatment of CA.

According to the risk of bias analysis, only the following studies related to the topic are considered high-quality studies: Martinelli *et al*, Rodríguez-Sanz *et al* and Scharfbillig *et al*.<sup>35 37 38</sup> These studies presented a score above 15 points on the NOS, which is considered high quality. The rest of the included studies had a score between 7 and 15 points, which is considered acceptable quality. Therefore, due to the quality of the included studies, the results of the present study should be taken into consideration.

### Limitation of ankle dorsiflexion

The most frequent intrinsic AF for CA demonstrated in this systematic review was the limitation of ankle dorsiflexion. This has previously been shown in studies from Scharfbillig *et al*,<sup>38</sup> Becerro-de-Bengoa-Vallejo *et al*<sup>7</sup> and Alfaro Santafé *et al*.<sup>15</sup> However, the study of James *et al*<sup>26</sup> concluded that patients with CA presented a great range of movement of the ankle joint. The authors explained that the different results may be due to the heterogeneous methods that were employed to assess the range of movement. Furthermore, the rest of the foot joints compensate for the lack of movement during walking and in sports practice under load.

Alfaro Santafé *et al*<sup>15</sup> demonstrated the relationship between the results of the lunge test and the presence of CA, also rejecting the association with the Jack test. The stress exerted by the gastrocnemius and soleus muscles is a factor commonly reported as a limitation that reduces the range of motion. This agrees with accelerated bone growth, which is much faster than muscle development, causing an excessive increase in the stress of the traction forces and muscle–tendon imbalances. Therefore, CA is a result of stress forces.<sup>14 15 40</sup>

### Foot alignment

Alterations in foot alignment have been described as another extrinsic AF,<sup>26 38</sup> demonstrating that children with CA presented higher scores in the Foot Posture Index than asymptomatic children. This suggests that pronated feet present higher levels of stress on the fascia and Achilles tendon.

### Stiffness and mobility of the midfoot

Children with and without CA presented similar results in terms of stiffness and mobility of the midfoot assessed by the Foot Mobility Magnitude<sup>41</sup> in load bearing conditions ( $p=0.045$ ). In this AF, the authors did not find statistically significant differences in midfoot mobility between children with and without CA.<sup>33</sup>

### Plantar pressures and ground reaction force

It is necessary to highlight the maximum plantar pressures as one of the consequences of the condition described in this systematic review; however, the conclusions of previous studies disagree.<sup>7 36</sup> Statistically significant differences in maximum plantar pressures in different areas of the feet while running or walking were not found between children with and

without CA. These results may be explained by the small sample size (n=28), which may not be sufficient to detect differences in the plantar pressures. Becerrode-Bengoa-Vallejo *et al*<sup>7</sup> included 56 participants in their study and concluded that plantar pressures were statistically significantly greater in children with CA. However, it was not possible to determine whether high plantar pressures are an RF for CA, or whether they are a consequence of the disease, agreeing with a previous study by the same author<sup>25</sup> and the study by James *et al*.<sup>42</sup>

The study from McSweeney *et al*<sup>43</sup> concluded that vertical ground forces were not an RF for CA. These results may be due to the relationship between CA and an increase in tension in the calf musculature.<sup>14 15</sup>

### Body mass index

Body mass index (BMI) was not an RF in the studies of Martinelli *et al*<sup>35</sup> and Scharfbillig *et al*,<sup>38</sup> with no statistically significant differences found between the groups. However, the study by James *et al*<sup>26</sup> concluded that children with CA present a higher BMI in comparison with healthy children, probably due to the intensity of physical activity. This conclusion agrees with previous studies, which demonstrated that higher BMI, weight and height are AFs for CA.<sup>18</sup>

### Age

The age of children from all included studies ranged from 6 to 15 years (as an RF). Some studies<sup>9 35 44</sup> concluded that CA appeared earlier in girls (11 years) than in boys (12 years).

### Gender

Previous studies have generated disagreements in terms of the gender distribution of CA<sup>5 9 13 14</sup> as an AF, but statistically significant differences were not found in this systematic review. The study of Ceylan and Caypinar<sup>44</sup> included 20 000 participants, most of them boys. The gender distribution may be influenced by sport and sports practice habits among boys and girls.<sup>9 44</sup>

### Osgood-Schlatter disease

Osgood-Schlatter disease leads to the appearance of CA according to the study of Watanabe *et al*.<sup>34</sup> The causes associated with this disease are similar to the AFs described in this systematic review: age of onset, joint limitation, muscle imbalance, pronated feet and microtrauma, among others. In addition, a high level of sports specialisation and overtraining contribute to its appearance.<sup>45</sup>

### Sport

The studies by Odgen *et al*<sup>8</sup> and Kvist and Heinonen<sup>9</sup> included high frequency and intensity of activity as an AF. However, Scharfbillig *et al*<sup>38</sup> concluded the opposite.

Martinelli *et al*<sup>35</sup> concluded that fewer training sessions per week and a lower activity level per session (<60 min) represent RF for CA. This may be explained by the fact that patients who are less trained and active

may have a low pain threshold. However, differences between the type of sport and the kinds of surfaces were not found.

### Strengths and limitations

One of the strengths of this review is the use of a protocol registered on PROSPERO. Also, the present review followed the current items of the PRISMA checklist. Finally, the use of specific checklists to evaluate the risk of bias (the NOS adapted version) is another strength of the present study.

To the best of our knowledge, this is the first systematic review that addresses the RFs, AFs and consequences of CA, including intrinsic and extrinsic factors. Previously, one literature review was published, but from a general point of view of the disease.<sup>39</sup>

The main limitation of the present systematic review is the number of included studies. Due to the nature of the review, only studies focused on the RFs, AFs and consequences of CA were included. All included studies were observational. The sample sizes were very heterogeneous and sometimes small, from 14 to 430 participants. In total, 1265 participants were included in the systematic review. Most of them were boys and three of the included studies only had male participants.<sup>7 15 37</sup>

### Clinical implications

Precisely determining the intrinsic and extrinsic RFs, AFs and consequences of CA will allow clinicians to identify the disease early as well as prevent and treat it in its early stages.

### Future research

Due to the diversity within the included studies, a larger number of more rigorous, prospective and cohort-type studies are needed. Studies must present an accurate methodology, including larger and more homogeneous sample sizes, in terms of age and gender, low risk of bias and uniform diagnostic criteria.

### CONCLUSIONS

Regarding the factors and consequences associated with CA (Sever's disease), ankle dorsiflexion limitation is the most frequent intrinsic factor studied, followed by peak plantar pressures and foot malalignment. However, disagreements between investigators of the included studies were found; in some cases, there is a lack of unanimity between different studies as to which factors are considered to be RFs, AFs and consequences. Higher-quality studies are necessary, with appropriate designs and adequate sample sizes.

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**Contributors** PN-G and LR-P contributed to study conception and design and drafted the review protocol. JG-C and GG-N designed the search strategy and carried out the search in the different databases and collected data. PN-G and JM-L independently carried out the review selection process. JG-C resolved any disagreement in the record selection process. MR-M and GG-N extracted data from the included records and contributed to data interpretation. LR-P assessed risk of bias and level of evidence and critically reviewed the manuscript for important intellectual content. LR-P did thorough proofreading of the whole manuscript,

including detecting and correcting any spelling mistakes and errors in the English grammar. PN-G is responsible for the overall content as the guarantor. All authors drafted the initial manuscript, and have read, contributed to and approved the final version of the manuscript.

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