

# The prognosis of ankle fractures: a systematic review

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- The aim of this study was to update the scientific evidence for ankle fracture prognosis by addressing radiographic osteoarthritis, time course and prognostic factors.
- A systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Studies were included if they were randomized controlled trials, controlled trials or observational studies, including case series and case-control studies investigating radiologically confirmed osteoarthritis in adults with a classified ankle fracture, treated with or without surgery, with a minimum follow-up of 1 year. Also included were studies examining prognostic factors predicting radiologically confirmed osteoarthritis. Tibial plafond and talus fractures were excluded.
- Thirty-four studies were included examining 3447 patients. Extracted data included study type, inclusion and exclusion criteria, age, number of patients, number of fractures according to the author-reported classification method, radiological osteoarthritis, follow-up period, prognostic factors, and treatment.
- Severe heterogeneity was visible in the analyses ( $I^2 > 90\%$ ), reflecting clinical heterogeneity possibly arising from the presence of osteoarthritis at baseline, the classifications used for the fractures and for osteoarthritis.
- The incidence of osteoarthritis was 25% (95% CI: 18–32) and 34% (95% CI: 23–45) for more severe fractures with involvement of the posterior malleolus.
- The severity of the trauma, as reflected by the fracture classification, was the most important prognostic factor for the development of radiographic osteoarthritis, but there is also a risk with simpler injuries.
- The period within which osteoarthritis develops or becomes symptomatic with an indication for treatment could not be specified.

## Keywords

- ▶ ankle fracture
- ▶ osteoarthritis
- ▶ prognosis

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## Introduction

Risks for the future are a source of concern for any trauma patient and are included in the settlement of personal injury claims. In the case of ankle fractures, this mainly concerns the risk of osteoarthritis and the resulting treatments in the years after the injury. Medical advisers and independent experts often consult *Medicolegal Reporting in Orthopedic Trauma* by Foy & Fagg (1). In this reference text, the incidence of osteoarthritis after ankle fractures is determined at 20–40%, depending on the extent of the fracture. In addition, it is stated that medical assessments are preferably postponed until 18–24 months after the trauma: if osteoarthritis starts to develop, it should already be visible radiologically. The scientific evidence for this statement is however only based on older publications by Willenegger (1961) and Lindsjø (1981) which allegedly found that most osteoarthritis occurs in

the first 12–18 months (2, 3). In fact, the last author found no (statistical) difference in the prevalence of osteoarthritis in 161 patients between their examination at 18 months and at 4 years since the accident. Furthermore, Foy & Fagg (1) refer to a study by Horisberger *et al.* (2009) who found a latent period between accident and end-stage osteoarthritis (arthrodesis or prosthesis) of 1–52 years (4). Because of this confusing lack of clear and recent evidence for the prognosis of ankle fractures, we performed a systematic review addressing the following questions:

1. What is the incidence of radiographic osteoarthritis in adults after an ankle fracture?
2. How long does the risk of radiological osteoarthritis persist since the accident?
3. Which prognostic factors are related to the development of radiological osteoarthritis after an ankle fracture?

## Methods

This report has been prepared in accordance with the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA) (5). The protocol of this systematic review was prospectively registered in the International Prospective Registry of Systematic Reviews (PROSPERO) under number CRD42021255718.

### Selection criteria

Studies were included if they were randomized controlled trials, controlled trials or observational studies, including case series and case-control studies investigating radiologically confirmed osteoarthritis in adults with an ankle fracture. All types of fractures were included, except for pilon fractures of the tibial plafond and talus fractures. The study had to describe which fracture was involved by a classification such as Weber, Lauge Hansen and AO/OTA (6, 7, 8) or otherwise radiological features of the fracture from which a classification could be derived. Also included were studies examining prognostic factors for radiologically confirmed osteoarthritis.

Other criteria for inclusion were a minimum mean follow-up of 1 year, osteoarthritis had to be radiologically confirmed and assessed by a systematic method, such as Van Dijk *et al.* or Kellgren and Lawrence (9, 10). The treatment the patient received (surgical or conservative) did not affect inclusion.

Case reports or studies on cadavers were excluded. Also excluded were studies with a combination of fractures including pilon fractures, the results of which were not reported separately.

### Outcome measures

Osteoarthritis has been defined as the radiological narrowing of the joint space. The results were derived from the method used in the article.

### Search method

Cochrane Central Register of Controlled Trials (CENTRAL), Medline, Embase and Cumulative Index to Nursing & Allied Health Literature (CINAHL) were searched on August 16, 2020. The search strategy for the topics of ankle fractures and osteoarthritis consisted of a combination of free text words, so-called keywords and MeSH terms combined with a filter for systematic review, randomized controlled trials and observational studies. The systematic review search was added to rule out the possibility of previous research similar to ours.

Study selection was performed by two investigators (B S, A v E) independently of each other. The selection was made in Covidence (9). Title and summary were first assessed. Potentially relevant references were searched for

as a full article and reviewed again. Discrepancies were discussed at consensus meetings.

### Data extraction

Predefined data were extracted by a first investigator (A v E) in Covidence and checked by a second investigator (B S). The following descriptive data were collected: study type, inclusion and exclusion criteria, age, number of patients, follow-up period, prognostic factors, treatment and number of fractures according to the author-reported classification method.

Different fracture classifications were used in the selected studies, most often the Weber classification (6). To facilitate analysis, we translated other fracture classifications such as Lauge Hansen (7) and AO/OTA (8) as much as possible to a Weber classification. Adjustments were made to the Weber B and Weber C categories to reflect the involvement of the posterior malleolus, and thus the severity of the trauma. This resulted in the Weber A, Weber B, Weber B+, Weber C and Weber C+ categories (+ meaning posterior malleolar fracture). For each study, the number of patients with radiological osteoarthritis (i.e. joint space narrowing) was reported.

For the third research question, prognostic factors were extracted that were significantly associated with radiological osteoarthritis.

### Risk of bias

Assessment of the risk of bias is an integral part of any systematic review. However, it was decided not to formally assess the risk of bias per study in this review. The instrument described by Hoy *et al.* 2012 is suitable for systematic reviews examining incidence data (10). Items from this instrument are either not applicable to this review or are part of the selection criteria that results in the item being scored as low in each study (Table 1).

### Statistical analysis

The incidence of osteoarthritis was assessed for every study (number of patients with osteoarthritis/total study population). A meta-analysis of incidence data of all fractures was performed according to a random effects model. Heterogeneity was examined by visual inspection of the forest plots and calculated with inconsistency statistics ( $I^2$ ).

The relationship between incidence and mean follow-up duration was investigated using meta-regression. When no mean follow-up period was indicated in the study, but a range, the arithmetic mean was arbitrarily taken. When only the median was presented, this was used as the mean follow-up.

In addition to the meta-regression, subgroup analyses were performed in which studies with a follow-up of up to

**Table 1** Risk of bias instrument according to Hoy *et al.* 2012 (10).

Item	Explanation
1. Was the study target population a good representation of the national population in relation to relevant variables?	Not applicable
2. Was the sample a true or accurate representation of the target population?	Not applicable
3. Was some form of random selection used to select the sample OR was a count performed?	Not applicable
4. Was the probability of non-response bias minimal?	Not applicable
5. Was the data collected directly from the subjects (as opposed to a proxy)?	Part of selection criteria
6. Was an acceptable case definition used in the study?	Part of selection criteria
7. Was the research instrument that measured the parameter in question valid and reliable?	Part of selection criteria
8. Was the same data collection method used for all subjects?	Part of selection criteria
9. Was the length of the shortest prevalence period appropriate for the parameter in question?	Not applicable
10. Were the numerator(s) and denominator(s) for the parameter of interest appropriate?	Part of selection criteria

2 years were analyzed separately from the studies with a follow-up longer than 2 years.

A meta-regression would also have been performed to investigate the prognosis per fracture type. However, insufficient data were available to perform an analysis per Weber classification. Therefore, Weber A, B and/or C fractures not involving the posterior malleolus were combined in comparison with fractures involving the posterior malleolus; Weber B+ and C+. A subgroup analysis was also performed for this. Finally, a subgroup analysis was performed, in which the fracture types were compared depending on the follow-up. All analyses were performed in Stata (11). No sensitivity analysis was planned.

*Quality of evidence*

The evidence of incidence data and prognostic factors (follow-up and fracture type) was examined according to Grading Recommendations Assessment, Development and Evaluation (GRADE) methodology (12).

**Results**

*Study selection*

The search identified 2224 references, of which 129 were assessed as a full-text article and 34 studies were included examining 3447 patients (Fig. 1) (13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47). The reasons for exclusion of 95 studies have been recorded. Most studies have been excluded because osteoarthritis had not been systematically studied (wrong outcome).

*Characteristics of the included studies*

The included studies were published between 1975 and 2020. Three studies had a randomized controlled study design. Other studies had an observational retrospective design. Follow-up ranged from 12 to 348 months with a mean of 81 (s.d. 75) months (Table 2).

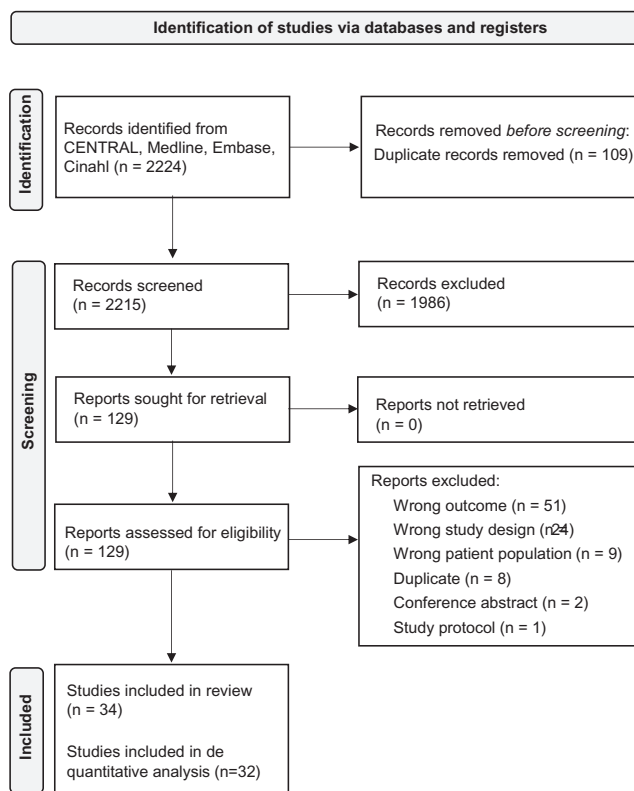
*Question 1. Incidence of osteoarthritis after an ankle fracture*

In a meta-analysis of all fractures from the selected studies regardless of the fracture type, the incidence of osteoarthritis was 25% (95% CI: 18–32) (Table 3).

The weight of evidence was lowered by two levels due to the severe heterogeneity and came out as low. Heterogeneity could not be sufficiently reduced by adjusting for follow-up and type of fracture. The GRADE profile is described in Table 4.

*Question 2. Follow-up moment*

When the results are sorted by follow-up time, both studies with a short and long follow-up showed a high incidence of osteoarthritis (Fig. 2). A regression analysis between the incidence of osteoarthritis and follow-up in months gave a nonstatistically significant regression coefficient of -0.0002 (95% CI: -0.0012 to 0.0; Pvalue=0.66).



**Figure 1** Flowchart of included studies.

**Table 2** Characteristics of the included studies.

Reference	Country	Follow-up* in months <sup>‡</sup>	Fracture classification according to Weber	Patients, n	Method to measure osteoarthritis	Osteoarthritis patients, n (%)
Abarquero-Diezhandino <i>et al.</i> (18)	Spain	33 (12–73) mo	Weber B+ and C+	45	Takakura Van Dijk	8 (18) 7 (16)
Bauer <i>et al.</i> (20)	Sweden	29 years	Weber A Weber B Weber C	15 61 11	Magnusson Magnusson Magnusson	1 (7) 4 (7) 1 (9)
Beris <i>et al.</i> (17)	Greece	8.6 (2–12) years	Weber B+ and C+ Weber B and C	56 64	Magnusson Unspecified*	20 (36) 5 (8)
Bois <i>et al.</i> (19)	Canada	9.4 years	Weber B+ and C+ Weber B+ and C+	66 17	Unspecified Kellgren and Lawrence	12 (18) 8 (67)
Day <i>et al.</i> (21)	Australia	10–14	Weber B, C, B+ and C+ Isolated posterior malleolus fracture	153 23	Philips Unspecified	19 (76) 1 (5)
Donken <i>et al.</i> (16)	Netherlands	20 (17–24) years <sup>†</sup>	Weber B+ and C+ Weber A, C, B+ and C+ Weber B, C, B+ and C+ Weber B, C, B+ and C+	131 145 56 82	Kellgren and Lawrence Magnusson Modified Knirk and Jupiter Magnusson	25 (19) 22 (28) 3 (7) 4 (5)
van Hooff <i>et al.</i> (45)	Netherlands	6.9 (2.5–15.9) y	Weber B+ and C+	130	Magnusson	23 (26)
Federici <i>et al.</i> (39)	Italy	6.2 years	Weber A, C, B+ and C+	61	Kellgren and Lawrence	16 (28)
Heim <i>et al.</i> (35)	Switzerland	7.3 (3.9–10.9) years	Weber B, C, B+ and C+	48	Kellgren and Lawrence	3 (6)
Hoelsbrenken <i>et al.</i> (36)	Norway	44 (24–72) mo; 41 (24–67) months	Weber B, C, B+ and C+	117	Takakura	17 (35)
Hoiness <i>et al.</i> (14)	Norway	3.7 ± 0.6 years (2.8–5.2)	Weber A, B, C, B+ and C+	7	Van Dijk	9 (18)
Kohake <i>et al.</i> (38)	Germany	6.6 (2–12) years	Weber B and B+	4	Unspecified	6 (86)
Kortekangas <i>et al.</i> (43)	Finland	4 years	Weber B and B+	14	Unspecified	1 (25)
Lambers <i>et al.</i> (40)	Netherlands	21 (9–35) years	Weber C and C+	7	Unspecified	8 (57)
Lange <i>et al.</i> (41)	Germany	2–9 years	Unknown Weber A Weber B Weber C	66 26 229	Unspecified Unspecified Unspecified Unspecified	5 (71) 4 (15) 27 (12) 22 (33)
Lindsjö (22)	Sweden	2–6 years	Weber B+ and C+ Weber B and B+ Weber C and C+	24 66 102	Unspecified Unspecified Kellgren and Lawrence	6 (86) 1 (25) 56 (55)
Lübbecke <i>et al.</i> (13)	Switzerland	12–22 years	Weber A, B, C, B+ and C+ Weber B, C, B+ and C+	48	Kellgren and Lawrence	1 (2)
May <i>et al.</i> (42)	Turkey	24.7 ± 12.0; 24.6 ± 9.1	Weber B, C, B+ and C+	48	Kellgren and Lawrence	23 (22)
McDaniel & Wilson (44)	United States	42 (12–180) months	Weber B+ and C+	51	Unspecified	32 (63)
Meijer <i>et al.</i> (33)	Netherlands	12.5–39.4 years	Weber A, B, C, B+ and C+	104	Van Dijk	23 (22)
Olerud & Molander (15)	Sweden	18–54 months	Weber B+ and C+	127	Unspecified	41 (32)
Regan <i>et al.</i> (34)	United States	11.6 (8.4–14.6) years	Weber B+ and C+ Weber A, B, C, B+ and C+	141	Van Dijk	26 (32)
Shih <i>et al.</i> (29)	Taiwan	1 year	Weber B+ and C+	72	Modified Kellgren–Lawrence	42 (58)
Stadler <i>et al.</i> (26)	Switzerland	3–4 years	Weber A, B, C, B+ and C+	216	Unspecified	75 (45)
Stufkens <i>et al.</i> (46)	Switzerland	12.9 years	Weber A, B, C, B+ and C+	109	AOFAS score	43 (39)
Sukur <i>et al.</i> (28)	Turkey	17.1 (12–24) months	Weber B+ and C+	14	Van Dijk	4 (29)
Tosun <i>et al.</i> (23)	Turkey	15 (12–51) months	Weber B+ and C+	64	Van Dijk	16 (33)
Veen & Zuurmond (31)	Netherlands	>6.5 years	Weber B, C, B+ and C+	59	Van Dijk	10 (17)
Verhaeg <i>et al.</i> (24)	Netherlands	9.6 (5–17) years	Weber A, B, C Weber B+ and C+	164 79	AOS AOS	5 (3) 13 (16)
Verhaeg <i>et al.</i> (37)	Netherlands	6.3 (2.4–15.9) years	Weber B+ and C+	327	Domic	26 (16)
Weigelt <i>et al.</i> (32)	Switzerland	7.9 (3.1–12.3) years	Weber B+ and C+	32	Van Dijk	18 (56)
Xu <i>et al.</i> (30)	China	55.7 (2.4–109) months	Weber A, B, C, B+ and C+	235	Van Dyk	6 (3)
Zhou <i>et al.</i> (27)	China	32.75 (24–44) months	Weber B+ and C+	34	Unspecified	0 (3)
Ziadek <i>et al.</i> (25)	Czech Republic	1 year	Weber A, B, C, B+ and C+	38	Kellgren and Lawrence	11 (29)

\*Unspecified, authors focused on joint space narrowing but did not refer to a formal classification; †value is median; ‡average value as indicated in study; †values as used in the analysis.

**Table 3** Results of the meta-analyses on the incidence of radiological osteoarthritis.

	% Osteoarthritis	95% CI	I <sup>2</sup>	Number of studies included in analysis
All fractures	25	18–32	94%	32*
Weber ABC	13	3–28	90%	5
Weber B+C+	34	23–45	92%	15

\*The number of included studies in the ‘all fractures’ category exceeds the sum of Weber ABC and Weber B+C+ because for this analysis we also included fractures that were not categorized in the original study.

This means that no relationship could be demonstrated between the incidence of osteoarthritis and the duration of follow-up. Therefore, a subgroup analysis did not seem useful.

### Question 3. Prognostic factors

There was insufficient data to perform separate subgroup analyses for Weber A, Weber B and Weber C fractures only. Subgroup analyses indicated that the incidence of osteoarthritis for Weber B+C+ was higher compared to Weber ABC without posterior malleolus involvement (Table 3). However, a regression analysis did not confirm a statistically significant relationship ( $\beta=0.18$ ; 95% CI:  $-0.06$  to  $0.42$ ;  $P=0.14$ ).

In the studies selected by us, insufficient homogeneous data were available for a (multiple) regression analysis of prognostic factors for the development of radiological osteoarthritis. In some of the studies, however, the authors had done their own research (Table 5).

## Discussion

Our research focused on three aspects of post-traumatic radiographic ankle osteoarthritis, namely incidence, time course and prognostic factors.

The incidence of osteoarthritis defined as joint space narrowing was 25% (95% CI: 18–32) for all fractures and 34% (95% CI: 23–45) for more severe fractures. Thus,

**Table 4** Quality of the evidence: GRADE Evidence profile. Incidence of radiologically confirmed osteoarthritis (follow up: range 12–348 months).

Certainty assessment	
Participants, <i>n</i>	2624
Studies, <i>n</i>	32
Risk of bias	Not serious
Inconsistency	Very serious <sup>a</sup>
Circumstantial evidence	Not serious
Inaccuracy	Not serious
Publication bias	Not found
Overall certainty of evidence	⊕⊕○○: Low
Summary results	
Number of events, % (95% CI)	25 (18–32)

<sup>a</sup>There was a very high degree of heterogeneity both clinically and statistically ( $I^2 > 90\%$ ).

trauma severity was associated with a higher incidence of radiographic osteoarthritis, which is not unexpected based on the pathogenesis, and is consistent with the prognostic factors found in some of our selected studies. However, osteoarthritis after a simpler ankle fracture cannot be ruled out. Stufkens *et al.* (2010) (46) pointed out the importance of osteochondral injuries such as can occur in simple Weber A fracture. These are usually not visible on the accident radiographs but are visible with arthroscopy, and in his research, they formed an independent predictive factor for the development of post-traumatic osteoarthritis.

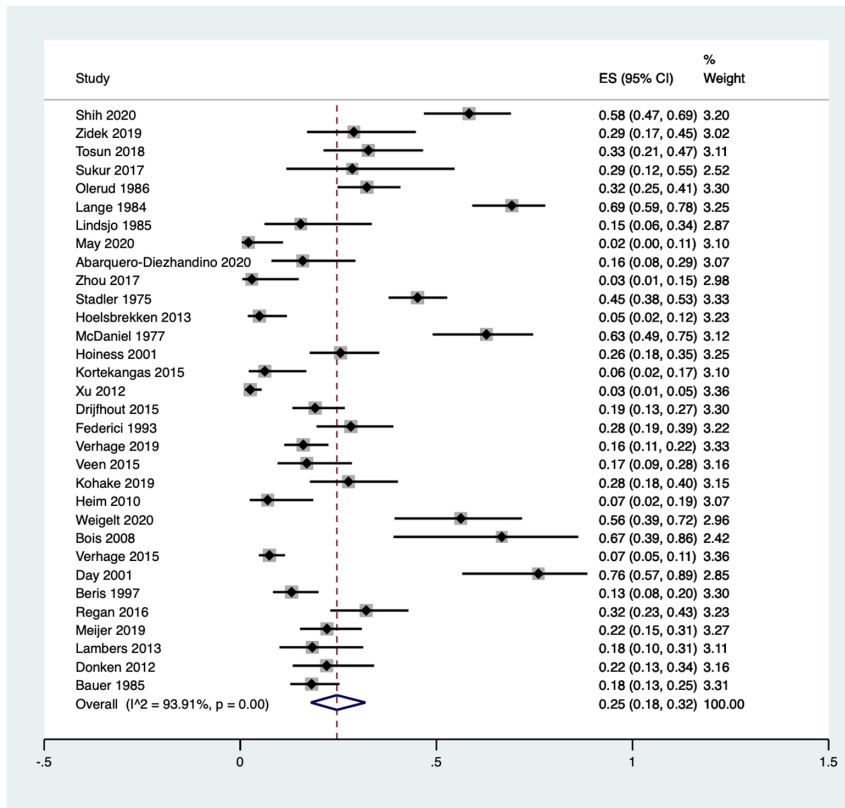
The strength of our study is that it is the first comprehensive systematic review of the incidence of post-traumatic radiologically confirmed ankle osteoarthritis.

However, the study also has several limitations. An important part of the current research was the classification of ankle fractures. Different fracture classifications were used in the selected studies. The interobserver variation in these classifications is considerable. Fonseca *et al.* (2018) (48) found a Kappa index of only 0.49 for the Danis–Weber classification, 0.32 for Lauge-Hansen and 0.38 for AO/OTA. An originally incorrect classified fracture might also incorrectly be classified in our translation to a Weber classification.

Various well-known and less common methods for staging radiological osteoarthritis were used in our selected studies. They lack consensus regarding the different radiological characteristics of osteoarthritis. For example, subchondral sclerosis is considered ‘normal’ in Van Dijk’s classification (49), while according to Kellgren and Lawrence (50), this is classified as grade III osteoarthritis. In addition, low-to-moderate interobserver agreements have been found for the most used classifications of Van Dijk, Takakura and Kellgren and Lawrence (51, 52). Therefore, we have chosen radiographic joint space narrowing as the most uniform and useful outcome parameter in our study. But even this parameter could have been dependent on the technique of the radiological examination: in most studies, no details are given about weight-bearing or not, and certainly before 2000 it was not common to take weight-bearing radiographs.

Two studies reported pre-existing osteoarthritis on accident radiographs (29, 43). We have corrected for this. The question remains, of course, whether there was actually no pre-existing osteoarthritis in all those studies in which this was not reported.

An important part in the settlement of the medical aspects of personal injury claims is the prognosis: how long does the risk of developing radiological osteoarthritis and its consequences persist. Our study could not confirm the position of Foy & Fagg that possible post-traumatic osteoarthritis becomes visible within 2 years (1). This position is only based on the thesis of Lindsjø (1981)



**Figure 2**

Forest plot of incidence of radiological osteoarthritis sorted from short follow-up (top) to long follow-up (bottom).

who found no statistically significant difference in the prevalence of radiological osteoarthritis between the study after 18 months (20.5%) and after 4 years (25.5%) since the accident (3). We have not been able to find a comparable study in the past 40 years. The number of studies with a follow-up of 2 years or less in our review was found to be limited to 4, and in addition, exceptionally high incidences were reported. There was even a study with 58% joint space narrowing after 12 months (29). That is unlikely and must be related to the radiological assessment.

Osteoarthritis can lead to complaints and medical treatment. Lübbeke *et al.* (2012) (13) found based on a hospital registry with a clinical and radiological follow-up of 12–22 years postoperatively that the time since the

accident was a continuous risk factor for the development of symptomatic advanced radiological (Kellgren and Lawrence grades 3 and 4) osteoarthritis; longer follow-up was thus associated with more severe osteoarthritis. Ankle osteoarthritis can lead to an end-stage with an indication for an arthrodesis or prosthesis. Papa and Meyerson (1992) (53) reported a mean time between trauma and ankle arthrodesis of 6 years (range: 1–24 years). Horisberger *et al.* (2009) (4) found a latent period between accident and end-stage osteoarthritis (arthrodesis or prosthesis) of 21 years on average (range: 1–52 years) with negative prognostic factors including a more severe fracture type (in their study also pilon fractures), postoperative complications and older age. So, ankle fractures can

**Table 5** Overview of prognostic factors mentioned by the authors in the study.

Reference	Prognostic factor
Abarquero-Diezhandino <i>et al.</i> (18)	Malleolus posterior fracture
Beris <i>et al.</i> (17)	Bi/trimalleolar, insufficient posterior malleolus reposition
Heim <i>et al.</i> (35)	Malleolus posterior fracture, cartilage injury
Lindsjø (22)	Sex (F), fracture type (posterior malleolus), reposition
McDaniel & Wilson (44)	Unrepaired posterior malleolus fracture > 25%
Regan <i>et al.</i> (34)	Luxation fracture after trauma
Verhage <i>et al.</i> (24)	Trimalleolar fracture (especially with medial malleolus fracture)
Verhage <i>et al.</i> (37)	Age, insufficient reposition of posterior malleolus fracture
Lübbeke <i>et al.</i> (13)	Age > 30 years, BMI, medial malleolus fracture, Weber C, time since trauma
Stufkens <i>et al.</i> (46)	Osteochondral lesions

have long-term consequences. Unfortunately, our study was unable to estimate the time at which radiological osteoarthritis develops after an ankle fracture. The data were insufficiently homogeneous to perform a regression analysis to establish a relationship between the onset of radiological osteoarthritis and the follow-up period since injury. This also implies that there is no time limit for insurers for the reservations they wish to make during the settlement procedure in injury claims for the development of osteoarthritis. If an insurance reservation applies to any treatment as a result of the ankle fracture, the reservation should be lifelong.

Very severe heterogeneity was visible in the analyses ( $I^2 > 90\%$ ). This probably reflects clinical heterogeneity arising from the possible presence of osteoarthritis at baseline, the classifications used for the fractures and for osteoarthritis. As mentioned earlier, there was insufficient data to perform the analysis in more homogeneous subgroups. The usefulness of systematic reviews and meta-analyses of observational studies that are based on different study populations, different data collection procedures, different statistical analysis strategies, different underlying assumptions and with bias adjustments for different sets of confounding factors has been debated (54).

## Conclusions

- One in four ankle fractures is followed by radiological osteoarthritis, and after more severe fractures even one in three.
- The severity of the trauma, as reflected by the fracture classification, is the most important prognostic factor for the development of radiographic osteoarthritis, but there is also a risk with simpler injuries.
- The period within which osteoarthritis develops or becomes symptomatic with an indication for treatment cannot be specified.

### ICMJE Conflict of Interest Statement

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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### Author contribution statement

Both authors were equally involved in all parts of the study.

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