Retrograde tibiotalocalcaneal nailing for the treatment of acute ankle fractures in the elderly: a systematic review and meta-analysis

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• Introduction: Fragility ankle fractures are traditionally managed conservatively or with open reduction internal fixation. Tibiotalocalcaneal (TTC) nailing is an alternative option for the geriatric patient. This meta-analysis provides the most detailed analysis of TTC nailing for fragility ankle fractures.

• Methods: A systematic search was performed on MEDLINE, EMBASE, Cochrane Library, and Web of Science, identifying 14 studies for inclusion. Studies including patients with a fragility ankle fracture, defined according to NICE guidelines as a low-energy fracture obtained following a fall from standing height or less, that were treated with TTC nail were included. Patients with a previous fracture of the ipsilateral limb, fibular nails, and pathological fractures were excluded. This review was registered in PROSPERO (ID: CRD42021258893).

• Results: A total of 312 ankle fractures were included. The mean age was 77.3 years old. In this study, 26.9% were male, and 41.9% were diabetics. The pooled proportion of superficial infection was 10% (95% CI: 0.06–0.16), deep infection 8% (95% CI: 0.06–0.11), implant failure 11% (95% CI: 0.07–0.15), malunion 11% (95% CI: 0.06–0.18), and all-cause mortality 27% (95% CI: 0.20–0.34). The pooled mean post-operative Olerud–Molander ankle score was 54.07 (95% CI: 48.98–59.16). Egger’s test ($P=0.56$) showed no significant publication bias.

• Conclusion: TTC nailing is an adequate alternative option for fragility ankle fractures. However, current evidence includes mainly case series with inconsistent post-operative rehabilitation protocols. Prospective randomised control trials with long follow-up times and large cohort sizes are needed to guide the use of TTC nailing for ankle fractures.

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Introduction

After the hip and distal radius, ankle fragility fractures (FFs) are the third most common type of fracture in the geriatric population, with an incidence of 184 cases per 100,000 population in the elderly per year (1). Despite occurring following low-energy injuries, ankle FFs lead to disproportionately high morbidity levels (2).

The management of ankle FFs poses specific challenges in the geriatric patient. In addition to being inherently unstable, ankle FFs occur in osteopenic bone, and the fracture-dislocation leads to significant soft tissue stripping (3). Conservative and surgical management options have both been utilised. Compared to surgery, closed contact casting has a reduced risk of infection and wound dehiscence; however, there is a higher risk of radiological malunion (4). The incidence of chronic pain 1 year following non-operative treatment can be as high as 79% (5). Despite a study by Makwana et al. reporting an anatomical fixation rate of 86% in patients over 55 (6), open reduction internal fixation (ORIF) have not produced satisfactory outcomes in some studies. Litchfield reported a 22.6% non-union rate (7/31) (7), whilst Beauchamp et al. reported a total complication rate of 50.1% and an anatomical fixation rate of 53.5% in patients over the age of 50 (8), which is a rather low

Keywords

- ankle fracture
- tibiotalocalcaneal nailing
- fragility fracture
- ORIF
- meta-analysis
cut-off age, especially for patients without comorbidities. Litchfield et al. suggested that inactivity is a risk factor for treatment failure, since those who were physically active pre-injury had the best chance of ORIF success (7). Nevertheless, the poor purchase in osteopenic bone and the need to add further soft tissue insult to a traumatised region make ORIF an unattractive option in the comorbid patient.

Tibiotalocalcaneal (TTC) nailing is a viable alternative to ORIF. This involves the insertion of an intramedullary nail through the plantar surface of the calcaneus, subtalar, and tibiotalar joints into the tibial canal. Advantages include its greater mechanical stability and decreased surgical trauma, allowing immediate weight-bearing. This is especially beneficial for the elderly, for whom prolonged periods of non-weight-bearing (NWB) can be challenging, often leading to pressure sores, vascular complications such as deep vein thrombosis, and lengthier hospital stays. Furthermore, the decreased soft tissue disruption with TTC lowers the chance of post-operative complications like surgical site infections, especially in those who are at risk of wound dehiscence or infection (9).

This study aims to provide a comprehensive review with a detailed meta-analysis of the current evidence for using a TTC nail as the primary surgical option to treat fragility ankle fractures in the elderly.

Methods

Search algorithm
This review was carried out according to the 2020 Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) statement protocol (10). A systematic search was performed on Ovid EMBASE, PubMed MEDLINE, Web of Science, and Cochrane Library from inception to 1 December 2021. The search contained variations of the terms ‘ankle fragility fracture’, ‘tibiotalocalcaneal nail’, ‘elderly’, ‘outcome’; a detailed search strategy is shown in Supplementary Table 1 (see section on supplementary materials given at the end of this article). A ‘snowball’ search was performed, whereby references of included studies, and studies that cited any included studies were independently searched, using Google Scholar to identify studies. All studies found by our search were imported into Mendeley and deduplicated. VL and MT independently completed title and abstract screening. A third reviewer (MK) was contacted for unresolvable disagreements.

Full-text screening was performed by VL and MT, based on the inclusion and exclusion criteria shown in Supplementary Table 2. A third reviewer (MK) was consulted for any disagreements. Inclusion and exclusion criteria were determined using the Population, Intervention, Comparison, Outcome, Study type model (11).

Data extraction
Data extraction was independently performed by VL and MT, with a third reviewer (MK) to resolve disagreements. Data were extracted into data tables created in a standardised excel spreadsheet for evidence synthesis and risk of bias analysis. Data from each study were split into six categories:

1. Study characteristics
2. Patient demographics
3. Patient selection
4. Intra-operative details
5. Clinical and functional outcomes
6. Post-operative complications

Missing data were retrieved by contacting the corresponding author of each study.

Data analysis
Quantitative data that were comparable across studies were selected for meta-analysis. This included post-operative complications and clinical outcomes such as percentage returned to pre-injury mobility and all-cause mortality. Extracted numerical data were rounded to three significant figures.

Meta-analyses were carried out using RStudio version 4.0.5 through the ‘metafor’ package (12). As we anticipated some between-study heterogeneity, a random-effects model was used. To pool effect sizes, the inverse-variance weighting method was used. For continuous data, the Wan et al. estimator (13) was used where mean ± s.d. was not given in the manuscript.

Knapp–Hartung adjustments were made when calculating the CI of pooled effect sizes, to reduce the chance of false positives (14). Higgins and Thompson’s I² statistic (15) and Cochran’s Q test (16) were used as measures of heterogeneity. Given the intrinsic limitations with Cochran’s Q test and the I² statistic (17, 18), prediction intervals were also included to provide a range into which future studies’ effect size can be expected to fall into. Subgroup analyses were performed according to (1) use of ankle fusion nail vs use of non-ankle fusion nails adapted for use in the ankle, (2) open vs closed fractures, (3) immediate post-operative full weight-bearing (FWB) vs post-operative NWB, and (4) majority of cohort are diabetics vs minority of cohort are diabetics. The Q test was used to determine if there is a difference in the true effect sizes between subgroups. A meta-regression was carried out using the REML estimator to determine how much of the heterogeneity variance various covariates can explain. Publication bias will be assessed using a funnel
plot and Egger’s test. For all analyses, a value of $P<0.05$ was used to determine statistical significance.

Risk-of-bias assessment was carried out independently by VL and MT using Cochrane’s RoB 2.0 tool for randomised trials containing five domains (19) and the methodological index for non-randomised studies (MINORS (Methodological Index for Non-Randomized Studies) tool) (20).

This review was prospectively registered in the International Prospective Register of Systematic Reviews PROSPERO (ID: CRD42021258893).

Results

A total of 1282 studies were identified from database searching. After deduplication, 1161 studies were identified for title and abstract screening, from which 125 full-text studies were reviewed. Thirteen studies were eligible for data synthesis. Searching studies that cited any of the included studies as well as references of the included studies yielded one extra study for inclusion, giving a total of 14 for qualitative and quantitative synthesis. To estimate interobserver reliability, a kappa coefficient of 0.84 was obtained, suggesting excellent agreement between reviewers. Twelve studies were retrospective case series (1, 2, 3, 21, 22, 23, 24, 25, 26, 27, 28, 29), one was a prospective case series (30), and one was a randomised control trial (31). Figure 1 presents a PRISMA flowchart.

Patient demographics

Table 1 presents the study characteristics and patient demographics. Seven studies were performed in the UK (2, 3, 22, 23, 24, 25, 28) and the majority were published in the last 5 years (1, 3, 21, 25, 26, 27, 28, 30, 31). Apart from 2 studies (22, 30), all studies collected patient data over a span of at least 3 years. A total of 312 fragility ankle fractures in 311 patients were included. The mean age was 77.3 years. A total of 84 patients (26.9%) were male and 228 (73.1%) were female. One study only included female patients (22). Fragility ankle fractures were defined as fractures that result from mechanical forces that would not ordinarily result in fracture, known as low-level (or ‘low energy’), according to the National Institute for Health and Care Excellence (NICE) guidelines (32). NICE defines these fractures as those that occur ‘following a fall from standing height or less’ (33). Only two studies reported BMI data (27, 28) and two studies reported smoking data (3, 28). The majority of fractures were closed (76.5%), with four studies including only closed fracture patients (2, 22, 29, 31). Despite an average of 23.5% of patients acquiring open fractures, patients sustained low-energy fractures, satisfying the NICE guideline’s definition for FFs.

Eight studies reported the number of diabetics (1, 2, 3, 21, 23, 26, 27, 28), with an average of 41.9%. One study included only diabetics in their study group (27). Since this study focused on ankle fractures in the geriatric population, we would assume that all study cohorts had some degree of comorbidity, yet only six studies reported comorbidities (3, 21, 23, 25, 28, 30). Lu et al. utilised the CCI, which gives a comorbidity-age combined risk score (28). Follow-up time was provided by all studies apart from 3 (23, 30), giving a mean of 18.5 months.

Intra-operative details

A hindfoot fusion/arthrodesis nail was used in six studies (1, 2, 26, 27, 28, 31), with the remaining utilising other types of nails such as a humeral nail (24), femoral nail (23, 25, 30), Gallagher nail (29), and an expandable nail (22) (Table 2). Joint preparation was only performed in one study (28). Five studies reported the total operative time, with a mean of 86.7 min (1, 21, 26, 27, 28). Seven studies reported the length of hospital stay, with a mean of 9.86 days (3, 21, 26, 27, 28, 30, 31). In the RCT performed by Georgiannos et al., a significantly shorter hospital stay...
was found in the TTC cohort than ORIF cohort (5.2 vs 8.4 days; \( P < 0.001 \)) (31).

### Outcomes and complications

The average time to weight-bearing and union was 22.2 weeks and 15.7 weeks, respectively (Table 3). Only Lu et al. provided a formal definition of union, namely the presence of bridging callus on anterior-posterior (AP) and lateral X-ray views, and painless FWB (28). Nine studies allowed immediate post-operative FWB (1, 2, 21, 22, 23, 28, 29, 30, 31), whilst the other five required patients to undergo a period of NWB (3, 24, 25, 26, 27). Pre-operative Olerud–Molander ankle scores (OMAS) were reported in five studies (1, 2, 22, 23, 31), and post-operatively in seven studies (1, 2, 22, 23, 24, 28, 31). OMAS was measured on a 0–100 scale, with lower scores indicating inferior ankle function. The pooled mean post-operative OMAS and standard mean difference between the pre-operative and post-operative OMAS are 54.07 (95% CI: 48.98–59.16; \( I^2 = 85\% \)) and −0.88 (95% CI: 0.50–1.25; \( P = 0.001 \)), respectively (Fig. 2A and B). Both the Foot and Ankle Outcome Score (26) and Parker score (30) were used in one study each. The former consists of 42 items on a scale of 0–100, with a lower score indicating worse function; the latter assesses mobility prior to fracture on a scale of 0–9, with a lower score indicating worse function. The pooled proportion for return to pre-operative mobility was 71% (95% CI: 0.6–0.8) (Fig. 2C).

Table 4 shows the complication profile. Surgical infection was reported in all 14 studies and had a pooled proportion of 13% (95% CI: 0.09–0.19; \( I^2 = 25\% \)) (Fig. 3A). Thirteen studies reported on superficial infection, with a pooled proportion of 10% (95% CI: 0.06–0.16; \( I^2 = 44\% \)) (Fig. 3B), and 12 studies reported on deep infection, with a pooled proportion of 8% (95% CI: 0.06–0.11, \( I^2 = 0\% \)) (Fig. 3C). Implant failure was reported in 11 and had a pooled proportion of 11% (95% CI: 0.07–0.15, \( I^2 = 0\% \)) (Fig. 3D). Implant failure was defined as broken/loose screws, nail breakages, or nail protrusions.

Twelve studies reported on malunion/non-union, with a pooled proportion of 11% (95% CI: 0.06–0.18; \( I^2 = 51\% \)) (Fig. 3E). Only Kulakli-Inceleme et al. (26) and Persigant et al. (30) provided a detailed definition of non-union and malunion, respectively.

Eleven studies reported patients returning to the operating theatre, with a pooled proportion of 12% (95% CI: 0.07–0.19, \( I^2 = 19\% \)) (Fig. 3F). This was usually as a consequence of deep infection requiring debridement, implant failure requiring removal, or peri-prosthetic fractures requiring re-fixation and revision nailing. Patients passed away in six studies due to medical complications (22, 23, 24, 25, 27, 31), including pneumonia occurring from 35 days (24) to 6 months post-surgery (23), and

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**Table 1. Study characteristics and patient demographics.**

| Reference                | Study Type          | Year studied          | Country  | Ankle number | Mean Age | Male n (%) | Follow-up time (months) | Comorbidities (mean #) | Diabetics (%) | Smoker (%) | BMI Mean | Male n (%) |
|--------------------------|---------------------|-----------------------|----------|--------------|----------|------------|-------------------------|------------------------|---------------|------------|---------|-----------|
| Amirfeyz et al. (27)     | RCS                 | 2010–2011             | UK       | 48           | 8 (14.6) | 11 (29.7) | 23                      | N/A                    | N/A           | N/A        | 3.3      | 38 (100) |
| Amirfeyz et al. (25)     | RCS                 | 2014–2015             | UK       | 10           | 9 (14.6) | 26 (35.2) | N/A                     | N/A                    | N/A           | N/A        | 2.4      | 15 (39.3) |
| Bouchard et al. (26)     | RCS                 | 2010–2015             | UK       | 16           | 16 (25)  | 66 (100)  | N/A                     | N/A                    | N/A           | N/A        | 2.8      | 38 (70%) |
| Georgiou et al. (22)     | RCS                 | 2009–2015             | Greece   | 43           | 83 (32)  | 78 (100)  | N/A                     | N/A                    | N/A           | N/A        | 3.3      | 15 (65.2) |
| Hansmann et al. (21)     | RCS                 | 2013                  | UK       | 30           | 85.2     | 84 (100)  | N/A                     | N/A                    | N/A           | N/A        | 3.3      | 30.1 (67.9–49.5) |
| Jansen et al. (20)       | RCS                 | 2012–2013             | USA      | 10           | 0        | 0 (100)   | N/A                     | N/A                    | N/A           | N/A        | 3.3      | 7 (55) |
| Kauer et al. (29)        | RCS                 | 2010–2013             | Austria  | 10           | 19 (38)  | 27 (63)   | N/A                     | N/A                    | N/A           | N/A        | 3.3      | 15 (31) |
| Kulakli-Inceleme et al.  | RCS                 | 2015–2019             | Turkey   | 10           | 100      | 1 (100)   | N/A                     | N/A                    | N/A           | N/A        | 3.3      | 10 (33.3) |
| Lemon et al. (28)        | RCS                 | 2012–2013             | France   | 12           | 84       | 72 (100)  | N/A                     | N/A                    | N/A           | N/A        | 3.3      | 8 (66.7) |
| Lu et al. (27)           | RCS                 | 2011–2016             | Germany  | 12           | 1 (100)  | 0 (100)   | N/A                     | N/A                    | N/A           | N/A        | 3.3      | 8 (66.7) |
| Martin et al. (30)       | RCS                 | 2015–2016             | France   | 20           | 9 (45)   | 9 (45)    | N/A                     | N/A                    | N/A           | N/A        | 3.3      | 15 (75) |
| Persigant et al. (22)    | RCS                 | 2016–2017             | France   | 14           | 3.3      | 6 (42.9)  | N/A                     | N/A                    | N/A           | N/A        | 3.3      | 10 (35.7) |
| Sune et al. (21)         | RCS                 | 2009–2012             | UK       | 31           | 84.3     | 14 (45.2) | N/A                     | N/A                    | N/A           | N/A        | 3.3      | 15 (48.3) |
| Taylor et al. (21)       | RCS                 | 2006–2012             | USA      | 31           | 63       | 14 (45.2) | N/A                     | N/A                    | N/A           | N/A        | 3.3      | 15 (48.3) |

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myocardial infarction occurring from 24 days (22) to 5 months (23) post-surgery. The pooled proportion all-cause mortality was 27% (95% CI: 0.20–0.34; $I^2 = 11\%$) (Fig. 3G). The pooled proportion of all surgical complications was 28% (95% CI: 0.20–0.39; $I^2 = 60\%$) (Fig. 3H).

**Subgroup analyses**

A subgroup analysis of open vs closed fracture studies shows that the rate of infection is lower in the latter ($P=0.0002$) (Table 5). Studies with a diabetic population of over 50% have a higher rate of infection ($P=0.0096$) than studies with a diabetic population below 50%.

Studies with diabetics in the majority also had a higher rate of implant failure ($P=0.034$). Although the proportion of patients returning to their pre-operative mobility was high in all studies, the value was higher in studies with a diabetic population below 50% compared with studies with a diabetic population of over 50% ($P=0.039$) (Table 6).

A subgroup analysis of studies that used an ankle fusion nail vs studies that adapted other nails for use in the ankle...
showed that the rate of malunion was lower in the former. Studies using an ankle fusion nail also had a lower rate of implant failure than those that did not. Subgroup analyses of studies that allowed immediate post-operative FWB vs those that did not fail to reveal any significant results. No significant difference was found between subgroups when comparing the pre-injury and post-operative OMAS differences (Table 6).

Meta-regression

Meta-regression analyses were done to explore sources of heterogeneity. Mean age was the only covariate that fit the regression model for post-operative OMAS ($P=0.0423$). Furthermore, a regression model using mean age and percentage of male patients as covariates produced an even stronger relationship ($P=0.026$). This was verified by the ANOVA model test, with an Akaike's information criterion of 36.88 for the full model and 42.2963 for the reduced model (Table 7).

Risk of bias

Publication bias was assessed with the funnel plot (Fig. 4). Egger’s test ($P=0.56$, intercept=0.54; 95% CI=−1.23 to 2.31) showed no statistically significant asymmetry in the funnel plot.

Risk of bias assessment was performed using the MINORS tool for each non-randomised study (Table 8A). The average score was 51.9% (31.3–68.8%). Only Persigant et al. performed prospective data collection (30). Although all studies besides one (29) stated some sort of aim, this was only properly done in two recently published studies (26, 28). Risk of bias assessment for the only randomised study in this review (31) was performed using the RoB 2.0 tool, giving an overall low risk of bias (Table 8B).

Discussion

This meta-analysis provides an in-depth analysis regarding the use of TTC nails for the treatment of fragility ankle fractures, evaluating patient selection, intra-operative variables, post-operative complications, patient reported outcome measures (PROMs), and mobility status. The overall complication rate was 28%, with 71% being able to return to their pre-operative mobility status. These results are favourable compared with conservative treatment, which reports a non-union rate of 48–73% (7, 8, 34, 35). Retrospective studies have reported that ORIF resulted in chronic pain in 56% of patients (5) and malunion in 19% (34). Makwana et al. performed an RCT between ORIF and conservative treatment of ankle fractures in patients above 55, which showed significantly higher post-operative OMAS ($P=0.03$) and increased accuracy of reduction.
in the ORIF cohort (P=0.03); however, the length of inpatient stay (P=0.01) and post-operative complications were greater in the ORIF cohort. Davidovitch et al. reported that in the absence of systemic comorbidities, the outcomes after ORIF for patients below and above 60 years old were similar; however, conservative treatment showed significantly inferior outcomes (36).

In addition to conservative treatment and ORIF performed according to the Association for Osteosynthesis/Association for the Study of Internal Fixation (AO/ASIF) manual (37), other joint preserving techniques have been described in a recent review (38). The trans-syndesmotic fixation technique is useful in osteoporotic patients, diabetic patients, and those with syndesmotic instability. It employs a ‘tibia pro fibula’ technique, which utilises the tibia for increased fibular fixation stabilisation (38).

Fixation can be augmented by bone cements such as polymethylmethacrylate or calcium phosphate cement, which can be loaded with antibiotics (39).

With 9 out of 14 included studies published in the last 5 years, this represents a significant increase in interest in the use of TTC nailing for ankle fracture management. In addition to satisfying the NICE guideline’s criteria for a FF, namely one that is caused by a low-energy mechanism such as a fall from standing height or less, many studies have outlined further indications for inclusion, namely elderly patients over 60 years (1, 24, 28, 30, 31), poor bone quality verified by radiological evidence of osteopenia or a history of FFs (1, 23, 24, 28, 30), poor pre-operative mobility (2, 23, 25, 30), and unstable fracture pattern defined by a medial clear space ≥ 5 mm on anteroposterior radiographs taken in dorsiflexion (28).

Figure 2
(A) Pooled mean post-operative OMAS. (B) Pooled standard mean difference between pre-injury and post-operative OMAS. (C) Overall proportion of return to pre-injury mobility status.
Table 4  Post-operative complications.

| Reference                      | Superficial infection (%) | Deep infection (%) | All infections (%) | Implant failure | Malunion or non-union (%) | Amputation (%) | Periprosthetic fracture (%) | Unplanned secondary surgery (%) | Other post-operative complications |
|--------------------------------|---------------------------|-------------------|-------------------|----------------|--------------------------|---------------|---------------------------|---------------------------------|----------------------------------|
| Al-Nammari et al. (23)         | 2 (4.2)                   | 1 (2.1)           | 3                 | 3 (6.3)        | 2 (4.2)                  | 1 (2.1)       | N/A                       | N/A                             | 3 cases of pneumonia; 5 cases of MI |
| Amirfeyz et al. (24)           | 1 (2.7)                   | 0                 | 1                 | N/A            | 1 (7.7)                  | N/A           | N/A                       | N/A                             | 1 case of pneumonia               |
| Armstrong et al. (3)           | 6 (28.6)                  | 0                 | 0                 | 0              | N/A                     | N/A           | N/A                       | N/A                             | Failure of SSG graft               |
| Baker et al. (25)              | 0                         | 0                 | 0                 | 0              | N/A                     | N/A           | N/A                       | N/A                             | 1 case of pneumonia               |
| El Baugh et al. (27)           | 3 (11.1)                  | 4                 | 3 (11.1)          | 3 (11.1)       | 2 (7.4)                  | N/A           | N/A                       | N/A                             | 1 case of pneumonia               |
| Georgiannos et al. (31)        | 1 (2.3)                   | N/A               | 1                 | 1 (2.3)        | 1 (5.9)                  | N/A           | 0                         | 0                               | 4 (14.8)                         |
| Herrera-Pérez et al. (1)       | 1 (5.9)                   | 0                 | 1                 | 1 (5.9)        | 1 (5.9)                  | N/A           | N/A                       | N/A                             | 1 case of DVT                     |
| Jonas et al. (2)               | 0                         | 0                 | 0                 | 0              | 0                       | N/A           | N/A                       | N/A                             | None                             |
| Kulakli-Inceleme et al. (26)   | 1 (10)                    | N/A               | 1                 | 1 (2.3)        | 1 (2.3)                  | N/A           | N/A                       | N/A                             | None                             |
| Lemon et al. (22)              | 0                         | 0                 | 0                 | N/A            | N/A                     | N/A           | N/A                       | N/A                             | None                             |
| Lu et al. (28)                 | 4 (20)                    | 0                 | 4                 | 4 (20)         | 0                       | 0             | 0                         | 0                               | 4 (20)                           |
| O’Daly et al. (29)             | 0                         | 0                 | 0                 | 0              | N/A                     | N/A           | N/A                       | N/A                             | None                             |
| Persignat et al. (30)          | 0                         | 0                 | 0                 | N/A            | N/A                     | N/A           | N/A                       | N/A                             | None                             |
| Taylor et al. (21)             | 2 (6.5)                   | 3 (9.7)           | 5                 | 3 (9.7)        | 3 (9.7)                  | 1 (3.2)       | N/A                       | N/A                             | None                             |

DVT, deep vein thrombosis; MI, myocardial infarction; N/A, not mentioned in study; SSG, split thickness skin graft.

(42) Especially with nails made from a titanium alloy (Ti-6Al-4V) such as the OxBridge Ankle Fusion Nail (1T4A4V) and the Fixion IM Expandable Intramedullary Nail (3T5A5V).
The oxide form, oxidation and corrosion are major concerns in diabetics, due to the acidic microenvironment and increased reactive oxygen species production \((44)\). The resulting corrosion products have a significant bearing on the biocompatibility and long-term stability of implants \((45)\).

A higher proportion of ankles treated with a non-ankle fusion nail used ‘off-label’ have implant failure than those that used nails specific for hindfoot stabilisation. Furthermore, short nails that do not cross the tibial isthmus were assumed to lead to periprosthetic fractures \((9)\), yet two of the earliest studies \((22, 24)\) that utilised
Table 5  Subgroup meta-analyses of association between TTC nailing and post-operative complications by study variables. Bold values indicate a P value <0.05.

| Variable                        | Number of studies | Number of ankles | Proportion (95% CI)     | Prediction interval          | I²   | Psubgroup |
|---------------------------------|-------------------|------------------|-------------------------|------------------------------|------|-----------|
| Infection                       |                   |                  |                         |                              |      |           |
| Type of nail                    |                   |                  |                         |                              |      |           |
| Ankle fusion nail               | 6                 | 148              | 0.1216 (0.0567; 0.2418) | (0.0533; -0.2542)            | 0    | 0.1441    |
| Non-ankle fusion nail           | 6                 | 112              | 0.0669 (0.0605; 0.0739) | (0.0600; 0.0745)             | 0.194|           |
| Post-op weight-bearing status   |                   |                  |                         |                              |      |           |
| FWB                             | 9                 | 225              | 0.1002 (0.0571; 0.1699) | (0.0342; 0.2592)             | 0.261|           |
| NWB                             | 5                 | 87               | 0.1842 (0.0938; 0.3300) | (0.0844; 0.3562)             | 0.001|           |
| Open/closed fracture            |                   |                  |                         |                              |      |           |
| Open                            | 2                 | 30               | 0.2465 (0.0168; 0.8626) | N/A                          | 0.066|           |
| Closed                          | 4                 | 95               | 0.0984 (0.0681; 0.1402) | (0.0678; 0.1408)             | 0.001|           |
| Diabetes                        |                   |                  |                         |                              |      |           |
| >50% of cohort                  | 3                 | 75               | 0.3046 (0.0020; 0.9896) | N/A                          | 0.411|           |
| ≤50% of cohort                  | 5                 | 130              | 0.1089 (0.0656; 0.1754) | (0.0362; 0.2848)             | 0.364|           |
| Malunion                        |                   |                  |                         |                              |      |           |
| Type of nail                    |                   |                  |                         |                              |      |           |
| Ankle fusion nail               | 6                 | 148              | 0.0532 (0.0334; 0.0803) | (0.0054; 0.3692)             | 0.57 |           |
| Non-ankle fusion nail           | 5                 | 96               | 0.1383 (0.0485; 0.3356) | (0.0151; 0.6272)             | 0    | 0.2591    |
| Post-op weight-bearing status   |                   |                  |                         |                              |      |           |
| FWB                             | 9                 | 225              | 0.0868 (0.0419; 0.1713) | (0.0126; 0.4150)             | 0.193|           |
| NWB                             | 3                 | 50               | 0.1547 (0.0234; 0.3833) | (0.0001; 0.9971)             | 0.649|           |
| Diabetes                        |                   |                  |                         |                              |      |           |
| >50% of cohort                  | 3                 | 75               | 0.0955 (0.0497; 0.1754) | (0.0131; 0.4554)             | 0    | 0.1367    |
| ≤50% of cohort                  | 4                 | 109              | 0.1883 (0.0446; 0.5351) | (0.0036; 0.9363)             | 0.594|           |
| Implant failure                 |                   |                  |                         |                              |      |           |
| Type of nail                    |                   |                  |                         |                              |      |           |
| Ankle fusion nail               | 6                 | 148              | 0.0646 (0.0635; 0.2295) | (0.0541; 0.0770)             | 0.63 |           |
| Non-ankle fusion nail           | 3                 | 78               | 0.1244 (0.0541; 0.0770) | (0.0635; 0.2295)             | 0    | 0.2125    |
| Post-op weight-bearing status   |                   |                  |                         |                              |      |           |
| FWB                             | 7                 | 204              | 0.0981 (0.0550; 0.1687) | (0.0534; 0.1732)             | 0    |           |
| NWB                             | 4                 | 74               | 0.1395 (0.0805; 0.2310) | (0.0658; 0.2717)             | 0    |           |
| Diabetes                        |                   |                  |                         |                              |      |           |
| >50% of cohort                  | 3                 | 75               | 0.2197 (0.0009; 0.9884) | N/A                          | 0.347|           |
| ≤50% of cohort                  | 5                 | 130              | 0.0897 (0.0575; 0.1371) | (0.0569; 0.1386)             | 0    |           |

Table 6  Subgroup meta-analyses of association between TTC nailing, mobility, and OMAS scores by study variables. Bold values indicate a P value <0.05.

| Variable                        | Number of studies | Number of ankles | Proportion (95% CI)     | Prediction interval          | I²   | Psubgroup |
|---------------------------------|-------------------|------------------|-------------------------|------------------------------|------|-----------|
| Return to pre-injury mobility status |                   |                  |                         |                              |      |           |
| Type of nail                    |                   |                  |                         |                              |      |           |
| Ankle fusion nail               | 6                 | 148              | 0.7571 (0.5369; 0.8934) | (0.2272; 0.9706)             | 0.6  |           |
| Non-ankle fusion nail           | 5                 | 98               | 0.6311 (0.5379; 0.7153) | (0.5239; 0.7267)             | 0    |           |
| Post-op weight-bearing status   |                   |                  |                         |                              |      |           |
| FWB                             | 7                 | 180              | 0.7244 (0.5575; 0.8458) | (0.3380; 0.9312)             | 0.511|           |
| NWB                             | 4                 | 66               | 0.6951 (0.4274; 0.8744) | (0.1164; 0.9753)             | 0.416|           |
| Diabetes                        |                   |                  |                         |                              |      |           |
| >50% of cohort                  | 3                 | 75               | 0.7110 (0.5682; 0.8213) | N/A                          | 0    |           |
| ≤50% of cohort                  | 5                 | 130              | 0.8124 (0.7345; 0.8715) | (0.3454; 0.9198)             | 0.483|           |
| Difference between pre-injury and post-operative OMAS scores* |                   |                  |                         |                              |      |           |
| Type of nail                    |                   |                  |                         |                              |      |           |
| Ankle fusion nail               | 4                 | 111              | 0.8772 (0.3348; 1.4196) | (1.1438; 1.6105)             | 0.308|           |
| Non-ankle fusion nail           | 2                 | 60               | 0.6875 (−2.0196 to 3.3946) | N/A                          | 0.213|           |

*Only six studies reported pre- and post-injury OMAS scores, from which detailed information about open fracture and diabetic patients can only be obtained from one study, precluding any subgroup analyses. All six studies allowed immediate post-operative FWB, also precluding subgroup analyses; †standard mean difference (95% CI).
short nails reported no periprosthetic fractures. However, small sample size and short follow-up time could be confounding factors.

**Infection**

The pooled proportion of all surgical infections in included studies was 13% (95% CI: 0.09–0.19). This is likely to be confounded by studies that included open fractures since they are associated with an increased infection risk due to wound contamination and significant soft tissue injury (46). Our subgroup analysis shows a significant difference in the proportion of surgical infections between an open fracture cohort (3, 28) and a closed fracture cohort (P=0.0002) (2, 22, 29, 31). There was only one case of infection amongst 95 ankle fractures in the 4 studies that only included closed fractures, which was reported in the RCT performed by Georgiannos et al. (31). The percentage of infections in their ORIF cohort was over five-fold greater (13.8% vs 2.7%). Studies utilising ORIF mentioned that the rate of infection is correlated with the ability to comply with post-operative NWB status (7, 8, 47), with Fong et al. reporting a deep infection rate of 12% decreasing to 0% after removing non-compliant patients from analysis (47). However, our subgroup analyses did not find a significant difference in the pooled proportion of surgical infection between studies that allowed immediate post-operative FWB and studies that insisted on a period of post-operative NWB.

Subgroup analysis of studies with a majority of diabetics has a higher pooled proportion of infection than studies with a minority of diabetics (P=0.0096). Apart from the study that included only open fractures (3), the two studies with the highest rate of surgical infections also contained the highest percentage of diabetics (21, 27). The hyperglycaemic environment favours immune dysfunction, and the infection itself can be a precipitating factor for inherent complications, in a vicious cycle that increases morbimortality (48). Nevertheless, the pooled rate of infection in diabetics is still lower than in studies utilising ORIF, which was reported to be as high as 50% (49). This could be because TTC nailing utilises small 1–2 cm incisions and avoids s.c. implants, with the nail being embedded in the medullary canal of the bone and locked proximally and distally. Nevertheless, increased post-operative wound care is still needed for diabetics who undergo TTC nailing to avoid surgical infections.

**Malunion/non-union, joint preparation, and arthritis**

One disadvantage of hindfoot fusion is the need to disturb the unprepared subtalar joint. Only one study included patients that had undergone formal joint preparation prior to nail insertion, i.e. cartilage was denuded down to the subchondral bone (28). Four studies specifically mentioned that the joints were not prepared (27, 24, 25, 27). Joint preparation is one of the most important modifiable factors influencing non-union rates (50). Yet some surgeons felt that formal joint preparation would devascularise the talar fragments and increase surgical insult, leading to an increased risk of wound healing complications, in exchange for arthrodesis union that is hard to achieve in a comorbid host (28). The low pooled proportion of fracture malunion/non-union (0.11; 95% CI: 0.06–0.18) could suggest that joint preparation may not be necessary for the low-demand geriatric patient. Furthermore, treatment is not indicated for asymptomatic non-union, as the nail will continue to act as a sturdy internal splint (9). Nevertheless, there was insufficient follow-up time in most studies to obtain a robust conclusion, and

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**Table 7** Meta-regression analyses of select co-variates for post-operative OMAS scores. Bold values indicate a P value <0.05.

| Co-variates       | I² (residual heterogeneity) | R² (heterogeneity explained) | Test of moderators (P-value) | Regression weight (95% CI) | Standard error |
|-------------------|-----------------------------|-----------------------------|-----------------------------|----------------------------|----------------|
|                   |                             |                             |                             |                            |                |
| Age               | 0.6747                      | 0.6737                      | 0.0423                      | −1.5983 (−3.1142 to 0.0824)| 0.5897         |
| Sample size       | 0.8505                      | 0.0048                      | 0.9064                      | 0.0202 (−0.4004 to 0.4409)| 0.1636         |
| % Male            | 0.8556                      | 0.0114                      | 0.8246                      | −0.0228 (−0.2740 to 0.2284)| 0.0977         |
| % Closed fracture  | 0.8629                      | 0.0619                      | 0.5914                      | 0.0391 (−0.1364 to 0.2147)| 0.0683         |
| Publication year  | 0.8641                      | 0.0319                      | 0.7045                      | −0.01686 (−1.2471 to 0.9100)| 0.4196         |
| Age & % Male      | 0.0554                      | 0.9907                      | 0.0263                      | −2.4996 (−4.0326 to 0.9665)| 0.5522         |
| Age % Male        |                             |                             | 0.0106                      | −2.1524 (−0.2944 to −0.0103)| 0.0512         |

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**Figure 4**

Contour-enhanced funnel plot for publication bias.
studies have failed to differentiate between radiographic and clinical union.

The unnecessary fixation of the unprepared subtalar joint is problematic and can increase the rate of symptomatic non-union and ankle arthritis. With the ankle mortise fused, the subtalar joint exerts a compensatory function so as to not concentrate the weight-bearing stress on the medial portion of the ankle and to retain motion and normal gait (51). Removing the compensatory function transfers motion to the midtarsal joints and promotes varus inclination of the subtalar joint, leading to increased medial stress concentration in the midtarsal joints causing arthritic changes (52). Mid-talar joint degeneration was most commonly found (60% of patients), with subtalar joint degeneration observed in 10% of patients (53). None of the studies included in this review reported arthritis, perhaps due to the short follow-up times (average of 18.6 months). Nevertheless, Childress et al. followed up 92 patients for 16 years and reported no degenerative changes; however, a narrow Steinman pin was used (54). Furthermore, fractures of the second metatarsal after ankle surgery have been reported in the literature (55), perhaps due to higher von Mises stresses in the second and third metatarsal bones after ankle fusion (56), yet none of the included studies reported such a finding.

**Mortality**

Our pooled all-cause mortality proportion was 27% (95% CI: 0.20–0.34), with the lowest at 11.8% with 20.9 months of follow-up (1). This is comparable to the mortality rate after hip fractures in the elderly (33%) (57). However, mortality in ORIF cohorts seems to be lower with one study reporting 5.4% with a 15-month follow-up (58). This may however not be a fair comparison since all-cause mortality is determined by many factors unrelated to the ankle fusion process itself, including age, comorbidities, and other injuries. Diabetics accounted for 8.7% of Shivarathre et al.’s cohort (58); our figure was 41.9%, which could have contributed to higher mortality. Nevertheless, co-management of geriatric patients by orthopaedic surgeons and geriatricians can lead to a shorter hospital stay and lower mortality and complication rates (59).

**Mobility and OMAS**

The measurement of pre-operative OMAS in five of the included studies may seem rather pointless since it was measured on the day of admission after an acute fracture. Nevertheless, pre-operative OMAS could provide a snapshot of the patient’s extent of disability and allows one to compare with their post-operative status. OMAS was created in 1984 from a cohort of 90 patients treated by Olerud and Molander (60). The overall score is the
The results of this meta-analysis show an overall lower complication rate with TTC nailing and improved OMAS when compared to studies utilising conservative treatment and ORIF (4, 7, 8, 34, 35). This could explain why TTC nailing is becoming more popular with the geriatric population, perhaps due to the underlying biomechanics of TTC nailing. They are sturdy internal splints that are biomechanically better than extra-medullary implants, which allows them to mediate fracture union. They have maximum leverage in the distal segment, which promotes a more reliable and rigid fixation system (68). Furthermore, the medullary canal is often reamed to a centimetre above the diameter of the nail. This creates a cancellous autograft, which encourages the formation of a local haematoma that is rich in inflammatory cells and mitogens, which recruits mesenchymal stem cells and promotes neovascularisation, all of which encourage osteoblast activity and bone formation (69). The biggest benefits come from two angles, the first being their load-sharing design makes the fracture site able to tolerate immediate weight-bearing, and the second being the minimal disruption and preservation of fracture biology upon insertion of a TTC nail, which decreases the risk of post-operative wound complications (9), especially in the comorbid host.

**Meta-regression**

An $I^2$ value below 60% suggests low or moderate heterogeneity (63). This was the case for all our pooled data, apart from post-operative OMAS ($I^2 = 85\%$). Hence, a meta-regression was used to determine potential covariates leading to heterogeneity. Age being inversely correlated with higher OMAS was not a surprising finding, given that ageing leads to physical and functional losses (64). What was more intriguing was that older males had a stronger inverse correlation with better OMAS. Some studies report no difference in PROMs between men and women (65, 66). However, studies on hip arthroplasty for osteoarthritic patients report that females achieved better outcomes than males (67), agreeing with our finding. More research is needed regarding the influence of gender on ankle surgery.
only one RCT available. In order to be able to make strong statements about preferred management strategies, we would need to perform studies which directly compare interventions; ideally, RCTs would be used. There is also poor consistency in post-operative rehabilitation protocols, and no studies evaluated fusion rates of the ankle and subtalar joints, or post-operative hindfoot alignment. Despite initial promising evidence that TTC nailing could be added to the paraphernalia for fragility ankle fracture management, prospective RCTs with long follow-up times and large cohort sizes are needed to create clear guidelines for the use of TTC nailing for ankle fractures.

Supplementary materials
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Availability of data and material
The authors confirm that the data supporting the findings of this study are available within the article (and/or) its Supplementary materials.

Author contribution statement
V L, M T, A Z, R P performed full text screening and data collection. V L wrote the manuscript. M F, A T, R P provided guidance on statistics and reviewed previous versions of the manuscript. M K conceptualised the study and edited previous versions of the manuscript. All authors have read and approve of the final version of the manuscript.

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