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Surgical interventions for treating distal tibial metaphyseal fractures in adults (Review)

Kuo LT, Chi CC, Chuang CH

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[Intervention Review]

Surgical interventions for treating distal tibial metaphyseal fractures in adults

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ABSTRACT

Background

The distal tibial metaphysis is located in the lower (distal) part of the tibia (shin bone). Fractures of this part of the tibia are most commonly due to a high energy injury in young men and to osteoporosis in older women. The optimal methods of surgical intervention for a distal tibial metaphyseal fracture remain uncertain.

Objectives

To assess the effects (benefits and harms) of surgical interventions for distal tibial metaphyseal fractures in adults. We planned to compare surgical versus non-surgical (conservative) treatment, and different methods of surgical intervention.

Search methods

We searched the Cochrane Bone, Joint and Muscle Trauma Group Specialised Register (9 December 2014), the Cochrane Central Register of Controlled Trials (2014, Issue 12), MEDLINE (1946 to November Week 3 2014), EMBASE (1980 to 2014 Week 48), the Airiti Library (1967 to 2014 Week 8), China Knowledge Resource Integrated Database (1915 to 2014 Week 8), ClinicalTrials.gov (February 2014) and reference lists of included studies.

Selection criteria

We included randomised and quasi-randomised controlled clinical studies comparing surgical versus non-surgical (conservative) treatment or different surgical interventions for treating distal tibial metaphyseal fractures in adults. Our primary outcomes were patient-reported function and the need for secondary or revision surgery or substantive physiotherapy because of adverse outcomes.

Data collection and analysis

Two authors independently selected studies, assessed the risk of bias in each study and extracted data. We resolved disagreement by discussion and, where necessary, in consultation with a third author. Where appropriate we pooled data using the fixed-effect model.

Main results

We included three randomised trials that evaluated intramedullary nailing versus plating in 213 participants, with useable data from 173 participants of whom 112 were male. The mean age of participants in individual studies ranged from 41 to 44 years. There were no trials comparing surgery with non-surgical treatment. The three included trials were at high risk of performance bias, with one trial also being at high risk of selection, detection and attrition bias. Overall, the quality of available evidence was rated as very low for all outcomes, meaning that we are very unsure about the estimates for all outcomes.

Although the pooled results of three different measures of foot and ankle function indicated a small difference in favour of nailing (standard mean difference 0.28, 95% CI -0.02 to 0.59; 172 participants, 3 trials), the results of individual trials indicated that this was very unlikely to be a clinically important difference. Pooled data (173 participants, 3 trials) for the need for reoperation or substantive physiotherapy for adverse events favoured nailing (4/90 versus 10/83; RR 0.37, 95% CI 0.12 to 1.12), but included the possibility of a better outcome after plating. Based on an illustrative risk of 100 re-operations for adverse outcomes within one year of plate fixation in 1000 people with these fractures, 63 fewer (95% CI 88 fewer to 12 more) people per 1000 would have re-operations after nailing. Similarly pooled data (173 participants, 3 trials) for the symptomatic nonunion or malunion, wound complications and fracture union favoured nailing but the 95% confidence intervals crossed the line of no effect and thus included the possibility of a better outcome after plating. Evidence from one trial (85 participants) showed no clinically important difference in pain between the two groups.

Authors' conclusions

Overall, there is either no or insufficient evidence to draw definitive conclusions on the use of surgery or the best surgical intervention for distal tibial metaphyseal fractures in adults. The available evidence, which is of very low quality, found no clinically important differences in function or pain, and did not confirm a difference in the need for re-operation or risk of complications between nailing and plating.

The addition of evidence from two ongoing trials of nailing versus plating should inform this question in future updates. Further randomised trials are warranted on other issues, but should be preceded by research to identify priority questions.

PLAIN LANGUAGE SUMMARY

Surgical interventions for treating distal tibial fractures (breaks of the lower end of the shin bone) in adults

Background

Breaks in the lower (distal) end of the shin bone (or tibia) are mostly caused by high-energy trauma, such as motor vehicle accidents. We set out to compare surgical treatment (such as putting the broken parts back into position and fixing these either by inserting a metal nail into the central cavity of the bone (nailing) or with a metal plate and securing it to the bone using screws (plating)) with non-surgical treatment (plaster cast immobilisation). We also set out to compare different methods of surgery such as nailing versus plating.

Study characteristics

We searched medical databases and trials registries in December 2014. We wanted to include studies in which receiving one surgical treatment or another surgical treatment was decided by chance. This research method, termed a randomised controlled trial (RCT), is the best way to ensure that any measured improvement is caused by the treatment itself and no other factors. We found three RCTs involving 213 adults (with results available from 173) that compared nailing versus plating for treating distal tibial fractures. Overall the studies included around twice as many males as females and the average age of the study participants was just over 40 years. We found no trials comparing surgery with non-surgical treatment.

Key results

We found no clear differences between the nailing and plating groups in terms of patient-reported functional outcomes, re-operations for adverse outcomes, troublesome non-healing of the bone or deformity, pain, wound problems such as infection, or the numbers of individuals with healed fractures.

Quality of the evidence

Only three trials were identified and the sample sizes were small, so the results are imprecise. Moreover, the results of one trial were very likely to be biased due to flawed methodology. We therefore judged the overall quality of evidence to be very low, which means that we are very unsure of these results.

Conclusions

Overall, the evidence is of very low quality and is insufficient to draw definite conclusions about the best method of surgery, including nailing versus plating, for treating breaks of the lower end of the shin bone in adults. Future updates of this review are likely to include evidence from currently ongoing research comparing nailing versus plating. Although other RCTs are needed to address key clinical questions on surgical methods for treating these fractures, these studies should be preceded by research to determine which questions should be prioritised.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Summary of findings: Surgical interventions for treating distal tibial metaphyseal fractures in adults

Surgical interventions for treating distal tibial metaphyseal fractures in adults

Population: individuals more than 18 years old with distal tibial metaphyseal fractures

Settings: hospitals (all linked with a university)

Intervention: intramedullary nailing

Comparison: plating

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Plating	Intramedullary nailing				
Patient-reported functional outcomes (pooled data)[1] 1. AOFAS score at 1 year 2. OMAS percentage of normal side at 2 years 3. OMAS score at 1 year	See comment	See comment	SMD 0.28 (-0.02 to 0.59)	172 (3 trials)	⊕⊝⊝⊝ **very low**[2]	0.2 SD represents a small difference, 0.5 SD a moderate difference and 0.8 SD a large difference. However, this does not mean that the 95% CI includes a clinically important effect. The separate results of two trials (87% of the data) showed no clinically important differences. Only the point estimate and wide CI of the third trial included the possibility of a clinically important effect.[3]
Need for a secondary/revision operation or substantive physiotherapy for adverse outcomes (e.g. non-union, malunion or infection) 1 year	**100 per 1000**[4]	**37 per 1000** (12 to 112)	**RR 0.37** (0.12 to 1.12)	173 (3 trials)	⊕⊝⊝⊝ **very low**[5]	

Symptomatic non-union or malunion, including limping 1 year	**67 per 1000**[4]	**49 per 1000** (12 to 188)	**RR 0.72** (0.18 to 2.80)	173 (3 trials)	⊕⊝⊝⊝ **very low**[6]	
Pain (0 to 40: no pain) 1 year	The mean pain score in the plating group was 31.5 points	The mean pain score in the nailing group was 1.00 higher (0.63 lower to 0.76 higher)	MD 1.00 (-0.63 to 2.63)	85 (1 trial)	⊕⊝⊝⊝ **very low**[7]	The CI is unlikely to include a minimal clinically important difference. Higher scores were better
Wound complications including superficial/deep wound infection and osteomyelitis 1 year	**147 per 1000**	**70 per 1000** (30 to 162)	**RR 0.47** (0.20 to 1.10)	173 (3 trials)	⊕⊝⊝⊝ **very low**[8]	
Fracture union 1 year	**934 per 1000**	**953 per 1000** (888 to 1000)	**RR 1.02** (0.95 to 1.09)	173 (3 trials)	⊕⊝⊝⊝ **very low**[9]	

*The basis for the **assumed risk** is provided in footnotes. The **corresponding risk** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

AOFAS: American Orthopaedic Foot and Ankle Surgery score; **CI:** confidence interval; **MD: m**ean difference; **OMAS:** Olerud and Molander Ankle Functional Score; **RR:** risk ratio; **SMD:** standardised mean difference

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very low quality: We are very uncertain about the estimate

1. Functional data were presented as AOFAS data in one trial, and OMAS data in the other two trials but in different ways, as described.
2. The evidence was downgraded two levels for study limitations in design and implementation (all three trials were at high risk of bias, including performance bias) and one level for inconsistency (mainly reflecting pooling of disparate outcome measures and timing of measurement).
3. Individual trial results:
a. AOFAS score (0 (worst) to 100 (best)) at 12 months: MD 2.20 favouring nailing, 95% CI -0.97 to 5.37; 85 participants
b. OMAS percentage of normal side at 24 months: MD 0.30, 95% CI -1.27 to 1.87; 64 participants
c. OMAS score (0 (worst) to 100 (best)) at 12 months: MD 15.80, 95% CI 0.80 to 30.80; 23 participants.
4. The basis for the assumed risk was the median plating group risk across studies.
5. The evidence was downgraded one level for study limitations in design and implementation (all three trials were at high risk of bias, in particular performance bias), one level for inconsistency ($Chi^2 = 2.17$, $df = 1$ (P value = 0.14); $I^2 = 54\%$), and one for imprecision (wide CIs and small numbers).

6. The evidence was downgraded one level for study limitations in design and implementation (all three trials were at high risk of bias, in particular performance bias) and two levels for serious imprecision (wide CIs and small numbers).
7. The evidence was downgraded two levels for study limitations in design and implementation (the trial was at high risk of selection, performance, detection and attrition biases) and one level for imprecision (wide CI and small numbers).
8. The evidence was downgraded two levels for study limitations in design and implementation (all three trials were at high risk of bias, in particular performance bias) and one level for inconsistency (Chi^2 = 4.55, df = 2 (P value = 0.10); I^2 = 56%).
7. The evidence was downgraded one level for study limitations in design and implementation (all three trials were at high risk of bias, in particular performance bias) and two levels for serious imprecision (there were few cases of non-union; if these had been pooled instead the result would have been 3/90 versus 4/83; RR 0.72, 95% CI 0.18 to 2.80).

BACKGROUND

Description of the condition

The lower (distal) end of the tibia (shin bone) of the lower leg articulates with the distal fibula (the other bone of the lower leg) and talus (the ankle bone) to form the ankle joint. An epidemiological study of fractures in adults showed that distal tibial fractures comprised 0.7% of all fractures with an annual incidence of 7.9 per 10,000 adults presenting to the Edinburgh Royal Infirmary in 2000 (Court-Brown 2006). These fractures are more common in young adults, usually males, but are becoming more common in older females. Court-Brown 2006 reported a male to female ratio of 57 to 43. In younger adults, the most common cause is high-energy trauma such as a motor vehicle accident or sports injury (Court-Brown 1995; Court-Brown 2005). Fractures in older adults often result from low-energy trauma, such as falls from standing height, which reflects underlying osteopenia and osteoporosis (Court-Brown 2005; Court-Brown 2006). The frequency of high-energy trauma and the relatively thin muscle coverage of the tibia increases the risk of an open fracture. The sparse muscle cover also makes fracture management more difficult. As with tibial fractures in general, these fractures and related complications, including non-union and infection, can lead to employment loss and other socioeconomic problems (Court-Brown 2005).

The distal tibia metaphysis is located in the distal part of the tibia. It lies above the plafond, which is the part of the tibia that articulates with the fibula and talus to form the ankle joint. Müller 1990 defined the distal tibial metaphysis by constructing a square, with the sides of length defined by the widest portion of the tibial plafond. Extra-articular fractures of the distal tibia correspond to type 43A according to the Arbeitsgemeinschaft für Osteosynthesefragen/Orthopaedic Trauma Association (AO/OTA) classification (AO/OTA 1996). The mechanism of injury and the prognosis of these fractures differ from those of pilon fractures, which are intra-articular fractures involving the plafond (Mast 1988; Ovadia 1986). Additionally, the proximity of the fracture to the ankle joint makes it technically demanding to achieve acceptable alignment and stable fixation using intramedullary nails, the most commonly used surgical technique for tibial shaft or diaphyseal fractures (Robinson 1995). Further, the subcutaneous and relatively exposed position of the metaphysis means that fractures in the distal tibia metaphysis, even following low-energy trauma, usually have more severe soft tissue injury than reported for fractures of the tibia diaphysis (Court-Brown 1990). Thus, the distal metaphysis is distinct from the diaphysis and a separate review of surgical interventions for treating distal tibia metaphyseal fractures is warranted.

Description of the intervention

Generally, undisplaced fractures are treated non-surgically, whereas most displaced or unstable fractures are treated surgically because of the risk of malunion or non-union. Most surgeons regard displacement as angulation of more than 5 degrees, shortening greater than 1 cm and rotation greater than 10 degrees (Petrisor 2010). Non-surgical or conservative treatment of displaced fractures generally comprises closed reduction (realignment of bone fragment without making an incision in the skin) and plaster cast immobilisation. Several surgical methods are available. Intramedullary nailing consists of a metal rod, inserted from the upper tibia into the inner cavity of the tibia, which is typically locked into place with screws. Plating is another treatment option. Traditionally, this required extensive exposure of the soft tissues to reduce (reposition) the fracture fragment(s) before fixation with plates. Minimally invasive percutaneous osteosynthesis (MIPO) is an alternative surgical method that causes less damage to tissue. Nowadays, precontoured locking plates are available, which are thinner, fit more closely to the bone and provide stronger support than traditional plates. External fixation is another alternative, especially for excessive soft tissue injury or comminuted fractures. Sometimes, two treatment methods may be used in combination; for example, nailing combined with plating.

How the intervention might work

Non-operative treatments for distal tibial fractures can lead to unfavourable results such as unacceptable deformity, shortening, rotation malunion and ankle stiffness (Digby 1982; Haines 1984). However, all methods of surgical fixation carry the risk of additional complications, including general complications from the operation itself.

The advantages of intramedullary nailing include the preservation of the soft tissue sleeve around the fracture site and the potential for early mobilisation of the adjacent joints (Whittle 2008). While intramedullary nails have become the mainstay for tibial diaphyseal fractures, there is a potential risk of propagation of the fracture into the ankle joint when introducing implants, and greater difficulties in aligning the distal fragment, which could lead to malalignment and malunion (Mosheiff 1999; Robinson 1995). Knee pain is also sometimes noted after nailing (Court-Brown 1997; Toivanen 2002).

Plating could provide improved alignment but has the disadvantages of wound complications, infection, implant prominence because of inadequate soft tissue coverage, and increased violation of soft tissue and blood supply during surgery (Borelli 2002; Im 2005; Obremskey 2004). With the evolution of implants, newly designed precontoured locking plates provide another treatment option for adult distal metaphyseal fractures. Combined with the MIPO technique, locking plates may provide greater biomechanical strength than conventional plates, and better reduction of the fracture with less violation of the soft tissue and periosteum (Ahmad 2010; Collinge 2010; Hasenboehler 2007; Redfern 2004). Because compression of the plate onto the bone is unnecessary, the periosteal blood supply and fracture hematoma are preserved, which enhances fracture healing (Wagner 2003).

External fixation is another treatment, often favoured for open fractures, excessive soft tissue injury or comminuted fractures (Court-Brown 2005). However, problems such as insufficient reduction, malunion, joint motion restriction and pin tract infections are frequently encountered (Babis 1997; Blauth 2001; Court-Brown 2005).

Why it is important to do this review

While relatively uncommon, distal tibial metaphyseal fractures are serious and clinically distinct injuries that may result in severe disability and are frequently treated surgically. A variety of surgical interventions are available but it is unclear which is the best method. A previous systematic review investigating the treatment of distal tibia fracture without articular involvement (Zelle 2006), which found no evidence from randomised controlled trials (RCTs), concluded that the optimal treatment for these fractures "remains controversial". Given this uncertainty and that RCTs have been conducted since the publication of this article, a review of the currently available best evidence is warranted in order to provide orthopaedic surgeons and individuals with such a fracture with a useful reference to inform their decision-making about the treatment of distal tibial metaphyseal fractures in adults.

OBJECTIVES

To assess the effects (benefits and harms) of surgical interventions for distal tibial metaphyseal fractures in adults.

We planned to compare surgical versus non-surgical (conservative) treatment, and different methods of surgical intervention.

METHODS

Criteria for considering studies for this review

Types of studies

RCTs and quasi-RCTs (in which the method of allocating participants to a treatment is not strictly random, e.g. by date of birth, hospital record number or alternation) evaluating surgical interventions or comparing surgical versus non-surgical interventions for treating distal tibial metaphyseal fractures in adults.

Types of participants

We included trials of skeletally mature people undergoing primary surgical fixation (surgical fixation of an acute fracture or early fixation following failure of conservative treatments, nominally within two weeks of injury) of fractures of the distal tibial metaphysis. While we accepted the definition and associated classification of the fracture as provided in trial reports, ideally the fractures should be entirely extra-articular and in the distal metaphysis of the tibia (thus the fracture will be within 4 cm of the tibia plafond (Bedi 2006) or be assigned as type 43A according to the AO/OTA classification (AO/OTA 1996)).

Since articular injuries behave so differently, we excluded trials with a primary focus on people with intra-articular (pilon) fractures or people with other fractures, except fibular fracture, affecting the same limb. We also excluded trials for which the primary focus was skeletally immature people; notably rigid intramedullary nailing cannot be performed in this group. Unless separate data for extra-articular fractures could be obtained, we excluded articles reporting mixed populations of intra-articular and extra-articular fractures if more than 25% of the fractures involved the plafond.

Types of interventions

We included trials comparing surgery with conservative treatment and trials comparing different surgical interventions: either different categories of surgical intervention (e.g. intramedullary nailing, plating or external fixation) or different methods of performing an intervention in the same category (e.g. different types or methods of plating).

Types of outcome measures

Primary outcomes

1. Patient-reported functional outcome, such as the American Orthopaedic Foot and Ankle Surgery (AOFAS) score (Kitaoka 1994) and the Olerud and Molander Ankle Functional Score (OMAS) (Olerud 1984)
2. Need for a secondary/revision operation or substantive physiotherapy for adverse outcomes (e.g. non-union, malunion and infection)

Timing of primary outcome measurement

Where available, we extracted outcome data for short-term follow-up (up to six weeks following treatment); intermediate follow-up (more than six weeks and up to six months after the end of treatment) and long-term follow-up (greater than six months after the end of treatment).

Secondary outcomes

1. Symptomatic non-union or malunion, including limping
2. Pain
3. Wound complications, including superficial wound infections, deep wound infections and osteomyelitis
4. Bone healing outcomes, including the proportion of fractures that united (fracture union) and healing time
5. Surgical details, including operation time, radiation time and any type of intraoperative complication such as fracture propagation

Search methods for identification of studies

Electronic searches

We searched the Cochrane Bone, Joint and Muscle Trauma Group Specialised Register (9 December 2014), the Cochrane Central Register of Controlled Trials (CENTRAL; 2014, Issue 12), MEDLINE (1946 to November Week 3 2014), MEDLINE In-Process & Other Non-Indexed Citations (4 December 2014), EMBASE (1980 to 2014 Week 48), the Airiti Library (1967 to 2014 Week 8) and the China Knowledge Resource Integrated Database (CNKI) (1915 to 2014 week 8). We did not apply any language restrictions.

In MEDLINE, we combined the subject-specific search strategy with the sensitivity-maximising version of the Cochrane Highly Sensitive Search Strategy for identifying randomised trials (Lefebvre 2011). The search strategies for *The Cochrane Library,* MEDLINE, EMBASE, Airiti Library and CNKI are listed in Appendix 1.

We also searched ClinicalTrials.gov (February 2014) for ongoing studies.

Searching other resources

We scanned the reference lists of included studies and relevant reviews. We contacted experts in this field and companies that manufacture intramedullary nails or plates for information on unpublished and ongoing studies.

Data collection and analysis

Selection of studies

We removed duplicate records of the search results. Two review authors (LTK and CHC) independently checked titles, abstracts and keywords from the searches to identify potentially eligible studies. The review authors were not blinded to the names of original researchers, journals or institutions. Upon obtaining the full texts of potentially eligible trials, the same two review authors performed independent study selection. We resolved disagreements by discussion and, where necessary, in consultation with a third review author (CCC).

Data extraction and management

Two review authors (LTK and CHC) independently extracted data from each trial, including trial methods, participants, interventions, outcomes and results, using a data extraction form. We resolved disagreements by discussion and, where necessary, in consultation with a third review author (CCC). One review author (LTK) entered the data into Review Manager software (RevMan 5.3; RevMan 2014), and another review author (CCC) rechecked the entered data.

Assessment of risk of bias in included studies

Two review authors (LTK and CHC) independently assessed each included trial for risk of bias using The Cochrane Collaboration's 'Risk of bias' tool (Higgins 2011). We resolved disagreements by discussion and, where necessary, by recourse to a third review author (CCC). We assessed the following:

1. random sequence generation;
2. allocation concealment;
3. blinding of participants and personnel;
4. blinding of outcome assessment (subjective (patient-reported) outcomes; re-operation and other objective outcomes);
5. incomplete outcome data (short-term follow-up; longer-term follow-up);
6. selective reporting (assessment dependent on availability of trial protocol);
7. other sources of bias: any other possible concerns about bias, such as major imbalances in baseline characteristics (e.g. age, open fractures, concomitant fibular fractures) and performance bias resulting in major differences in care programmes, including the treatment of concomitant fibular fractures, or experience with the interventions under investigation by the operating surgeons. Upon recommendation from editorial feedback at the review stage, we also considered sponsorship bias.

We judged each of the above domains as being at low risk of bias, high risk of bias or unclear risk of bias (indicating either lack of information or uncertainty over the potential for bias).

Measures of treatment effect

We expressed the treatment effects for dichotomous outcomes as risk ratios (RRs) and 95% confidence intervals (CIs). We expressed the treatment effects for continuous outcomes as mean differences (MDs) and 95% CIs for single studies or for two or more studies with comparable outcome measures. We used standardised mean differences (SMDs) and 95% CIs for data from disparate outcome measures. Where appropriate, we planned to express the dichotomous results as number needed to treat for an additional beneficial outcome (NNTB) and number needed to treat for an additional harmful outcome (NNTH) for outcomes where the RR was statistically significant.

Unit of analysis issues

We used the individual participant as the unit of analysis. For trials including bilateral fractures, we planned to follow the analytic methods stated in section 16.3 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). However, we found no trials including bilateral fractures.

Dealing with missing data

Where necessary, we contacted trial researchers to request missing data. We planned to conduct intention-to-treat analyses to include all participants randomised where possible. If participant dropout led to missing data for dichotomous outcomes, we planned to conduct a sensitivity analysis where participants with missing data would be viewed as treatment failures and included in the analysis. We planned not to impute data for continuous outcomes for either missing participants or results; however, we planned to derive missing standard deviations where standard errors, 95% CIs, or exact P values were reported instead (Higgins 2011).

Assessment of heterogeneity

We assessed statistical heterogeneity by visual inspection of the forest plot (analysis) and the I^2 statistic (Higgins 2003). We assessed clinical heterogeneity arising from the interventions, participants and outcome measures. We undertook meta-analyses if the I^2 statistic was less than 75%, and there was acceptable clinical homogeneity.

Assessment of reporting biases

We planned to investigate publication bias by using a funnel plot (Egger 1997) if at least 10 studies were available for meta-analysis of a primary outcome. Had there been pooled data from a mixture of one very large trial and several small trials, we planned to explore the presence of small study bias in the overall meta-analysis by checking if the random-effects estimate of the intervention effect varied significantly from the fixed-effect estimate.

Data synthesis

Where pooling was considered clinically appropriate, we initially pooled data using the fixed-effect model. We planned to use the random-effects model, especially if there was unexplained and substantial heterogeneity. Where it was not appropriate to pool data, we summarised the data for each trial in the text and tables.

Subgroup analysis and investigation of heterogeneity

Where sufficient data are available in future updates, we plan to explore the following potential sources of heterogeneity using subgroup analyses (Higgins 2004).

- Open fracture versus closed fracture (different soft tissue injury)
- Combined injury versus isolated injury (concurrent tibial and fibular fractures versus tibial fracture only)
- Delayed surgery after conservative treatment versus surgery started immediately

- Müller's definition versus other definitions of the distal tibia metaphysis
- Different methods of the same category of surgery (e.g. MIPO versus open surgery for plate fixation; locked versus conventional (non-locking) plate fixation).

We will investigate whether the results of subgroups are significantly different by inspecting the overlap of CIs and performing the test for subgroup differences available in RevMan.

Sensitivity analysis

If sufficient data had been available, we would have conducted sensitivity analyses to examine the effects of various aspects of trial and review methodology, including study susceptibility to selection and performance biases, the effects of missing data and the use of different models (fixed-effect versus random-effects for pooling data where there was heterogeneity). In future updates, we plan also to examine the effects of including trials that include intra-articular fractures.

'Summary of findings' tables

We summarised the results for the only comparison investigated by the trials included in this review in a 'Summary of findings' table. We used the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach to assess the quality of evidence related to each primary outcome and the first four secondary outcomes listed in the section Types of outcome measures (Higgins 2011; section 12.2).

RESULTS

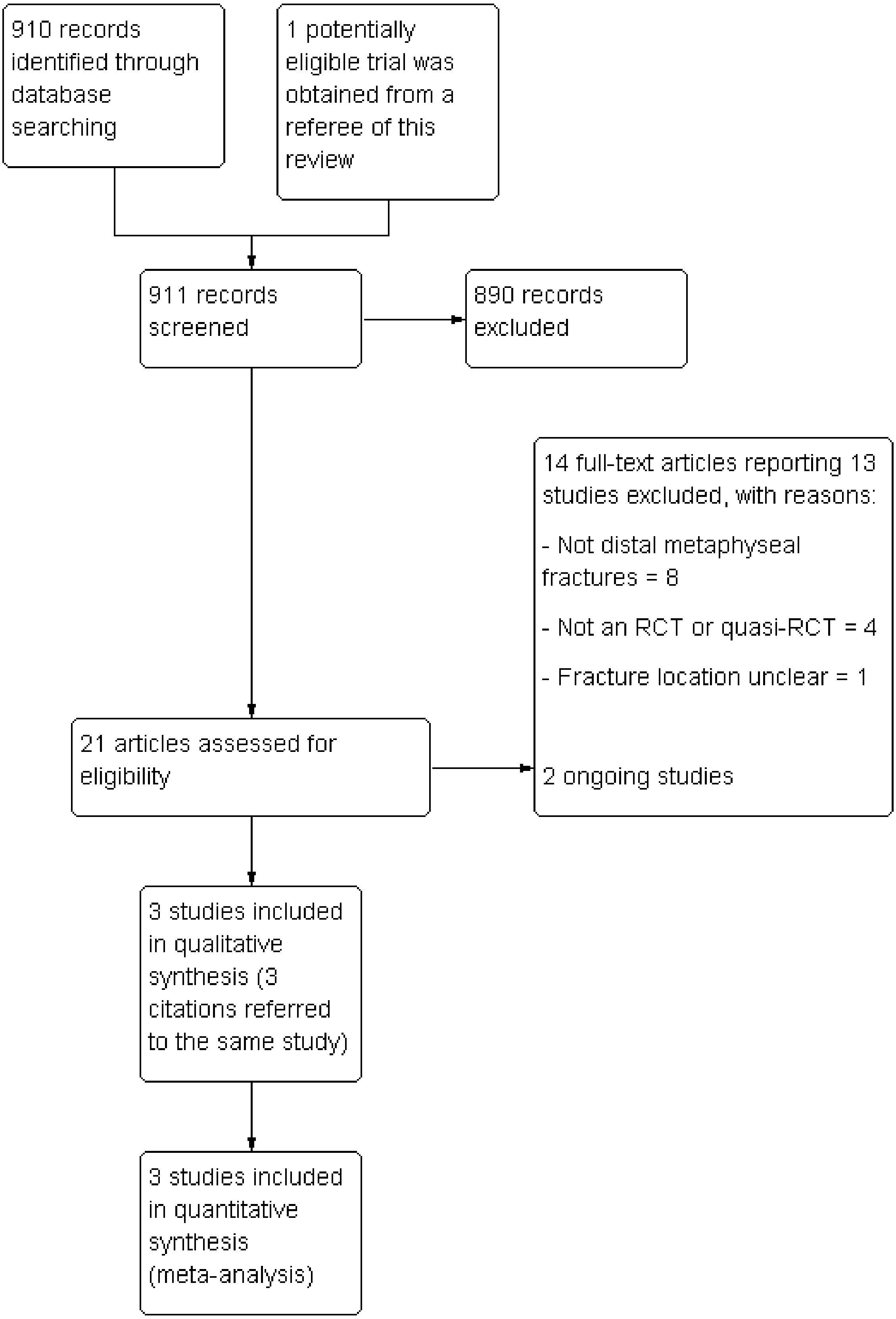
Description of studies

See the Characteristics of included studies, Characteristics of excluded studies and Characteristics of ongoing studies tables.

Results of the search

We completed the search in December 2014 (see Figure 1). We screened a total of 910 records from the following databases: Cochrane Bone, Joint and Muscle Trauma Group Specialised Register (11 records); CENTRAL (45), MEDLINE (149), EMBASE (211), Airiti Library (90), CNKI (402), ClinicalTrials.gov (2). We obtained one potentially eligible trial from a referee of this review.

Figure 1. Study flow diagram



We identified 21 potentially eligible articles. Following study selection, we included three trials in the review: Guo 2010; Im 2005; and Mauffrey 2012 , which was reported in 3 articles. All three included studies were reported in English. We excluded 13 studies (Cheng 2011; Dai 2009; Hontzsch 2014 (2 articles); Li 2014; Liu 2014; Ristiniemi 2011; Shon 2012; Sun 2014; Vallier 2011; Vallier 2012; Yang 2006; Zou 2012; Zou 2013). We identified two ongoing studies (ISRCTN99771224; NCT01047826). No studies await classification.

Included studies

All three included studies compared two types of surgical devices for internal fixation. None compared surgical versus non-surgical treatment. Details of the methods, participants, interventions and outcome measures of individual trials are provided in the Characteristics of included studies table.

Study design

All three studies were single-centre RCTs with two parallel groups.

Setting

The included trials were conducted in single hospitals in China (Guo 2010), Korea (Im 2005) and the UK (Mauffrey 2012).

Participants

Guo 2010 randomised 111 participants and included 85 participants in the final analyses. Im 2005 randomised 78 participants and included 64 participants in the final analyses. Mauffrey 2012 randomised 24 participants and included all of them in the final analyses. In total, the three studies randomised 213 participants with 213 fractures, and 173 participants were included in the final analyses.

Of the 173 participants included in the final analyses, 112 were men and 61 were women. The mean age of participants in individual studies ranged from 41.1 (Im 2005) to 44.3 years (Guo 2010). The type of distal tibial metaphyseal fractures included was either closed fracture or Gustilo open type I fracture. Im 2005 included 51 closed fractures and 13 open fractures. The other two trials (Guo 2010; Mauffrey 2012) did not provide details of the number of open fractures. Two trials (Guo 2010; Im 2005) used the AO/OTA classification type 43 to define distal tibial metaphyseal fracture. Mauffrey 2012 defined distal tibial metaphysis as the area within two Müller squares of the ankle joint, in which the proximal and the distal segments of long bones were defined by a square whose sides had the same length as the widest part of the epiphysis (Müller 1990). Im 2005 additionally used the Tscherne classification (Oestern 1984) to assess the extent of the soft tissue injuries in closed fractures.

Interventions

One trial (Im 2005) compared intramedullary nailing versus plating with non-locking screws, while the other two (Guo 2010; Mauffrey 2012) compared intramedullary nailing versus plating with fixed-angle locking screws. Guo 2010 used the MIPO technique in all cases, whereas Mauffrey 2012 used MIPO only in some cases (the exact number was not reported).

Outcomes

The length of follow-up ranged from one year in two trials (Guo 2010; Mauffrey 2012) to two years in Im 2005. All three trials recorded patient-reported functional outcome. In terms of foot and ankle function scores, Guo 2010 reported the AOFAS score at 12 months after surgery, and Im 2005 and Mauffrey 2012 reported OMAS results. However, Im 2005 reported OMAS for the injured side as a percentage of the OMAS for the normal side at 24 months after surgery. Mauffrey 2012 reported OMAS at 3, 6 and 12 months after surgery. Mauffrey 2012 also recorded Disability Rating Index (DRI) scores and EuroQol EQ-5D questionnaire and scale results at the same follow-up times. All three trials provided details of secondary/revision operations, symptomatic non-union/ malunion, wound complications and fracture union; Guo 2010 and Im 2005 reported time to fracture union using the same criteria to determine union. Only Guo 2010 reported pain level at one year after surgery, using the pain component of the AOFAS score. Guo 2010 and Im 2005 provided data on operation time; Guo 2010 provided details of radiation time; and Im 2005 reported an intra-operative complication.

Excluded studies

Thirteen studies were excluded for reasons stated in the Characteristics of excluded studies table. Four studies (Dai 2009; Ristiniemi 2011; Shon 2012; Yang 2006) were neither RCTs nor quasi-RCTs. The other nine trials included either no or insufficient numbers of participants with distal tibial metaphyseal fractures: eight trials (Cheng 2011; Hontzsch 2014; Li 2014; Liu 2014; Sun 2014; Vallier 2012; Zou 2012; Zou 2013) primarily included individuals with distal diaphyseal fractures of the tibia, and one trial (Vallier 2011) included individuals with fractures 4 cm to 11 cm from the tibia plafond.

Ongoing studies

We found two ongoing studies on distal tibial metaphyseal fractures: ISRCTN99771224, which is comparing nailing with locking plate fixation, aims to recruit a minimum of 320 participants; and NCT01047826, which is comparing intramedullary nailing with plate fixation, aims to recruit 180 participants.

Risk of bias in included studies

We present 'Risk of bias' assessments for individual studies in 'Risk of bias' tables in the Characteristics of included studies and have summarised these assessments in Figure 2 and Figure 3.

Figure 2. 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included studies

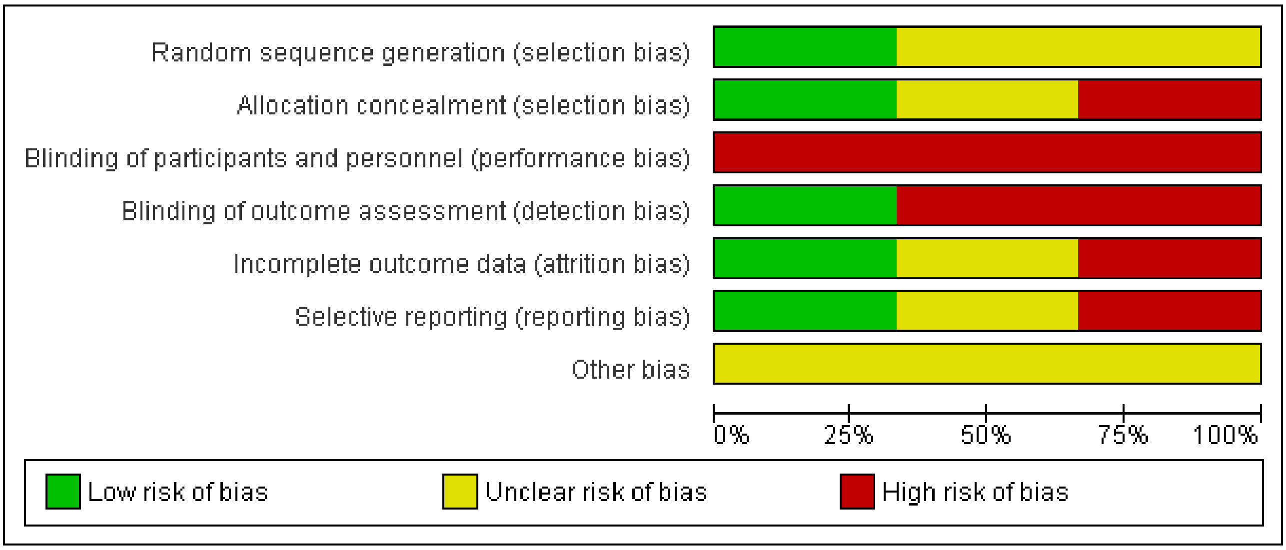
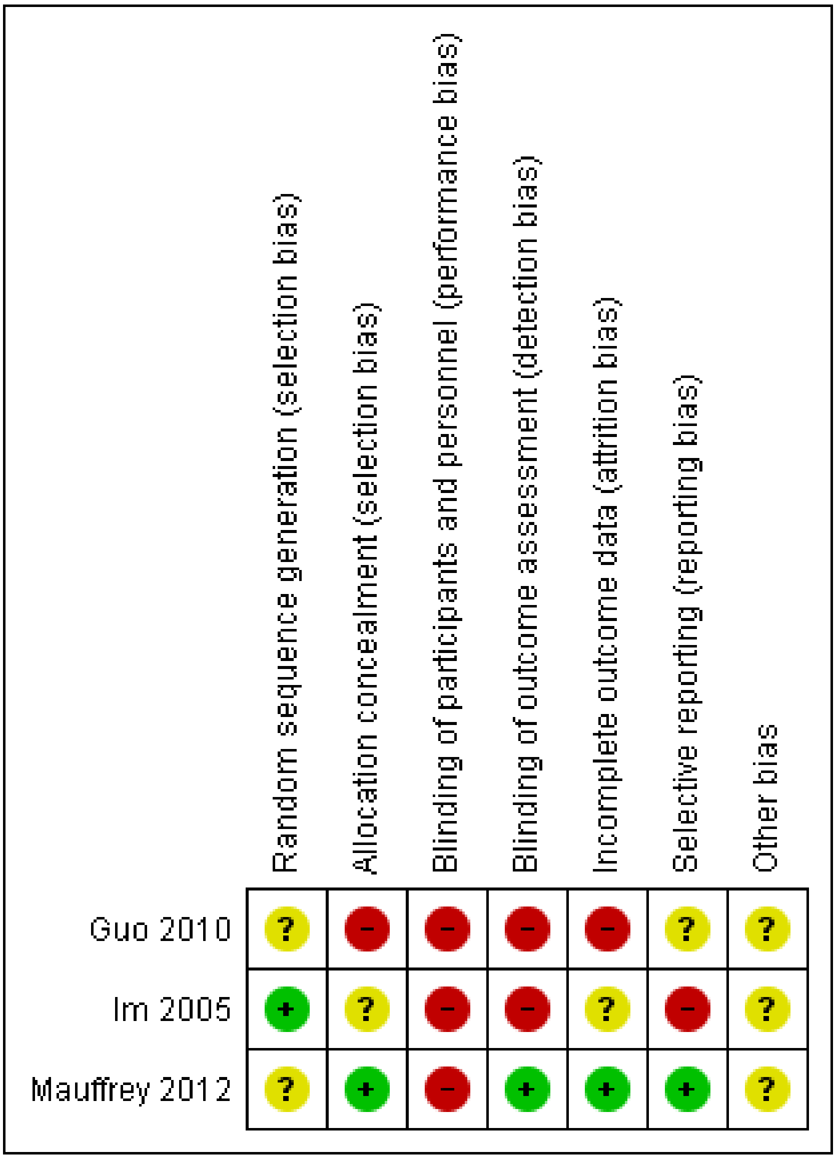


Figure 3. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study



Allocation

We judged Guo 2010, which described neither the method of random sequence generation nor allocation concealment, as being at unclear risk of bias relating to sequence generation and at high risk of bias relating to lack of allocation concealment. We judged Im 2005, which described drawing envelopes from a box, at low risk of bias relating to random sequence generation but at unclear risk of bias relating to lack of allocation concealment as there was no mention of safeguards. We judged Mauffrey 2012, which described a "pseudo-random number sequence" as being at unclear risk of bias relating to random sequence generation but at low risk of bias relating to allocation concealment, reflecting the remote and independent administration of allocation.

Blinding

None of the three trials reported any details about blinding of participants and personnel. However, blinding of surgeons and participants in this condition is not possible since the surgical incisions in nailing and plating are very different and the metalwork is easily palpable. Thus, we judged the three trials to be at high risk of performance bias.

Guo 2010, where outcomes were assessed by doctors who were also involved in the treatment, we judged to be at high risk of detection bias. Im 2005 described outcome assessment at two years by "an independent physician". However, as this and other assessments (e.g. of complications) were not blinded, we judged this trial to be at high risk of detection bias. We judged Mauffrey 2012 to be at low risk of detection bias, reflecting the use of an outcome assessor who was blinded to treatment allocation.

Incomplete outcome data

In judging the risk of bias for this item, we considered a less than 80% completion rate in the treatment group to indicate a high risk of bias. We also assessed whether missing data were balanced between the two groups and whether an intention-to-treat analysis had been reported for the primary outcome. All three trials (Guo

2010; Im 2005; Mauffrey 2012) provided data on dropouts/loss to follow-up and 23.4%, 15.3% and 8.3% participants, respectively, were excluded from the outcome analyses of these trials. We also judged Guo 2010 to be at high risk of attrition bias, reflecting contradictory statements in the report in terms of the post-randomisation exclusion of participants whose fibular fracture had been fixed. We judged Im 2005 to be at unclear risk of attrition bias. Since the trialists of Mauffrey 2012 provided us with raw data, we judged the study to be at low risk of attrition bias.

Selective reporting

Neither trial registration documents nor protocols were available for any of the three trials. We obtained raw data from trialists of one study (Mauffrey 2012), which we thus judged as being at low risk of bias. We judged Guo 2010 as being at unclear risk of reporting bias and Im 2005 at high risk given the disparity between the methods and results in how OMAS data were reported.

Other potential sources of bias

While we considered Guo 2010 and Im 2005 to be at low risk of performance bias relating to surgeon experience and comparability of care programmes, there was an unclear risk of bias relating to a lack of data on baseline characteristics for all trial participants. The comparability of care programmes was not established in Mauffrey 2012, which we also judged to be at unclear risk of other bias because the mean age of the nailing group was older than that of the plating group. While the trial authors performed a linear regression analysis to adjust for the effects of age, only the adjusted data for DRI at six months of follow-up were reported. In addition, while similar numbers in Im 2005 and Mauffrey 2012 underwent fixation of fibula fractures, we considered that any differences between groups in the decision to fix these fractures were a potential source of other bias. We found no evident sponsorship from manufacturers of intramedullary nails or plates.

Effects of interventions

See: **Summary of findings for the main comparison** Summary of findings: Surgical interventions for treating distal tibial metaphyseal fractures in adults

All three included trials compared intramedullary nailing versus plating (Guo 2010; Im 2005; Mauffrey 2012). There were no trials comparing surgery with non-surgical treatment.

Intramedullary nailing versus plating

The three trials recruited a total of 213 participants and reported data for 173 participants at follow-up. Due to the clinical heterogeneity across available trials and the lack of relevant data, we were unable to perform prespecified subgroup analyses, including of different methods of the same category of surgery.

Primary outcomes

Patient-reported functional outcome

All three trials reported patient-reported functional outcome relating to the ankle, but used different measures (Guo 2010: AOFAS scores at one year; Im 2005: OMAS, percentage of normal side at two years; Mauffrey 2012: OMAS scores at one year). Standard deviations were calculated from exact P values presented in Guo 2010 and Im 2005, and from individual participant data provided for Mauffrey 2012. Pooled data from these three trials were in favour of the nailing group (SMD 0.28, 95% CI -0.02 to 0.59; 172 participants; Analysis 1.1). Separate data for these outcomes and for DRI data (direction reversed in the Analysis to present a direction of benefit consistent with the other scores) reported for Mauffrey 2012 are shown in Analysis 1.2. It is notable that all results favour the nailing group, although all CIs cross the line of no effect, with the exception of those for OMAS at 12 months in Mauffrey 2012. Mauffrey 2012 reported that the minimal clinically important difference for the DRI is 8 points. Hence, although the effect size is less than 8 points, the wide CIs at all three time points for this outcome include the potential for a clinically important effect both in favour of nailing and, to a lesser extent, of plating (e.g. at 12 months, the MD was 3.90 in favour of nailing (95% CI -19.22 to 27.02)). Mauffrey 2012 also found no significant differences in the EQ-5D scores between the two groups at all follow-up times (data not presented).

Need for a secondary/revision operation or substantive physiotherapy for adverse outcomes (e.g. non-union, malunion and infection)

Pooled data from the three trials showed a lower incidence in the nailing group than in the plating group of participants undergoing or waiting for a secondary operation for adverse outcomes (4/90 versus 10/83; RR 0.37 favouring nailing, 95% CI 0.12 to 1.12; 173 participants; Analysis 1.3). These data were moderately heterogeneous (Chi^2 = 2.17, df = 1 (P value = 0.14); I^2 = 54%). The details of the revision operations for each trial are listed in Table 1. Not included in Analysis 1.3 are fasciotomies performed for compartment syndrome in one participant in each group included in Mauffrey 2012; this is because it is unclear whether these participants had a subsequent complication. Notably, no secondary surgeries were performed in Guo 2010 during the 12-month follow-up period. However, similar numbers (23 in the nailing group versus 24 in the plating group) of participants had their implants removed after the end of follow-up (mean 15.5 months). The main factors contributing to the decision for implant removal were prominence of the plate and pain. Guo 2010 observed that all nails were removed without difficulty, but that difficulties were encountered with the removal of locking screws in nine participants in the plating group.

Secondary outcomes

Symptomatic non-union or malunion, including limping

Pooled data from the three trials (Guo 2010; Im 2005; Mauffrey 2012) showed no significant differences in symptomatic non-union or malunion between the nailing and plating groups (3/90 versus 4/83; RR 0.72 favouring nailing, 95% CI 0.18 to 2.80; Analysis 1.4). Mauffrey 2012 reported that one participant in the nailing group had a malunion (10 degrees valgus) but did not mention whether this was symptomatic.

Pain

Only Guo 2010 reported on pain (scale 0 to 40: highest score = no pain); however, this measure was part of the AOFAS score. Guo 2010 found little difference in pain between the nailing and plating groups at one year after operation (MD 1.00 favouring nailing, 95% CI -0.63 to 2.63; 85 participants; Analysis 1.5).

Wound complications including superficial wound infections, deep wound infections and osteomyelitis

Pooled data from the three trials (Guo 2010; Im 2005; Mauffrey 2012) showed a lower incidence of wound complications in the nailing group than in the plating group (7/90 versus 14/83; RR

0.47 favouring nailing, 95% CI 0.20 to 1.10; 173 participants; Analysis 1.6). Overall, 19 participants had a superficial wound infection, one of whom required a skin graft (Table 1), and two participants, both of whom had plating, had a deep infection requiring debridement and other treatment (Table 1). These data were moderately heterogeneous (Chi^2 = 4.55, df = 2 (P value = 0.10); I^2 = 56%) but no data on risk factors for wound complications such as open fractures and delayed surgery were available for subgroup analyses to explore this.

Bone healing outcomes including fracture union and healing time

Pooled data from the three trials (Guo 2010; Im 2005; Mauffrey 2012) found no significant differences between the two intervention groups in the proportion of fractures that united (87/90 versus 79/83; RR 1.02 favouring nailing, 95% CI 0.95 to 1.09; Analysis 1.7). Pooled data from the two trials reporting on time to fracture union showed no significant differences between the two groups (MD 0.09 weeks, 95% -1.46 to 1.44 weeks; 149 participants; Analysis 1.8).

Surgical details, including operation time, radiation time and any type of intraoperative complications

Pooled data from two trials (Guo 2010; Im 2005) showed a shorter mean operation time in the nailing group than in the plating group (81.23 minutes versus 97.90 minutes; MD -16.78 minutes favouring nailing, 95% CI -24.67 to -8.88 minutes; 149 participants; Analysis 1.9). Guo 2010 reported a shorter total radiation exposure time in the nailing group than in the plating group (2.2 minutes versus 3.0 minutes; MD -0.80 minutes, 95% CI -1.31 to -0.29 minutes; Analysis 1.10). Im 2005 also reported a case of intraoperative fracture comminution in the nailing group that needed further screw fixation.

DISCUSSION

Summary of main results

In this review, we included three RCTs that compared the effects of nailing versus plating in treating distal tibial metaphyseal fractures in adults. These trials provided outcome data for a maximum of 173 participants with 173 mainly closed fractures. We found no trials comparing surgery with non-surgical treatment, or trials comparing other surgical methods. Overall, the quality of available evidence was rated as very low for all outcomes; this means that we are very uncertain about the estimates and that further research is very likely to have an important impact on the estimates of effect. A summary of the results of the comparison of nailing versus plating is presented in Summary of findings for the main comparison.

Although the pooled SMD results (172 participants, 3 trials), which crossed the line of no effect, from three different measures of foot and ankle function indicated a small difference in favour of nailing, the results of individual trials indicated that this was very unlikely to be a clinically important difference. Pooled data (173 participants, 3 trials) for the need for re-operation, symptomatic non-union or malunion, wound complications and fracture union all favoured nailing, but the 95% CIs crossed the line of no effect and thus included the possibility of a better outcome after plating. For example, based on an illustrative risk of 100 re-operations for adverse outcomes within one year of plate fixation in 1000 people with these fractures, 63 fewer (95% CI 88 fewer to 12 more) people per 1000 would have had re-operations after nailing. Evidence from one trial (85 participants) showed no clinically important difference in pain between the two groups.

Overall completeness and applicability of evidence

There is evidence available from a total of only 173 adults with distal tibial metaphyseal fractures for one surgical comparison only. Although the three trials compared nailing with plating, the two types of intervention differed between trials. In particular, one trial (Im 2005) used conventional plating with non-locking screws, whereas the other two (Guo 2010; Mauffrey 2012) involved plating with locking screws. Open surgery was used in Im 2005, whereas the MIPO technique was used in all cases in Guo 2010 and in at least some cases in Mauffrey 2012. The age and sex distributions of participants in the three trials were comparable and similar to that reported in Court-Brown 2006. The fracture populations also appeared comparable; however, there were insufficient data to determine how many of the fractures in Guo 2010 and Mauffrey 2012 were open. As all three trials excluded open fractures other than Gustilo type 1 fractures, our findings may not apply to more severe open fractures. In such fractures, especially Gustilo types 2 and 3, debridement is important, and a temporary external fixator is usually used for stabilisation. Additional concerns about infection extending to the intramedullary canal during procedures mean that plating may be used in preference to nailing.

Developments in plating could also affect the findings of this review. The technique and experience of individual surgeons can affect outcomes, and surgeons often choose what they are familiar with. Nonetheless, there is a trend towards the increased use of locking plate fixation. In addition, the MIPO technique should cause less tissue damage and, hence, could theoretically achieve better outcomes. This may also be influenced by the use of precontoured locking plates. Both of the ongoing trials we have identified use locking plates and one specifically uses the MIPO technique. The planned enrolment of the ongoing trial (ISRCTN99771224) for which recruitment is confirmed as ongoing is over 320 participants. This highlights the limitations of the currently available evidence in terms of sample size and current practice.

Quality of the evidence

A summary of the 'Risk of bias' judgements for each domain across the included studies shows a mixed picture but one in which at least one trial was at high risk of bias for five of seven domains (see Figure 2).

Overall, the quality of the evidence assessed using GRADE was very low, which means that we are very uncertain about the estimates for all six outcomes presented in our 'Summary of findings' table (Summary of findings for the main comparison). Although, our main reasons for downgrading the evidence varied, we usually downgraded one or two levels for study limitations that reflected the high risk of bias of the included studies. We further downgraded for imprecision (wide CIs and small sample size) and for inconsistency where there was clear heterogeneity.

Potential biases in the review process

With the exception of a few items (detailed in the section Differences between protocol and review) we conducted the review following the prespecified protocol. A comprehensive database search was performed but it is possible that we have missed unpublished studies and study findings. We tried to contact authors of all included trials for detailed data, but only the authors of Mauffrey 2012 responded; they provided us with their original data. We calculated missing standard deviations from P values for both Guo 2010 and Im 2005, and calculated means and standard deviations from individual patient data provided for Mauffrey 2012. Especially for Mauffrey 2012, we assumed a normal distribution for all outcomes. This assumption may be less appropriate where the sample sizes are small.

Agreements and disagreements with other studies or reviews

We have identified two recently published systematic reviews, both of which include a broader range of study designs that include retrospective studies. One review (Xue 2014), including 14 studies of mixed design that compared nailing with plating for distal tibial metaphyseal fractures, found nailing to be associated with better functional scores (reported P value = 0.01), a lower risk of infection (P value = 0.02) and comparable pain scores (P value = 0.33), total complication rates (P value = 0.53) and times to union (P value = 0.86) than plating. Conversely, the malunion rate was lower in the plating group (P value < 0.0001). The second review (Kwok 2014) included eight studies testing the same comparison of nailing versus plating for distal tibial fractures. This also found the malunion rate to be lower in the plating group than in the nailing group (reported P value = 0.001). Kwok 2014 found no difference in the fracture union rate and in wound complications between the two groups. As well as differences in the inclusion criteria, both reviews included studies with fractures (generally AO/OTA type 42) other than those included in our review.

AUTHORS' CONCLUSIONS

Implications for practice

Overall, there is either no or insufficient evidence to draw definitive conclusions on the best surgical treatment for distal tibial metaphyseal fractures in adults. The current available evidence, which is of very low quality, suggests there are no clinically important differences in functional or pain outcomes, and does not confirm a difference in the need for major re-operations or risk of complications between nailing and plating. There is no evidence available from RCTs to inform on the use of surgery for less serious fractures or on the relative effects of other surgical interventions.

Implications for research

In future updates of this review, the addition of evidence from the two ongoing trials identified will help to inform the selection of optimal treatments in managing distal tibial metaphyseal fractures. Further RCTs are needed but, in order to optimise research efforts, these should be preceded by research that aims to identify priority questions that can then be tested in large multicentre trials. Key clinical questions include the use of different plating techniques such as the minimally invasive percutaneous osteosynthesis technique, the fixation or not of fibula fractures, locking bolts and other techniques of nailing, and the use of the external fixation. In such trials, full data on functional outcomes, pain, complications, re-operations and cost outcomes should be reported.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Guo 2010

Methods	Randomisation: participants were allocated a sequential study number but there was no mention of method otherwise Assessor blinding: there was no assessor blinding Length of follow-up: 12 months
Participants	First Affiliated Hospital of Soochow University, Suzhou, China Period of study: July 2005 to January 2008 111 participants each with distal metaphyseal fracture of the tibia. There were 26 participants "who had not reached one year by the time of the study." Sex (of 85): 35 female, 50 male Age: mean 44.3 years, range 23 to 70 Fracture type: AO/OTA 43-A1:26, 43-A2: 28, 43-A3: 31 Unknown number of open fractures (Gustilo type I). Most participants had a fractured fibula (19 that were surgically fixed were excluded) **Inclusion criteria** 1. Distal metaphyseal fracture of tibia 2. Presence of a distal fragment of at least 3 cm in length with no articular incongruity (OTA type 43-A fracture) **Exclusion criteria** 1. Individuals with pathological fractures, non-osteoporotic osteopathies such as endocrine disorders, rheumatologic disorders, diabetes mellitus, renal disease, immunodeficiency states, mental impairment or difficulty in communication 2. Those with open fractures according to Gustilo and Anderson type II or type III or fractures with a displaced intra-articular fragment **Assigned**: 57/54 participants (intramedullary nail/plate) **Analysed**: 44/41 (12 months)
Interventions	1. Closed reduction and intramedullary nailing (IMN) (S2 nailing system; Stryker, Schönkirchen, Germany). Nails were inserted after reaming. Static locking applied in all cases. 2. Closed reduction and locking compression plate (LCP) (LCP; Synthes, Bettlach, Switzerland) applied with minimally percutaneous plate osteosynthesis (MIPO) technique. Operation was usually performed on day of injury. However, operations were delayed 5 to 10 days in 5 plate group participants because of excessive swelling or bruising. Other care: All received prophylactic antibiotics. Same postoperative care for both groups. Sutures removed after 14 or 15 days. Ankle was immobilised on a short-leg cast or splint for 3 weeks. Range of motion ankle exercises were encouraged. Timing of partial and full weight-bearing was on an individual basis.
Outcomes	• AOFAS functional score • Re-operation • Delayed union, non-union, malunion (malalignment) • Pain • Function • Wound problem including delayed wound healing and superficial wound infection

Guo 2010 *(Continued)*

	• Time to union • Radiation time, operation time • Implant removal questionnaire. Implant removal after the end of the follow-up period was also reported
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Participants were allocated a sequential study number. There was no mention how this was done.
Allocation concealment (selection bias)	High risk	Participants were allocated a sequential study number. Thus it appears that the sequence was predictable and allocation was not concealed. It was stated there were "no exclusions after randomisation" but then stated that "If the associated fibular fracture was fixed, the patient was excluded from the study". This applied to "ten patients in the IMN group and nine in the LCP group". reported that 19 participants whose associated fibular fracture was fixed surgically were excluded.
Blinding of participants and personnel (performance bias) All outcomes	High risk	The difference between the two methods means that blinding is not possible for the surgeon and unlikely for the participants. There was no statement on blinding.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcomes were assessed by the two of the three operating surgeons involved in the treatment.
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "The remaining 26 patients had not reached one year by the time of the study." "Ten patients in the IMN group and nine in the LCP group were excluded due to fixation of fibular fracture." Contradictory statements mean that it is unclear how many were excluded from the trial.
Selective reporting (reporting bias)	Unclear risk	Protocol unavailable and results reported in a different way between abstract and text. Subsequent correction published.
Other bias	Unclear risk	Since the baseline characteristics of 26 participants (23% of 111) were not provided, we cannot tell if the baseline characteristics were balanced. Similar numbers in the 2 groups who had surgically fixed fibular fractures (10 in nail group and 9 in plate group) but these people were excluded; it is unclear whether these were counted in the 111 participants. All operations were carried out by the three senior surgeons. Postoperative care was reported to be comparable.

Im 2005

Methods	Randomised trial, allocation by drawing from a box of envelopes Assessor blinding: one physician who had not been involved in the treatment performed an independent evaluation of all trial participants at 24 months Length of follow-up: 24 months

Im 2005 *(Continued)*

Participants	Dongguk University Hospital, Goyang, Korea Period of study: July 1998 to June 2001 78 participants, each with a distal metaphyseal fracture of the tibia. Two died and 12 did not complete the study at 2 years follow-up; these were excluded from the trial analyses and baseline characteristics Sex (of 64): 18 female, 46 male Age: mean 41.1 years, range 17 to 65 Fracture type: AO/OTA 43-A1: 26, 43-A2: 19, 43-A3: 9, 43-C1: 10 13 open fractures (Gustilo type I) and 51 closed fractures; 35 also had fibula fractures **Inclusion criteria** 1. Distal metaphyseal fractures of tibia 2. In all of the included cases, the centre of the fracture was in the distal metaphysis of tibia and either entirely extra-articular (A1, A2, and A3) or with minimally displaced extension into the ankle joint (C1) **Exclusion criteria** 1. Open fractures of Gustilo-Anderson type II or III 2. Fractures with displaced intra-articular fragments 3. Based on the preoperative roentgenograph examination, two distal screw fixations were found to be not feasible (this applied to one case) **Assigned:** ?/? participants (intramedullary nail/plate) **Analysed:** 34/30 (24 months)
Interventions	1. Closed reduction and intramedullary nailing (ACE tibial nails (ACE Depuy, El Segundo, California) used in 16 cases; or cannulated tibial nails (Mathys, Bettlach, Switzerland) used in 18 cases). Nails were inserted after reaming. Static locking applied in all cases. 2. Open reduction and fixation with anatomic plates (Waldermar-Link, Hamburg, Germany) and screws. Eleven of the 35 fibular fractures were fixed with small dynamic compression plates (6 in the nail group versus 5 in the plate group). Other care: A long leg plaster cast was applied. After wound swelling had subsided, ankle joint mobilisation was encouraged under physiotherapist supervision. Timing of weight-bearing was on an individual basis. A short leg cast was applied for participants with minimally displaced intra-articular fractures.
Outcomes	• Olerud and Molander Ankle Functional Score (OMAS) • Re-operation or surgery for complication • Fracture non-union, tibia malalignment • Complications including superficial and deep wound infection, • Fracture healing time • Operation time, intraoperative fracture comminution • Ankle range of motion
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"The treatment method was chosen at random by drawing from the box containing an equal number of envelopes with either of the methods"

Im 2005 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	"The treatment method was chosen at random by drawing from the box containing an equal number of envelopes with either of the methods". Adequate safeguards not described.
Blinding of participants and personnel (performance bias) All outcomes	High risk	The difference between the two methods means that blinding is not possible for the surgeon and unlikely for the participants. There was no statement on blinding.
Blinding of outcome assessment (detection bias) All outcomes	High risk	"To limit the bias inherent in all clinical examinations and manual tests, the final follow-up examination, 2 years after the operation, was performed by an independent physician who had not been involved in the actual treatment of any of the patient." However, this was not blinded and blinding of outcome assessment was not reported for other time points prior to 2 years after the operation.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Treatment allocation and outcome were not provided for 14 participants (18% of 78), 2 of whom had died and 12 who were lost to follow-up.
Selective reporting (reporting bias)	High risk	No protocol provided and the OMAS results only reported in the abstract and not in a way described in the methods.
Other bias	Unclear risk	Since the baseline characteristics of 14 participants were not provided, we cannot tell if the baseline characteristics were balanced. Although similar numbers in the 2 groups had surgically fixed fibular fractures (6 in nail group and 5 in plate group), we cannot be sure that the decision to operate was comparable in the 2 groups. Experience with both methods was stated; all operations were carried out or supervised by one senior surgeon.

Mauffrey 2012

Methods	Randomised trial, allocation using computer-generated random number sequence Assessor blinding: one physician blinded to treatment allocation performed evaluation of all participants Length of follow-up: 12 months
Participants	Warwick Orthopaedics, University of Warwick, Warwick, United Kingdom Period of study: March 2008 to August 2009 24 participants with 24 distal metaphyseal fracture of the tibia Sex: 8 female, 16 male Age: mean 41.5 years Fracture type: All fractures were closed or Gustilo type 1 fracture **Inclusion criteria** 1. Adults aged 18 years or over with a closed or Gustilo I extra-articular fracture of the distal tibia 2. The distal tibia was defined as the area within two Müller squares of the ankle joint, in which the proximal and the distal segments of long bones are defined by a square whose sides have the same length as the widest part of the epiphysis **Exclusion criteria** 1. Open fractures of Gustilo-Anderson type II or III 2. Fractures with displaced intra-articular fragments

Mauffrey 2012 *(Continued)*

	3. Individuals were excluded if they had other injuries that could affect the primary outcome measure, such as polytrauma or vascular or neurological injuries, if the fracture was too distal to achieve fixation of four cortices with distal interlocking screws, if the individual had a history of peripheral vascular disease or had a contraindication to anaesthesia **Assigned:** 12/12 participants (intramedullary nail/plate) **Analysed:** 12/11 (12 months)
Interventions	1. Intramedullary nails were secured using a minimum of two distal non-locking screws 2. Plate with a fixed-angle screws (locking plate) was applied using indirect reduction techniques and bridge-plating However, the surgeons were given the freedom to adapt these techniques as required by the configuration of the fracture and in accordance with their preferred technique and surgical approach.
Outcomes	Patient-reported outcome (Disability Rating Index: DRI), Olerud and Molander Ankle Functional Score (OMAS), EuroQol (EQ-5D), non-union, delayed union, tibia malalignment, wound complications including superficial and deep infections, reoperation, need for hardware removal, broken hardware, compartment syndrome
Notes	One participant in the intramedullary nail group receiving conservative treatment was included in the intention-to-treat analysis Individual participant data, characteristics and outcomes received from trialists (20 May 2013)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"Treatment allocation was determined using a computer-generated pseudo-random number sequence" We are not sure why a pseudo-random rather than random number sequence was used.
Allocation concealment (selection bias)	Low risk	Treatment allocation was administered by an independent trial co-ordinator (KMG) who was contacted by telephone"
Blinding of participants and personnel (performance bias) All outcomes	High risk	The difference between the two methods means that blinding is not possible for the surgeon and unlikely for the participants.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The outcome data were collected by an experienced research physiotherapist (KMG) blinded to treatment allocation, at 6 weeks, 3 months, 6 months and 12 months postoperatively
Incomplete outcome data (attrition bias) All outcomes	Low risk	All data reported, and the trialists provided us with the raw data.
Selective reporting (reporting bias)	Low risk	No protocol but no selective reporting was found, and the trialists provided us with the raw data.
Other bias	Unclear risk	Participants in the plate group were younger than those in the nail group (mean age 33 versus 50 years) Two fibulae were fixed in the nail group, whereas none was fixed in the plate group. No mention of the reason why fibulae were fixed.

Mauffrey 2012 *(Continued)*

	Although surgery was carried out by experienced surgeons, this was a pragmatic trial and the small numbers mean that variation in the postoperative rehabilitation regimens may have resulted in some important lack of comparability in the care programmes.

AOFAS: American Orthopaedic Foot and Ankle Surgery
AO/OTA: Arbeitsgemeinschaft für Osteosynthesefragen/Orthopaedic Trauma Association

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Cheng 2011	Fracture location is on the distal third of the tibia diaphysis, which is outside of the scope of review
Dai 2009	The study design was not explicitly stated with no description of allocation method. It seems to be a retrospective study. Also, the fracture location was not clearly defined: the study included AO/OTA type A, B and C fractures, without mentioning whether type 42 or type 43 fracture was included. If type 42 fractures were included, they are outside the scope of this review. If type 43 fractures were included, a high proportion of intra-articular fractures (type B+C, 21/25 versus 15/20) were present, which are also outside the scope of this review
Hontzsch 2014	This RCT of two types of locking systems for intramedullary nailing included 75 participants in the experimental group and 67 participants in the control group. However, only 3/75 versus 0/67 were classified as AO/OTA 43 fractures; the rest being AO/OTA 42 fractures, which are outside the scope of this review
Li 2014	The study focused on distal tibial shaft (AO 42) fractures, which was beyond the scope of review
Liu 2014	The fracture location of the study was not clearly defined: the study included AO/OTA type A, B and C fractures, without mentioning whether type 42 or type 43 fracture was included. If type 42 fractures were included, they are beyond the scope of this review. If type 43 fractures were included, a high proportion (> 25%) of intra-articular fractures (type B+C/total: 26/68) was present; which also is a reason for exclusion
Ristiniemi 2011	Retrospective study design. The study design is outside the scope of review
Shon 2012	Retrospective cohort study design. The study design is outside the scope of review
Sun 2014	The study focused on distal tibial shaft (AO 42) fractures, which are outside the scope of review
Vallier 2011	This was an RCT but the fracture location was 4 cm to 11 cm from the distal tibia plafond; which is outside the scope of this review
Vallier 2012	The study focused on extra-articular distal tibia shaft fractures (OTA 42), which was beyond the scope of review
Yang 2006	Retrospective study design. The study design is outside the scope of this review
Zou 2012	RCT but the trial included distal tibial shaft fractures (AO/OTA types 42 A, 42B, and 42C fractures), which are outside the scope of this review
Zou 2013	RCT but the trial included distal tibial shaft fractures (AO/OTA types 42 A, 42B, and 42C fractures), which are outside the scope of this review

AO/OTA: Arbeitsgemeinschaft für Osteosynthesefragen/Orthopaedic Trauma Association
RCT: randomised controlled trial

Characteristics of ongoing studies *[ordered by study ID]*

ISRCTN99771224

Trial name or title	'UK FixDT - A Randomised Controlled Trial for patients with a displaced fracture of the distal tibia, is there a clinical and cost-effectiveness difference between 'locking' plate fixation and intramedullary nail fixation'
Methods	Multicentre randomised clinical trial
Participants	Inclusion criteria: • Aged 16 years or over, either sex • Any fracture which involves the distal tibial metaphysis – defined as a fracture extending within 2 Muller squares of the ankle joint • In the opinion of the attending surgeon, the individual would benefit from internal fixation of the fracture Exclusion criteria: • Current exclusion criteria as of 03/02/2014: a. In the opinion of the attending surgeon, there is a contraindication to intramedullary nailing b. The fracture is open c. There is a contraindication to anaesthesia d. There is evidence that the individual would be unable to adhere to trial procedures or complete postal questionnaires • Previous exclusion criteria: a. In the opinion of the attending surgeon, there is a contraindication to intramedullary nailing b. The fracture is open with a Gustillo grade of more than 1 c. There is a contraindication to anaesthesia d. There is evidence that the individual would be unable to adhere to trial procedures or complete postal questionnaires
Interventions	1. Intramedullary nailing The intramedullary nail is inserted at the proximal end of the tibia and passed down the centre of the bone in order to hold the fracture in the correct (anatomical) position. The reduction technique, the surgical approach, the type and size of the nail, the configuration of the proximal and distal interlocking screws and any supplementary device or technique will be left entirely to the discretion of the surgeon as per standard clinical practice. 2. Locking plate fixation The locking plate is inserted at the distal end of the tibia and passed under the skin on the surface of the bone. Again, the details of the reduction technique, the surgical approach, the type and position of the plate, the number and configuration of fixed-angle screws and any supplementary device or technique will be left to the discretion of the surgeon. The only stipulation is that fixed-angle screws must be used in at least some of the distal screw holes – this is standard practice with all distal tibia locking plates.
Outcomes	Primary outcome Disability Rating Index at 6 months after injury Secondary outcomes 1. Early functional status at 3 months and later functional status at 12 months; Olerud and Molander Ankle Functional Score (OMAS) which is a self-administered questionnaire 2. Radiological outcomes: non-union, malalignment and shortening

ISRCTN99771224 *(Continued)*

	3. Health-related quality of life in the first year after the injury. EuroQoL (EQ-5D)-3-level 4. Complication rate in the first year after the injury; including malunion, delayed/non-union, infection, wound complications, vascular and neurological injury, and venous thromboembolism. Any other surgery required in relation to the index fracture, including removal of any metalwork 5. Resource use, costs and comparative cost effectiveness of the two interventions
Starting date	Recruitment start date: 01/03/2013 Recruitment end date: 28/02/2017
Contact information	Prof Matthew Costa, +44 (0)24 7615 1721 (UK) matthew.costa@warwick.ac.uk
Notes	Enrolment target: minimum 320 Ongoing

NCT01047826

Trial name or title	Intramedullary nailing vs. M.I.P.O. in fractures of the tibia; a randomised controlled trial
Methods	Randomised controlled trial

Participants	Inclusion criteria:
	
	• Males and females aged from 18 to 60 years
	• Closed tibia fracture
	• Tibia fracture Müller AO Class 43-A
	
	Exclusion criteria:
	
	• Intra-articular fractures
	• Open fractures
	• Individuals with documented Marfan's syndrome or Ehlers-Danlos syndrome or Hajdu-Cheney syndrome.
	• Postorgan transplant recipients (except corneal transplant)
	• Individuals on immunosuppressive medications
	• Individuals diagnosed with
	  ○ osteogenesis imperfecta
	  ○ osteopetrosis
	  ○ Paget disease of bone
	  ○ renal osteodystrophy
	• Individuals diagnosed with neoplasms or mitotic illnesses
	• Individuals receiving growth hormone
	• Individuals unable to comply with postoperative rehabilitation e.g. head injury
	• Individuals with impending compartment syndrome

Interventions	1. Minimally invasive percutaneous osteosynthesis (MIPO) using locked plates 2. Intramedullary nail group using the Expert Tibial Nail
Outcomes	Primary outcome measures: 1. Rate of malunion (time frame: 6 months) 2. Any healing that occurs with any one of the following: more than 5 degree angulation in the anterior-posterior or lateral view or rotation of more than 10 degrees or shortening of more than 1 cm

NCT01047826 *(Continued)*

	Secondary outcome measures: 1. Short Form (12) Health Score (SF-12v2®) (time frame: every 3 months until healing or 24 months) 2. Blood loss (time frame: during the time of surgery) 3. Radiation exposure (time frame: during the time of surgery) 4. Duration of surgery 5. Infection rate (time frame: every 3 months until healing or 24 months) 6. Hospital stay (time frame: after surgery) 7. Time of fracture healing (time frame: 6 months) 8. Clinical criteria: no pain or tenderness while weight bearing or palpating the fracture site. 9. Radiological criteria: bridging of the fracture site in anterior-posterior and lateral views. Trialists will use these two criteria to measure healing time
Starting date	Start date: December 2010 Estimated completion date: December 2014
Contact information	Principal Investigator: Husam A AL-Rumaih, MD (Saudi Arabia) +96612520088 ext 14119 rumai-h@me.com
Notes	Estimated enrolment: 180 Status unknown (2/12/2014)

DATA AND ANALYSES

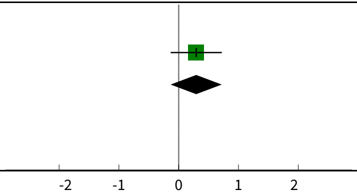
Comparison 1. Nailing versus plating

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Patient-reported functional outcome (pooled data)	3	172	Std. Mean Difference (IV, Fixed, 95% CI)	0.28 [-0.02, 0.59]
1.1 American Orthopaedic Foot and Ankle surgery score at 12 months	1	85	Std. Mean Difference (IV, Fixed, 95% CI)	0.29 [-0.13, 0.72]
1.2 OMAS % of normal side at 24 months	1	64	Std. Mean Difference (IV, Fixed, 95% CI)	0.09 [-0.40, 0.58]
1.3 Olerud and Molander Ankle Score at 12 months	1	23	Std. Mean Difference (IV, Fixed, 95% CI)	0.83 [-0.03, 1.69]
2 Patient-reported functional outcome	3		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.1 American Orthopaedic Foot and Ankle surgery score at 12 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.2 OMAS % of normal side at 24 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.3 Olerud and Molander Ankle Score at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.4 Olerud and Molander Ankle score at 6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.5 Olerud and Molander Ankle Score at 12 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.6 Disability Rating Index at 3 months (0 = full ability, 100 = maximal disability)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.7 Disability Rating Index at 6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.8 Disability Rating Index at 12 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Need for a secondary/revision operation or substantive physiotherapy for adverse outcomes (e.g. nonunion, malunion, and infection)	3	173	Risk Ratio (M-H, Fixed, 95% CI)	0.37 [0.12, 1.12]
4 Symptomatic nonunion or malunion, including limping	3	173	Risk Ratio (M-H, Fixed, 95% CI)	0.72 [0.18, 2.80]
5 Pain (0 to 40: no pain) at 12 months	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6 Wound complications including superficial/deep wound infection and osteomyelitis	3	173	Risk Ratio (M-H, Fixed, 95% CI)	0.47 [0.20, 1.10]
7 Fracture union	3	173	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.95, 1.09]
8 Fracture union time (weeks)	2	149	Mean Difference (IV, Fixed, 95% CI)	0.09 [-1.46, 1.65]
9 Operation time (minutes)	2	149	Mean Difference (IV, Fixed, 95% CI)	-16.78 [-24.67, -8.88]
10 Radiation time (minutes)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Analysis 1.1. Comparison 1 Nailing versus plating, Outcome 1 Patient-reported functional outcome (pooled data).

Study or subgroup	Nailing N	Nailing Mean(SD)	Plating N	Plating Mean(SD)	Std. Mean Difference Fixed, 95% CI	Weight	Std. Mean Difference Fixed, 95% CI
1.1.1 American Orthopaedic Foot and Ankle surgery score at 12 months							
Guo 2010	44	86.1 (7.4)	41	83.9 (7.4)		49.85%	0.29[-0.13,0.72]
Subtotal ***	**44**		**41**			**49.85%**	**0.29[-0.13,0.72]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.34(P=0.18)							



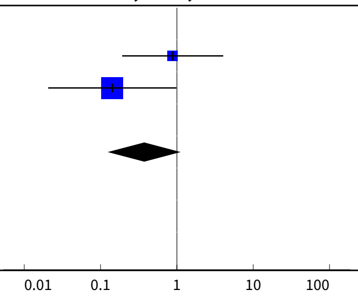
Study or subgroup	Nailing N	Nailing Mean(SD)	Plating N	Plating Mean(SD)	Std. Mean Difference Fixed, 95% CI	Weight	Std. Mean Difference Fixed, 95% CI
1.1.2 OMAS % of normal side at 24 months							
Im 2005	34	88.5 (3.2)	30	88.2 (3.2)		37.81%	0.09[-0.4,0.58]
Subtotal ***	**34**		**30**			**37.81%**	**0.09[-0.4,0.58]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.37(P=0.71)							
1.1.3 Olerud and Molander Ankle Score at 12 months							
Mauffrey 2012	12	81.3 (17.9)	11	65.5 (18.8)		12.34%	0.83[-0.03,1.69]
Subtotal ***	**12**		**11**			**12.34%**	**0.83[-0.03,1.69]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.9(P=0.06)							
Total ***	**90**		**82**			**100%**	**0.28[-0.02,0.59]**
Heterogeneity: Tau²=0; Chi²=2.15, df=2(P=0.34); I²=6.94%							
Test for overall effect: Z=1.84(P=0.07)							
Test for subgroup differences: Chi²=2.15, df=1 (P=0.34), I²=6.94%							
				Favours plating	-2 -1 0 1 2	Favours nailing	

Analysis 1.2. Comparison 1 Nailing versus plating, Outcome 2 Patient-reported functional outcome.

Study or subgroup	Nailing N	Nailing Mean(SD)	Plating N	Plating Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
1.2.1 American Orthopaedic Foot and Ankle surgery score at 12 months						
Guo 2010	44	86.1 (7.4)	41	83.9 (7.4)		2.2[-0.97,5.37]
1.2.2 OMAS % of normal side at 24 months						
Im 2005	34	88.5 (3.2)	30	88.2 (3.2)		0.3[-1.27,1.87]
1.2.3 Olerud and Molander Ankle Score at 3 months						
Mauffrey 2012	12	57.5 (15.3)	11	47.7 (17.2)		9.8[-3.55,23.15]
1.2.4 Olerud and Molander Ankle score at 6 months						
Mauffrey 2012	12	67.1 (18.4)	11	55.5 (23.2)		11.63[-5.58,28.84]
1.2.5 Olerud and Molander Ankle Score at 12 months						
Mauffrey 2012	12	81.3 (17.9)	11	65.5 (18.8)		15.8[0.8,30.8]
1.2.6 Disability Rating Index at 3 months (0 = full ability, 100 = maximal disability)						
Mauffrey 2012	12	-42.3 (20.7)	11	-46.3 (18.7)		4[-12.1,20.1]
1.2.7 Disability Rating Index at 6 months						
Mauffrey 2012	12	-32.1 (26.4)	11	-39.2 (22.4)		7.1[-12.86,27.06]
1.2.8 Disability Rating Index at 12 months						
Mauffrey 2012	11	-23.4 (28.6)	11	-27.3 (26.7)		3.9[-19.22,27.02]
				Favours plating	-40 -20 0 20 40	Favours nailing

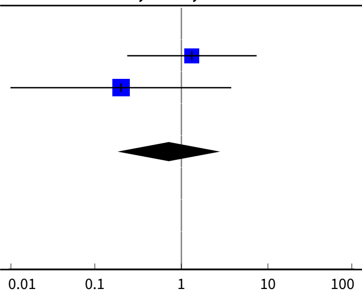
Analysis 1.3. Comparison 1 Nailing versus plating, Outcome 3 Need for a secondary/revision operation or substantive physiotherapy for adverse outcomes (e.g. nonunion, malunion, and infection).

Study or subgroup	Nailing n/N	Plating n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Guo 2010	0/44	0/41			Not estimable
Im 2005	3/34	3/30		31.29%	0.88[0.19,4.05]
Mauffrey 2012	1/12	7/12		68.71%	0.14[0.02,0.99]
Total (95% CI)	**90**	**83**		**100%**	**0.37[0.12,1.12]**
Total events: 4 (Nailing), 10 (Plating)					
Heterogeneity: Tau²=0; Chi²=2.17, df=1(P=0.14); I²=53.88%					
Test for overall effect: Z=1.75(P=0.08)					



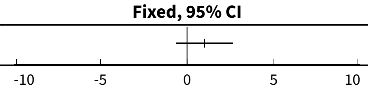
Analysis 1.4. Comparison 1 Nailing versus plating, Outcome 4 Symptomatic nonunion or malunion, including limping.

Study or subgroup	Nailing n/N	Plating n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Guo 2010	0/44	0/41			Not estimable
Im 2005	3/34	2/30		45.95%	1.32[0.24,7.4]
Mauffrey 2012	0/12	2/12		54.05%	0.2[0.01,3.77]
Total (95% CI)	**90**	**83**		**100%**	**0.72[0.18,2.8]**
Total events: 3 (Nailing), 4 (Plating)					
Heterogeneity: Tau²=0; Chi²=1.21, df=1(P=0.27); I²=17.62%					
Test for overall effect: Z=0.48(P=0.63)					



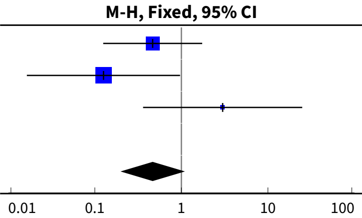
Analysis 1.5. Comparison 1 Nailing versus plating, Outcome 5 Pain (0 to 40: no pain) at 12 months.

Study or subgroup	Nailing N	Nailing Mean(SD)	Plating N	Plating Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
Guo 2010	44	32.5 (3.8)	41	31.5 (3.8)		1[-0.63,2.63]

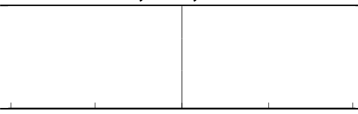


Analysis 1.6. Comparison 1 Nailing versus plating, Outcome 6 Wound complications including superficial/deep wound infection and osteomyelitis.

Study or subgroup	Nailing n/N	Plating n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Guo 2010	3/44	6/41		42.4%	0.47[0.12,1.74]
Im 2005	1/34	7/30		50.77%	0.13[0.02,0.97]
Mauffrey 2012	3/12	1/12		6.83%	3[0.36,24.92]
Total (95% CI)	**90**	**83**		**100%**	**0.47[0.2,1.1]**

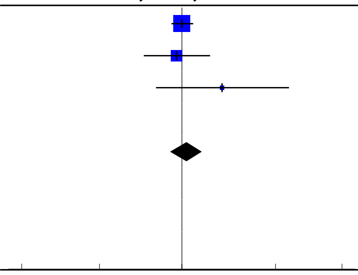


Study or subgroup	Nailing n/N	Plating n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Total events: 7 (Nailing), 14 (Plating)					
Heterogeneity: Tau²=0; Chi²=4.55, df=2(P=0.1); I²=56.09%					
Test for overall effect: Z=1.74(P=0.08)					



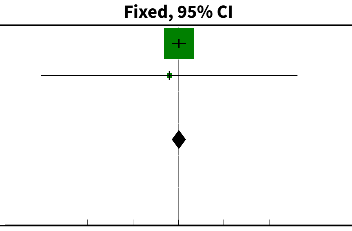
Analysis 1.7. Comparison 1 Nailing versus plating, Outcome 7 Fracture union.

Study or subgroup	Nailing n/N	Plating n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Guo 2010	44/44	41/41		51.61%	1[0.96,1.05]
Im 2005	31/34	28/30		35.77%	0.98[0.85,1.13]
Mauffrey 2012	12/12	10/12		12.62%	1.19[0.89,1.59]
Total (95% CI)	**90**	**83**		**100%**	**1.02[0.95,1.09]**
Total events: 87 (Nailing), 79 (Plating)					
Heterogeneity: Tau²=0; Chi²=1.93, df=2(P=0.38); I²=0%					
Test for overall effect: Z=0.46(P=0.65)					



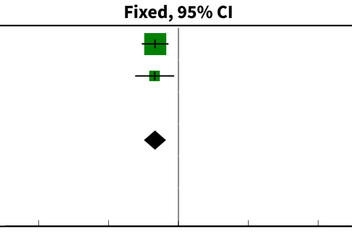
Analysis 1.8. Comparison 1 Nailing versus plating, Outcome 8 Fracture union time (weeks).

Study or subgroup	Nailing N	Nailing Mean(SD)	Plating N	Plating Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Guo 2010	44	17.7 (3.7)	41	17.6 (3.7)		99.7%	0.1[-1.45,1.65]
Im 2005	34	18 (57.5)	30	20 (57.5)		0.3%	-2[-30.22,26.22]
Total ***	**78**		**71**			**100%**	**0.09[-1.46,1.65]**
Heterogeneity: Tau²=0; Chi²=0.02, df=1(P=0.88); I²=0%							
Test for overall effect: Z=0.12(P=0.91)							



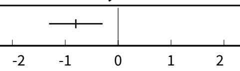
Analysis 1.9. Comparison 1 Nailing versus plating, Outcome 9 Operation time (minutes).

Study or subgroup	Nailing N	Nailing Mean(SD)	Plating N	Plating Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Guo 2010	44	81.2 (22.5)	41	97.9 (22.5)		67.98%	-16.67[-26.25,-7.09]
Im 2005	34	72 (28.4)	30	89 (28.4)		32.02%	-17[-30.95,-3.05]
Total ***	**78**		**71**			**100%**	**-16.78[-24.67,-8.88]**
Heterogeneity: Tau²=0; Chi²=0, df=1(P=0.97); I²=0%							
Test for overall effect: Z=4.16(P<0.0001)							



Analysis 1.10. Comparison 1 Nailing versus plating, Outcome 10 Radiation time (minutes).

Study or subgroup	Nailing		Plating		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI	Fixed, 95% CI
Guo 2010	44	2.2 (1.2)	41	3 (1.2)		-0.8[-1.31,-0.29]



ADDITIONAL TABLES

Table 1. Details of secondary/revision surgery for complications

Trial ID	Group	Reasons for revision operation	Secondary procedures
Guo 2010		None[1]	None
Im 2005	Nailing	3 non-union	2 exchange nailing and autogenous bone grafting; 1 bone grafting
	Plating	1 non-union	1 autogenous bone grafting
		1 non-union with deep infection	1 plate removal and debridement, then change to external fixator, revision plate osteosynthesis after infection control
		1 superficial wound infection	1 skin grafting
Mauffrey 2012	Nailing	1 hardware impingement	1 removal of hardware
		1 compartment syndrome	1 fasciectomy
	Plating	2 non-union	1 exchange nailing, 1 awaiting surgery
		3 hardware impingement	3 removal of hardware
		1 compartment syndrome	1 fasciectomy
		1 deep infection	1 debridement, antibiotics and plate removal upon fracture union

1. 47 implants were removed (23 in the nail group versus 24 in the plate group) after end of follow-up (mean 15.5 months). The main factors contributing to the decision for implant removal were prominence of the plate and pain.

APPENDICES

Appendix 1. Search strategies

CENTRAL (Wiley Online Library)

#1 MeSH descriptor: [Tibial Fractures] explode all trees and with qualifier(s): [Surgery - SU] (157)
#2 MeSH descriptor: [Fracture Fixation] this term only (346)
#3 MeSH descriptor: [Fractures, Bone] this term only (1209)
#4 #2 or #3 (1508)

#5 MeSH descriptor: [Tibia] this term only (394
#6 #4 and #5 (8)
#7 tibia*:ti (865)
#8 (fracture*):ti,ab,kw (10116)
#9 (metaphyseal or metaphysis or distal*):ti,ab,kw (5665)
#10 #7 and #8 and #9 (62)
#11 #1 or #6 (163)
#12 #11 and #9 (27)
#13 #10 or #12 (67)
#14 MeSH descriptor: [Internal Fixators] this term only (151)
#15 MeSH descriptor: [Bone Screws] this term only (578)
#16 MeSH descriptor: [Fracture Fixation, Internal] this term only (730)
#17 MeSH descriptor: [Bone Plates] this term only (372)
#18 MeSH descriptor: [Bone Nails] this term only (357)
#19 (pin* or nail* or screw* or plate* or fix* or prosthes* or ream* or unreamed):ti,ab,kw (40579)
#20 MeSH descriptor: [External Fixators] this term only (136)
#21 MeSH descriptor: [Orthopedic Fixation Devices] this term only (70)
#22 MeSH descriptor: [Ilizarov Technique] this term only (12)
#23 (minimally invasive plate osteosynthesis):ti,ab,kw (23)
#24 (Mipo near/1 technique):ti,ab,kw (3)
#25 #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 (40583)
#26 #25 and #13 (45) [Trials]

MEDLINE (Ovid Online)

1 exp Tibial Fractures/su [Surgery] (7561)
2 Fracture Fixation/ (16836)
3 Fractures, Bone/ (49111)
4 2 or 3 (61539)
5 Tibia/ (27992)
6 4 and 5 (1015)
7 tibia$.ti. (19699)
8 fracture$.tw. (182445)
9 (metaphyseal or metaphysis or distal$).tw. (193452)
10 7 and 8 and 9 (1366)
11 (1 or 6) and 9 (1509)
12 10 or 11 (2027)
13 Internal Fixators/ or Bone Screws/ or Fracture Fixation, Internal/ or Bone Plates/ or Bone Nails/ (51151)
14 (pin$1 or nail$ or screw$1 or plate$1 or fix$ or prosthes$ or ream$ or unreamed).tw. (515370)
15 External Fixators/ or Orthopedic Fixation Devices/ or Ilizarov Technique/ (10663)
16 ((Mipo adj1 technique) or (minimally adj invasive adj plate adj osteosynthesis)).tw. (159)
17 13 or 14 or 15 or 16 (534345)
18 12 and 17 (1434)
19 Randomized controlled trial.pt. (401553)
20 Controlled clinical trial.pt. (90822)
21 randomized.ab. (321810)
22 placebo.ab. (164757)
23 Drug therapy.fs. (1789870)
24 randomly.ab. (230217)
25 trial.ab. (335714)
26 groups.ab. (1446586)
27 or/19-26 (3545656)
28 exp Animals/ not Humans/ (4099183)
29 27 not 28 (3046502)
30 18 and 29 (149)

EMBASE (Ovid Online)

1 Tibia Fracture/ or Distal Tibia Fracture/ (11859)
2 exp Fracture Fixation/ (64556)
3 Fracture/ (64075)
4 2 or 3 (120598)
5 Tibia/ (28724)

6 4 and 5 (3014)
7 tibia$.ti. (19998)
8 fracture$.tw. (201566)
9 (metaphyseal or metaphysis or distal$).tw. (218297)
10 Metaphysis/ (4182)
11 9 or 10 (219269)
12 7 and 8 and 11 (1500)
13 (1 or 6) and 11 (2469)
14 12 or 13 (2804)
15 exp Fixation Device/ (44587)
16 exp Surgical Equipment/ (277456)
17 (pin$1 or nail$ or screw$1 or plate$1 or fix$ or prosthes$ or ream$ or unreamed).tw. (558152)
18 ((Mipo adj1 technique) or (minimally adj invasive adj plate adj osteosynthesis)).tw. (175)
19 or/15-18 (830183)
20 14 and 19 (1691)
21 Randomized controlled trial/ (353243)
22 Clinical trial/ (834048)
23 Controlled clinical trial/ (388219)
24 Randomization/ (63897)
25 Single blind procedure/ (19033)
26 Double blind procedure/ (116034)
27 Crossover procedure/ (40609)
28 Placebo/ (247319)
29 Prospective study/ (266630)
30 ((clinical or controlled or comparative or placebo or prospective$ or randomi#ed) adj3 (trial or study)).tw. (776337)
31 (random$ adj7 (allocat$ or allot$ or assign$ or basis$ or divid$ or order$)).tw. (191602)
32 ((singl$ or doubl$ or trebl$ or tripl$) adj7 (blind$ or mask$)).tw. (164277)
33 (cross?over$ or (cross adj1 over$)).tw. (70703)
34 ((allocat$ or allot$ or assign$ or divid$) adj3 (condition$ or experiment$ or intervention$ or treatment$ or therap$ or control$ or group $)).tw. (251970)
35 RCT.tw. (15276)
36 or/21-35 (1936765)
37 Case Study/ or Abstract Report/ or Letter/ (933293)
38 36 not 37 (1897787)
39 Animal/ or Animal Experiment/ or Nonhuman/ (6197012)
40 Human/ (15089379)
41 39 and 40 (1298730)
42 39 not 41 (4898282)
43 38 not 42 (1745667)
44 20 and 43 (211)

Airiti Library

1 tibia* (2955)
2 fracture* (22544)
3 1 and 2 (1358)
4 distal* (4540)
5 3 and 4 (229)
6 proximal* (3621)
7 5 not 6 (90)

CNKI

1 tibia or tibial (9245)
2 fracture or fractures (38782)
3 1 and 2 (4162)
4 metaphyseal or metaphysis or distal (15683)
5 3 and 4(724)
6 plate or nail (21986)
7 5 and 6 (402)

WHAT'S NEW

Date	Event	Description
3 April 2015	Amended	Missing paragraph reinserted into Abstract: Main results

CONTRIBUTIONS OF AUTHORS

- Conceiving the review: LTK
- Link with the editorial base and co-ordinating the review: CCC
- Drafting the protocol: LTK and CCC
- Identifying relevant titles and abstracts from the searches: LTK and CHC
- Obtaining copies of the trials: LTK
- Selecting the trials: LTK and CHC
- Extracting the data: LTK, CHC and CCC
- Writing to authors of papers for additional information: LTK
- Entering data into RevMan: LTK
- Rechecking the data entered into RevMan: CCC
- Analysis of data: LTK and CCC
- Interpreting the data: LTK and CCC
- Drafting the final review: LTK with contributions from CCC

DECLARATIONS OF INTEREST

Liang Tseng Kuo: none known
Ching-Chi Chi: none known
Ching-Hui Chuang: none known

SOURCES OF SUPPORT

Internal sources

- Chang Gung Memorial Hospital, Chiayi, Taiwan.

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

- We have made minor edits to the Background section, to improve clarity.
- In the protocol, under 'Types of interventions', we said that we would make the more traditional method the 'control' group in any comparison; however, the final three included trials all compared the effect of intramedullary nailing and plating. Since, neither intervention was more traditional than the other, we made plating the control group.
- We have clarified, under 'Types of studies', that we were interested in studies comparing surgical with non-surgical interventions as well as studies comparing different interventions.
- We have included sponsorship bias in the section 'Other potential sources of bias'.
- We have added 'Different methods of the same category of surgery (e.g. MIPO versus open surgery for plate fixation; locked versus conventional (non-locking) plate fixation)' to subgroup analyses.

INDEX TERMS

Medical Subject Headings (MeSH)

Bone Plates; Epiphyses [injuries] [surgery]; Fracture Fixation, Intramedullary [adverse effects] [*methods]; Randomized Controlled Trials as Topic; Reoperation [statistics & numerical data]; Tibial Fractures [*surgery]

MeSH check words

Adult; Female; Humans; Male