Treatment of open fractures of the shaft of the tibia

A SYSTEMATIC OVERVIEW AND META-ANALYSIS

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We have systematically reviewed the effect of alternative methods of stabilisation of open tibial fractures on the rates of reoperation, and the secondary outcomes of nonunion, deep and superficial infection, failure of the implant and malunion by the analysis of 799 citations on the subject, identified from computerised databases. Although 68 proved to be potentially eligible, only eight met all criteria for inclusion. Three investigators independently graded the quality of each study and extracted the relevant data.

One study (n = 56 patients) suggested that the use of external fixators significantly decreased the requirement for reoperation when compared with fixation with plates. The use of unreamed nails, compared with external fixators (five studies, n = 396 patients), reduced the risk of reoperation, malunion and superficial infection.

Comparison of reamed with unreamed nails showed a reduced risk of reoperation (two studies, n = 132) with the reamed technique. An indirect comparison between reamed nails and external fixators also showed a reduced risk of reoperation (two studies) when using nails.

We have identified compelling evidence that unreamed nails reduced the incidence of reoperations, superficial infections and malunions, when compared with external fixators. The relative merits of reamed versus unreamed nails in the treatment of open tibial fractures remain uncertain.

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The treatment of open tibial fractures remains controversial. The precarious blood supply and lack of soft-tissue cover of the shaft of the tibia make these fractures vulnerable to nonunion and infection. The rate of infection may be as high as 50% in grade-IIIB open fractures.^{1,2} Attempts to reduce these complications have led to aggressive protocols which include immediate intravenous antibiotics, repeated soft-tissue debridement, stabilisation of the fracture, early soft-tissue cover and prophylactic bone grafting.^{3,4}

The choice of technique for stabilisation of open tibial fractures has not been analysed. External fixation has been popular because of the relative ease of application and the limited effect on the blood supply of the tibia, but these advantages have been outweighed by the high incidence of pin-track infection, difficulties relating to soft-tissue management and the potential for malunion.⁵ The use of unreamed intramedullary (IM) nails avoids pin-track infection but potentially may compromise stability at the site of the fracture.^{6,7}

The use of reamed IM nails in the management of open tibial fractures is contentious. While reamed nails offer improved stability of the fracture, their use carries a theoretical risk of increasing infection and nonunion as a consequence of disturbing the endosteal blood supply.⁸

A number of randomised trials have compared the results of open fractures of the shaft treated either by external fixators or plates, external fixators or unreamed IM nails or reamed or unreamed IM nails.⁹⁻¹⁶ These trials have overcome the limitations of earlier studies by reducing bias through randomisation and blinding. Small sample sizes and wide confidence intervals, however, have limited the power of the conclusions. Previous clinical reviews have considered the treatment of closed tibial fractures,¹⁷ or have attempted to clarify the role of IM nailing in the treatment of grade-IIIB open injuries.¹⁸

We have undertaken a meta-analysis of comparative studies to evaluate the clinical results of external fixation, plating and reamed and unreamed IM nailing on the rates of reoperation, nonunion and infection in the treatment of open tibial fractures. A systematic approach to the literature, with the potential of statistical pooling, allows stronger recommendations to be made to guide clinical practice.¹⁹

Materials and Methods

Eligibility. We identified articles which met the following criteria:

Target population. Patients with open fractures of the tibial diaphysis.

Intervention. External fixation, plate fixation, IM nails inserted without reaming, or IM nails inserted with reaming.

Primary outcome. Reoperation: any subsequent surgery such as for bone grafting, revision of an IM nail for nonunion or breakage of an implant.

Methodology. Published or unpublished, randomised or quasi-randomised studies, i.e., those in which there is potential for the investigator to determine the allocation of the next eligible patient such as the use of even/odd days or hospital chart numbers.

Study identification. Studies were identified from a Medline search (1969 to 1998), a SCISEARCH, a COCHRANE database search, and hand searches of major orthopaedic journals and orthopaedic proceedings. Content experts were asked to identify additional potentially relevant studies.

Quality assessment. The quality of the method of each study was assessed with respect to randomisation (present and concealed); blinding of patients, clinicians and those assessing outcomes; the proportion of patients lost to follow-up; and the appropriateness of the statistical methods (sample size calculations, confidence intervals, appropriate tests). A 21-point quality assessment scale provided an additional rating.²⁰ The overall quality score calculated for each study was graded to a percentage.

Data extraction. Two authors extracted all the relevant information regarding the population, intervention and outcome from each article. In addition to the rates of reoperation we extracted data concerning bony union, such as failure of the progression of fracture healing over a period of at least two months, pain at the fracture site, inability to bear full weight and the requirement of secondary procedures, including revision IM nailing or bone grafting. The rates of infection, both deep and superficial, were collected, including pin-track sepsis, and the incidence of implant failure and malunion (anteroposterior or mediolateral angulation $>5^\circ$, or $>10^\circ$ rotation, or >1 cm shortening). An author of each study received summary data extraction sheets with a request to verify their accuracy. Five authors authenticated the accuracy^{10,12,13,15,16} and the other three did not reply.

Data analysis. We used kappa statistics to assess agreement among reviewers for inclusion in the study.²¹⁻²³ A kappa value of 0.65 was considered to show adequate agreement.²³ The quality of the study was evaluated by the intraclass correlation coefficient.²³

We pooled the data from the different studies and calculated risks and associated 95% confidence intervals for each outcome using the random-effects model of Der Simonian and Laird.²⁴ Homogeneity or consistency of the estimates

across studies was provided by the Breslow-Day test.²⁵

We found no studies which directly compared reamed nails with external fixators in the treatment of open tibial fractures. We therefore relied on indirect comparisons of the effect of treatment. The model described by Bucher et al²⁶ provided an overall estimate for the relative risk of outcome for the indirect comparison of reamed IM nails and external fixators. Potential sources of heterogeneity, or differences in the apparent effect of size across the various studies^{27,28} were assumed to reflect the differences in the methods of study of patients, treatments, outcome measurement and follow-up. We compared the relative risks of reoperation between different categories for each potential determinant of heterogeneity.

Results

Literature search. We identified 799 citations: 786 from MEDLINE, ten from content experts and three from manual searches of major orthopaedic journals or the programmes of orthopaedic meetings. Only 12 studies proved eligible. The weighted kappa statistics on overall agreement, based upon the application of study inclusion criteria to study titles, was 0.82 (95% confidence interval (CI) 0.79 to 0.85). We excluded one of these studies²⁹ because it described the same patients as in a subsequent report, and another three because there was no randomisation.³⁰⁻³² This left five studies comparing external fixation with unreamed IM nailing, two articles comparing reamed and unreamed IM nailing and one comparing plate fixation with external fixation.⁹⁻¹⁶ We were unable to locate any studies which compared reamed IM nailing with external fixation.

Study characteristics. Table I summarises the quality of the method of the study. Six provided details concerning the management of the soft tissues and characteristics of the fractures (Tables II and III). Most utilised planned bone-grafting procedures as part of their treatment of the fracture (Table II). Agreement for the overall study quality score was good (intraclass correlation coefficient 0.68, 95% CI 0.37 to 0.99). Kappa statistics for the various components of the design of the study such as randomisation and blinding of patients, clinicians and those assessing outcomes, the conduct of the statistical analysis and follow-up, ranged from 0.48 to 1.0.

Plates versus external fixators. One quasi-randomised trial compared plate fixation with external fixation for the treatment of open tibial fractures⁹ (Tables I and II). Of the 26 patients managed with plates, 13 (50%) needed reoperation and of the 30 managed with external fixators, two (6.7%) required a further procedure. Despite the limited sample size ($n = 56$), the low rate of reoperation with external fixation reached conventional levels of statistical significance (relative risk (rr) 0.13, 95% CI 0.03 to 0.54, $p < 0.01$). External fixation did not significantly alter the risk of nonunion (rr 0.52, 95% CI 0.21 to 1.28), deep infection (rr 0.39, 95% CI 0.13 to 1.11), failure of fixation

Table I. Study characteristics

Author/s	Sample size				Design†	I-III A (%)	III B (%)	Intervention*	Outcomes‡	Follow-up (%)	Quality (%)
	UR	R	EF	P*							
Keating et al ¹⁶	44	50	-	-	RCT	88.3	11.7	R nail/UR nail	NU,MU,IF,IFN,P,CS,FO,RO	94	67
Finkemeier et al ¹⁵	23	15	-	-	RCT	93.4	6.6	R nail/UR nail	NU,MU,IF,IFN,P,CS,RO	84	67
Henley et al ¹²	104	-	70	-	QRT	85.1	14.9	UR nail/EF	NU,MU,IF,IFN,RO	100	71
Tornetta et al ¹³	15	-	14	-	QRT	0.0	100.0	UR nail/EF	NU,MU,IFN,RO	100	52
Tu et al ¹⁴	18	-	18	-	RCT	56.0	44.0	UR nail/EF	NU,MU,IF,IFN,RO	100	37
Swanson et al ¹¹ §	50	-	50	-	RCT	ID¶	ID	UR nail/EF	NU,MU,IF,IFN,RO	ID	18
Holbrook et al ¹⁰	29	-	28	-	QRT	71.9	28.1	UR nail/EF	NU,MU,IFN,RO,FO	90	48
Bach and Hansen ⁹	-	-	30	26	QRT	71.0	29.0	Plate/EF	NU,MU,IFN,IF	95	38

* R = reamed intramedullary nails; UR = unreamed intramedullary nails; EF = external fixator; P = plate

† RCT = randomised controlled trial, QRT = quasi-randomised trial

‡ NU = nonunion; MU = malunion; IF = implant failure; IFN = infection; P = pulmonary complications; CS = compartment syndrome; FO = functional outcome; RO = reoperation

§ abstract

¶ insufficient data

Table II. Method of managing soft-tissue injuries associated with tibial fractures

Author/s	Time to OR* (hrs)	Irrigation/debridement		Antibiotics		Coverage procedures	Delayed bone graft
		Immediate	Repeat	Type†	Duration (hrs)		
Keating et al ¹⁶	10* (3.7 to 29)	Yes	ID‡	Ceph/Gent	72	Yes	Yes
Finkemeier et al ¹⁵	<8 (89%)	Yes	Yes	Ticar/Clav	72	Yes	ID
Henley et al ¹²	<8	Yes	Yes	Ceph	48	3 to 10 days	Yes
Tornetta et al ¹³	<8	Yes	Yes	Ceph/Gent	72	3 to 10 days	Yes (4 to 10 wks)
Tu et al ¹⁴	<8	Yes	ID	Ceph/Gent	3 to 7 days	7 days	Yes (3 to 6 wks)
Swanson et al ¹¹ §	Immediate	Yes	Yes	Yes	ID	Yes	Yes (6 wks)
Holbrook et al ¹⁰	Immediate	Yes	Yes	Ceph/Gent	ID	Yes	ID
Bach and Hansen ⁹	<14	Yes	Yes	Ceph	48 to 72	Yes	Yes

* operating room

† Ceph = cephalosporin, Gent = gentamycin, Ticar = ticarcillin, Clav = clavulanic acid

‡ ID = insufficient data

§ abstract

Table III. Characteristics of the patients and fractures

Authors/s	Age (yrs)	Men (%)	Location in diaphysis				Pattern*				Comminution†		
			Prox	Middle	Distal	Multi-level	Spiral	Trans	Oblique	Seg	0	1 to 2	3 to 4
Keating et al ¹⁶	37 (16 to 68)	85	3	81	9	7	6	30	52	12	10	67	23
Finkemeier et al ¹⁵	34 (16 to 88)	82	7	47	46	NA‡	OTA A	54	B 31	C 15	NA	NA	NA
Henley et al ¹²	33 (14 to 77)	79	4	78	10	8	AO A	26	B 51	C 23	6	39	55
Tornetta et al ¹³	39 (19 to 86)	69	NA	NA	NA	NA	Stable	34	Unstable	66	NA	NA	NA
Tu et al ¹⁴	39 (16 to 55)	83	14	28	33	25	NA				NA	NA	NA
Swanson et al ¹¹ §	NA	NA	NA	NA	NA	NA	NA				NA	NA	NA
Holbrook et al ¹⁰	26 (15 to 66)	NA	NA	NA	NA	NA	NA				NA	NA	NA
Bach and Hansen ⁹	37 (14 to 71)	71	NA	NA	NA	NA	NA				NA	NA	NA

* OTA = Orthopaedic Trauma Association classification; AO = ASIF classification

† comminution classified by Winquist-Hansen

‡ NA = no available data from manuscript or abstract

§ abstract

Table IV. Outcomes after unreamed IM nailing and external fixation

Outcome	Sample size*		Unreamed nails		External fixators	
	UR nail	EF	Number	Percent	Number	Percent
Reoperation	216	180	43	20	67	37
Nonunion	216	180	34	15.7	43	24
Deep infection	216	180	22	10.2	29	16.1
Superficial infection	216	180	13	6.0	76	42.2
Malunion	216	180	28	13.0	60	33.3

* UR = unreamed, EF = external fixator

Table V. Results of statistical pooling among studies

Outcome	Unreamed nails v external fixators			Reamed v unreamed nails		
	Relative risk (CI)	p value	Homogeneity p value	Relative risk (CI)	p value	Homogeneity p value
Reoperation	0.51 (0.37 to 0.69)	<0.0001	0.83	0.75 (0.43 to 1.32)	0.32	0.74
Nonunion	0.69 (0.46 to 1.03)	0.067	0.27	0.70 (0.24 to 1.67)	0.24	0.80
Deep infection	0.60 (0.36 to 1.01)	0.054	0.58	1.02 (0.22 to 4.67)	0.98	0.86
Superficial infection	0.24 (0.08 to 0.73)	0.012	0.01	NA*	NA	NA
Malunion	0.42 (0.25 to 0.71)	0.0013	0.70	NA	NA	NA
Implant failure	NA	NA	NA	0.32 (0.17 to 0.89)	0.025	0.88

*not available

(rr 0.58, 95% CI 0.10 to 3.20) or malunion (rr 2.6, 95% CI 0.29 to 23.5). The point estimates of the relative risk, however, favoured external fixation with regard to nonunion, deep infection and failures of fixation, and plates with regard to malunion.

Unreamed nails versus external fixators. Five randomised trials (n = 396 patients) provided detailed information regarding rates of reoperation, nonunion and deep infection (Tables IV and V). The risks of reoperation, nonunion and infection with nails inserted without reaming in comparison with external fixators were, respectively, 0.51 (95% CI 0.37 to 0.69), 0.69 (95% CI 0.46 to 1.03) and 0.60 (95% CI 0.36 to 1.01) (Fig. 1). The weighted absolute risk of reoperation in the patients treated with external fixation was 37.2%, implying that the risk difference for reoperation was 18%. Therefore for every six patients treated with an IM nail inserted without reaming, an orthopaedic surgeon would avoid one reoperation (1:0.18).

All trials provided data on secondary outcomes (n = 396). While unreamed nails did not show significant rates of nonunion and deep infection compared with external fixators, they did offer significant advantages in reducing the risks of superficial infection (rr 0.24, 95% CI 0.08 to 0.73) and malunion (rr 0.42, 95% CI 0.25 to 0.71). The weighted risks of superficial infection and malunion in patients treated by external fixation were 42% and 33.3%, respectively, implying risk differences of 31% and 19.3%. This suggested that after using an unreamed IM nail, an

orthopaedic surgeon would avoid one superficial infection with every three patients treated and one malunion with every five. The heterogeneity in results of studies with respect to superficial infection call for further study of the possible reasons. None of our hypotheses (study quality, completeness of follow-up, the method of randomisation and the presence of grade-IIIB soft-tissue injury) explained this heterogeneity (Table VI).

Information on nonunion and deep infection in tibial fractures of grade IIIB was available in 45 patients in randomised trials of unreamed nails and external fixators. Unreamed nails did not significantly alter the relative risk of nonunion (rr = 0.70, 95% CI 0.24 to 2.43) or deep infection (rr 1.95, 95% CI 0.39 to 9.89) when compared with external fixators.

Reamed versus unreamed nails. Two randomised trials provided information regarding the rates of reoperation, nonunion and infection (n = 132 patients). Table V presents the results of the pooled statistical analyses. The use of reamed IM nails did not significantly decrease the risk of reoperation when compared with unreamed nails (rr 0.75, 95% CI 0.43 to 1.32). Moreover, reaming did not significantly alter the risks of nonunion or of deep infection in comparison with non-reaming (rr 0.70, 95% CI 0.24 to 1.67; and rr 1.02, 95% CI 0.22 to 4.67, respectively). Detailed information regarding secondary outcomes was available only for rates of implant failure. The use of reamed nails significantly reduced the risk of this (rr =

Table VI. Sensitivity analysis for unreamed nails *versus* external fixators with regard to reoperation

Outcome	Number of studies	Relative risk	95% CI	Homogeneity p value
Quality				
Quality score >50	2	0.50	0.34 to 0.73	0.60
Quality score <50	3	0.56	0.25 to 1.24	0.51
Follow-up				
Complete follow-up	3	0.55	0.39 to 0.78	0.24
Incomplete follow-up	2	0.36	0.18 to 0.73	0.48
Open fracture				
Grade IIIB only	1	0.76	0.36 to 1.60	1.00
All open grades	4	0.51	0.15 to 0.69	0.29
Randomisation				
Randomised	2	0.36	0.01 to 11.45	0.07
Quasi-randomised	3	0.19	0.04 to 0.87	0.80

0.32, 95% CI 0.17 to 0.89). The weighted absolute risk of implant failure with unreamed nails was 23.4% implying a risk difference of 15.9%. Thus, for every seven patients treated by a reamed nail, one implant failure was avoided (1:0.13).

Information on nonunion and deep infection in tibial fractures of grade IIIB was available for 11 patients in randomised trials of treatment with reamed and unreamed nails. The use of reamed IM nails did not significantly alter the risk of nonunion (rr 1.14, 95% CI 0.15 to 8.99) or of deep infection (rr 1.88, 95% CI 0.09 to 37.63) when compared with unreamed nails. The number of patients is, however, small.

Reamed nails *versus* external fixators. Indirect comparisons for reoperation, nonunion and risks of deep infection between reamed IM nails and external fixators were conducted from the available studies of five randomised trials comparing unreamed nails with external fixators and two randomised trials comparing reamed with unreamed nails. As with unreamed nails, the use of reamed nails significantly reduced the risk of reoperation when compared with external fixators (rr 0.43, 95% CI 0.19 to 0.95, homogeneity p value = 0.04), but did not significantly reduce the risk of nonunion or deep infection (rr 0.56, 95% CI 0.25 to 1.26, homogeneity p value = 0.02; and rr 0.34, 95% CI 0.11 to 1.09; homogeneity p value = 0.04, respectively).

Statistically significant heterogeneity appeared in all of the analyses of reoperation, nonunion and deep infection between reamed nails and external fixators. The quality of the study, the completeness of the follow-up and the presence of soft-tissue injury of grade IIIB did not significantly alter the risks of reoperation, nonunion or deep infection after reamed IM nailing.

Discussion

Rates of reoperation have varied between 4% and 48% in studies which include a variety in the severity of soft-tissue damage and patterns of fracture.⁹⁻¹⁶ Although formal criteria for establishing the prognosis after open tibial fracture remain unavailable, surgeons can generally identify patients at low risk (5% to 10%) and at high risk (>50%) for reoperation. Those at high risk include cases in which there is significant comminution at the site of the fracture, bone loss or an extensive soft-tissue injury.³³

Given the current pooled estimates for reoperation with unreamed IM nails against those for external fixators, there is persuasive evidence in favour of unreamed nails. For instance, an orthopaedic surgeon would have to treat 41 low-risk patients (5%) with unreamed nails instead of an external fixator (rr 0.51) to avoid a single reoperation. In a high-risk population, however, unreamed nailing would reduce the need for reoperation from 50% to 25% when compared with external fixators. Clinicians would thus

Fig. 1

The effects of unreamed nails *versus* external fixators and unreamed nails *versus* reamed nails on the rates of reoperation. The use of unreamed nails significantly reduced the risk of reoperation when compared with external fixators (rr 0.51, 95% CI 0.37 to 0.69, homogeneity p value = 0.83). However, insignificant differences in the risk of reoperation were observed between unreamed and reamed nails, but the point estimates revealed better results with reamed IM nails.

have to treat three high-risk patients (1:0.25) with an unreamed nail instead of an external fixator to avoid a single reoperation.

In our meta-analysis, six of the eight eligible studies had, as part of their treatment protocol, a bone-grafting procedure six to eight weeks after the initial surgery. If the number of reoperations solely reflected the patients who received bone grafts to promote fracture healing, our results would have indicated no difference in the rates of reoperation between treatment groups (i.e., $rr = 1.0$). This, however, was not the case; the differences in the effect of treatment were most often the result of nonunion (despite prophylactic bone grafting), infection or malunion (Table V).

Meta-analysis combines data from different studies which address a similar question, using accepted statistical methods, to obtain a more reliable estimate of the overall effect of treatment. The conclusion from statistical pooling, however, is only as valid as the component studies which contribute to the analysis. Our meta-analysis met most of the criteria for a research overview.^{19,27,34-37} While this strengthens the inferences from our work, it suffers from the limitations common to all such studies. Despite rigorous search, there is the possibility that not all randomised trials describing treatment alternatives for open tibial fractures were included. This may be because there is either a publication bias³⁸ against studies which did not report a significant difference in effect between two treatments or a selection bias³⁹ against choosing those studies which favoured a particular treatment.

A number of meta-analyses have provided results which have contradicted the findings from subsequent large, randomised controlled trials.⁴⁰ These reservations suggest that findings from meta-analyses must be interpreted in the light of our understanding of the underlying biology.⁴¹ For example, in those studies comparing unreamed nails with external fixation, rates of reoperation were significantly reduced with unreamed nails ($rr\ 0.51$, $p < 0.001$). This significant effect is understandable, considering that the point estimates of the risk of nonunion, deep infection, superficial infection and malunion with unreamed nails are also decreased, and the magnitude of the effect is similar ($rr\ 0.69$, 0.60 , 0.24 and 0.42 , respectively). In general, the results of meta-analyses should be interpreted conservatively. A clinician can gain an indication of the degree of uncertainty regarding benefit by calculating standard confidence limits.

Yusuf⁴² has suggested that meta-analyses of small randomised trials can generate hypotheses for more reliable, and larger, randomised trials. Our study provides strong enough evidence that IM nails offer benefit over external fixators in the treatment of open tibial fractures and that further trials may be a poor investment of resources. On the other hand, trends in favour of reamed over unreamed nails were associated with wide confidence intervals. These findings, together with those showing an apparent benefit of reamed nails in closed fractures,⁴³ suggest the need for a

large, randomised trial of reamed *versus* unreamed IM nails in the treatment of open tibial fractures.

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