TRAUMA

Exchange nailing for nonunion of diaphyseal fractures of the tibia

OUR RESULTS AND AN ANALYSIS OF THE RISK FACTORS FOR FAILURE


From Royal Infirmary of Edinburgh, Edinburgh, United Kingdom

Aims
The aim of this study was to identify risk factors for the failure of exchange nailing in nonunion of tibial diaphyseal fractures.

Patients and Methods
A cohort of 102 tibial diaphyseal nonunions in 101 patients with a mean age of 36.9 years (15 to 74) were treated between January 1992 and December 2012 by exchange nailing. Of which 33 (32%) were initially open injuries. The median time from primary fixation to exchange nailing was 6.5 months (interquartile range (IQR) 4.3 to 9.8 months).

The main outcome measures were union, number of secondary fixation procedures required to achieve union and time to union.

Univariate analysis and multiple regression were used to identify risk factors for failure to achieve union.

Results
Multiple causes for the primary nonunion were found for 28 (27%) tibiae, with infection present in 32 (31%). Six patients were lost to follow-up. Further surgical procedures were required in 35 (36%) nonunions. Other fixation modalities were required in five fractures. A single nail exchange procedure achieved union in 60/96 (63%) of all nonunions. Only 11 out of 31 infected nonunions (35.4%) healed after one exchange nail procedure. Up to five repeated exchange nailings, with or without bone grafting, ultimately achieved union in 89 (93%) fractures. The median time to union after exchange nailing was 8.7 months (IQR 5.7 to 14.0 months). Univariate analysis confirmed that an oligotrophic/atrophic pattern of nonunion (p = 0.002), a bone gap of 5 mm or more (p = 0.04) and infection (p < 0.001), were predictive for failure of exchange nailing. Multiple regression analysis found that infection was the strongest predictor of failure (p < 0.001).

Conclusion
Exchange nailing is an effective treatment for aseptic tibial diaphyseal nonunion. However, in the presence of severe infection with a highly resistant organism, or extensive sclerosis of the bone, other fixation modalities, such as Ilizarov treatment, should be considered.

Take home message: Exchange nailing is an effective treatment for aseptic tibial diaphyseal nonunion.

Cite this article: Bone Joint J 2016;98-B:534–41.
Exchange nailing for aseptic diaphyseal nonunion the rate of successful union ranges from 76% to 98%.9,15 However other studies have reported that to achieve union a significant number require additional surgical procedures.9-14 Factors associated with failure in exchange nailing include cortical bone loss,10,12 comminution13 and segmental bone loss.11 There is currently no consensus in the literature with regard to the use of exchange nailing for tibial diaphyseal fracture nonunion in the presence of infection.15

This study aimed to identify the principal risk factors for the failure of exchange nailing in the treatment of tibial diaphyseal fracture nonunions.

Patients and Methods
The study did not require Ethics Committee review as it fulfilled the criteria for continued audit of clinical outcomes.

We identified all patients from a trauma database over the age of 16 years who had undergone exchange nailing for the management of tibial diaphyseal fracture nonunion at our institution between January 1992 and December 2012. We included patients who were referred following initial treatment within our hospital and tertiary referrals. The rate of nonunion for tibial diaphyseal fractures in our institute during this period was 5%.17 We excluded patients who had their index nailing for any cause other than trauma and pathological fractures. We also excluded patients who had failed other surgical interventions prior to exchange nailing. In total 101 patients (102 nonunions) were included in our study. The mean age of the patients at the time of exchange nailing was 36.9 years (15 to 74). The median time to exchange nailing from primary fixation was 6.5 months (interquartile range (IQR) 4.3 to 9.8 months). The mean time to exchange nailing was 8.5 months (5.7 to 14.0). Characteristics of the patients, injury and primary surgery are presented in Table I.

Following high-energy injuries (falls > 2 m high, road traffic and industrial accidents) we defined primary fracture nonunion as no radiological or clinical signs of union after six months, with no evidence of progression in the previous three months. Following low energy fractures (falls < 2 m high, sporting injuries) we defined nonunion as no radiological evidence of callus formation by 12 to 16 weeks.

Information was obtained from the patient records, radiographs and laboratory results. The initial fractures were all classified as subtypes of AO/OTA 42-A, 42-B and 42-C18 and according to the Gustilo and Anderson classification.8 The information was recorded in the trauma database and was checked by the primary author and two senior authors. We analysed the patient records to identify risk factors for nonunion including host factors, mechanical factors, bone defect at the site of nonunion and infection. Infection was deemed to be present if there was evidence of a sinus or frank pus at the fracture site, or if positive cultures were obtained or had previously been obtained from intra-operative specimens at the site of the nonunion in addition to clinical and/or serological suspicion. If there was clinical evidence of infection, such as the presence of a sinus, formal debridement was undertaken with biopsy samples from the fracture site sent for microbiology culture, if infection was suspected serologically but with no cutaneous evidence only intra-operative reamings were

<table>
<thead>
<tr>
<th>Table I. Patient, injury and primary surgery characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age at time of exchange nailing (yrs; range) 36.9 (15 to 74)</td>
</tr>
<tr>
<td>Median time to exchange nailing (mths) (IQR) 6.5 (4.3 to 9.8)</td>
</tr>
<tr>
<td>Mean time to exchange nailing (mths) (range) 8.5 (5.7 to 14.0)</td>
</tr>
<tr>
<td>Mechanism of injury</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Gustilo Classification (n)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Primary fixation (n)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Primary IM nail (n = 102) (n)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

* converted to intramedullary (IM) nail at later date prior to exchange nail procedure
sent. In total, six patients had samples taken at wound exploration and debridement following primary fixation prior to the exchange nail procedure. Samples were sent only in those cases with clinical or serological suspicion of infection. An inappropriate mechanical environment was determined by failure of fixation or a hypertrophic pattern of nonunion on radiographs. A nonunion with minimal or no callus response was classified as an oligotrophic/atrophic nonunion. A bone defect at the site of nonunion was recorded if there was a distraction gap of 5 mm or more or bone loss of more than 50% of the tibial circumference at the nonunion site on plain radiographs. All of the risk factors that were present in each case were included in the statistical analysis.

Operative technique. The patient was positioned either on a traction table or a standard operating table with a radiolucent top, as used for a primary nailing procedure, and the original nail and cross-screws were removed through the original surgical incisions.

If a significant bone defect had been identified preoperatively the nonunion site was exposed and the sclerotic bone was excised with minimal dissection of the periosteum from the surrounding healthy bone. Autogenous iliac crest bone graft was packed into the nonunion site. In patients with bone defects, as a result of Gustilo and Anderson\textsuperscript{8} IIIB fractures, the soft tissues were elevated by a plastic surgeon with bone defects, as a result of Gustilo and Anderson\textsuperscript{8} IIIB fractures, the soft tissues were elevated by a plastic surgeon to allow bone grafting via an anterior approach. The posterior Harmon approach\textsuperscript{20} was only used if the condition of the anterior soft tissues was unsatisfactory. The Masquelet technique\textsuperscript{21} is not used at our institution.

The intramedullary canal was initially reamed with a drill bit of the same size as the extracted nail. Sequential reaming was undertaken in 0.5 mm increments to remove endosteal fibrous tissue, until there was ‘bony chatter’ during reaming and healthy bone was seen on the tip of the withdrawn reamer. In young patients this usually occurred at a diameter of 1 mm larger than the diameter of the original nail. When possible, reaming was continued to a diameter 2 mm greater than the original nail, to allow insertion of a revision nail at least 1 mm larger than the original. The new nail was locked proximally to prevent backing out.

In the early part of the series, to prevent coronal deformity arising from nonunion involving the distal third of the diaphysis, the exchange nails were locked proximally and distally. In more recent cases, the nails were first locked distally, then tapped backwards with the nail removal apparatus to compress the nonunion site prior to static proximal locking.

Fibular osteotomies were not routinely performed unless it was felt that the intact fibular was causing distraction at the fracture site. In this cohort only two fibular osteotomies were performed, both at the time of the primary nail exchange. No antibiotic-loaded spacers were used in the treatment of infected nonunions. Systemic antibiotic choice was based on organism sensitivity. Where no positive microbiological cultures were available empirical antibiotics were started in accordance with local antimicrobial policies.

When wound closure was not possible soft tissue coverage was achieved using skin grafts, local fasciocutaneous flaps or free flaps under the care of the local plastic surgery department.

Post-operatively all patients were encouraged to become mobile, bearing full weight without a supportive cast or crutches.\textsuperscript{10} Use of elbow crutches was permitted in the early post-operative period to assist with mobility.

Outcome measures. These included radiographic fracture union, failure of the exchange nailing to achieve union and time to union. Union was defined using well recognised radiographic criteria; i.e. when radiographs demonstrated bridging callus of at least three cortices on standard anteroposterior and lateral radiographs. Failure of the exchange nail was defined as the requirement for further surgical intervention to achieve union. Time to union was determined as the time, in days, from initial exchange nailing to radiographic union as defined above.

Statistical analysis. Data were analysed using SPSS statistical software (version 21.0 IBM, Armonk, New York). The probabilities of union and associated comparisons were estimated using the Kaplan-Meier test and log-rank analysis. Risk factor analysis was performed using a chi-squared test for categorical data, Pearson’s correlation for continuous data and multiple regression modelling. A p-value < 0.05 was considered statistically significant. Risk factors analysed were age at time of exchange nailing, time to exchange nailing from primary fixation, Gustilo-Anderson grade\textsuperscript{8} at initial injury, cigarette smoking, excessive alcohol use, excessive NSAID use, Weber and Cech classification\textsuperscript{22} of primary nonunion, presence of a mechanical cause for nonunion, presence of host cause(s) for nonunion, presence of a bone defect, and infection. A univariate analysis of the risk factors was initially performed followed by multiple regression analysis of significant factors.

Results
A total of six fractures in six patients were lost to follow-up, at a mean of 13 months (three to 58 months) and excluded from the outcome analysis. The causes attributed to fracture nonunion are presented in Figure 1. Multiple causes of the primary nonunion were found in 28 of the 102 fractures (27.2%), infection was found to be a cause in 32 of the 102 fractures (31.4%).

Bone grafting was used during seven of the 96 (7.3%) primary exchange nailing procedures. Subsequent, further surgery was required to promote union in 35 fractures (36.5%), the majority of these were repeat exchange nailing, and 17 (17.7%) also required additional bone grafting. Up to five revision nailing procedures were performed per patient.

Plastic surgical intervention to achieve soft-tissue cover following debridement and exploration of fracture site, in the form of a skin graft or fasciocutaneous flap, was required in four patients. A revision flap was required in one patient. The exchange nail was revised for varus mal-
alignment in one patient and one required incision and drainage for a post-operative infected haematoma at the proximal entry site.

Following fracture union, 24 of the 96 (25.0%) fractures required removal of symptomatic metalwork.

Fracture union was achieved in 89 of 96 patients (92.7%) with one of more exchange nailing procedures, with or without bone grafting. A further five patients (5.2%) were converted to another fixation modality and two patients (2.1%) failed to unite (Fig. 2). The median time to union was 8.7 months (IQR 5.7 to 14.0 months) (Fig. 3).

Univariate analysis identified factors which were predictive of failure of exchange nailing. These were an
oligotrophic/atrophic pattern of nonunion, a bone defect and infection (Table II). The timing of exchange nailing was not predictive.

Multiple regression analysis was run to predict failure of exchange nailing from oligotrophic/atrophic patterns of nonunion, a bone defect and presence of infection. These variables successfully predicted the number of further fixation procedures required to achieve union (F (3, 98) = 9.70, p < 0.001, R = 0.48). Only the presence of infection added statistically significantly to the prediction, p < 0.001. The multiple regression model used found that infection carried a coefficient factor 0.72 (95% CI 0.37 to 1.07, p < 0.001). A bone defect > 5 mm was found to approach statistical significance with a coefficient factor 0.38 (95% CI -0.03 to 0.80, p = 0.068).

Post hoc analyses revealed that in 31 fractures (31 patients) with known infection, 19 (61.3%) experienced failure of the initial exchange nailing. Further exchange nailing was performed in 16 fractures, of which nine included bone grafting, which all went on to unite. An alternative modality of fixation was used in three fractures: two fine wire circular frames (Ilizarov / Taylor Spatial Frame Smith & Nephew, Hull, United Kingdom), and one internal plate and screws. Ultimately 27/31 (87.1%) infected nonunions healed with exchange nailing with or without bone grafting and systemic antibiotics alone.

No further risk factors could be found on univariate or multi-regression analyses.

Post hoc analyses of the aseptic tibial diaphyseal nonunions revealed that 16/65 (24.6%) fractures in 64 patients experienced failure of the initial exchange nailing. Further exchange nailing was successful in 13 patients, of these eight included bone grafting. The use of other fixation modalities was required to achieve union in two fractures. Of these, one was converted to internal fixation with a plate and screws and one to a fine-wire circular frame. One fracture went on to a chronic nonunion. Ultimately 62 out of 65 (95.4%) aseptic tibial nonunions healed with

<table>
<thead>
<tr>
<th>Factor</th>
<th>(RRR) / Pearson's correlation</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.123†</td>
<td>0.22</td>
</tr>
<tr>
<td>Time to exchange nailing</td>
<td>0.063†</td>
<td>0.54</td>
</tr>
<tr>
<td>Open injury</td>
<td>1.24*</td>
<td>0.73</td>
</tr>
<tr>
<td>Smoking</td>
<td>0.71*</td>
<td>0.29</td>
</tr>
<tr>
<td>Alcohol excess</td>
<td>0.70†</td>
<td>0.47</td>
</tr>
<tr>
<td>Oligotrophic/atrophic pattern of nonunion</td>
<td>3.10†</td>
<td>0.002</td>
</tr>
<tr>
<td>Host factor</td>
<td>0.98†</td>
<td>0.95</td>
</tr>
<tr>
<td>Bone defect (5 mm or more)</td>
<td>1.86†</td>
<td>0.04</td>
</tr>
<tr>
<td>Bone defect (3 mm or more)</td>
<td>1.37†</td>
<td>0.29</td>
</tr>
<tr>
<td>Infection</td>
<td>2.60*</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Multiple causes</td>
<td>1.56*</td>
<td>0.11</td>
</tr>
</tbody>
</table>

* Relative risk ratio (RRR)
† Pearson’s correlation
Bold text indicates significance

Fig. 3
Kaplan-Meier curve of united fractures following exchange nailing for diaphyseal nonunion of the tibia.

Table II. Univariate analysis results with associated relative risk ratio (RRR) / Pearson’s correlation factor for exchange nail failure and significance levels
exchange nailings with or without bone grafting. Univariate and multi-regression analyses were unable to demonstrate any additional risk factors for exchange nail failure in aseptic tibial diaphyseal nonunion.

The median time to union following exchange nailing was 10.7 months (IQR 5.6 to 18.0 months) for infected nonunions and 7.6 months (IQR 5.7 to 10.8 months) for aseptic tibial diaphyseal nonunions, this difference was statistically significant (log-rank, p = 0.008) (Fig. 4). The sole intervention of exchange nailing, with or without bone grafting, was successful in achieving union in 62/65 (95.4%) aseptic nonunions and 27/31 (87.1%) infected nonunions.

Discussion
This study found a failure rate following exchange nailing for tibial diaphyseal nonunion of 35/96 (36.5%). The presence of infection, a bone gap of more than 5 mm and an atrophic/oligotrophic pattern of nonunion were statistically significant risk factors for failure of exchange nailing. Infection increased the median time to union by approximately three months and had an increased chance of requiring a second procedure, to achieve bony union, of 60%. The strongest predictor of failure of exchange nailing was infection. Ultimately, repeat nailing, with or without bone grafting, achieved union in 62/65 (95.4%) of non-infected cases and 27/31 (87.1%) in the infected nonunions.

As far as we are aware this is the largest cohort of tibial diaphyseal nonunions treated with exchange nailing. All were from a single institution, the Royal Infirmary of Edinburgh, which has used the procedure of exchange nailing for tibial diaphyseal nonunions for over 20 years. A further strength is the low numbers, six (5.9%), lost to follow-up. A weakness of the study is that some of the cohort predates contemporary understanding of the prognosis of tibial diaphyseal fractures following intramedullary nailing. During the 20 years our cohort of patients presented, technological and ideological treatment concepts have evolved. The initial failure rate of exchange nailing, particularly when dealing with infected nonunions, may have been reduced with the use of newer treatment strategies and technologies, such as staged exchange nailing with antibiotic-loaded cement spacers or antibiotic-impregnated nails.

Some of the earlier patients in this cohort may have undergone exchange nailing too soon. The SPRINT trial\textsuperscript{23} results have suggested that, prior to six months, some interventions for tibial diaphyseal fracture nonunion may be unnecessary. However, the SPRINT study carried out exchange nailing for the following criteria a fracture gap of $\geq$ 1 cm and at least 50% circumferential bone loss or failure of progression of fracture healing for at least two months, accompanied by clinical symptoms of delayed union (pain, difficulty with weight-bearing), which are similar to the current criteria in our unit. The overall rate of exchange nailing or bone grafting in the SPRINT study was 5%, which again was similar to the overall rate in our unit.\textsuperscript{17}

The reported rates of exchange nail failing to achieve union range between 4% and 21.4\%,\textsuperscript{9,10,14,15,24} which are comparable with this study’s rate of exchange nail failure in aseptic primary nonunion (24.6%). Previous studies have attempted to identify risk factors for exchange nail failure. Court-Brown et al\textsuperscript{10} and Oh et al\textsuperscript{24} suggested that a distraction gap of more than 2 cm or bone loss of more than 50% of the tibial circumference resulted in failure of exchange nailing. Elsewhere a smaller gap (3 mm or more) has been found to predispose to nonunion.\textsuperscript{25} In our analysis we found that a gap of this magnitude was not significantly associated with failure of exchange nailing. However, a gap of 5 mm or more was statistically significant (relative risk ratio (RRR) 1.86, p = 0.04). Of the 18 fractures with a clinically significant bone defect, two underwent bone grafting at the primary exchange nail procedure, with one requiring no further fixation surgery to achieve union and the second requiring further bone grafting to achieve union. Of the remaining 16 fractures with a recorded bone defect, a further six underwent bone grafting during subsequent revision procedures.

The presence of multiple causes of nonunion was found to have a relative risk (RR) 1.56, which approached statistical significance (p = 0.11). This may suggest that although exchange nailing is a successful procedure, all modifiable risk factors for nonunion (e.g. smoking, use of NSAIDs) should, if possible, be identified and addressed prior to the exchange nailing. This approach improved the success rate of primary exchange nailing for Swanson et al\textsuperscript{9} who reported a union rate of 98% for exchange nailing of aseptic tibial nonunions.

Oligotrophic/atrophic patterns of nonunion were found to be predictive of exchange nail failure, but on univariate analysis only. Previous studies have found exchange nailing to be equally effective in the treatment of both hypertrophic and atrophic lower limb diaphyseal nonunions.\textsuperscript{14,24,26}
However, in the cohort reported by Oh et al., two out of eight atrophic nonunions of the tibia required further fixation procedures to achieve union. In this study oligotrophic/atrophic patterns of nonunion had a RR 3.10 (p < 0.01) for exchange nail failure.

Currently the use of exchange nailing in the treatment of infected long-bone nonunion is controversial. The results of this study support the view that infection is a risk factor for failure of exchange nailing, with a RR 2.60 (p < 0.001) on univariate analysis. Previous studies have found that infection was not associated with failure if organism-specific antibiotics were started from the time of exchange nailing. A more recent study by Petrisor, Anderson and Court-Brown found that 11 of 18 infected tibial nonunions, treated with the protocol described by Court-Brown et al. required additional operative intervention. Brinker and Connor suggested that infected nonunions could be treated using a planned series of surgical procedures. It has been suggested that antibiotic-impregnated polymethylmethacrylate nails could be implanted to provide temporary internal splinting and elute high concentrations of an antimicrobial drug in the medullary canal until exchanged for a definitive locked nail. Treatment using the Ilizarov method has been found to be associated with union rates close to 100%. A recent study Bose et al. reported the results of a heterogeneous series from a limb reconstruction unit of 67 infected long bone nonunions, of which 49 involved the tibia. The majority of this cohort (54 patients out of 64) were treated with bony debridement, antibiotics, and external fixation, with union achieved following a single procedure in 54 patients out of 64 (84.3%) and a mean time to union nine months. However, in the 21 patients previously managed with an intramedullary nail, ten needed further surgery for either infection or nonunion, i.e., the failure rate of the first operation in this group was 48%. The previous use of internal fixation was found to be associated with a higher rate of persistent nonunion and recurrence of infection. It is important to recognise that tibial exchange nailing for infected nonunions using standard uncoated tibial nails, in the cohort reported here, has a 65% failure rate. After a second procedure a further nine of the infected nonunions had healed i.e., 20 of the 31 infected nonunions had healed with exchange nailing thus the overall failure rate had fallen to 12 patients out of 31 (38.7%). The median time to union was 4.9 months (IQR 3.5 to 18.0 months) for one exchange nail and 9.8 months (IQR 7.7 to 14.0 months) if a second exchange nail was required. This should be compared with the time reported to obtain union following an Ilizarov procedure of between nine and 11 months. The Ilizarov treatment also requires a second procedure to remove the frame and several years to regain function after frame removal. It is important to counsel the patients of their likely outcomes when considering their management options.

In conclusion, this study demonstrated that exchange nailing is an effective treatment for aseptic tibial diaphyseal nonunion. However, if there is known infection, or extensive sclerosis of the bone ends, other treatment modalities, such as Ilizarov treatment, should be the preferred option.

Author contributions:
S. T. J. Tsang: Study conception, data collection, data analysis, writing of manuscript.
L. A. Mills: Study conception and editing of manuscript.
J. Frantzias: Data collection.
J. P. Baren: Data collection.
J. F. Keating: Study conception, performed surgeries, and editing of manuscript.
A. H. R. W. Simpson: Study conception, performed surgeries, and editing of manuscript.

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

This article was primarily edited by E. Moulder and first proof edited by G. Scott.

References


