Factors affecting rates of infection and nonunion in intramedullary nailing

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We report a retrospective study over five years to determine the incidence of infection and nonunion after intramedullary nailing in fractures of 214 long bones; 122 femoral, 75 tibial and 17 humeral. The indications for nailing were trauma (n = 161), pathological fracture (n = 30) and nonunion (n = 23). There were 30 open fractures. The overall rates of deep infection and nonunion were 3.8% and 14.2%, respectively.

Using multiple logistic regression analysis, we determined the relationships between deep infection and nonunion and the pre- and peri-operative factors of age, ASA score, indication for nailing, the use of reaming, the use of antibiotics, whether the fracture was open and the operating time. Open fractures were found to be significantly associated with deep infection. The length of the operation may also affect the outcome. Opening of the fracture at the time of surgery and the ASA score were found to be significantly associated with the development of nonunion after intramedullary nailing.

We have compared our findings with previously published data from large teaching hospital units.

Intramedullary [IM] nailing has become a standard procedure for the treatment of closed fractures of long bones, offering excellent healing potential and a low complication rate. However, the question as to whether to ream the medullary canal before insertion of the nail and the place of nailing in open fractures remains controversial.

Reaming allows the insertion of a tighter fitting nail across the isthmus of a long bone thereby giving greater stability and a lower rate of implant failure than with unreamed nails. It provides an internal bone graft, which acts locally to stimulate union of the fracture. Concerns have been raised that reaming destroys the endosteal blood supply and may delay union, although published data on this subject are equivocal. Intravasation of fat and marrow contents into the venous circulation with subsequent embolisation to the lungs occurs during reaming and can activate fibrinolytic and coagulation cascades. Unreamed nailing does not have this effect, but no clinical study has shown a convincing difference in cardiorespiratory complications between the two methods of nailing.

Unreamed nailing does not have this effect, but no clinical study has shown a convincing difference in cardiorespiratory complications between the two methods of nailing. Advocates of the unreamed nail suggest that the risk of infection increases with reaming as a result of disturbing the endosteal blood supply, especially in open tibial fractures in which the precarious blood supply and lack of soft-tissue cover predispose to nonunion and infection.

There is a lack of randomised, controlled trials in the literature which compare the rates of infection and nonunion in unreamed and reamed IM nailing. Studies which have been published have small sample sizes and large confidence intervals. Most published data from large teaching hospital units quote rates for nonunion and infection in nailed tibial fractures which range from 0% to 12% and 0% to 11%, respectively, with the higher figures relating to open type-IIIB tibial fractures. In a recent systematic review of the literature, no difference in the rates of infection was found after reamed or unreamed nailing of closed or open tibial fractures. The rate of nonunion was lower, the healing time was shorter and the incidence of implant failure was lower in reamed compared with unreamed nailing.

Quoted rates for nonunion and infection in femoral fractures treated by IM nailing range from 0% to 7.5% and 0% to 5%. The difference between the two methods is less distinct except for polytrauma patients at risk of respiratory complications in whom the unreamed femoral nail is probably to be preferred since it is quicker to insert and causes less embolic phenomena.
Reamed IM nailing is advocated as the treatment of choice by many authors for nonunion in the lower limb.\textsuperscript{18,19} It offers the advantages of stable fixation, a localised endosteal bone graft, realignment and compression at the site of nonunion by early weight-bearing. Rates of union of 78\% to 100\% and infection of 0\% to 7.5\% are quoted for uninfected nonunions, with the higher rates of infection occurring in groups in which more fracture sites were opened at the time of revision surgery.

Several methods of treatment are commonly used for the management of diaphyseal humeral fractures: a long arm cast, functional bracing, compression plating and IM nailing using either an ante- or retrograde method. Studies comparing plate fixation with IM nailing show no difference in complication rate apart from slightly higher rates of nonunion and substantial increases in shoulder pain and stiffness with the latter.\textsuperscript{20}

Pathological diaphyseal fractures and metastases of long bones are commonly regarded as an indication for IM nailing since they offer immediate stability, relatively minor soft-tissue trauma and protection against further fracture from the pathological process.\textsuperscript{1}

We report our findings of a retrospective study over five years to determine the incidence of infection and nonunion after IM nailing of a fracture of a long bone.

**Patients and Methods**

The Royal Preston Hospital is a designated district accident centre. It has a 24-hour flying-squad service and a catchment area that covers a large part of the north west of England, from Manchester in the south to the Lake District in the north and the Irish Sea in the west. The Accident and Emergency Department sees 55 000 new patients per year and all sub-regional specialties except cardiothoracics are present on site.

Between 1995 and 1999 we performed a retrospective study of our IM nailing practice of long bones. All patients were identified from the operating theatre logbooks. All the case notes were retrieved. The outcomes of interest were deep infection and union of the fracture. The potential risk factors for infection or nonunion were as follows: age, gender, site, indication for surgery, use of medullary reaming, whether the fracture was open at the time of injury or at surgery, operating time, the use of peroperative antibiotics and the American Society of Anaesthesiologists (ASA) score. The latter is a score of the patients’ general pre-operative condition on a five-point scale with high scores corresponding to a poor physiological condition.\textsuperscript{21}

Infection was classified into two groups; either superficial infective complications or deep infection requiring further surgery or removal of the implant. Union was defined by the clinical and radiological findings at follow-up.

Of the 226 operations using IM nailing initially identified for the study, completed data were found for 211. There were 109 men and 102 women with a mean age of 40 years and a median age of 34 years (15 to 92).

### Statistical analysis.

For each outcome of interest, namely infection or nonunion, we used multiple logistic regression analysis to identify significant risk factors and to estimate the resulting probabilities of an unfavourable outcome.

We used backward selection from a full main effects model to eliminate non-significant terms successively, based on a likelihood ratio test at each stage to obtain a reduced model which showed overall significance by comparison with the null model and in which all retained risk factors were individually significant or nearly so. We then investigated whether adding interaction terms to the reduced model led to any improvement in significance. All the tests were performed at the conventional 5\% level of significance. Our justification for retaining marginally non-significant terms in the reduced model is that in a relatively small study it is important to retain terms which may be clinically significant, but are estimated with low precision. The widths of the confidence intervals (CI) associated with such terms act as warnings against over-interpretation.

### Results

The median ASA score was 2 and the mean ASA score was 2.1 (1 to 5). The median length of the operation was 154 minutes and the mean 137 minutes (30 to 613). All patients except one had received intravenous antibiotics before and after operation. In this single exception a reamed humeral nail had been used for a closed fracture, which subsequently healed without complication.

Table I lists the number of nails inserted for each indication.

<table>
<thead>
<tr>
<th>Indication</th>
<th>Femur</th>
<th>Tibia</th>
<th>Humerus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trauma</td>
<td>91</td>
<td>58</td>
<td>12</td>
</tr>
<tr>
<td>Revision</td>
<td>9</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td>Pathological</td>
<td>22</td>
<td>0</td>
<td>5</td>
</tr>
</tbody>
</table>

In the trauma group there were ten open fractures of the femur, 18 open fractures of the tibia and three open fractures of the humerus. Table III lists the Gustilo grading\textsuperscript{15} of the fractures and the rates of deep and superficial infection. All open fractures which required soft-tissue cover had this done on site within five days. Of the total of seven type-III B fractures only two fractures of the tibia developed deep infection. One was managed by exchange nailing and subsequently developed chronic osteomyelitis and a discharging sinus. The other was revised to an above-knee amputation.

For infection, the full main effects model showed that fractures which were open at presentation were associated with an increased risk of deep infection (p = 0.022). The backward elimination procedure led to the reduced model summarised in Table IV in which open fracture and length...
of operation were retained as risk factors. The overall significance of the reduced model was 2.2% (chi-squared = 7.64; p = 0.022). Adding an interaction term to the reduced model gave a non-significant result (chi-squared = 0.11; p = 0.74). Both retained terms are marginally not significant. Further reduction to a model with either open fracture or length of operation as a single risk factor rendered the effect of the retained term unequivocally significant (2.3%, p = 0.023 and 2.5%, p = 0.025 for retained terms open and length, respectively).

For nonunion, the reduced model is summarised in Table V in which open at surgery, ASA score and indication for surgery are retained as risk factors. The reduced model is highly significant overall (chi-squared = 25.28; p < 0.001) and the retained terms are all individually significant. It should be noted from Table V that the significance of the indication risk factor stems primarily from the contrast between trauma and pathological indications with a non-significant difference between indications for revision and trauma. Adding pairwise interaction terms to this model
gave unequivocally non-significant results in all cases. Table VI gives the estimated probabilities for nonunion of a fracture for various ASA scores, indications for surgery and opening of the site of the fracture at the time of surgery.

Discussion

Our results correspond reasonably well to those of previously published reports from other large trauma units. The rates of deep infection and nonunion are higher, however, for all indications. This may reflect the varied case mix of both patients and surgeons of all grades included in the data. Previous studies have not usually commented on superficial infection although our study has shown a high rate of occurrence when both pre- and post-operative intravenous antibiotics have been given. We used multiple logistic regression analysis to establish which risk factors were significantly predictive of each outcome.

Open fractures were found to be significantly associated with deep infection. The reduced statistical model in Table IV gives the overall conclusion that openness of a fracture is an important predictive factor for infection, the estimated odds ratio between open and closed fractures being 2.7. The time taken for the operation may also affect the outcome, but is less important. The estimated odds ratio corresponding to an additional hour of operating time is 1.2. If the reduced model is fitted first for openness and then adding length of operation, the additional effect of fitting length is non-significant (chi-squared = 3.06, p = 0.080).

A simple explanation is that surgery on open fractures tends to take longer than that on closed fractures (mean lengths 174 and 131 minutes, respectively; 95% CI 0.949 to 7.660) so that including the open factor takes partial account of the effect of length.

From this model, the probabilities of deep infection for closed and open fractures, each with an operation lasting 137 minutes (the overall mean for all patients in the study) are 0.087 and 0.204, respectively. For an operation lasting 30 minutes (the shortest among all patients) these probabilities reduce to 0.063 and 0.154, while for that lasting 613 minutes (the longest) they increase to 0.188 and 0.547, respectively.

This would suggest that it is very important to have an experienced surgeon present to perform the operation or to supervise junior surgeons to make sure that an appropriate nailing procedure is performed within a reasonable operating time. Of interest is the fact that reaming of the medullary canal was shown not to be associated with deep infection of either closed or open fractures. Recent studies support this finding.\(^4\)\(^9\)\(^14\)

Opening of the fracture at the time of surgery and ASA score were found to be significantly associated with the development of nonunion after nailing. The reduced model in Table V shows that opening the fracture at surgery reduces the probability of successful union with an odds ratio of 0.26. Pathological fractures are the least likely to progress to union with an odds ratio of 0.33; revisions are not significantly different from fresh fractures with an estimated odds ratio of 0.70 not statistically different from 1 (p = 0.594). A high ASA score also indicates a poor prognosis with an estimated odds ratio per unit increase in ASA of 0.46. Table VI gives the estimated probabilities of nonunion for various combinations of ASA score, indication for operation and whether the site of the fracture was opened at surgery.

These results suggest that opening the site of the fracture should be avoided if possible. The presence of an experienced trauma surgeon at the time of operation could help to avoid this in many cases. An increased probability of nonunion with increasing ASA score probably reflects the poorer physiological, and often nutritional state, of patients with scores above 3.\(^2\)\(^3\)\(^2\)\(^3\) In our study reaming appeared to offer no added benefit with regard to the development of union. This remains a controversial point since there have been recent studies which both confirm and refute this point.\(^4\)\(^9\)\(^14\)

Our study is limited since it is a retrospective analysis of suspected risk factors for the development of nonunion and deep infection secondary to IM nailing. It does suggest, however, that strategies for risk management to avoid these complications can be developed. What is required is a randomised, controlled trial prospectively collecting these data. This is on-going at our hospital.

Table VI. Estimated probabilities of nonunion for all combinations of open/closed, indication and ASA score based on the reduced model summarised in Table V. The model is: Log (p/(1-p)) = -4.0188 + 1.3442 x open + 0.7815 x ASA + 1.1180 x pathological + 0.3539 x revision where p denotes the probability of nonunion, open = 1 for open at surgery, 0 otherwise, ASA is the ASA score on a five-point scale, pathological = 1 for a pathological indication, 0 otherwise and revision = 1 for a revision indication, 0 otherwise.

<table>
<thead>
<tr>
<th>Indication</th>
<th>ASA 1</th>
<th>ASA 2</th>
<th>ASA 3</th>
<th>ASA 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Closed trauma</td>
<td>0.038</td>
<td>0.079</td>
<td>0.158</td>
<td>0.291</td>
</tr>
<tr>
<td>Closed revision</td>
<td>0.053</td>
<td>0.109</td>
<td>0.211</td>
<td>0.368</td>
</tr>
<tr>
<td>Closed pathological</td>
<td>0.107</td>
<td>0.208</td>
<td>0.364</td>
<td>0.556</td>
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<tr>
<td>Open at surgery trauma</td>
<td>0.131</td>
<td>0.248</td>
<td>0.418</td>
<td>0.611</td>
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<tr>
<td>Open at surgery revision</td>
<td>0.177</td>
<td>0.319</td>
<td>0.506</td>
<td>0.691</td>
</tr>
<tr>
<td>Open at surgery pathological</td>
<td>0.315</td>
<td>0.502</td>
<td>0.687</td>
<td>0.881</td>
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</table>
References


