Noninvasive Technologies for Fracture Repair

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Case scenario

A 32 year old man, who was otherwise healthy, sustained a comminuted open tibial shaft fracture as a result of a motor vehicle accident. After initial debridement and irrigation, the fracture was fixed by an unreamed interlocking nail. Radiographs showed no sign of callus formation 6 months after surgery (Figure 72.1). There was no clinical, biochemical, or radiographic evidence of deep infection or osteomyelitis.

Relevant anatomy

Fracture healing of locked tibial nailing is controlled by many factors such as stability, gap, and vascularity of fracture site (level II–V). Therefore comminuted open tibial shaft fractures are potentially at risk of developing delayed healing (level II).1–5

Importance of the problem

Of the estimated 5.6 million fractures occurring annually in the United States, it is believed that 5–10% demonstrated delayed union or nonunion (level II).6 Acceleration of fracture healing is important to reduce the socioeconomic loss by shortening the period of fracture treatment.

Top five questions

1. What are the predictors of nonunion?
2. What kinds of noninvasive biophysical technologies can be available for noninfected delayed union and nonunion?
3. Does low-intensity pulsed ultrasound (LIPUS) accelerate fracture healing and improve the patient’s health-related quality of life (QOL)?
4. Does pulsed electromagnetic fields (PEMF) accelerate fracture healing and improve the patient’s health-related QOL?
5. Does extracorporeal shock wave therapy (ESWT) accelerate fracture healing and improve the patient’s health-related QOL?

Question 1: What are the predictors of nonunion?

Case clarification

The patient’s radiograph reveals a comminuted tibial shaft fracture fixed by a relatively small unreamed intramedullary (IM) nail. Subsequent radiographs showed no bridging callus with existence of visible fracture line (Figure 72.1). If we know the probability of this open tibial fracture developing to established nonunion, this information will help us to determine when additional treatment or therapy is needed to achieve union.

Relevance

Evaluation of predictors for nonunion will help us to recognize the risk of delayed union or nonunion earlier, and early treatment can help patients avoid prolonged periods of pain and disability.

Current opinion

Predictors of nonunion of open tibial fracture treated by using IM nail are Gustilo grades, postoperative fracture gap, unreamed IM nailing, and dynamization.

Finding the evidence

- PubMed (www.ncbi.nlm.nih.gov/pubmed/) advanced search with meta-analysis, clinical trial, randomized
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could not be determined because of the inadequate description

Findings
Court-Brown et al. have analyzed the mean time to union for different Gustilo grades of open fracture. These results indicated that the risk of nonunion increased with Gustilo grades (level II).  

Drosos et al. studied factors affecting fracture healing after tibial nailing for closed and grade I open fractures, and reported that the risk of failure of union increased by 2.38 times for highly comminuted fractures, by 3.14 times when nail dynamization was applied, and by 1.65 times when the locking screws failed (level II). They also showed that the risk of nonunion increased if the postrduction gap was 3 mm or more in fractures with no or only minimal comminution (level II).  

Bhandari et al. identified that postoperative fracture gap is one of the predictors of reoperation following operative treatment of tibial shaft fracture (level II).  

Meta-analyses of prospective RCTs have suggested large reductions in the risk of nonunion in association with the use of reamed IM nailing (RR 0.44; 95% CI 0.21–0.93) (level I–II).  

A well-designed randomized trial with a large number of participants demonstrated that overall nonunion rate was 4.6% and there is a possible benefit for reamed IM nailing in patients with closed fractures (RR 0.67; 95% CI 0.47–0.96) (level I).  

Recommendations
• Risk factors for nonunion in tibial shaft fractures include: (1) open fractures with high-grade Gustilo classification [overall quality: moderate]; (2) fixation with unreamed nails [overall quality: moderate]; and (3) fixation with large fracture gap between main fragments [overall quality: moderate]

• In these situations, some sort of additional intervention would be needed to avoid nonunion [overall quality: moderate]

Question 2: What kinds of noninvasive biophysical technologies can be available for noninfected delayed union and nonunion?

Case clarification
Some noninvasive technologies would be worth trying before surgical interventions for delayed union and nonunion.

Relevance
Some type of bone growth stimulation can be widely applied for acceleration of fracture healing as an adjuvant therapy and/or alternative therapy.
Current opinion
LIPUS, PEMF, and ESWT have been widely used to enhance fracture healing.

Finding the evidence
See Question 1.

Quality of the evidence
Level I
• 3 meta-analyses (2 for LIPUS and 1 for PEMF)
• 1 RCT for ESWT

Findings
LIPUS and PEMF have been most popular devices for the adjuvant and/or alternative treatment of choice for surgical intervention to enhance fracture healing (level I–III).\textsuperscript{15–17} Currently the effectiveness of ESWT for hypertrophic nonunions has been confirmed by RCT.

Recommendation
• Noninvasive biophysical stimulation may be available for possible tibial nonunion, and LIPUS, PEMF, and ESWT are recommended methods

Question 3: Does LIPUS accelerate fracture healing and improve the patient’s health-related QOL?

Case clarification
Before surgical intervention is considered for delayed or nonunion after tibial fracture, there is a chance to achieve union by LIPUS.

Relevance
How much is fracture healing accelerated by using LIPUS? What is the overall union rate for delayed union/nonunion by LIPUS? Does LIPUS improve QOL of the patient with a tibial fracture?

Current opinion
The use of LIPUS is considered to augment fracture healing in those fracture types at risk for nonunion such as open or comminuted fracture and/or compromised patients with smoking and malnutrition.

Finding the evidence
See Question 1.

Quality of the evidence
Level I
• 7 meta-analyses

Findings
Most meta-analyses included several kinds of bone and fractures, not focusing on tibial nonunion. Heckman et al. concluded that LIPUS shortened the time to healing fracture by 38% and significantly reduced the incidence of delayed union for the relatively simple closed or Gustilo I open tibial shaft fracture immobilized by a cast (level I).\textsuperscript{18} Leung et al. investigated the effect of LIPUS on fracture healing for open and/or severely comminuted tibial shaft fractures immobilized by IM nail or external fixator (level I).\textsuperscript{19} They concluded that the LIPUS-treated group showed statistically significant better healing, as demonstrated by all assessments. Emami et al., however, concluded that LIPUS did not shorten healing time in fresh tibial fractures treated with a reamed and statically locked IM nail (level I).\textsuperscript{20} Limited information for tibial shaft fracture from these three RCTs suggested that LIPUS probably enhances or accelerates fracture healing in tibial fractures (Figure 72.2), although the results of these three trials were heterogeneous (level I).\textsuperscript{17}

The benefits of LIPUS for delayed and nonunion were also investigated by cohort studies, which revealed that the overall success rate of LIPUS for delayed union and nonunions of tibia/tibia-fibula or fibula is approximately 88% (Table 72.1) (level II).\textsuperscript{21–24} Unfortunately, there is little literature that studies the improvement of health-related QOL of the patient (level II).\textsuperscript{25}

Recommendation
• LIPUS is likely to accelerate fracture healing in a fresh fracture as well as in delayed union or nonunion [overall quality: high]

Question 4: Does PEMF accelerate fracture healing and improve the patient’s health-related QOL?

Case clarification
Before surgical intervention is considered for delayed or nonunion after tibial fracture, there is a chance to achieve union by PEMF.

Relevance
How much does the use of PEMF accelerate fracture healing? What is the overall union rate for delayed union/
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nonunion by PEMF? Does PEMF improve QOL of the patient with tibial fractures?

Current opinion
The use of PEMF is considered to augment fracture healing in those fracture types at risk for nonunion such as open or comminuted fractures and/or compromised patients with smoking and malnutrition.

Finding the evidence
See Question 1.

Quality of the evidence
Level I
• 4 meta-analyses

Findings
For fracture healing, three types of electrical stimulation are available: (1) direct current stimulation using electrodes; (2) electromagnetic stimulation by inductive coupling; (3) capacitive coupling stimulation (level II).

Sharrard (level I)\(^2\) and Simonis et al. (level I),\(^2\) in a placebo-controlled randomized trial, examined the efficacy of PEMF on tibial delayed or nonunions. Both reports indicated that a greater proportion of patients in the treatment group achieved union (Table 72.2), and PEMF increased the chance of union by 3.8 or 1.8 times. However, the 95% confidence interval suggested that the increase could be as low as 1.1-fold (level III).\(^2\) Baker et al., in a placebo-controlled randomized trial, showed a negative effect of PEMF for tibial nonunion conservatively treated by cast (Table 72.2) (level II);\(^2\) however, the number of participants seemed to be too small.

Cohort studies or case series without control group showed that PEMF showed a high union rate (87–93%) of long-bone nonunions with non-weight-bearing treatment (level IV).\(^3\)\(^,\)\(^4\)

No evidence was available for improvement of the patient’s QOL.

Table 72.1 Success rate of LIPOUS for long bone fractures

<table>
<thead>
<tr>
<th>Study</th>
<th>Delayed or nonunion</th>
<th>Overall of long bones</th>
<th>Humerus</th>
<th>Radius/ radius-ulna</th>
<th>Femur</th>
<th>Tibia/tibia-fibula or fibula</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Success rate %</td>
<td>Success rate %</td>
<td>Success rate %</td>
<td>Success rate %</td>
<td>Success rate %</td>
</tr>
<tr>
<td>Mayr et al. 2000</td>
<td>Delayed</td>
<td>90 (525/584)</td>
<td>76 (49/52)</td>
<td>94 (85/98)</td>
<td>87 (350/380)</td>
<td></td>
</tr>
<tr>
<td>Rubin et al. 2001</td>
<td>Nonunion</td>
<td>84 (216/256)</td>
<td>69 (21/22)</td>
<td>95 (57/66)</td>
<td>86 (105/120)</td>
<td></td>
</tr>
<tr>
<td>Nolte et al. 2001</td>
<td>Nonunion</td>
<td>81 (179/195)</td>
<td>69 (21/22)</td>
<td>95 (57/66)</td>
<td>86 (105/120)</td>
<td></td>
</tr>
<tr>
<td>Gebauer et al. 2005</td>
<td>Nonunion</td>
<td>91 (1921)</td>
<td>100 (4/5)</td>
<td>80 (4/5)</td>
<td>80 (10/10)</td>
<td></td>
</tr>
<tr>
<td>Subtotal</td>
<td>Nonunion</td>
<td>89 (1580/1856)</td>
<td>69 (21/22)</td>
<td>95 (57/66)</td>
<td>86 (105/120)</td>
<td></td>
</tr>
</tbody>
</table>

Table 72.2 Effect of pulsed electromagnetic fields on increasing chance of union for tibial nonunion

<table>
<thead>
<tr>
<th>Study</th>
<th>Active</th>
<th>Placebo</th>
<th>Increased chance of union</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>United</td>
<td>Not united</td>
<td>United</td>
</tr>
<tr>
<td>Sharrard 1990</td>
<td>9</td>
<td>11</td>
<td>3</td>
</tr>
<tr>
<td>Simonis 2003</td>
<td>16</td>
<td>2</td>
<td>8</td>
</tr>
</tbody>
</table>

Recommendation
• PEMF is likely to improve healing rate in delayed union or nonunion [overall quality: high], but no evidence was available for acceleration of fracture healing in fresh fracture.

Question 5: Does ESWT accelerate fracture healing and improve the patient health-related QOL?

Case clarification
Before surgical intervention is considered for delayed or nonunion after tibial fracture, there is a chance to achieve union by ESWT.
Relevance
How much is fracture healing accelerated by using ESWT? What is the overall union rate for delayed union/nonunion by ESWT? Does ESWT improve QOL of the patient with tibial fractures?

Current opinion
Predictors of open tibial fracture treated by IM nailing are Gustilo grades, postoperative fracture gap, unreamed IM nailing, and dynamization.

Finding the evidence
See Question 1.

Quality of the evidence
Level II
• 1 systematic review of case series

Findings
A shock wave is defined as a sonic pulse characterized by a high peak pressure (500 bar = 100 kPa), a short life cycle (10 ms), fast pressure rise (<10 ns), and broad frequency spectrum (16–20 MHz) (level IV). Elster et al. currently reported the result of 192 tibial nonunions treated by ESWT coupled with post-treatment immobilization, external fixation, or ESWT alone (level IV). They stated that 138 of 172 (80.2%) patients demonstrated complete fracture healing at the time of last follow-up, and that mean time from first shock wave therapy to complete healing was 4.8 ± 4 months.

Cacchio et al. prospectively compared the results of ESWT produced by two different devices (with 400 impulses of shock waves with an energy flux density of 0.40 mJ/mm² (group 1) or 0.70 mJ/mm² (group 2) with those of surgical treatment for long-bone hypertrophic nonunions (group 3) (level IV). At 6 months, 70% of the nonunions in group 1, 71% of the nonunions in group 2, and 73% of the nonunions in group 3 had healed. They concluded that ESWT is as effective as surgery in stimulating union of long-bone hypertrophic nonunions.

Zelle et al. reviewed 10 case series and reported that the overall union rate in patients with delayed union/nonunion was 76% (95% CI 73–79%) and ranged from 41% to 85%. The union rate in atrophic nonunions was 29% as compared with 76% in hypertrophic nonunions (RR 2.6; 95% CI 1.6–4.7; p < 0.0001).

Recommendation
• ESWT is likely to be the alternative treatment of choice for hypertrophic long-bone nonunion [overall quality: low]

Summary of recommendations
• Risk factors for nonunion in tibial shaft fractures include (1) open fractures with high-grade Gustilo classification, (2) fixation with unreamed nails, and (3) fixation with large fracture gap between main fragments. In these situations, some sort of additional intervention would be needed to avoid nonunion
• Noninvasive biophysical stimulation may be available for possible tibial nonunion, and LIPUS, PEMF, and ESWT are among the recommended methods
• LIPUS is likely to accelerate fracture healing in fresh fracture as well as in delayed union or nonunion
• PEMF is likely to improve healing rate in delayed union or nonunion, but no evidence was available for acceleration of fracture healing in fresh fracture
• ESWT is likely to be the alternative treatment of choice for hypertrophic long-bone nonunion

References
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