Time to Union as a Measure of Effectiveness

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Time to fracture union is commonly reported in orthopaedic clinical research even though there is no accepted reference standard for the radiological diagnosis of union, and radiographic diagnosis of union has not been shown to be reliable or precise. Studies have noted inconsistent definitions and measure of union both in orthopaedic scientific publications as well as in a survey of orthopaedic traumatologists. Several studies have also questioned the intra- and inter-observer reliability of radiographic diagnosis of union for various fractures. The growing consensus that time to union is an unreliable and imprecise measure of the effectiveness of fracture treatment would be corroborated by identification of variance in the average time to union in studies of comparable fractures similarly treated.

In this study we catalogue the last 10 years’ studies that use time to union as an outcome measure, recording diagnostic criteria and comparing mean time to union for comparable fractures with comparable treatment.

Methods

Pubmed was searched for English Language articles published during the 10-year period between 1997 and 2007 using the following terms: “time to union,” time AND union, time AND bony AND healing, time AND fracture AND healing, time AND unite AND fracture, time AND bone AND unite. Exclusion criteria were (1) nonhuman studies, (2) studies of the treatment of ununited fractures, osteomyelitis, or peri-prosthetic fractures (3) case reports and (4) pediatric fractures.

The papers were evaluated in three ways. First, the following data were extracted: the method for diagnosing union; mean and range of “time to union”; the number of patients; fracture site and treatment; and the statistical methods used to evaluate time to union. Second, in order to evaluate variations in average “time to union” for comparable treatments of nearly identical fractures at identical anatomic sites, we selected sets of three or greater papers evaluating similar fracture treatment. Finally among all papers providing enough data to perform statistical comparisons, the average time to union was evaluated for statistically significant differences across studies using one-way analysis of variance. P values <0.05 were considered significant. For each statistically significant difference, post-hoc pair wise comparisons of the selected studies were performed using the Tukey test.

Results

One hundred twenty-seven studies met the inclusion criteria. Because of the number of studies and many anatomical areas, the areas were categorized by AO location. The following anatomical areas were involved: Ankle (3 studies); calcaneus (1); clavicle (3); distal femur (2); distal radius (1); tibial pilon (5); distal femur (21); floating knee (1); forearm (9); hip (13); humerus (10); long bones (2); mallet finger (1); metacarpal (1); metatarsal (1); proximal phalanx (1); scaphoid (6); segmental tibia (2); talus (1); tibial
shaft (39), tibial plafond (4) and 1 trans-scaphoid perilunate fracture-dislocation.

**Diagnosis of Fracture Union**

There was variation in the diagnostic criteria for fracture union as follows: Bridging callus (39 studies), bridging callus at three different cortices (30), bridging callus in two different views (25), and bridging callus or obliteration of the fracture line (13), presence of callus (2), absence of osteonecrosis (1), absence of displacement (1), and hardware failure or loosening (1). The diagnostic criteria were not clearly stated in 27 studies.

**Variation in Reported Time to Union for Specific Fractures**

Most studies don’t mention the interval time between follow-up appointments. Others have a monthly interval for follow-up, and some have a two-weekly follow-up. Ten specific fracture types had three or more studies addressing time to fracture union, comprising a total of 66 studies. The anatomical regions covered included: Upper extremity fractures: Clavicle (3); Forearm (3); Humerus (6) and Scaphoid (4); Lower extremity fractures: Distal Tibia (6); Femur (9); Hip (12); Tibia (8); Tibial plafond (3), and open tibia fractures. (12) There was substantial variance in mean time to union for all fractures.

**Upper Extremity Fractures**

The average mean time to union was 12.8 ± 2.6 weeks (range 9.6 – 16.4 weeks) among the three studies of clavicle fractures; 10.9 ± 2.7 weeks (range 7.8 – 16 weeks) among the six studies addressing humeral fractures treated with nailing or plating; 13.6 ± 5.2 weeks (range 6.4 – 20 weeks) among the three studies addressing forearm fractures; and 12.0 ± 5.0 weeks (range 6.1 – 18.2 weeks) among the four studies addressing operative management of scaphoid fractures.

**Lower Extremity Fractures**

The average mean time to union among seven studies addressing operative treatment of intertrochanteric femur fractures was 14.0 ± 3.1 weeks (range 10.2 – 19.5 weeks). The average mean time to union among three studies of the operative management of subtrochanteric femur fractures was 14.9 ± 0.7 weeks (range 14 – 15.7 weeks). The average mean time to union among nine studies of operative treatment of diaphyseal femur fractures was 18.2 ± 7.1 weeks (range 11.4 – 39.4 weeks).

The average mean time to union among three studies addressing tibial plafond fractures was 19.9 ± 2.6 weeks (range 16.5 – 22.8 weeks). The average mean time to union among eight studies addressing diaphyseal tibia fractures was 18.5 ± 3.6 weeks (range 13.6 – 25.7 weeks). The average time to union among 12 studies addressing surgical treatment of open diaphyseal tibia fractures was 32.1 ± 7.4 weeks (range 19 – 47.8 weeks). Among six studies addressing distal tibia fractures, the average time to union was 20.9 ± 5.8 weeks (range 14.7 – 35 weeks).

**Statistical Comparison of Time to Union for Specific Fractures**

Among studies that provided sufficient data to perform a statistical comparison, there were statistically significant differences in average time to union among two studies evaluating plate fixation of clavicle fractures (mean 11.5 ± 1.8 weeks; p=0.03), three studies evaluating unreamed nailing of femur fractures (mean 25.9 ± 10.0 weeks, p <0.01; Post hoc Tukey--all significantly different from one another), and three studies evaluating reamed nailing of femur fractures (mean 19.3 ± 7.0 weeks, p <0.01; Post hoc Tukey--all significantly different from one another). There were no differences in four study groups evaluating plate and screw fixation of intertrochanteric femur fractures (mean 10.9 ± 0.6 weeks, P=0.29), three studies describing plating of distal tibia fractures (mean 20.0 ± 0.6 weeks; p=0.92), or three studies comparing intramedullary nailing of femur fractures (mean 17.1 ± 3.0 weeks; p=0.23).

Three studies compared unreamed nailing
techniques in closed tibia fractures. There was no significant difference between the studies of Larsen and colleagues\(^{10}\), Uhlin and colleagues\(^{11}\), and Karladani and colleagues\(^{12}\) (mean 21.2 ± 3.2 weeks; \(p = 0.07\)). There was a significant difference between the four studies reporting time to union in tibia fractures treated with reamed nailing (mean 15.8 ± 1.5 weeks; \(p < 0.01\)). Post hoc Tukey HSD analysis found a significant difference between Emami and colleagues\(^{13}\) and Tigani and colleagues\(^{14}\); Larsen and colleagues\(^{10}\) and Tigani and colleagues\(^{14}\); and between Braten and colleagues\(^{15}\) and Tigani and colleagues\(^{14}\).

## Discussion

This study and prior structured reviews\(^{1,16}\) note that there is no reference standard for the radiographic diagnosis of fracture union. Furthermore, our analysis demonstrated substantial variation in reported time to union for comparable fracture types with comparable treatments and statistically significant differences between several comparable studies that provided adequate data for statistical comparison. Combined with analyses that question the precision and reliability of the diagnosis of fracture union\(^{2,3}\), these findings bring into question the role of time to union as a useful and meaningful measurement of treatment effectiveness in studies of fracture treatment.

The observed variations in average time to union are likely the result of multiple factors, including, but not limited to: (1) variations in diagnostic criteria for union; (2) intra- and interobserver variation in the diagnosis of union; and (3) variations in the details of management. One must also consider differences in the number, spacing, and regularity of the office appointments to assess fracture healing as well as differences in the statistical technique for evaluating union.

Until there is a consensus technique for the diagnosis of fracture union that is reliable and precise, it is misleading to report measurements of time to union. Other measures of successful fracture healing, such as the absence of loosening or failure of implants a minimum one year after surgery, may prove more valid and reliable for the diagnosis of fracture union and are probably more applicable and relevant. The imprecision of time to union as a measure of treatment effectiveness makes it particularly susceptible to bias and therefore inadequate for scientific investigation.

## References


**Appendix A: Papers Used for Analysis**


73. Leung F, Chow SP. A prospective, randomized trial comparing the limited contact dynamic compression plate with the point contact fixa-


96. Raschke M, Rasmussen MH, Govender S et al. Effects of growth hormone in patients with tibial fracture: a randomised, double-blind, pla-


117. Trumble TE, Gilbert M, Murray LW et al. Displaced scaphoid fractures treated with open reduction and internal fixation with a cannulated