Ability and Limitation of Radiographic Assessment of Fracture Healing in Rats

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Abstract The purpose of the present study was to assess whether clinicians are actually able to evaluate the mechanical status of fracture healing from radiograms. Fifteen orthopaedic surgeons evaluated the radiograms of experimentally produced femur fractures in rats and predicted mechanical strength (%) of the affected side compared to the unaffected control side. Following this, actual mechanical strength of the affected and control side was determined by a three-point bending test. The median of the strength in the transverse fracture model predicted from radiograms was 33% (2 weeks), 72% (4 weeks), 88% (6 weeks), 84% (8 weeks), and 89% (12 weeks). The actual measured recovery ratio of mechanical strength (exp/control $\times$ 100) was 36%, 76%, 93%, 89%, and 106% in each observation period respectively. The tendency was almost the same in a comminuted fracture model. The mean recovery rate determined by interpretation of the surgeons correlated linearly to the actual measured mechanical strength determined by mechanical testing (R^2 : 0.80 in transverse fracture, 0.60 in comminuted fracture). Clinicians demonstrated that a comparatively good evaluation of the mechanical status of fracture healing is possible from

radiograms up to approximately 80% recovery. However, they tended to make less accurate, weaker assessments at the final stages. In conclusion, radiograms may be inadequate for evaluation of fracture healing completion.

Introduction

Biomechanically, the goal of fracture healing can be defined as the restoration of the mechanical properties, such as strength and stiffness, of fractured bone [10] because the healed fracture must achieve and maintain mechanical characteristics similar to those of the bone before fracture. Prediction of mechanical strength of healing bone is clinically quite important because it directly affects the progress in permissible activity of daily living of the patient after injury. However, nobody can know its actual mechanical strength by noninvasive means.

How do clinicians evaluate fracture healing? We consider the intervals after injury, check for clinical symptoms such as pain and tenderness, evaluate the patient's ability to weight bear without pain, and look at radiograms. Bhandari et al. [1] reported a cross-sectional survey of 577 orthopaedic surgeons on the assessment of fracture healing and concluded a lack of consensus in the assessment of fracture healing in tibial shaft fractures among orthopaedic surgeons, but it would seem that primary emphasis is placed on radiographic examination.

We hypothesized that an orthopaedic surgeon has the ability to predict mechanical strength of healing fracture by interpretation of radiograms. First of all, the present study attempted to evaluate the agreement between surgeon assessment based on radiogram and mechanical assessment for transverse fractures. Second, the present study attempted to evaluate the agreement between surgeon

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assessment based on radiogram and mechanical assessment for comminuted fractures.

Materials and Methods

Forty 7-week-old female Sprague-Dawley rats were employed in this study. All experimental protocols were conducted according to the “Guiding Principles for the Care and Use of Animals in the field of Physiological Sciences,” published by the Physiological Society of Japan. Under intraperitoneal anesthesia (30 mg/kg pentobarbiturate), the left femur was exposed and fixed with a specially designed unilateral external fixator and then experimental transverse and comminuted fractures were made in the midshaft (Fig. 1). Midshaft of the femur was cut by using a small radial arm saw to produce the transverse fracture model. Midshaft of the femur was fragmented by using a small bone rongeur to produce a comminuted fracture model (Fig. 1A–B). The rats were euthanized at 2, 4, 6, 8, and 12 weeks ($n = 4$, for each interval in each group) after fracture. The external fixator was removed, and both sides of the femur were dissected free from the soft tissue and

anterior-posterior and lateral views of radiographs were taken. These radiographs were shown to 15 orthopaedic surgeons and they were asked to rate the degree of healing in comparison to a normal control, as predicted recovery ratio (%) of bending strength. They received a detailed briefing on the mechanical test performed after radiographic evaluation, and ordered to answer the recovery ratio from 0% to 200% in 5% increments. To measure the actual bending strength, the fractured bones were subjected to a quasi-static three-point bending test using a mechanical testing machine (Shimadzu, EZ Graph, Japan) at a cross-head speed of 0.1 mm/min to measure ultimate strength. The control bones were also tested for comparison, and an actual recovery ratio (%) was calculated. Actual recovery ratio was expressed as percentage to strength of the control. There must be some discrepancy between the actual recovery and the estimated recovery from mechanical test because there must be some error associated with the mechanical testing itself. Because this potential error will probably be small, the actual recovery ratio was defined as above in this study.

The median was used as measure of central tendency, because the predicted recovery ratio is not continuous scale and the results of mechanical testing were asymmetrically distributed. The median recovery ratio in each interval group was represented as a measure of central tendency, and the Kruskal-Wallis test was used to examine the effect of healing time on predicted recovery ratio and actual recovery ratio. Coefficient of determination (R^2) between actual and predicted recovery ratio was also calculated. Statistical differences were considered significant for $p < 0.05$.

Results

In the transverse fracture, both the predicted and actual recovery ratio increased with time of healing (Kruskal-Wallis test, $p < 0.0001$), but the predicted recovery ratio showed no useful information after 6 weeks (Fig. 2A). Median of predicted recovery ratio in the transverse fracture model was 33% at 2 weeks, 72% at 4 weeks, 88% at 6 weeks, 84% at 8 weeks, and 89% at 12 weeks, respectively. Median of actual recovery ratio in the transverse fracture model was 36% at 2 weeks, 76% at 4 weeks, 93% at 6 weeks, 89% at 8 weeks, and 106% at 12 weeks, respectively (Fig. 2B). Mechanical strength increased with time of healing (Kruskal-Wallis test, $p < 0.0001$), and at 12 weeks the affected bone was actually stronger than the normal control. All specimens were broken at the original or near the original osteotomy site. Three specimens in the 2-week model showed ductile behavior. The broken line macroscopically extended to the adjacent pin holes in three specimens.

Fig. 1A–B Models of transverse fractures and comminuted fractures were used. Experimental fractures were made in the midshaft of the femur. The fractures were fixed with a specially designed unilateral external fixator. Anteroposterior view and lateral view of the same femur were shown. The (A) transverse fracture 2-week model showed 18% recovery rate in mechanical test and the (B) comminuted fracture 2-week model showed 8% recovery rate in mechanical test.

Fig. 2A–B Changes in recovery ratio of the transverse fracture model. Actual mechanical strength increased with time of healing during experimental periods, but the predicted strength from radiograms reached a plateau at 6 weeks following the experimentally produced transverse fracture. **(A)** Recovery ratio was predicted by radiograms. **(B)** Actual recovery ratio was measured by mechanical test.

In the comminuted fracture, both the predicted and the actual recovery ratio increased again with time of healing (Kruskal-Wallis test, $p < 0.0001$). Median of predicted recovery ratio in the comminuted fracture model was 16% at 2 weeks, 77% at 4 weeks, 84% at 6 weeks, 87% at 8 weeks, 91% at 12 weeks, respectively (Fig. 3A). Median of actual recovery ratio in the comminuted fracture model was 4% at 2 weeks, 86% at 4 weeks, 101% at 6 weeks, 107% at 8 weeks, and 108% at 12 weeks, respectively (Fig. 3B). Mechanical strength increased with time of healing (Kruskal-Wallis test, $p < 0.0001$), and it increased conspicuously over the first 6 weeks. All specimens were broken at the original comminuted fracture site. Five specimens in the 2-week model and three in the 4-week model showed ductile behavior. The broken line macroscopically extended

Fig. 3A–B Changes in recovery ratio of comminuted fracture model are shown. The tendency of fracture healing was almost the same in comminuted fracture model with the transverse fracture model, but there is a greater degree of variance at each interval among comminuted fracture than in transverse fractures. **(A)** Recovery ratio was predicted by radiograms. **(B)** Actual recovery ratio was measured by mechanical test.

to the adjacent pin holes in one specimen. There was a greater degree of variance at each interval among comminuted fractures than transverse fractures.

The median values of predicted recovery ratio in each specimen correlated linearly to the actual recovery ratio determined by mechanical testing ($R^2 = 0.80$, $p < 0.0001$) (Fig. 4A). The median of R^2 value for each participating surgeon was 0.73 (range: 0.14–0.84, 95% CI: 0.58–0.78). Association of predicted recovery ratio by the observer surgeons to actual recovery ratio measured by mechanical testing showed a clearly correct trend overall ($R^2 = 0.62$, $p < 0.0001$) (Fig. 4B). The median R^2 value for each participating surgeon was 0.59 (range: 0.35–0.68; 95% CI: 0.49–0.63).

Fig. 4A–B Association of predicted recovery ratio to actual recovery ratio is shown. The median values of predicted recovery ratio in each specimen correlated linearly to the actual recovery ratio determined by mechanical test. Solid lines represent regression line and dotted line is one $X = Y$. The value of R^2 was 0.80 in the transverse fracture model ($p < 0.0001$) and 0.62 in the comminuted fracture model ($p < 0.0001$). (A) Transverse fracture and (B) comminuted fracture models are shown.

Discussion

This study was conceived to assess a surgeon's ability to judge the extent of fracture healing from radiographs. There is no ready substitute for radiograms for monitoring fracture healing clinically, although many kinds of monitoring systems have been developed [3–5, 8, 10]. Radiographic examination is an excellent diagnostic tool for evaluating the type of fracture and consequently for planning the surgery, but it sometimes fails to provide sufficient information about the mechanical status of the healing fracture [6].

There are several limitations of this study. Compared to human bone, the size of bone is very small in rats.

Therefore, it is difficult to interpret radiograms in a rat fracture model. In addition, there appears a large variation in the surgeons' ability to predict the likely bending strength. It is therefore important to establish a correlation between the transverse and the comminuted fracture for the individual surgeon. However, only five surgeons evaluated both models by radiograms, therefore we could not evaluate this important matter. Furthermore, we did not examine the correlation between predicted strength of the healing fractures and other mechanical parameters such as axial and torsional stiffness. We only tested our fractures in three point bending.

In this study, mechanical tests showed that an increase in bending strength is observed over time with both transverse and comminuted fractures. However, there is a greater degree of variance at each interval among comminuted fractures than in transverse fractures. This result, therefore, indicated that the interval alone does not provide us with enough information to adequately evaluate healing for clinical use, especially with comminuted fractures.

The coefficient of determination between the actual and predicted recovery ratio was calculated in the present study. Coefficient of determination was 0.80 for the transverse fracture and 0.62 for the comminuted fracture. This result showed that around 80% of fractured bone's mechanical competence typically can be explained by variations from interpretation of the radiographic image in the transverse fracture, but the clinician's ability to evaluate mechanical strength from interpretation of the radiographic image was reduced to around 60% in comminuted fractures. Panjabi et al. [7] studied correlations of radiographic analysis of healing fractures with strength by using experimental osteotomies in rabbits, and reported that cortical continuity was the best single predictor of strength of a healing fracture. They reported that its correlation coefficient was 0.80, which is equivalent to 0.64 of coefficient of determination. The clinician's ability to predict the strength of healing fractures from radiographs was comparable with the best predictor analyzed under laboratory conditions.

Hammer et al. [2] reported that conventional roentgenographic examinations as a means of assessing the stage of union are generally inconclusive. Sano et al. [9] stated the amount of callus on a radiogram is not related to stiffness. In the present study, for the first 6 weeks we saw an excellent correlation between the surgeon's subjective evaluation and actual mechanical measurements. After 6 weeks, however, the surgeon was no longer able to make an accurate assessment from the radiograph. In other words, clinicians demonstrated that a comparatively good evaluation of the mechanical status of fracture healing is possible from radiographs up to approximately 80% of recovery of fractured bone. In comparison, we recognize

that the surgeons tended to make less accurate, weaker assessments at the final stages of fracture healing. Thus, clinicians cannot help taking time after injury into account to decide whether to allow patients to bear full weight. In conclusion, radiograms may be inadequate for evaluation of fracture healing completion.

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