

Ultrasound treatment for accelerating fracture healing of the distal radius. A control study¹

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ABSTRACT

PURPOSE: To investigate the accelerating effects of low-intensity pulse ultrasound stimulation (LIPUS) on the fracture healing of distal radius.

METHODS: A total of 81 patients with distal radius fracture were randomly divided into two groups: the ultrasound treatment group and the control group. Patients in the ultrasound treatment group were immobilized in a below-elbow cast and received LIPUS treatment 15 min/day, while the control group were immobilized by a plaster support and cast. The patients were followed up every week and took X-ray films. The initial and healed X-ray films and the gray value of fracture site were analyzed by Photoshop software. The effect of reposition was evaluated based upon Steward recommended by Dienst, combining with Aro's measuring method.

RESULTS: Clinical fracture healing time in ultrasound group was significantly shorter than that in the control group ($32.04 \pm 2.58d$ vs. $40.75 \pm 5.12d$, $p < 0.01$). In addition, the grey value changes of fracture sites of the ultrasound group were much higher than that of the control group. The reposition effects of fracture healing had no difference between the two groups ($p > 0.05$).

CONCLUSION: Low-intensity pulse ultrasound stimulation could accelerate fracture healing of the distal radius and promote local bone formation.

Key words: Ultrasonography. Radius Fractures. Fracture Healing. Osteogenesis.

Introduction

Fracture healing is a homeostatic process that depends on many factors, including specialized cell activation and bone immobility during repair¹. About 5%-10% of fractures lead to delayed union (even nonunion) and require corrective secondary surgery because of the impairments in healing process^{2,3}. Various physical and biologic methods are developed for enhancing fracture healing including, laser, direct current, microcurrent, ultrasound, electrical magnetic field, and capacitive coupled electrical stimulation⁴⁻⁶. Low-intensity pulsed ultrasound (LIPUS) is a form of ultrasound that transmitted into connective tissues as an acoustic wave. As a non-invasive therapy, LIPUS has been used to promote fracture healing for 30 years, and is studied and applied in many clinical studies⁷⁻⁹.

LIPUS can stimulate the differentiation of bone-forming cells which contribute to bone formation, fracture healing and recovery of strength at the healing site¹⁰. It has been proved that LIPUS can promote formation of the medullary canal and cortex in a gap-healing model, which then leads to earlier restoration of the structural integrity of the healing site¹¹. Many clinical studies indicate that LIPUS can enhance the healing of fresh fractures, delayed unions, nonunions, distraction osteogenesis and congenital pseudoarthroses^{7,8,12,13}.

In this study, we designed a prospective, randomized study to assess the effect of LIPUS on distal radius fracture, and to investigate the ability of LIPUS to accelerate fracture healing of the distal radius on radiographs.

Methods

Patient inclusion and exclusion criteria

The study was approved by the Ethics Committee of Shuguang Hospital and the informed consent was obtained from each patient.

From October 2005 to March 2008, eighty-one outpatients with a fracture at distal radius which were dorsally angulated and displaced were enrolled in this study. The inclusion criteria were (i) fractures involving radiocarpal joint or distal ulnoradial joint, or (ii) involving ulnar styloid process. The exclusion criteria were (i) patients with Smith's fracture and Barton's fracture, and (ii) patients accompanied with systemic diseases such as heart, brain, liver, and kidney.

Experimental design

The patients' characteristics including sex, age, causes of injury, fracture severity and symptom of pressure on the nerve were recorded. The angulations of palm obliquity, ulna deviation and height of radius were measured by X-ray. The classification of Lidstrom was defined as: I° (no deformity, no dorsal angulation and radius was shortened less than 3 mm), II° (light deformity, 1°-10° of dorsal angulation and radius was shortened 3-6 mm), III° (mild deformity, 11°-15° of dorsal angulation and radius was shortened 7-12 mm), and IV° (severe deformity, more than 15° of dorsal angulation and radius was shortened more than 12 mm). Patients were closely reduced and immobilized with cast in the position of palmar flexion. All patients were randomly divided into two groups with the random number table: the ultrasound treatment group (n=41) and the control group (n=40). In ultrasound group, a 'window' of 2.5 cm in diameter was cut on the dorsal side of fracture site. Ultrasonic probe was applied on the fracture site through the window. The ultrasound treatment was given with 15 min/day with the low-intensity pulsed therapeutic ultrasonic device (Shanghai Dahu Medical Instrument Plant, including the electropult of ultrasound and ultrasonic probe). The intensity of LIPUS was 30 mW/cm² (1.5 MHz frequency and 200µs pulse duration). The first time of ultrasound treatment was performed in hospital by doctors, and then patients manipulated the treatment themselves according to instructions given by doctor. The patients took the entopic and lateral X-ray films at a follow-up examination every week. Two weeks later, the patients in the ultrasound group were immobilized with a below-elbow plaster cast, while the patients in the control group were immobilized with plaster support and cast until clinical union of bone. Then functional training was performed on patients directed by doctors.

In order to initial determine the conditions of bone healing, all patients were re-examined by knocking the 2, 3, 4 metacarpal heads of affected hand after around four weeks. If patients felt pain, then immobilization was continued and a reassessment was done one week later. When patients felt no pain, the plaster cast was removed, and then tenderness and abnormal movement was examined by doctor. The fracture was judged as clinical healing when the affected hand could raise 1 kg levelly for 1 minute in functional test, and the fracture was not obvious according the X-ray film¹⁴ (the fracture line was faint in X-ray film). The clinical healing time of each patient was defined as the time from fracture to clinical union. The clinical healing time was assessed by three experienced doctors (blinded to the treatment method).

The initial and final X-ray films of each patient were

captured with Casio digital camera (5 million pixels). The grey level of X-ray films were analyzed by the Photoshop software according to a imaging analysis method describe previously¹⁵. On the anterior posterior (AP) view of the film, an area of 2.0×0.5 cm along the fracture line was selected, meanwhile, the mean value of the grey level in the area was investigated by the order of histogram. The selected area of initial film should be closed to the proximal end of the fracture line, and this can reflect the normal grey level of the bone and avoid the error from fracture site overlapped. The selected area of the film after union was just on the fracture line. The films were also assessed by three experienced doctors who were blinded to the treatment method.

The dorsal inclination of the fracture, drift angle of ulna, and height of radius of primary fracture were measured by X-ray film after fracture healing. Then the effect of manipulation was evaluated based upon Steward recommended by Dienst, combining with Aro's measuring method (Table 1).

TABLE 1 - The score chart for reposition accuracy of the distal radius fracture after union.

Graded items	0	1	2	3
Dorsal inclination (°)	0	1-10	11-14	>14
Decrease of drift angle of ulna (°)	0-4	5-9	10-14	>14
Shortening of radius (mm)	0-3	4-6	7-11	>11

Notes: The sum of the three items being 0 was marked perfect, 1-3 good effect, 4-6 improvement, and 7-12 bad effect.

Statistical analysis

The chi-square test was used for comparing values of binary variables, student *t*-test was used for comparing means of continuous variables, and the Mann Whitney U test was used for comparing distributions of ordinal variables. *P* value less than 0.05 was considered to be significant.

Results

Statistics for all patients showed that the average time from fracture to beginning ultrasound treatment was 3.4 days. There was no significant difference ($p < 0.05$) in sex, age, and various parameters relating to fracture between two groups (Table 2). The mean time to clinical fracture-healing was 32.04 ± 2.58 days in ultrasound group and 40.75 ± 5.12 days in control group. The clinical healing time in the ultrasound group were less than that in the control group. The change of grey level in the ultrasound group was more than that in the control group (Table 3 and Figure 1). Dorsal inclination and shortening of the radius were similar in two groups ($p > 0.05$, Tables 4, 5).

TABLE 2 - Comparison of the primal data between the two groups.

Comparability	Treatment group	Control group	p
Sex			>0.05
Male (n)	4	5	0
Female (n)	37	35	0
Average age (years)	67.90±5.58	65.70±6.09	>0.05
Fracture of processusstyloideus ulnae (n)	24	21	>0.05
Involving radiocarpal articular surface (n)	19	21	>0.05
Involving distal ulnoradial joint (n)	21	19	>0.05
Comminuted fracture (n)	22	20	>0.05
Lidstrom's type			>0.05
I°	12	8	
II°	4	6	
III°	8	12	
IV°	17	14	



FIGURE 1 - X-ray film in the present study. A. The original X-ray film of a 61year-old male patient; B. After LIPUS therapy for 1month, bone density at fracture site enhance significantly; C. The cast for LIPUS therapy.

TABLE 3 - Comparison of the average time of union and the average ratio of the grey level between the two groups.

Comparability	Treatment group	Control group	p
The average time of union (days)	32.04±2.58	40.75±5.12	<0.01
The average ratio of the grey level	1.109±0.147	1.029±0.096	<0.05

TABLE 4 - Assessment of the degree of dorsal inclination.

	0°	1-10°	11-14°	>14°
Treatment group	10	15	5	1
Control group	8	24	8	0

TABLE 5 - Assessment of the shortening of the radius.

	0-3 mm	4-6 mm	7-11 mm	>11 mm
Treatment group	7	26	6	2
Control group	5	25	9	1

In the 81 cases of distal radius fracture, 49 cases got good accuracy of reposition, 29 cases showed a little improvement in reposition accuracy and three cases had poor accuracy of reposition. The reposition accuracy of fracture healing was graded and no difference were found in reposition between the two groups ($p > 0.05$, Table 6).

TABLE 6 - Comparison of the reposition accuracy between the two groups.

Comparability	Treatment group	Control group	p
Grade			>0.05
Marked effect	3	2	
Good effect	23	21	
Improvement	13	16	
Bad effect	2	1	0
Sum	41	40	>0.05

Discussion

The histological or biomechanics method could not be used for comparing fracture healing of distal radius in clinical trials. The grey levels of the fracture site were corrected to eliminate error coming from different conditions of taking the X-ray film. The grey level of X-ray film could indirectly reflect the changes of bone mineral density. Thus, we could compare the grey level of X-ray film to assess bone mineral density of fracture site in this study. The result indicated that the bone mineral density in the ultrasound group was statistically higher than that in the control group ($p < 0.05$), and it meant that LIPUS could promote bone formation at local site.

LIPUS has already been used to promote the fracture healing in both animal fracture models and clinical trials^{7,9,13,16,17}. Fracture healing involves inflammation, soft callus formation, hard callus formation, and bone remodeling¹⁸. Several studies indicate that LIPUS can be applied to accelerate the fracture healing by influencing all four stages of fracture healing¹⁸⁻²². The mechanical stresses resulting from LIPUS can manipulate the expression and functioning of various cells as well as molecules involved in the fracture healing process. Rawool *et al.*²³ found that LIPUS can increase the local blood flow of fracture site promoting the bone union. Tsumaki *et al.*²⁴ demonstrated that LIPUS accelerates callus maturation after opening-wedge high tibial osteotomy by hemicallotaxis. LIPUS can stimulate the expression of integrins and facilitates adhesion of osteoblasts at the fracture site^{20,21}. In addition, LIPUS upregulate the expression of master transcription factors directing osteogenic differentiation of pluripotent cells including Runx2, Msx2, Dlx5, osterix and bone sialoprotein, which are essential for fracture healing^{25,26}. However, fracture healing is very intricate, and many factors could advance or slow the process. Moreover, the underlying mechanism by which LIPUS accelerates bone union is not fully understood.

The objective of this study was to evaluate the effect of LIPUS on fracture healing of distal radius. The times (15 min/day for at least 12 weeks) to clinical healing in the LIPUS group was significantly shortened compared with that in the control group. This result indicated that LIPUS could increase bone formation at the fracture site (Figure 1) and accelerate the fracture healing of distal radius. In terms of the application of LIPUS to forearm fractures, Kristiansen *et al.*¹² perform a randomized, controlled trial of 85 patients with metaphyseal fractures of the distal radius treated with LIPUS. The mean time to fracture healing was significantly reduced by 34% in the LIPUS group. In the present study, the values of reduction time by LIPUS were 20% for clinical healing. Moreover, there was no difference in reposition between the two groups ($p > 0.05$) in the present study, and the therapeutic effects of LIPUS were not satisfactory. The possible reasons were not difficult to explore. Firstly, the mean age of patients was more than 60 years and many of them were osteoporotic. Although the reposition efficacy was good initially, the bone might be shorten or translocated during fracture healing process. Secondly, some patients suffered from severe injuries and the fracture was unstable, the fixation with plaster could not maintain the position. In addition, the reposition efficacy was also determined by good reposition at the moment of fracture, firm external fixation, bone mineral density at the fracture and the fracture type. Thus, there was no different in reposition efficacy in the ultrasound treatment group.

The intensity of therapeutic ultrasonic device was 30 mW/cm² in the present study. As a kind of energy and wave, the intensity and frequency are the most important parameters of ultrasound. Moreover, time of treatment have an important influence on the therapeutic effect. In most experiments and clinical studies, the ultrasound (intensity of 30-50 mW/cm²) is used to accelerate fracture healing. It has been indicated that lower intensities of ultrasound therapy is used for fracture healing because the higher intensities may cause tissue damage²⁷. Tsai found that the ultrasound with intensity 1.0 W/cm² can inhibit rabbit fibula healing²⁸. However Yang and colleagues find that the average maximum torque and average torsional stiffness were significantly increase when treated with ultrasound with an intensity of 50 mW/cm².²⁹ Watson T report that the effective dose of LIPUS is lower (30 mW/cm²) than ultrasound doses used for soft tissue healing³⁰. In general, the ultrasound intensities for acute conditions should be between 10 and 30 mW/cm², and the intensity is chosen based on the target.

The 0.5-1.5MHz ultrasound is the most commonly used frequency to accelerate fracture healing in experiments and clinical studies. Tsai prove that 1.5 MHz ultrasound can increase endogenous PGE2 and have the best effect of accelerating bone healing³¹. Wang *et al.*³² suggest that the effect of 1.5 MHz on fracture healing is better than that of 0.5 MHz on fracture healing with biochemical tests. Thus, based on the previous data, the frequency of therapeutic ultrasonic device was 1.5 MHz in our study. Most researchers applied ultrasound 15-20 min daily. The total treatment times were determined according to the fracture site and condition of patients, until fracture healing. However, there were also some limitations in this study, such as small simple size, patients' age, the confirming method for bone healing, and image analysis technique. Thus, a more optimized research is needed for the further investigation.

Conclusions

Low-intensity pulse ultrasound stimulation therapy was beneficial to bone healing after the fracture of distal radius. LIPUS might provide an early return to activity and work for patients undergoing fracture.

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