



Follow-up evaluation with ultrasonography of peripheral nerve injuries after an earthquake

Man Lu¹, Yue Wang², Linxian Yue¹, Jack Chiu³, Fanding He¹, Xiaojing Wu², Bin Zang², Bin Lu², Xiaoke Yao², Zirui Jiang⁴

1 Department of Ultrasound, Sichuan Provincial People's Hospital, Chengdu, Sichuan Province, China
2 Department of Orthopedics, Sichuan Provincial People's Hospital, Chengdu, Sichuan Province, China
3 Department of Radiology, University Hospital, University of Western Ontario, Ontario, Canada
4 Chengdu Jiaxiang Foreign Languages School, Chengdu, Sichuan Province, China

Corresponding author:

Yue Wang, M.D., Ph.D., Department of Orthopedics, Sichuan Provincial People's Hospital, Chengdu 610072, Sichuan Province, China, wangyue@medmail.com.cn.

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Abstract

Published data on earthquake-associated peripheral nerve injury is very limited. Ultrasonography has been proven to be efficient in the clinic to diagnose peripheral nerve injury. The aim of this study was to assess the role of ultrasound in the evaluation of persistent peripheral nerve injuries 1 year after the Wenchuan earthquake. Thirty-four patients with persistent clinical symptoms and neurologic signs of impaired nerve function were evaluated with sonography prior to surgical repair. Among 34 patients, ultrasonography showed that 48 peripheral nerves were entrapped, and 11 peripheral nerves were disrupted. There was one case of misdiagnosis on ultrasonography. The concordance rate of ultrasonographic findings with those of surgical findings was 98%. A total of 48 involved nerves underwent neurolysis and the symptoms resolved. Only five nerves had scar tissue entrapment. Preoperative and postoperative clinical and ultrasonographic results were concordant, which verified that ultrasonography is useful for preoperative diagnosis and postoperative evaluation of injured peripheral nerves.

Key Words: nerve regeneration; earthquake; Wenchuan; ultrasound; peripheral nerve; nerve injury; repair; follow-up; 863 Program; neural regeneration

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Introduction

On May 12, 2008 at 14:28, an earthquake of magnitude 8 occurred in Wenchuan in Sichuan Province, China. The earthquake occurred in a densely populated area, with approximately 374,643 injured^[1-5]. Although many patients had undergone surgery or rehabilitation, 1 year later, many orthopedic patients continued to have symptoms of nerve injury including motor weakness, sensory loss, paresthesia, and pain.

In the past, nerve impairment has been diagnosed on the basis of clinical findings and electrodiagnostic test results. Electrodiagnostic studies, including nerve conduction studies and electromyography, are useful adjuncts to help detect abnormal nerves. However, these methods do not provide information about the morphology or anatomy of nerves, or the pathophysiology of the nerve injury to allow for treatment planning and postoperative care^[6]. There have been significant improvements in imaging techniques applied to peripheral nerves, such as magnetic resonance imaging (MRI)^[7-8]. Although MRI is a superior method for evaluation of soft-tissue injury, it is limited by spatial reso-

lution and cannot easily assess small nerves and partial and full-thickness disruption^[9]. Ultrasonography now enables visualization of the fascicle, perineurium, epineurium, and surrounding tissues of the peripheral nerves and has been proven to be efficient in various clinical settings to evaluate peripheral nerve lesions^[10-26].

Multiple previous studies of earthquake injuries have focused mainly on crush syndrome, fractures, infections, and rhabdomyolysis^[1, 15, 27]. Published data on peripheral nerve injury are very limited^[28-29] and there is no report of the findings on ultrasonographic scans. This study sought to assess the sonographic features of peripheral nerve injuries 1 year following the Wenchuan earthquake, and to compare the follow-up ultrasonography with clinical outcomes 6 months after surgery, so as to evaluate the role of ultrasound in the diagnosis and surgical treatment planning of traumatic neural injuries.

Results

Quantitative analysis and characteristics of subjects

A total of 211 outpatients and inpatients from the Sichuan

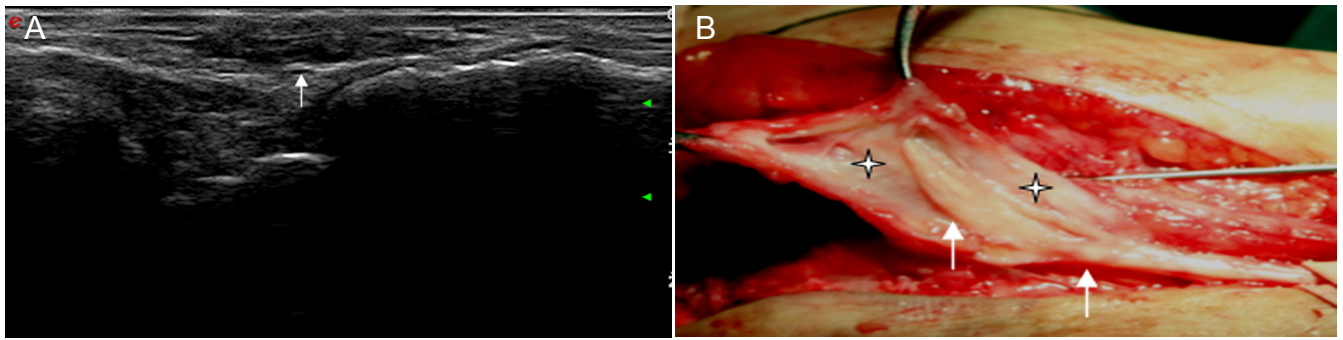


Figure 1 Forearm of a 21-year-old woman 12 hours after a crush injury.

(A) High-frequency sonogram shows focal encasement of the radial nerve by an ill-defined hypoechoic mass (arrow) due to scar tissue. The nerve's fascicular echotexture is unclear within the callus. (B) Surgical image shows the nerve to be swollen but still continuous (arrows) within the mass (stars).

Table 1 Preoperative and postoperative data in patients according to clinical outcome

Type	Preoperative				Postoperative				χ^2	P value
	Severe	Moderate	Mild	Normal	Severe	Moderate	Mild	Normal		
Entrapment	28	20	0	0	3	5	22	18	91.3	< 0.001
Disruption	9	2	0	0	4	3	4	0	5.79	< 0.05
Total	37	22	0	0	7	8	26	18	89.6	< 0.001

Provincial People's Hospital and Mianzhu Municipal People's Hospital with signs of impaired peripheral nerves 1 year following the Wenchuan earthquake underwent clinical examination, electrodiagnostic testing, and sonography. Thirty-four patients met enrollment criteria, including 13 patients aged 5–20 years (13/34, 38%), 9 patients aged 21–40 years (9/34, 26%), 10 patients aged 41–60 years (10/34, 29%), and 2 patients aged 61–80 years (2/34, 6%). All patients had suffered tissue compression injuries ranging over a period of time from several minutes to 4 days. Clinical examination results were abnormal, with findings including motor weakness, sensory loss, paresthesia, and pain.

A total of 37 nerves were defined as severe and 22 nerves were defined as moderate.

Nerve conduction and abnormal electromyography in patients with peripheral nerve injuries

Compound muscle action potential is the evoked response recorded from the surface of the muscle. The time it takes from stimulation to generation of the compound muscle action potential is the conduction speed. All patients showed poor or absent evoked responses in muscles innervated by the injured nerves.

Results of sonographic diagnosis in patients with peripheral nerve injuries

Preoperative sonography showed that 34 patients experienced 59 nerve injuries, including 6 median nerves, 5 ulnar nerves, 7 radial nerves, 21 peroneal nerves, 8 tibial nerves, 5 sciatic plexi, 6 brachial plexi, and 1 femoral nerve. Five patients had 1 injured peripheral nerve, 15 patients had 2 injured peripheral nerves, and 8 patients had 3 or more in-

jured peripheral nerves.

Forty-three peripheral nerves were entrapped by scar tissue (Figure 1A). Four peripheral nerves were entrapped by an injured pronator muscle (Figure 2A), the collum fibulae, piriform muscle, and arcade of Frohse, respectively. Ultrasonography revealed that the nerves were flattened at the compression points and markedly swollen proximal to the level of entrapment. Twelve peripheral nerves had suffered partial-thickness tears or complete disruptions. Ultrasonography showed the nerves were discontinuous, with globular hypoechoic terminal neuromas developing at the ends (Figure 3A, B), or surrounded by scar tissue.

Treatment of patients with peripheral nerve injuries after the earthquake

Surgical findings showed 48 entrapped peripheral nerves and 11 disrupted peripheral nerves. There was 1 case (1 peripheral nerve injury) of misdiagnosis on ultrasonography among the 59 peripheral nerve injuries. A swollen nerve with thickness circumferential scar was diagnosed as neuroma secondary to partial-thickness tear. The concordance rate of ultrasonography findings with those of surgical results was 98%.

Forty-eight nerves in 34 patients were treated with neurolysis to free the nerves from entrapping tissues (Figure 1B), such as scar and thickened tendons. Of the 11 nerves with complete disruptions, 2 of these nerves were treated by transplantation (Figure 3C), and 9 of these nerves underwent repair.

Six-month postoperative evaluation

Six months after surgery, clinical, ultrasonographic, and

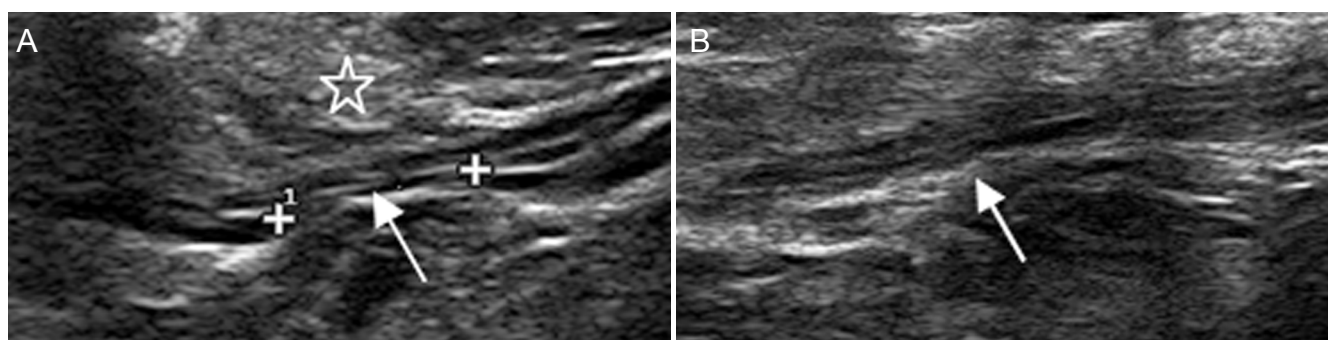


Figure 2 Surgically proven median nerve injury in a 43-year-old woman 40 hours after crush injury.

(A) High-frequency sonogram shows the median nerve entrapped (calipers) by the heads of pronator teres (stars). The nerve is flattened at the entrapped site (arrow) and the distal nerve is thickened (arrow). (B) After surgical repair, the medial nerve appears normal in diameter at the entrapped site (arrow).

Table 2 Kappa test for the concordance between changes in clinical outcomes and ultrasonographic outcomes

Type	Clinical outcomes (moderate and severe, <i>n</i>)		Ultrasonographic outcomes (<i>n</i>)		Kappa	<i>P</i> value
	Prior	Post	Prior	Post		
Entrapment	48	8	48	5	0.915	< 0.001
Disruption	11	7	11	5	0.895	< 0.001
Total	59	15	59	10	0.862	< 0.001

electrodiagnostic follow-up was carried out to assess for improvement. Clinical examination revealed outcomes of being cured in 18 nerves, much better in 26 nerves, slightly better in 8 nerves, and no change in 7 nerves. The chi-squared test showed significant improvement in post-operative clinical outcome in patients independent of type of injury ($P < 0.01$), disruption type ($P < 0.05$) and total ($P < 0.01$; Table 1).

Ultrasonography displayed that only five nerves were still entrapped by scar tissue after an operation. Among the 11 completely disrupted nerves, fascicular and epineurial continuity were found in 6 nerves (Figure 3D), epineurial continuity and whole fascicular discontinuity (represented as an uneven hypoechoic lesion that may be a scar) in 5 nerves including 1 never transplanted. Overall, postoperative ultrasound follow-up revealed that the majority of patients (86.2%) had a good recovery. The Kappa test was applied to determine the concordance between clinical outcomes and ultrasonographic outcomes (Table 2). Concordance was found between the two methods for entrapment type, disruption type and total (Kappa = 0.894, 0.769, 0.811, respectively).

Electrodiagnostic data revealed that the compound muscle action potentials of 13 nerves were still low or absent. Seventy-eight percent of patients had partial to full recovery.

Discussion

Peripheral nerve injuries are quite common, and may result from traction, contusion, or penetrating trauma in accidents occurring during daily living^[30-31]. There are more than 500,000 earthquakes each year^[32]. Most nerve injuries during earthquakes are due to collapsed buildings or flying debris

such as stones, bricks, or other falling objects. In addition to direct injury to vital organs, crush injuries cause damage to the body and limbs by prolonged pressure^[2, 33-34]. Previous studies have shown that the highest incidence of peripheral nerve injuries is seen in the lower limb^[1, 35-37].

Direct injury, ischemia/reperfusion injury, or compartment syndrome due to primary compression and secondary muscle swelling can lead to nerve injuries^[1, 38]. An acute increase in crushing can lead to muscle necrosis, compartment syndrome, swelling of the involved limbs, intense pain, diminishing sensation and muscle strength, and even paralysis^[39-40]. Peripheral nerve tissue is exquisitely sensitive to the changes in oxygen tension. Consequently, peripheral nerve function may be lost within 30 to 90 minutes after the onset of ischemia^[41]. The combination of muscle and nerve ischemia can result in worsening of nerve conduction, endoneurial ischemia, and consequent structural damage^[15, 42-43]. There is a positive correlation between the time spent under debris and the degree of nerve injury^[44].

The location and duration of compression of the peripheral nerves also significantly affect the severity and prognosis of neural injury. In this study, all patients had tissue compression from crush injuries ranging from several minutes to 4 days. Ultrasonography showed that more than half of the injured nerves were in the lower limb; all the extensively damaged nerves adhered to surrounding subcutaneous tissues and muscles. Compared with the traction, contusion, and penetrating trauma occurring during daily living, the findings in earthquake-associated peripheral nerve injuries include multiple nerve injuries (in 1 patient), multiple injuries to a single nerve, and adherence to surrounding scar tissue or nerve compression by scar tissue. Uzun et al.^[45]

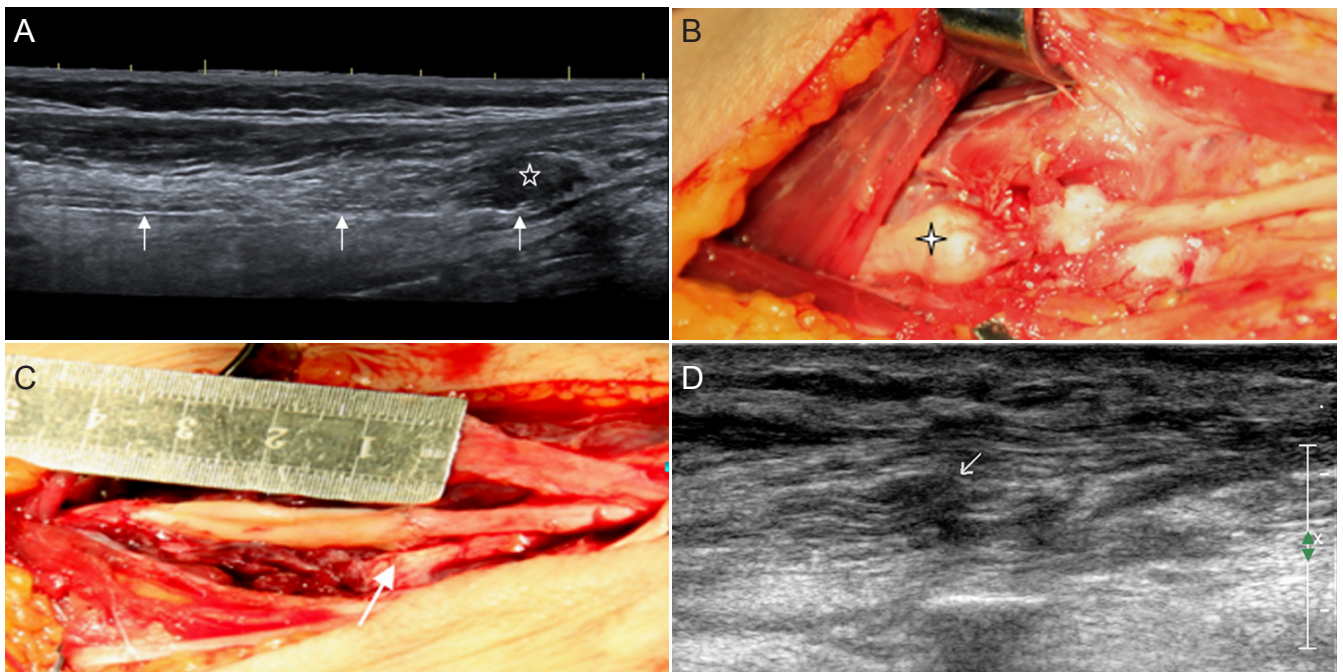


Figure 3 Complete median nerve tear in the forearm of a 52-year-old woman 30 hours after crush injury.

(A) High-frequency sonography shows the median nerve (arrow) that is completely disrupted with a hypoechoic terminal neuroma (star) at the ending of the proximal stumps. (B) Surgical image shows gap and neuromas (star) at both ends of the nerve. (C) Surgical correlation. After surgical repair the sural nerve graft is seen interposed between the nerve ends (arrow). (D) High-frequency sonography shows the surgical repair site (arrow) after nerve repair. Hypoechoic thickening is observed at the proximal and distal sites of anastomosis: this should be regarded as a normal finding.

studied 75 subjects with electromyography following the 1999 Marmara earthquake. Their study showed pathology in the form of apraxia and axon crush injury; only half of the patients recovered without treatment. Our results indicate that damage to nerves and surrounding tissues by crush, infection and/or surgery, such as those induced by postoperative scar adhesion or humeral fracture plate-induced nerve compression, are common, with the inevitable formation of extensive scar tissue. Being compressed by scars, the reduced nerve blood flow ultimately leads to ischemic damage to neurons and subsequent structural damage and neuropathy. Under these circumstances, fibroblastic response with scar tissues replacing normal tissues may serve to inhibit the longitudinal movement of nerves. With limb movement, the peripheral nerve may be compromised by adjacent scar proliferation, which leads to constant traction and delayed recovery of nerve function^[46-50]. Excessive intraneural connective tissue formation or scarring may not only compromise remyelination, but also axonal nerve regeneration.

Injured patients may benefit from early medical interventions. Once infections are controlled, patients should be subjected to fasciotomy, fracture repair operations, primary repairs of traumatic nerve damage, and amputations, if necessary. Most of the patients with peripheral nerve injury were found to have recovered rapidly after being treated conservatively. Regeneration can occur within months^[46]. Campbell et al.^[51] found that operations done earlier have a better outcome than those done later. However, peripheral nerve reconstruction is often done in the second phase

of nerve injury because of concomitant injuries and the uncertainty of the extent of nerve damage. Wu et al.^[52] confirmed that the total number of regenerating nerve fibers decreased after repair, because of a reduced size match between the proximal and distal nerve stumps in delayed repair. In this study, ultrasonography showed the continuities of fascicles and the epineurium in seven completely disrupted nerves after nerve suture; the clinical outcomes were markedly improved in four nerves and slightly improved in three nerves. The tension and the gap between nerve stumps in the direct delayed nerve suture are two more important factors to impact nerve regeneration. The epineurium continuity and the whole fascicles discontinuity appeared on ultrasonography as an uneven hypoechoic lesion in four nerves, including one never transplanted; however, nerve function was not recovered due to scar formation. The poor recovery is attributed to the longer scarring in the distal nerve stump and larger neuroma in the proximal nerve stump. In our study, it should be noted that 81.3% of patients recovered. Delayed surgical intervention was useful in treating the injured nerves.

Based on previous reports, electromyography examinations are a reliable and feasible method for the diagnosis of severe peripheral nerve injury and recovery^[45]. However, ultrasound is being used more frequently in various clinical settings to evaluate the injury and recovery phases of nerve, thus influencing the diagnosis and clinical care of symptomatic patients^[13, 53-55]. The sudden onset and severity of the earthquake led to peripheral nerve injuries in many unique cases, which allowed us to evaluate the natural his-

tory of these injuries and the impact of surgical treatments in the recovery of these nerves. We could also evaluate ultrasound's suitability as a diagnostic tool in nerve reconstruction.

There was one case of misdiagnosis on ultrasonography. In that case, spindle-shaped masses near the right ulnar nerve at the elbow were diagnosed as neuromas secondary to a partial-thickness tear. However, later surgical results showed the ulnar nerve was swollen due to a thick surrounding scar. This case demonstrates that in the assessment of nerve injury, attention should be paid to the possibility of scar tissue formation.

The most important limitation of this study may be the short period of assessment, which was only 6 months after surgery. To verify the recovery of transplantation by ultrasound, animal experiments may be valuable.

In summary, ultrasonography is useful for locating the injured nerve as well as for qualitative diagnosis, follow-up, and postoperative evaluation, so that appropriate management can be instituted early.

Subjects and Methods

Design

A prospective single-center study.

Time and setting

Experiments were performed in the Department of Ultrasound, Sichuan Provincial People's Hospital and Mianzhu Municipal People's Hospital, China from May 2009 to June 2010.

Subjects

A total of 211 patients (outpatients and inpatients from the Sichuan Provincial People's Hospital and Mianzhu Municipal People's Hospital in China) with clinical signs of impaired peripheral nerves wounded in the Wenchuan earthquake underwent clinical examination, electrodiagnostic tests, and sonography. Patients with peripheral nerve injuries were enrolled according to the following criteria.

Inclusion criteria: (a) Patients with injuries from the earthquake who, after undergoing initial surgery or rehabilitation, continued to have persistent daily sensory symptoms, including hypoesthesia, burning pain, tingling, or numbness. (b) Peripheral nerve injuries were confirmed based on the results of clinical examination and electrodiagnostic tests. (c) All patients' surgical explorations and the duration between ultrasound examination and surgery were within 1 month, and the follow-up clinical examination and sonography were conducted 6 months after surgery.

According to the abovementioned criteria, 34 patients were eligible (21 men, 13 women, mean age 33 years; range, 5–75 years). All patients provided informed written consent for their inclusion in this research. This study followed the *Declaration of Helsinki* on medical protocol and ethics.

Methods

Ultrasound examination

High-resolution sonography was performed with 7–13 MHz

linear-array transducers connected to either a MyLab 90 system (Esaote, Genoa, Italy) or an iU22 ultrasound system (Philips, Bothell, WA, USA). Patients were positioned according to the region to be examined. Special care was taken to obtain a stable position of the limb by using supportive cushions. For the examination of nerves running superficially, a standoff gel pad was positioned between the probe and the skin surface. The examination included the level of suspected damage and at least 10 cm above and below this level, especially at the level of pressure marks or postoperative cutaneous scar.

The shape, echotexture, diameter, and overall integrity of the nerve and its fascicle, perineurium, epineurium, and peripheral tissues of the peripheral nerves were examined in transverse and longitudinal planes, and were compared with the non-affected side^[6]. When a scar was identified, the relationship between the abnormal nerve structures and the scar tissue was observed. The preoperative ultrasonographic results were compared with intraoperative and postoperative findings.

All ultrasonographic examinations were performed by a single ultrasonographer who had over 10 years of experience in sonography of small parts and was blinded to the results of electrodiagnostic tests and clinical examination.

Nerve conduction studies and electromyography

Nerve conduction studies and needle electromyography examinations were performed with a Keypoint® workstation (Medtronic Functional Diagnostic A/S, Skovlunde, Denmark) for each patient to determine the presence of peripheral nerve damage. Electrophysiological data analyzed included electromyography recruitment and compound muscle action potential amplitude recorded from surface electrodes. Based on reports in the facial nerve literature that a compound muscle action potential amplitude of 10% or greater predicts a good prognosis^[56], we set the compound muscle action potential amplitude at 50% or greater to predict partial recovery. All nerve conduction studies and electromyography examinations were performed by one physician, blinded to the results of clinical examination, before the ultrasound examinations.

Clinical outcome assessment

The clinical outcome assessment included observation of the presence of sensory deficits according to the classification of the British Medical Research Council^[56] by two examiners in a blinded manner and by consensus and the patient's overall satisfaction. The severity of peripheral nerves was defined as normal, mild, moderate, or severe. The functional changes of peripheral nerves were defined as no change, slightly better, much better, and cured at 6 months postoperatively.

Statistical analysis

We studied the distribution of preoperative and postoperative clinical and ultrasonographic variables in all patients. All statistics were performed using GraphPad Prism 5.0

(Graphpad Software, Inc., San Diego, CA, USA). Chi-square tests were used to evaluate the difference between preoperative and postoperative data. Kappa statistics was calculated for the concordance between clinical and ultrasonographic outcomes postoperation at each site. *P* values of less than 0.05 were considered statistically significant.

Author contributions: Lu M and Wang Y designed the study. Lu M, He FD, Wu XJ, Zang B, Lu B and Yao XK implemented the study. Lu M, Wang Y, Wu XJ, Zang B, Lu B and Yao XK evaluated the study. Lu M, Yue LX, He FD, Wu XJ, Zang B, Lu B, and Yao XK collected the data. Lu M wrote the manuscript. Wang Y and Chiu J were in charge of manuscript authorization. All authors approved the final version of the paper.

Conflicts of interest: None declared.

Peer review: Ultrasonography can rapidly identify the position and degree of peripheral nerve injuries. Thus, ultrasonography was considered as the first-choice method to diagnose peripheral nerve injuries. This study retrospectively analyzed the data of 34 patients with peripheral nerve injuries from Wenchuan earthquake in China, and confirmed that ultrasonography was an effective method in the prompt and subsequent evaluation of earthquake-induced peripheral nerve injuries.

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