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High-Energy Extracorporeal Shock Wave Treatment of Nonunions

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Forty-three consecutive patients who did not have healing of tibial or femoral diaphyseal and metaphyseal fractures and osteotomies for at least 9 months after injury or surgery were examined prospectively for use of high-energy extracorporeal shock waves. Former treatment modalities (cast, external fixator, plate osteosynthesis, limitation of weightbearing) remained unchanged. In all cases a ^{99m}Technetium dicarboxyphosphonate regional two-phase bone scintigraphy was performed before one treatment with 3000 impulses of an energy flux density of 0.6 mJ/mm^2. Radiologic and clinical followups were done at 4-week intervals starting 8 weeks after shock wave treatment. The success criterion was bridging of all four cortices in the anteroposterior and lateral radiographic views, in oblique views, or by conventional tomography. An independent observer described bony consolidation in 31 of 43 cases (72%) after an average of 4 months (range, 2–7 months). Twenty-nine of 35 (82.9%) patients with a positive bone scan had healing of the pseudarthrosis compared with two of eight (25%) patients with a negative bone scan. Six of these eight patients with negative scans were heavy smokers. No complications were observed. High-energy shock wave therapy seemed to be an effective noninvasive tool for stimulation of bone healing in properly selected patients with a diaphyseal or metaphyseal nonunion of the femur or tibia. Additional controlled studies are mandatory.

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The central event in bone repair is the formation of a fracture exudate. Size, duration, and biochemical activity of this exudate are decisive for the rate and success of healing, if established conservative or operative methods have been used.[17] Currently, the treatment of delayed bone healing is aimed at restarting the regenerating system by creating new bone injury through survey, various types of grafts, and fixation.[25] For humeral, femoral, or tibial nonunions success rates between 86% and 93% have been reported,[4,26,29,34,36,38,39] with better results for scintigraphically active pseudarthroses compared with inactive pseudarthroses.[35] However, the rate of disturbances in bone healing has stayed on a relatively constant level of approximately 5% in traumatology, and 1% to 2% in elective surgery. Moreover, donor site morbidity ranges from 6% to 20%.[24,41] Accordingly, alternatives of treatment have been sought that would allow induction of fracture healing nonsurgically. Several positive physical factors have been identified such as electrical stimulation, electromagnetic fields, capacitive coupling, direct current, piezoelectricity or low-intensity pulsed ultrasound[1,2,11,23] none of which have been adopted universally in clinical practice.

In the early part of the decade, by the use of extracorporeal shock wave therapy for conditions other than stones in the renal and biliary tracts, a new biophysical factor was introduced. A shock wave is characterized by a steep rise time, typically on the order of tens of nanoseconds, followed by an exponential decrease in pressure. This curve is distinguished easily from that of an ultrasound pulse, which is sinusoidal in nature, propagating at discrete frequencies with positive compressive and negative tensile components of pressure. One cannot directly compare waves produced during extracorporeal shock wave therapy or produced by ultrasound. Additional contrasts are apparent on examination of the frequency spectrum of shock waves. The presence of lower frequency components allows shock waves to pass through fluid and body tissues with less energy loss than ultrasound. Therefore, shock waves are expected to be superior to ultrasound in penetrating tissues and delivering adequate pressures for stone destruction or stimulation of bone growth.[21]

On an experimental basis, effects regarding possible osteogenetic stimulation have been published in various fracture or osteotomy models.[6,9,13,18,19] In a metaanalysis for human shock wave application, Heller and Niethard[16] found one preliminary prospective, noncontrolled study on treatment of nonunions with an adequate number of patients, a reproducible rating system, and clear followup criteria. A success rate of 52% in an inhomogenous patient collective was reported.[32] The current authors focused on nonunions of the femur or tibia after fracture or corrective osteotomy.

MATERIALS AND METHODS

An opportunity to participate in the current study was offered to all skeletally mature men and nonpregnant women who presented to the authors' institution from 1992 to 1998 with a bony nonunion of the long bones of the lower extremity. Inclusion of the patients was discussed with the local ethical committee. A randomized, placebo-controlled study was not permitted.

Twenty women and 23 men (mean age, 39.5 ± 8.5 years; range, 18–74 years) entered the current prospective cohort study. Seventeen patients had pseudarthroses after fracture, and 26 had pseudarthroses after corrective osteotomies. A pseudarthrosis was diagnosed when a minimum of 9 months had elapsed since the last operation, and no radiologic bridging of the four cortices of bone was observed on the anteroposterior (AP) and lateral radiographs. An average of 1.9 ± 0.7 (range, 1–6) unsuccessful operations had been performed previously to attain union (Table 1).

Anteroposterior (AP) and lateral radiographs, and, when visualization of the gap was difficult, oblique views or conventional tomography were obtained before deciding on shock wave treatment.

Exclusion criteria included insufficiently stable situations, that is, loosening of screws or plates; a bone gap more than 0.5 cm after surgery; local infection; pathologic fracture; patients receiving steroids, anticoagulants, nonsteroidal antiinflammatory medication, diphosphonate therapy, calcium channel blockers, immunosuppressive therapy; and patients with a history of thrombophlebitis or vascular insufficiency; drug addiction; hepatitis; and human immunodeficiency virus infection.

After the patients had agreed to participate in the study and had given informed consent, a regional ^{99m}Technetium dicarboxyphosphonate (^{99m}TcDCP) two-phase bone scintigraphy was done to differentiate between active and inactive pseudarthroses. The scintigraphy was done with a Picker Dyna Camera 4 (Marconi Medical Systems, Cleveland, OH). The ipsilateral side was compared with the contralateral side. The evaluation of the blood-pool phase started within 2 minutes after application of 550 MBq ^{99m}TcDCP and evaluation of the mineralization phase began 3 hours after nucleide application. Tracer accumulation was analyzed visually by a physician specialized in nuclear medicine and assessed either as little or none (inactive pseudarthrosis) or as significant (hyperemia, hypermineralization, that is, an active pseudarthrosis).

High-energy shock wave treatment then was applied within 14 days after scintigraphy using a Siemens Osteostar machine (Siemens AG, Erlangen, Germany), integrating an electromagnetic shock wave generator in a mobile fluoroscopy unit. In all patients the treatment was done under regional anesthesia during a 3-day hospital stay. Once the nonunion was localized in the shock wave

TABLE 1. Epidemiological Data of the Patients

Patient Number	Age (years)	Gender	Localization	Nonunion after	Number of Operations	Period of Nonunion (months)
1	34	M	T	O	2	9
2	33	M	T	O	3	13
3	33	M	T	O	1	12
4	47	M	T	Fx, short oblique	2	17
5	49	F	T	O	1	9
6	65	F	T	O	2	9
7	51	F	Fe	Fx, short oblique	3	13
8	18	F	Fe	O	1	9
9	18	F	Fe	O	1	9
10	40	M	T	Fx, transverse	2	10
11	32	F	T	Fx, comminuted	3	36
12	19	F	T	O	1	18
13	50	F	T	Fx, comminuted	5	14
14	33	F	T	O	1	11
15	70	M	Fe	Fx, short spiral	2	14
16	37	M	T	Fx, short oblique	2	12
17	21	F	Fe	Fx, short oblique	1	9
18	34	M	Fe	Fx, short spiral	1	9
19	27	M	Fe	O	1	9
20	73	F	Fe	Fx, comminuted	4	9
21	53	M	T	O	1	9
22	64	M	Fe	Fx, short spiral	3	14
23	27	M	Fe	O	2	13
24	58	F	T	O	1	9
25	62	F	Fe	O	3	13
26	25	F	Fe	O	1	9
27	28	M	Fe	Fx, short spiral	2	9
28	32	F	Fe	O	1	12
29	18	F	Fe	O	1	9
30	27	F	Fe	O	1	9
31	43	M	Fe	Fx, comminuted	3	11
32	49	M	T	O	1	13
33	79	F	Fe	Fx, transverse	2	9
34	51	M	Fe	O	1	10
35	32	F	Fe	O	4	9
36	21	F	Fe	O	1	10
37	54	M	T	O	2	9
38	27	M	T	Fx, transverse	2	9
39	18	F	Fe	O	1	9
40	53	M	Fe	O	2	9
41	35	M	T	Fx, comminuted	3	11
42	33	F	Fe	O	1	15
43	22	M	T	Fx, transverse	1	11

M = male; F = female; T = tibia; Fe = femur; Fx = fracture; O = osteotomy.

focal center, the unit was docked to the skin by means of a water-filled cylinder. Ultrasound gel was used as a contact medium between cylinder and skin. In all patients 3000 impulses of an energy flux density of 0.6 mJ/mm^2 were administered, the shock wave focus being targeted to the gap and to the adjacent cortical structures. The topographic anatomy was respected and major vascular and neural bundles were avoided in the focal area. The treatment lasted between 50 and 75 minutes. The regime before treatment (limitation of weightbearing, cast) remained unchanged.

All patients subsequently were evaluated 8 weeks after shock wave application and monthly thereafter until 9 months after shock wave application or until adequate bony healing was determined. Standardized AP and lateral radiographs were obtained with the same machine, the same exposure setting, and with a comparable positioning of the leg.

All radiographs were assessed in blind review by an independent radiologist. A pseudarthrosis was judged healed when four cortices were bridged or if no gap could be detected using conventional tomography. On each radiographic evaluation at each time, four cortices (two on the AP radiograph, and two on the lateral radiograph; rarely on oblique views) were evaluated for the amount of cortical bridging. On occasion when the radiologist was uncertain whether union actually had occurred, conventional tomography was done.

RESULTS

All patients were followed up for 9 months and complied with the followup protocol. At an average of 4.0 ± 0.6 months, in 31 of 43 (72.1%) pseudarthroses all four cortices were judged bridged and full weightbearing was allowed (Table 2; Figs 1–3).

Before shock wave treatment, 17 of 31 (54.8%) successfully treated patients had a distinct hyperemia in the region of the nonunion in the blood-pool phase of the technetium scintigraphy, compared with three of 12 (25%) who did not respond to treatment.

Before shock wave treatment, 25 of 31 (80.6%) bony unions had shown a significant tracer uptake in the mineralization phase, compared with four of 12 (33.3%) among failures.

Twenty-nine of 35 (82.9%) patients with a positive bone scan had healing of the pseudarthrosis compared with two of eight (25%) patients with a negative bone scan. Six of those eight patients were heavy smokers (more than 20 cigarettes per day).

In the current series a success rate of 50% of eight tibial and 66% of nine femoral postfracture nonunions was achieved. Regarding postosteotomy pseudarthrosis, consolidation occurred in 82% of 11 tibias and 80% of 15 femurs.

Besides transient local hematoma no adverse effects were observed after high-energy shock wave therapy. The authors did not observe any effects on the osteosynthesis implants by the shock waves.

DISCUSSION

Pulsed ultrasound results in an increase in vascularization, increased soft callus, and faster enchondral ossification.[8,23,33]

To date, the working mechanism of shock waves on bones is not understood. Histologic studies after shock wave application produced evidence for stimulation of osteogenesis, but no quantitative analysis has been published.[6,9,12,22,27] Reports on slowing of bone healing after shock wave treatment of experimentally produced defects were disturbing.[9,18,40] In part this inconsistency of results may be attributed to the fact that the lithotripter machines that were used could not be compared with each other. Ideally, shock wave generators should be classified with acoustic measurements. Theoretically, they can be defined by the rise time, peak positive and negative pressure, duration of impulse, spectrum of frequencies, size of focal area, and acoustic energy of every impulse. Currently, there are no standardized hydrophones available to produce reliable measurements of these parameters. Another reason for the large variation in results is the use of different animal models (dog, sheep, rabbit) with various kinds of bone injury and subsequent fixation.

Unlike pulsed ultrasound where excellent prospective clinical studies showed acceleration of bone healing in fresh fractures and pseudarthrosis,[10,15,20] (Xavier CAM, Duarte LR: Treatment of non-unions by ultrasound stimulation: First clinical applications. Presented at the meeting of the American Academy of Orthopaedic Surgeons, San Francisco 1987.) the published preliminary examinations on shock wave therapy did not meet this

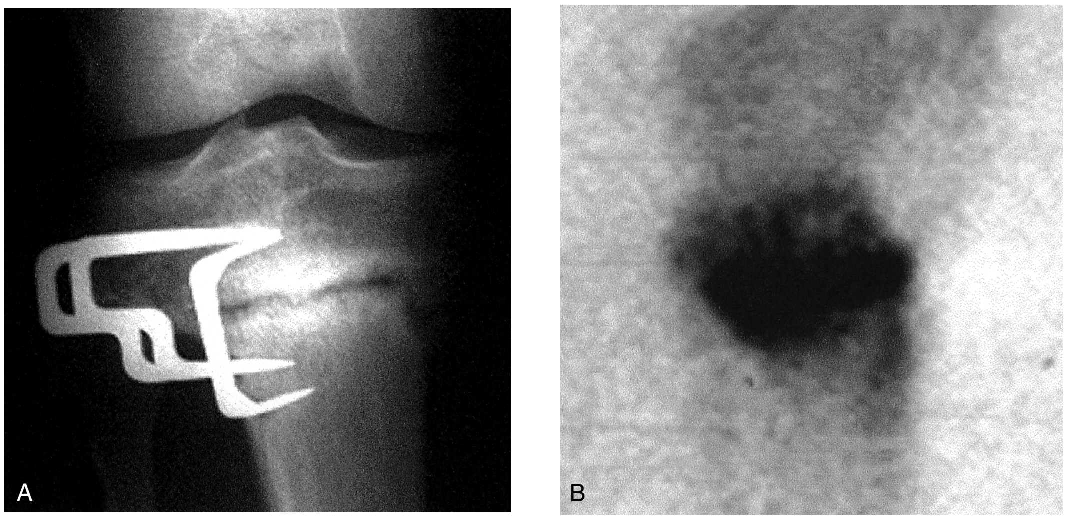
TABLE 2. Consolidation of Nonunion After Shock Wave Therapy

Patient Number	Scintigraphy	Bony Union	Period to Bony Union (months)	Smoker
1	A	Y	4	N
2	A	Y	2	N
3	A	Y	3	N
4	A	Y	5	Y
5	A	Y	3	N
6	IA	Y	3	Y
7	IA	N		Y
8	A	Y	4	Y
9	A	N		N
10	A	N		N
11	A	Y	6	Y
12	A	Y	4	N
13	IA	N		Y
14	A	N		N
15	A	Y	5	N
16	A	N		N
17	A	Y	5	Y
18	A	Y	5	Y
19	A	Y	5	N
20	IA	N		N
21	A	Y	3	N
22	A	Y	6	Y
23	IA	Y	4	Y
24	A	Y	3	N
25	A	N		Y
26	A	Y	5	N
27	A	Y	4	N
28	A	Y	4	N
29	A	Y	3	N
30	A	Y	4	N
31	IA	N		Y
32	A	Y	3	N
33	A	Y	4	N
34	A	Y	7	Y
35	A	Y	4	N
36	A	Y	7	Y
37	IA	N		Y
38	A	Y	5	N
39	A	N		Y
40	A	Y	5	Y
41	IA	N		Y
42	A	Y	5	Y
43	A	Y	4	N

A = active pseudarthrosis; IA = inactive pseudarthrosis; Y = yes; N = no.

quality standard. Accordingly, the results after shock wave therapy still must be regarded with great care.

Initial data were reported by Valchanou and Michailov[31] who began shock wave treatment of pseudarthrosis and delayed union in 1988. Of 82 treatments, 70 were successful but patient history, concomitant treatment, and followup were not exactly specified. Bürger et al[5] reported a lower success rate, observing complete union in 35% and callus formation in 21% of 37 patients who were treated. How-



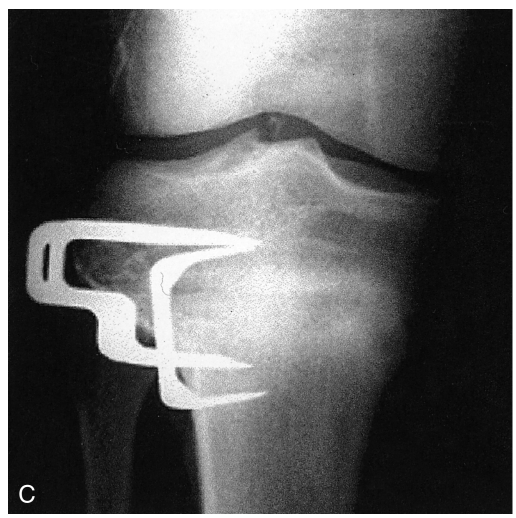
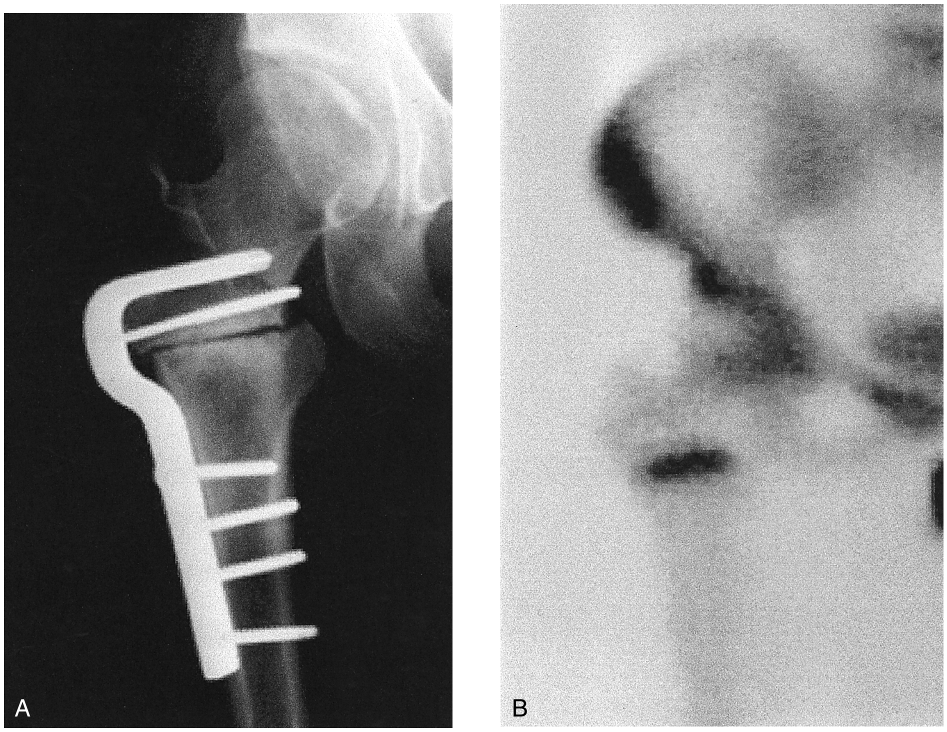


Fig 1A–C. (A) In Patient 32, this AP radiograph was obtained 13 months after correcting valgization osteotomy for medial gonarthrosis. (B) The lateral scintigraph shows significant tracer uptake in the mineralization phase. (C) An AP radiograph obtained 3 months after high-energy extracorporeal shock wave therapy shows complete bony healing.

ever, modalities of shock wave application were not standardized, a problem also observed in the studies of Haupt[14] and Diesch and Haupt,[7] who reported 76% and 66% consolidation in 30 and 172 patients with pseudarthrosis. Wirsching et al[37] treated 115 patients with a nonunion at an average of 34 months after the last operation. Their treatment concept with the Osteostar shock wave device was to administer 500 impulses at each 5 mm distance of the nonunion gap, using an energy flux density of 0.84 mJ/mm^2. The previous stabilization procedure (external fixator, plate, nail, cast) remained unchanged. In patients with insufficient bony healing, one to three shock wave treatments (average, 1.1 treatments) were performed additionally. Eighty-one percent of the nonunions were healed at a mean followup of 36 months. Of 52 tibial pseudarthroses, all 24 hyperthrophic pseudarthroses healed, and 57% of the 28 avascular nonunions healed. The total success rate in these patients was 77%. In patients with an avascular defect pseudarthrosis, Wirsching et al[37] recommended a combination of spongeous grafting plus extracorporeal shock wave



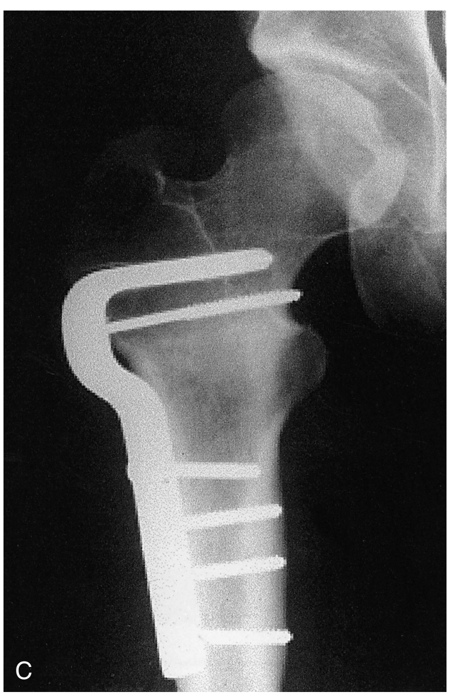


Fig 2A–C. (A) In Patient 42, this AP radiograph was obtained 15 months after intertrochanteric varization osteotomy. (B) The AP scintigraph shows positive tracer uptake in the mineralization phase. (C) An AP radiograph obtained 5 months after high-energy extracorporeal shock wave therapy shows complete bony healing.

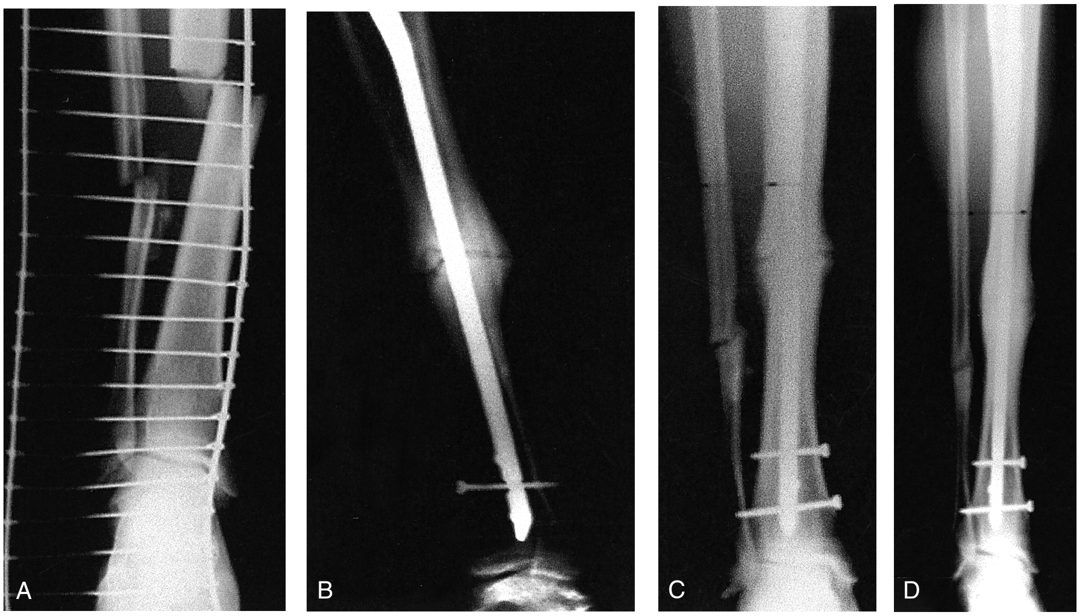


Fig 3A–D. (A) Anteroposterior radiograph shows a closed fracture of tibia and fibula in Patient 43. (B) Anteroposterior and (C) lateral radiographs obtained 11 months after intramedullary nailing. (D) Anteroposterior radiograph obtained 4 months after high-energy extracorporeal shock wave therapy shows compete bony healing

therapy. Rodriguez et al treated three patients successfully with high-energy shock waves. (Rodriguez de Oya R, Sanchez Benitez de Soto J, Garcia Munilla M: Treatment of nonunion with extracorporeal shockwaves. Presentation at the Second International Congress of the European Society for Musculoskeletal Shockwave Therapy, London 1999.) Wang reported shock wave application in 40 patients with postfracture nonunion of the long bones. (Wang C: Treatment of fracture non-union with shockwave application. Presentation at the Second International Congress of the European Society for Musculoskeletal Shockwave Therapy, London 1999.) All patients only received one treatment, with 6000 shock waves applied to the femur or the tibia, 2000 shock waves applied to the radius, and 1000 shock waves applied to metacarpal and metatarsal bones. At 6-month followup, 28 patients did not have pain and the average bone gap decreased from 4.5 mm to 1.6 mm. In 80% of the patients, significant callus formation was observed. Gerdesmeyr et al treated 25 patients prospectively during 1 year. All patients were treated two times within 6 weeks. (Gerdesmeyer L, Bachfischer K, Peters P, Gradinger R: The indication of the application of high energetic extracorporeal shock waves in the treatment of pseudarthrosis: Clinical and radiological results. Presentation at the Second International Congress of the European Society for Musculoskeletal Shockwave Therapy, London 1999.) Two thousand shock waves were applied with an energy flux density of 0.5 mJ/mm^2. A bony consolidation was observed in 16 patients (64%) within 6 months and in three patients callus formation was observed without bony consolidation. They concluded that high-energy extracorporeal shock wave therapy was an excellent noninvasive treatment for pseudarthrosis and should be used as primary treatment method. Beutler et al[3] reported that the nonunions in 11 of 27 patients healed (41%) 3 months after shock wave therapy after two treatments with 2000 impulses at 18 kV. Schaden reported a success rate of 75.4% in 49 nonunions and of 75% in 15 infected nonunions. He suggested that shock waves had a stimulating effect on osteoformation. (Schaden W: Single application of extracorporeal shock waves in 97 patients with nonunions or delayed healing fractures. Presented at the Sixty-Seventh Annual Meeting of the American Academy of Orthopaedic Surgeons, Orlando, FL 2000.)

The current observational cohort study focused on the treatment of nonunions of the femur or tibia, being defined as a fracture or osteotomy in which no radiologic signs of cortical bridging occurred for at least 9 months after the last operative intervention. Stringent exclusion criteria were applied, shock wave treatment was standardized, and adjunct treatment remained unchanged. An independent observer made the decision whether bony healing had occurred. A radiologic success was seen in 72% of the patients, and a clear connection with a positive tracer uptake in the mineralization phase of bone scintigraphy. Therefore, now patients with a scintigraphically inactive pseudarthrosis are excluded. Six of eight patients with an inactive pseudarthrosis and subsequent treatment failure after extracorporeal shock wave therapy smoked more than 20 cigarettes per day. With the knowledge of a possible direct relationship between the development of a nonunion and the presence of nicotine,[28] the authors recommend that patients stop smoking before starting with high-energy extracorporeal shock wave therapy.

Several weak points of the current study deserve attention. First, as reported by Taylor,[30] the suggestions of the Food and Drug Administration panel from 1986 for the definition of a pseudarthrosis were only partially adopted: the determination of visible progressive signs of healing for 3 months was excluded because according to the radiologic department involved in the current study, this criterion should not be used as a success parameter because of the wide range of interobserver variability in its assessment. It was thought that if cortical consolidation had not appeared after 9 months in long bones, spontaneous union had to be regarded as improbable, even in hypertrophic, hypervascular nonunions as shown in Figure 3. One may wonder whether the nonunion would have united spontaneously. However, in this case, as in all the others, it was an independent observer who diagnosed a nonunion, and operative revision could have been suggested at this time. Second, the authors attempted to select a homogenous group of patients. It is evident that there may be differences between healing times of posttraumatic and postosteotomy nonunions. With the small number of patients available, an individual statistical comparison of the two groups would not have given adequate statistical information. Nevertheless, better results were observed after postosteotomy than after postfracture nonunions. Third, there is no control group. Whenever a new method of treatment is suggested, it must be compared with an adequate set of controls. A study design with a placebo control had been dismissed as unethical. The alternative must be the comparison of high-energy extracorporeal shock wave therapy versus a standardized operative or conservative procedure. The authors strongly favor a multicenter study. With the small number of patients available in one department, an additional subdivision into two treatment groups would not have given adequate information from the statistical point of view.

Beyond the preliminary clinical studies, the authors are not aware of any other studies that document the effectiveness of high-energy extracorporeal shock wave therapy in the treatment of pseudarthrosis. The authors think that additional clinical corroboration of the stimulation of bone healing with use of standardized high-energy extracorporeal shock waves should be done, and may lead to useful application of shock waves in the treatment of pseudarthroses, and a determination of the total energy most likely to accomplish healing.

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