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● *Original Contribution*

# EXTRACORPOREAL SHOCK WAVE THERAPY FOR MANAGEMENT OF CHRONIC ULCERS IN THE LOWER EXTREMITIES

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**Abstract—Management of chronic ulcers in the lower extremities is still a challenge for patients and health providers. Recent studies showed extracorporeal shock waves (ESW) as effective in stimulating growth factors, inducing angiogenesis and healing of fractures and injuries. This study was planned to investigate the opportunity of introducing the ESW in the treatment of chronic wounds. Thirty consecutive patients with chronic posttraumatic, venous and diabetic ulcers, unresponsive to conservative or advanced dressing treatments, were counseled about the use of ESW as alternative treatment for their wounds. Thirty-two wounds were treated and 16 wounds healed completely within six sessions of ESW. In all of the nonhealed wounds, decrease of the amount of exudates, increased percentage of granulation tissue compared with fibrin/necrotic tissue and decrease of wounds' size were statistically significant after four to six sessions of ESW ($p < 0.01$). Significant decrease of pain was reported ($p < 0.001$). Comparison with a control group of 10 patients with chronic ulcer treated on the basis of regular dressings confirmed the statistical significant improvement in the healing process ($p < 0.01$). ESW therapy seems to be a safe, feasible and cost-effective treatment for chronic ulcers in the lower extremities. Further research and clinical trials are necessary to evaluate dose and time intervals of sessions to standardize a protocol of treatment in the management of chronic wounds. (E-mail: nicolo.scuderi@uniroma1.it) © 2008 World Federation for Ultrasound in Medicine & Biology.**

***Key Words*: Extracorporeal shock waves therapy, Shock waves, Chronic ulcers, Chronic wounds, Difficult wounds, Lower extremities ulcers.**

## INTRODUCTION

Chronic ulcers are complex wounds that do not heal spontaneously and usually have multiple causative factors, local or systemic, for the nonhealing process (Broughton et al. 2006; Lazarus et al. 1994; Nwomeh et al. 1998).

Chronic ulcers are also known as "difficult wounds" that challenge medical and nursing teams, requiring specialized care. As the average age of the population is increasing, the frequency of these complex wounds is becoming a major social and economic problem in the health care system worldwide (Ferreira et al. 2006).

Current treatment of chronic ulcers are mechanical/surgical debridement followed by skin grafting (Hierner et al. 2005) or flap coverage (Gonzalez et al. 2002), use of conventional or advanced dressings (Attinger et al. 2006; Fleck 2006), medical or surgical correction of inadequate blood supply (Muhs et al. 2006; Schultz et al. 2003) and use of recent wound healing adjuvants (Argenta et al. 2006; Braakenburg et al. 2006; Hess et al. 2003).

These treatments, because of the complex etiology and the several local and systemic factors, are not always successful and require variable time–cost period in supporting the healing process.

Almost 30 years ago, extracorporeal shock waves (ESW) were introduced successfully in urology and gastroenterology as lithotripsy (Chaussy et al. 1980; Delhaye et al. 1992; Iro et al. 1992; Sauerbruch et al. 1986). In the last decade, shock waves were introduced to treat different pathologies of the musculoskeletal system, including nonunion bone, plantar fasciitis, epicondylitis of the elbow and calcifying or noncalcifying tendonitis (Biedermann et al. 2003; Gerdesmeyer et al. 2003; Pettrone and McCall 2005; Thomson et al. 2005). In 2000, the Food and Drug Administration approved ESW therapy (ESWT) for chronic plantar fasciitis and in 2003 for chronic lateral epicondylitis (Henney 2000; Rompe 2003).

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Fig. 1. ESWT: a single-layer sterile gauze and ultrasound transmission gel were applied between the wound and the hand-handle ESWT probe.

Previous studies demonstrated that ESW may be effective in stimulating numerous growth factors endogenously, inducing angiogenesis and healing of fractures, injuries and wounds (Belcaro et al. 2005; Chen et al. 2004; Dyson et al. 1976; Wang et al. 2003, 2005; Haupt and Chvapil 1990; Young and Dyson 1990a, 1990b, 1990c; Webster et al. 1978, 1980).

ESWT also demonstrated effects on nerve conduction, with reduction of pain in chronic degenerative pathologies and potential bactericide action against *Staphylococcus aureus* (Gerdesmeyer et al. 2005; Ohtori et al. 2001; Takahashi et al. 2006).

With the noninvasive nature of the shock waves and their seemingly low complication rate, ESWT may be a valid alternative support to conservative and surgical treatments in patients with chronic wounds (Speed 2004).

This preliminary study was planned to investigate the opportunity of introducing ESWT in the treatment of

Table 1. ESWT group. Patients and ulcers data

| | | | | | | | | | Granulation tissue % | | Fibrin/necrotic tissue % | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Patient N/Sex | Age (y) | Ulcer type | Site | Duration (mo) | NBS Pre | NBS Post | Exudate Pre-ESWT | Exudate Post-ESWT | Pre | Post | Pre | Post |
| 1/M | 76 | V | Ant | 3 | 5 | 5 | Heavy | Moderate | 70 | 80 | 30 | 20 |
| 1/M | 76 | V | Ant | 4 | 6 | 5 | Minimal | Healed | 75 | 0 | 25 | 0 |
| 2/F | 58 | V | Mal | 5 | 6 | 6 | Heavy | Moderate | 75 | 90 | 25 | 10 |
| 2/F | 58 | V | Mal | 6 | 8 | 5 | None | Healed | 70 | 0 | 30 | 0 |
| 3/M | 56 | V | Mal | 7 | 5 | 4 | Moderate | Healed | 65 | 0 | 35 | 0 |
| 4/M | 57 | V | Mal | 8 | 8 | 6 | None | Healed | 70 | 0 | 30 | 0 |
| 5/F | 50 | V | Mal | 8 | 8 | 6 | Moderate | Moderate | 65 | 80 | 35 | 20 |
| 6/M | 51 | V | Mal | 6 | 6 | 5 | Minimal | Minimal | 60 | 100 | 40 | 0 |
| 7/M | 49 | V | Mal | 5 | 7 | 5 | Minimal | Minimal | 70 | 85 | 30 | 15 |
| 8/F | 58 | V | Mal | 5 | 7 | 6 | None | Minimal | 80 | 85 | 20 | 15 |
| 9/M | 62 | V | Mal | 4 | 6 | 4 | Minimal | Minimal | 75 | 100 | 25 | 0 |
| 10/F | 71 | V | Mal | 3 | 5 | 3 | Moderate | Minimal | 60 | 85 | 40 | 15 |
| 11/M | 24 | T | Cal | 3 | 5 | 5 | Heavy | Minimal | 30 | 75 | 70 | 25 |
| 12/F | 59 | T | Cal | 4 | 6 | 4 | Heavy | Minimal | 20 | 65 | 80 | 35 |
| 13/M | 45 | T | Mal | 5 | 7 | 4 | None | Healed | 50 | 0 | 50 | 0 |
| 14/M | 54 | T | Mal | 6 | 8 | 5 | Minimal | None | 30 | 85 | 70 | 15 |
| 15/F | 62 | T | Mal | 4 | 6 | 6 | None | Healed | 58 | 0 | 42 | 0 |
| 16/F | 78 | T | PD | 5 | 7 | 5 | None | Healed | 51 | 0 | 49 | 0 |
| 17/M | 42 | T | Mal | 6 | 8 | 6 | None | Healed | 45 | 0 | 55 | 0 |
| 18/M | 39 | T | Mal | 7 | 8 | 6 | None | Healed | 45 | 0 | 55 | 0 |
| 19/M | 73 | T | Mal | 8 | 8 | 7 | Minimal | None | 35 | 70 | 65 | 30 |
| 20/F | 65 | T | PD | 4 | 6 | 6 | None | Healed | 35 | 0 | 65 | 0 |
| 21/M | 77 | T | PD | 4 | 6 | 5 | None | Healed | 40 | 0 | 60 | 0 |
| 22/F | 63 | T | Ant | 4 | 6 | 4 | Heavy | None | 30 | 75 | 70 | 25 |
| 23/M | 61 | T | LP | 4 | 6 | 4 | Minimal | Healed | 35 | 0 | 65 | 0 |
| 24/M | 59 | T | LP | 8 | 8 | 5 | None | Healed | 60 | 0 | 40 | 0 |
| 25/F | 47 | T | LP | 8 | 6 | 4 | None | Healed | 45 | 0 | 55 | 0 |
| 26/M | 64 | T | Mal | 7 | 8 | 6 | None | Healed | 65 | 0 | 35 | 0 |
| 27/F | 79 | D | Cal | 7 | 8 | 6 | Heavy | None | 45 | 85 | 55 | 15 |
| 28/F | 55 | D | Ant | 6 | 8 | 5 | Minimal | None | 60 | 100 | 40 | 0 |
| 29/M | 37 | D | Ant | 4 | 6 | 5 | Minimal | None | 40 | 85 | 60 | 15 |
| 30/M | 68 | D | LP | 3 | 5 | 3 | Minimal | Healed | 55 | 0 | 45 | 0 |
| Mean | 58.5 | | | 5.34 | 6.65 | 5.03 | | | 53.4 | 84.1* | 46.6 | 15.9 |

V = venous ulcer; T = posttraumatic ulcer; D = diabetic ulcer; Ant = anterior aspect lower leg; Mal = malleolar region; Cal = calcaneal region; PD = posterior distal aspect lower leg; LP = lateral and plantar region of the foot.

* Mean percentage of granulation tissue in nonhealed ulcers.

Table 2. Control group patients and ulcers data

| Patient N/Sex | Age (y) | Ulcer type | Site | Duration(mo) | NBS Pre | NBS Post | Exudate Pre | Exudate Post (8 wk) | Granulation tissue % | | Fibrin/necrotic tissue % | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | Pre | Post | Pre | Post |
| 1/M | 78 | V | Ant | 3 | 6 | 5 | Heavy | Moderate | 40 | 60 | 60 | 40 |
| 2/F | 67 | V | Mal | 4 | 6 | 6 | Heavy | Moderate | 70 | 80 | 30 | 20 |
| 3/M | 62 | V | Ant | 5 | 4 | 5 | Moderate | Moderate | 65 | 50 | 35 | 50 |
| 4/M | 56 | V | Mal | 8 | 6 | 6 | Minimal | Healed | 80 | 0 | 20 | 0 |
| 5/F | 78 | V | Mal | 7 | 8 | 7 | Moderate | Moderate | 60 | 80 | 40 | 20 |
| 6/M | 68 | T | Mal | 6 | 6 | 6 | Minimal | Minimal | 80 | 100 | 20 | 0 |
| 7/M | 55 | T | Ant | 5 | 7 | 6 | Minimal | None | 70 | 85 | 30 | 15 |
| 8/F | 59 | D | Mal | 5 | 8 | 6 | None | Minimal | 80 | 65 | 20 | 35 |
| 9/M | 65 | D | LP | 5 | 6 | 4 | Minimal | Minimal | 45 | 60 | 55 | 40 |
| 10/F | 78 | D | Cal | 4 | 5 | 4 | Moderate | Minimal | 60 | 80 | 40 | 20 |
| Mean | 66.6 | | | 5.2 | 6.2 | 5.5 | | | 65 | 57.5 | 35 | 22.5 |

NBS = pain self-assessment numeric box scale, from 0 (no pain) to 10 (worst imaginable pain); V = venous ulcer; T = posttraumatic ulcer; D = diabetic ulcer; Ant = anterior aspect lower leg; Mal = malleolar region; Cal= calcaneal region; PD = Posterior distal aspect lower leg; LP = lateral and plantar regione of the foot.

chronic wounds evaluating the outcomes of this therapy in a consecutive series of patients with chronic ulcers in the lower extremities.

## MATERIALS AND METHODS

Between September 2005 and August 2006, all consecutive patients ranging between 18 and 85 y, presenting a history of chronic ulcers from more than three months that were unresponsive to conservative or advanced dressing treatments or mechanical debridement, were counseled about the use of ESWT as alternative treatment for their wounds.

ESWT, used in the present study, consisted of 100 impulses at 0.037 mJ/mm$^2$ each per cm$^2$ of the row wound area (Evotron, High Medical Technologies, Lengwil, Switzerland). The focal volume of the hand-handled probes (Trode) was 10–15 mm in diameter and the total energy applied for each impulse was 3.5 mJ, with a frequency of 4 Hz or 240 impulses/min.

Exclusion criteria were arrhythmias, presence of pacemaker, coagulopathies, tumors, pregnancy, presence of growth cartilage, local acute inflammation, exposed bone and wound size area <1 cm$^2$ or more than 10 × 20 cm.

The wounds were classified on the basis of the location, width (cm), length (cm), row surface area (cm$^2$), percentage of granulation tissue, percentage of fibrin tissue or necrotic tissue, presence of exudates, bacterial colonization (positive culture swabs or tissue scrapings) and pain.

Presence of exudates was determined as: none, minimal, moderate and heavy, adapted from the wound bed preparation score developed by Falanga (2000) (Falanga et al. 2006).

Pain suffering parameter was assessed on the basis of a pain self-assessment numeric box scale (NBS) rang-

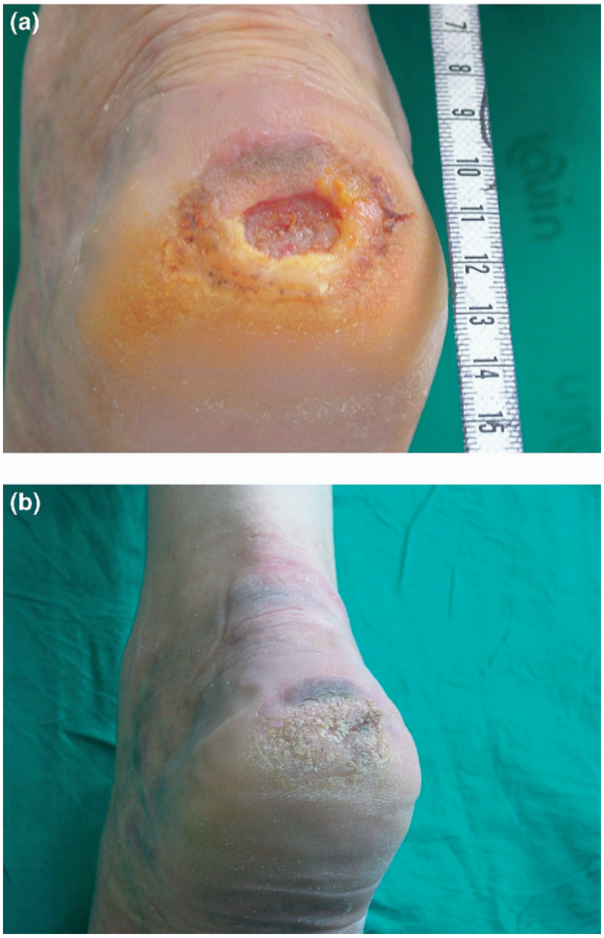


Fig. 2. (a) Male patient (58 y) with a 5-mo posttraumatic calcaneal ulcer of the left foot, 2.1 × 1.2 cm. (b) Complete closure of the wound after six sessions (12 wk) of ESWT.

Table 3. Pre and post-ESW treatment posttraumatic ulcers dimensions and row surface

| Patient No. | Ulcer type | Pre-ESWT ulcer dimensions (cm) | Post-ESWT ulcer dimensions (cm) | Pre-ESWT ulcer surface ($cm^2$) | Post-ESW ulcer surface ($cm^2$) |
|---|---|---|---|---|---|
| 11 | T | 1.5 × 2.5 | 1 × 0.5 | 3.7 | 1.5 |
| 12 | T | 3.4 × 2.2 | 3.4 × 1.6 | 7.5 | 5.44 |
| 14 | T | 2.8 × 1.7 | 1.3 × 2.5 | 4.7 | 3.25 |
| 19 | T | 3.4 × 1.2 | 3.1 × 0.7 | 3.9 | 2.17 |
| 22 | T | 2.8 × 3.5 | 3.5 × 2 | 9.7 | 7.04 |
| 13 | T | 2.1 × 1.2 | Healed | 2.5 | Healed |
| 15 | T | 3.4 × 1.2 | Healed | 4 | Healed |
| 16 | T | 2.5 × 1.3 | Healed | 3.2 | Healed |
| 17 | T | 2.1 × 0.5 | Healed | 1 | Healed |
| 18 | T | 3.5 × 1.1 | Healed | 3.8 | Healed |
| 20 | T | 3.3 × 0.7 | Healed | 2.3 | Healed |
| 21 | T | 2.7 × 1.4 | Healed | 3.7 | Healed |
| 23 | T | 3.2 × 2.1 | Healed | 6.7 | Healed |
| 24 | T | 2.9 × 2.3 | Healed | 6.6 | Healed |
| 25 | T | 2.5 × 1.4 | Healed | 3.5 | Healed |
| 26 | T | 2.8 × 2.1 | Healed | 5.8 | Healed |

ing between 0 (no pain) and 10 (worst imaginable pain) (Jorgensen et al. 2006).

Following the natural history of the wounds, chronic ulcers in this series were classified as: posttraumatic ulcers (previous history for trauma in the area where wound developed in absence of other causative factors), venous ulcers (caused by chronic venous insufficiency in the lower extremities) and diabetic ulcers (chronic wounds developed in diabetic patients in the lower extremities).

All associated pathologies such as peripheral arterial insufficiency, vasculitis, rheumatoid arthritis, severe kidney disease, heart disease, gastrointestinal bleeding, serious heart/liver insufficiency, hypertension, thrombocytopenia, asthma or other allergic symptoms were documented. Patients who were under salicylic acid or other NSAIDs therapy were allowed to take concomitant pain medication but were required to keep the medication constant during the study period. Smoking habits were recorded as well.

All patients who fulfilled the inclusion criteria joined the study after a strict selection and consent/protocol form acceptance following local ethical committee approval.

Every patient underwent single sessions every two weeks, with a minimum of four and a maximum of 10 sessions for a complete treatment. No general or local anesthesia or other injections were used.

After disinfection of the wound with polyvinylpyrrolidone, a single-layer sterile gauze and ultrasound transmission gel were applied between the wound and the probe (Fig. 1). After each session, the probes were cleaned with chlorhexidine for surgical instruments sterilization. Because of the ESWT direct microtraumatic effects, the possibility of bleeding, petechiae, hematoma and/or seroma formation and painful sensation was documented (Haake et al. 2002; Sistermann and Katthagen 1998).

The NBS self-assessment pain scale was administered to the patient to quantify the painful sensation before, during and after the session's treatment and to evaluate improvement of the pain threshold. Between ESW treatment sessions, the patients continued the previous conservative treatment. All the pretreatment gathered data were updated continuously within photographic digital documentation and single-time session.

Row surface area of the nonhealed wounds, percentage of granulation tissue and fibrin tissue/necrotic tissue, amount of exudates and scores from the NBS were compared before and after treatment with the Wilcoxon matched pairs rank sum test considering a statistical significance of $p < 0.05$.

A group of 10 consecutive patients, randomly recruited, with chronic ulcers in the lower limb treated on the basis of regular conservative dressings have been used as a control group to evaluate efficacy of the ESWT.

## RESULTS

During the study period, 40 consecutive patients affected by chronic ulcers of the lower extremities were selected (range of wounds duration between 3 to 8 mo, mean 5.3 mo). Average age of the patients was 60.4 y (range 24 to 78 y).

Thirty patients (18 men, 12 women) were treated with ESWT (Table 1) and 10 patients (6 men, 4 women) were treated with conservative dressings representing the control group (Table 2). Two patients had bilateral ulcers; thus the ESWT group included 32 wounds.

In the ESWT group, 17 ulcers were in the malleolar region, five were in the anterior aspect of the medial third of the leg, three were in the posterior aspect of the distal


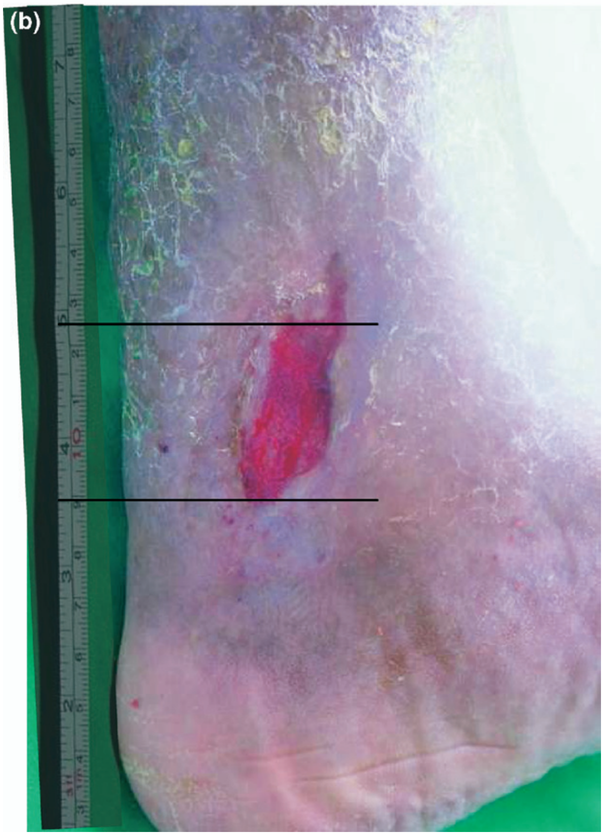


Fig. 3. (a) Male patient (62 y) with a 6-mo venous ulcer of the medial malleolar region of the left foot, 5.4 × 2.8 cm. (b) Decrease of wound row surface of 70% after six sessions (12 wk), 3.1 × 1.2 cm. Other four sessions were performed without further reduction of the wound's row surface area.

third of the leg, four were in the lateral/plantar side of the foot and three were in the calcaneal region. Eight patients were smokers. Eleven patients had venous insufficiency in the lower limbs. Four patients were diabetics, 18 patients had referred arterial hypertension controlled by medication.

Before ESWT, wounds' dimensions ranged from 1.2 × 2 × 5.4 × 2.8 cm, with a mean row surface area of 5.29 cm$^2$.

Initially, the wounds showed a percentage of granulation tissue and fibrin/necrotic tissue varying between 20–80% of the wounds' row surface area, with a mean of 53.4% and 46.6%, respectively.

The amount of exudates was recorded as: none in 13 ulcers, minimal in 10 ulcers, moderate in three ulcers and severe in six ulcers. Only one ulcer was positive for *Staphylococcus aureus* bacterial growth on culture swabs.

Before ESWT, NBS for pain evaluation showed a mean score of 6.65 ranging from 5–8. Average time session was 16.84 (range 12 to 24) min. Sixteen chronic ulcers were posttraumatic, 12 were chronic venous ulcers and four were chronic ulcers in diabetic patients. Among the 16 posttraumatic ulcers (Fig. 2), 11 healed completely (69%). In eight cases, the wounds healed after four sessions, and in the other three cases after six sessions.

The five ulcers that did not heal after 10 sessions demonstrated a mean wound row surface area of 3.88 cm$^2$, with a range between 1.5–7.04 cm$^2$. Mean percentage of wounds' size decrease was 37.5%, with a range between 22–60% (Table 3).

Among the 11 venous ulcers (Fig. 3), four healed completely (36%), and the remaining demonstrated a mean wound row surface area of 5.22 cm$^2$, with a range between 3.38–7.7 cm$^2$ decrease of percentage of the row surface area of the wound varying from 32–70%, with a mean of 45% (Table 4).

Among the four diabetic patients (Fig. 4), all smokers, one ulcer healed (25%) after ESWT. The nonhealed wounds' sizes demonstrated a 50% decrease of the row surface area, and complete disappearing of the exudate was documented in all of these wounds (Table 5).

In all of the 16 nonhealed wounds, an increasing percentage of granulation tissue varying from 5–45% was demonstrated (Fig. 3a and b). In three ulcers, presence of moderate exudates was observed, whereas a minimal amount was observed in seven ulcers after ESWT.

One patient with a 30-year history of chronic wound in the posterior aspect of the lower third in the right leg showed a slight decrease from moderate to minimal presence of exudates and an increased percentage of granulation tissue compared with the pretreatment condition. The ESWT was considered not effective. This

Table 4. Pre and post-ESW treatment venous ulcers dimensions and row surface

| Patient No. | Ulcer type | Pre-ESWT ulcer dimensions (cm) | Post-ESWT ulcer dimensions (cm) | Pre-ESWT ulcer surface ($cm^2$) | Post-ESWT ulcer surface ($cm^2$) |
|---|---|---|---|---|---|
| 1 | V | 2.6 × 2.5 | 1.7 × 2 | 6.5 | 3.38 |
| 2 | V | 5.4 × 2.8 | 3.1 × 1.5 | 15.1 | 4.5 |
| 5 | V | 4.1 × 2 | 1.9 × 2.5 | 8.2 | 4.75 |
| 6 | V | 3.3 × 2.7 | 2.4 × 2 | 8.9 | 4.8 |
| 7 | V | 3.3 × 3.4 | 2.5 × 2.2 | 10.6 | 5.5 |
| 8 | V | 4 × 2.5 | 2.6 × 2.5 | 10 | 6.5 |
| 9 | V | 3.8 × 3 | 3.5 × 2.2 | 11.3 | 7.7 |
| 1 | V | 3.4 × 1.3 | Healed | 4.4 | Healed |
| 2 | V | 3.2 × 1.4 | Healed | 4.4 | Healed |
| 3 | V | 3.3 × 1.9 | Healed | 6.2 | Healed |
| 4 | V | 1.4 × 2 | Healed | 2.8 | Healed |

patient had a posttraumatic wound from World War II because of a bullet injury. Pretreatment and posttreatment culture swabs were negative for bacterial growth. After failure of ESWT, an excision biopsy of the entire wound and $^{99}$mTc-mononuclear leukocyte scintigraphy demonstrated presence of osteomyelitis of the right fibula. *Staphylococcus aureus* colonization was identified on microbiologic assessment of the surgical specimen. Removal of the infected bone, covered with a local perforator flap (Masia et al. 2007; Top et al. 2005) and selective antibiotic therapy with meropenem, led to a complete healing of the wound. Twelve months after surgery no complications arose.

At the end of the study period, 16 ulcers healed completely (50%). Complete healing was documented within the first fourth to sixth sessions. Wilcoxon matched pairs rank sum test applied on differences between the row surface area of the nonhealed wounds, calculated before and after ESWT, showed a significant statistical decrease ($p < 0.01$). In all of the wounds, the amount of exudates decreased considerably and the increasing percentage of granulation tissue compared with the fibrin/necrotic tissue was statistically significantly different ($p < 0.01$). At the end of the study period, in the nonhealed ulcers, a considerable improvement in the wound bed blood supply was documented. Improvement of all these parameters was noted within the first fourth to sixth sessions (Fig. 5).

Among the 30 patients in the ESWT group, 22 referred no increase of pain during the ESWT sessions and only eight referred a single point increase of pain at NBS during scattered sessions. After treatment, 24 patients reported a 1 to 3-point decrease of pain at NBS assessment. Six patients did not report improving in pain threshold after treatment. Statistical analysis on NBS scores showed significant decrease of pain after ESWT ($p < 0.001$).

During all treatments no adverse effects such as bleeding, petechiae, hematoma or seroma formation arose.

In the control group, only one wound completely healed after eight weeks (Table 6). No statistically significant differences were found between the row surface area of the wounds, the amount of exudates, percentage of granulation tissue compared with the fibrin/necrotic tissue and pain threshold assessed with the NBS scale, before and after eight weeks of regular dressings (Fig. 6).

Wilcoxon matched pairs rank sum test applied on differences between the two groups showed a statistical significant decrease of row surface area of the wounds, increase of granulation tissue compared with fibrin/necrotic tissue and pain threshold ($p < 0.01$).

## DISCUSSION

Chronic ulcers are a challenge to problem-solve, even in specialized centers (Gottrup 2004). In these wounds, the healing process is altered by local or systemic factors, which prevent closure of the skin defect and scar formation. In the present series, all chronic wounds were older than three months and unresponsive to previous topical conservative therapy with conventional or advanced dressings.

ESW are considered a viable treatment modality for urologic and orthopaedic ailments (Biedermann et al. 2003; Chaussy et al. 1980; Delhaye et al. 1992; Gerdesmeyer et al. 2003; Iro et al. 1992; Pettrone and McCall 2005; Sauerbruch et al. 1986; Thomson et al. 2005). Despite an increasing clinical use, the mechanisms by which ESW generate a therapeutic effect are not yet understood. The mechanistic differences in various devices and their efficacy might be dependent on shock waves' acoustic and cavitation outputs (Ogden et al. 2001).

Shock waves are single-impulse with high-amplitude and short-length sound waves from a transient pressure disturbance that propagate in 3-D space, with a sudden rise from ambient pressure to its maximum pressure at the wave front. There are three main techniques through which the shock waves can be generated: electrohydraulic, electromagnetic and piezoelectric. Regard-

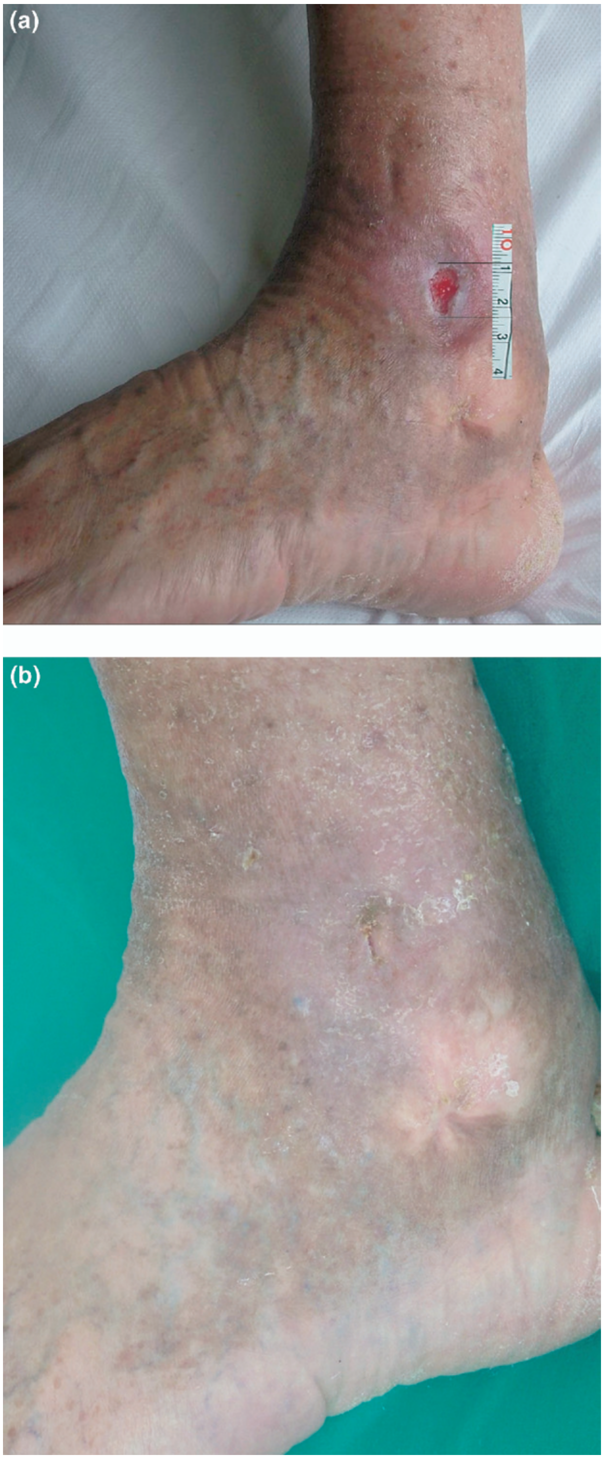

Fig. 4. (a) Female patient (68 y) with a 4-mo diabetic ulcer of the lateral malleolar region of the left foot, 1.4 × 0.8 cm. (b) Complete closure of the wound after four sessions (8 wk) of ESWT.

less of the generation technique, shock waves are concentrated on a target site of 2–8 mm in diameter. The shock wave energy per unit area, energy flux density, is measured in mJ/mm$^2$ and divided in three levels by Mainz (Speed 2004). ESWT is performed according to the number of shocks administrated, the generator frequency and energy level setting.

In this series, the same energy was used for every wound. This was done to reduce the confounding variables during assessment of the results.

We feel that a different amount of energy or number of sessions with lesser interval of time may influence the outcomes and, on the basis of these preliminary results, further studies are already underway.

ESWT demonstrated an effective action within the first four to six sessions of treatment. In the following sessions, until the tenth, no significant improvement was noticeable (Fig. 5a–c). This may be related to dose-dependant effect according to the different etiology of the wounds.

Shock waves' biological mechanisms have been studied *in vitro* and *in vivo* on soft tissue, but a clinical series of wounds treated with this therapy is still lacking (Gambihler et al. 1990; Haupt and Chvapil 1990; Young and Dyson 1990a, 1990b, 1990c; Webster 1978, 1980). To our knowledge, ESWT was used on burned skin, but chronic wounds have not been evaluated as to wounds regeneration effects and/or supporting therapy (Meirer et al. 2005a).

Histologically, in chronic ulcers there is a disorganized endothelial proliferation, presence of parakeratotic keratinocytes, connective tissue not organized in fibrils, increased number of lymphocytes and granulocytes with alterations of proteins, electrolytes and cytokines (Cullen et al. 2002).

Direct and indirect effects of ESW may stimulate endothelial organization, with increased deposition of connective tissue and stimulation of epithelialization (Meirer et al. 2005a; Wang 2003).

Previous studies on shock waves demonstrated rearrangement of the endothelial cells and basal laminae, significant rise of local growth factors, such as nitric oxide synthase, proliferating cell nuclear antigen inducing neovascularization and transforming growth factor-$\beta$1 (Wang 2003; Wang et al. 2003, 2005; Wang et al. 2002). Other studies *in vitro* and in animal models (Young and Dyson 1990b; Webster et al. 1978, 1980) suggested that ESWT can be useful in accelerating the inflammatory and early proliferative stages of repair, stimulating macrophages to synthesize and secrete fibroblast mitogenic factors. Collagen synthesis is apparently stimulated to the same extent as general protein synthesis.

Most of the previous clinical studies were focused on orthopedic use of shock waves, whereas only recently, this therapeutic approach was investigated on animals from a reconstructive surgery perspective (Meirer et al. 2005a, 2005b, 2007). Studies on the effects

Table 5. Pre and post-ESW treatment diabetic ulcers dimensions and row surface

| Patient No. | Ulcer type | Pre-ESWT ulcer dimensions (cm) | Post-ESWT ulcer dimensions (cm) | Pre-ESWT ulcer surface ($cm^2$) | Post-ESWT ulcer surface ($cm^2$) |
|---|---|---|---|---|---|
| 1 | D | 2.7 × 1.1 | 2.5 × 0.6 | 3 | 1.5 |
| 2 | D | 2.6 × 1.2 | 1.2 × 2 | 3.1 | 1.5 |
| 3 | D | 3 × 2.4 | 2.5 × 1.4 | 7.2 | 3.5 |
| 4 | D | 1.4 × 0.8 | Healed | 1.1 | Healed |

of ESW in enhancing skin flap survival, reducing ischemic necrosis in rats, demonstrated encouraging results (Huemer et al. 2005; Meirer et al. 2005b, 2007).

The available results from the present study demonstrated a significant effect of ESWT in improving the healing process of chronic ulcers in the lower extremities. This was more noticeable in the treatment of posttraumatic chronic ulcers than in the venous or diabetic ulcers, which had been refractory to other nonoperative treatment modalities. The significant improvement in the

Fig. 5. (a) Female patient (62 y) with an 8-mo posttraumatic lateral calcaneal ulcer of the left foot, 3.4 × 1.2 cm. (b) Wound almost closed after four sessions (8 wk) of ESWT. (c) Final clinical result after 10 sessions (20 wk) of ESWT. It is noticeable that no significant improvement occurred after the fourth session of ESWT.



Fig. 6. (a) Male patient (55 y) from control group with a 7-mo posttraumatic ulcer on the anterior aspect of the right lower leg, 4 × 2.6 cm. (b) No significant improvement after eight weeks of regular dressings.

healing process was observed and confirmed in the non-healed wounds as well.

The exact mechanism of action for ESW remains uncertain but it was found to be successful in increasing the release of endogenous angiogenic factors from endothelial cells and fibroblasts, which may be useful in the possible stimulation of the healing process in chronic ulcers. ESW seems to stimulate revascularization, release of local growth factors and recruitment of appropriate stem cells to the target area (Meier et al. 2003; Rompe et al. 1998; Wang 2003; Wang et al. 2003, 2007). ESW may stimulate not only a single agent or factor, but the interactions between physical shock wave energy and biological responses, within the complexity of etiology and healing process, may act on a cascade of interacting growth factors, resulting in support of closure of difficult wounds.

In this series, a complete closure of the chronic wound was obtained in 50% of the wounds. In the nonhealed wounds, all the compared parameters showed a significant statistical difference before and after treatment. These results pointed out the fact that ESWT was effective in enhancing the healing process to definitely close some wounds, in particular the posttraumatic wounds, to improve the outcome of the remaining wounds.

Probably, the major results observed within the posttraumatic wounds demonstrated the effective action on neo-angiogenesis and growth factors stimulation, which in these wounds, may be less altered or more respondent than those in patients with diabetes and venous insufficiency.

In the present study, a significant decrease of pain threshold was demonstrated. This result may confirm the reported efficacy of shock waves on hyperstimulation analgesia and long-term pain relief (Rompe et al. 1996a, 1996b, 1998). Alteration of chemical pain mediators, modulation of pain signal and disruption of cell membranes (Schelling et al. 1994), with blockade of impulse transmission and realizing of Substance P have all been proposed as possible generators of this analgesic effect (Maier et al. 2003).

Even if ESWT was postulated to cause microtrauma and hematoma formation, depending on location of treatment and amount of energy (Haake et al. 2002; Sistermann and Katthagen 1998), during all the study period no complications were encountered. ESWT seems to be a safe method to improve wound healing in chronic wounds.

This preliminary study was performed on a limited series of chronic wounds, which showed various patterns of etiology. However, the statistical significant improvement in wound healing parameters and pain threshold of the ESWT group compared with a control group treated with regular dressings for eight weeks demonstrates the efficacy of the ESWT in the healing process of chronic ulcer in the lower extremities.

In patients who have had failure of conventional treatment, ESWT seems to be a valid support to accelerate the healing process of these chronic wounds. ESWT used without local anesthesia may be a safe, feasible and cost-effective treatment in the management of chronic wounds in the lower extremities. However, prospective randomized studies on the mechanisms and effects of shock waves on soft tissues are needed to define more accurate indications and to optimize therapeutic outcomes. Further research and clinical trials are needed to evaluate dose and time intervals of sessions and to standardize a protocol of use of ESWT in the management of chronic ulcers in the lower extremities.

Table 6. Control group. Pre and post (8 weeks) ulcers dimensions and row surface

| Patient No. | Ulcer type | Site | Pre-ulcer dimensions (cm) | Post-ulcer dimensions (cm) | Pre- ulcer surface ($cm^2$) | Post-ulcer surface ($cm^2$) |
|---|---|---|---|---|---|---|
| 1 | V | Ant | $4.2 \times 2$ | $3.7 \times 2$ | 8.4 | 7.4 |
| 2 | V | Mal | $3.3 \times 2.7$ | $2.8 \times 2.2$ | 8.9 | 6.1 |
| 3 | V | Ant | $3.6 \times 3.4$ | $3 \times 3$ | 12.2 | 9 |
| 4 | V | Mal | $2.4 \times 1.6$ | $2.6 \times 2$ | 3.8 | 5.2 |
| 5 | V | Mal | $1.6 \times 1.2$ | Healed | 1.9 | Healed |
| 6 | T | Mal | $3 \times 2$ | $2.7 \times 1.4$ | 6 | 3.7 |
| 7 | T | Ant | $3 \times 1.4$ | $2.3 \times 0.8$ | 4.2 | 1.8 |
| 8 | D | Mal | $2.9 \times 1.6$ | $1.3 \times 2.5$ | 4.6 | 3.2 |
| 9 | D | LP | $3.5 \times 1.2$ | $2.7 \times 0.8$ | 4.2 | 2.1 |
| 10 | D | Cal | $2.8 \times 2.5$ | $3 \times 2.6$ | 7 | 7.8 |

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