Extracorporeal Shock Wave Therapy as an Adjunct Wound Treatment: A Systematic Review of the Literature

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Abstract

Standard care procedures for complex wounds are sometimes supported and reinforced by physical treatment modalities such as extracorporeal shock wave therapy (ESWT). To evaluate available evidence of ESWT effectiveness in humans, a systematic review of the literature was conducted using MEDLINE, PubMed, Scopus, EBSCOhost, and PEDro databases. Of the 393 articles found, 13 met the publication date (year 2000–2013), study type (clinical study), language (English only), and abstract availability (yes) criteria. The 13 studies (n = 919 patients with wounds of varying etiologies) included seven randomized controlled trials that were evaluated using Cochrane Collaboration Group standards. Only studies with randomization, well prepared inclusion/exclusion criteria protocol, written in English, and full version available were analyzed. An additional six publications reporting results of other clinical studies including a total of 523 patients were identified and summarized. ESWT was most commonly applied once or twice a week using used low or medium energy, focused or defocused generator heads (energy range 0.03 to 0.25 mJ/mm^2; usually 0.1 mJ/mm^2), and electrohydraulic or electromagnetic sources. Few safety concerns were reported, and in the controlled clinical studies statistically significant differences in rates of wound closure were reported compared to a variety of standard topical treatment modalities, sham ESWT treatment, and hyperbaric oxygen therapy. Based on this analysis, ESWT can be characterized as noninvasive, mostly painless, and safe. Controlled, randomized, multicenter, blind clinical trials still are required to evaluate the efficacy and cost-effectiveness of ESWT compared to sham control, other adjunctive treatments, and commonly used moisture-retentive dressings. In the future, ESWT may play an important role in wound care once evidence-based practice guidelines are developed.

Keywords: extracorporeal shock wave therapy, soft tissue wounds, wound healing, physical therapy, systematic review

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Management of soft tissue wounds remains a medical problem and a challenge, not only for internal medicine, dermatology, trauma, surgery, and angiology specialists, but also for physiotherapists in their daily rehabilitation practice.[1]

Chronic wounds are defined as wounds that have not proceeded toward healing in an orderly and timely (more than 3 months) fashion through tissue repair to reconstitute anatomic and functional integrity.[2] The most common types of chronic wounds include venous leg ulcers (VLU), diabetic foot ulcers (DFU), pressure ulcers (PU), and arterial insufficiency ulcers (AIU). Acute wounds involve sudden skin disturbance and are expected to progress through the phases of normal healing, resulting in wound closure. Acute wounds include burn wounds (BW), postsurgical wounds (SW), and post-traumatic wounds (TW).[1,3,4]

The primary aim in the treatment of these two pathologically distinct types of wounds is to promote tissue granulation and reepithelialization to achieve wound closure. Wound

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care modalities for chronic wounds include offloading (when the leg is involved), cleansing with sterile normal saline solution, surgical wound debridement, topical treatment (eg, antiseptic silver-containing dressing, silver sulfadiazine cream), antibiotic treatment, split-thickness skin grafting, and compression therapy — gold standards for the treatment of soft tissues that can be successfully supported and promoted using a variety of physical methods.[5-8]

Biophysical basics and clinical efficiency of extracorporeal shock wave therapy. Extracorporeal shock wave therapy (ESWT) is an adjunct medical procedure aimed to improve the skin condition of patients with chronic and acute soft tissue wounds. ESWT is defined as a sequence of biphasic, high-energy acoustic pulses that generate transient pressure disturbance and propagate rapidly in three-dimensional space; this therapy is associated with a sudden rise of pressure applied directly into tissues without any damaging effect.[9-11]

ESWT utilizes two basic types of generators: radial and focused. They differ in terms of shock wave propagation and the physical characteristics of the energy. Radial ESWT is produced by pneumatic devices located inside the generator that create linear pressure with low energy values. The energy is produced by the pressure wave, while compressed air accelerates the cartridge strikes at the top of the applicator.[12] The energy generated by the pressure wave is absorbed into the skin approximately 3 cm deep and spreads a wider beam to a larger target area (see Figure 1). Focused ESWT is generated by electromagnetic, electrohydraulic, and piezoelectric sources. Pressure pulses rise rapidly in range of 10–100 MPa and concentrate the acoustic energy beam with a penetration depth of approximately 12 cm (see Figure 2).[9,12,13]

Some authors describe a third type of defocused ESWT: an acoustic planar wave generated by electromagnetic and electrohydraulic devices. It is characterized by lower energy values delivered into the soft tissues and a superficial and quite large (3–5 cm^2) impact zone.[14,15] ESWT types have been differentiated on the basis of the level of energy applied at the focal point per one pulse during treatment session — ie, energy flux density (EFD), which is determined as low energy when <0.12 mJ/mm^2 and high energy when >0.12 mJ/mm^2.[13] Table 1 summarizes the basic characteristics of focused and radial ESWT.

Because of ESWT's direct microtraumatic effects, the possibility exists for bleeding, petechiae, hematoma and/or seroma formation, and pain. A randomized, placebo-controlled, single-blind, multicenter study[16] conducted among 272 patients with lateral epicondylitis to analyze potential side-effects after application of shock waves found transitory reddening of the skin (21.1%), pain (4.8%), and small hematomas (3.0%) most commonly occurred. Migraine was registered in four and syncope in three instances after ESWT. The possibility of migraine being triggered by ESWT and the risk of syncope should be taken into account in the future.

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Key Points

- Extracorporeal shock wave therapy (ESWT) is a physical, adjunctive wound treatment modality.
- The authors conducted a systematic literature review to evaluate the available evidence of clinical studies using ESWT in the management of acute and chronic wounds.
- Available literature, including seven randomized controlled clinical studies, suggests ESWT facilitates healing compared to control treatments studied.
- The authors conclude that additional, well-designed controlled clinical studies are needed to confirm the efficacy, evaluate the cost-effectiveness, and develop evidence-based practice guidelines for the use of ESWT in wound care.

Application of ESWT in general usage, including wound treatment, can be performed with local anesthesia (LA). However, two prospective, randomized, observer-blinded pilot trials[17,18] found ESWT is less effective when patients received LA. Regardless of these initial findings, the use of LA is justified, especially among patients who are unable to tolerate the procedure because of pain during the ESWT session.[19] Klonschinski el al's[20] randomized, clinical, nonblinded study that included 20 healthy participants (10 male, 10 female; mean age 27 years, range 17–36 years) investigated whether the biological effects of ESWT differ between application with and without LA. Focused ESWT (2,000 pulses) was performed in three single sessions with different EFD levels: 0.06 mJ/mm^2, 0.09 mJ/mm^2, or 0.18 mJ/mm^2. The results indicated that increasing EFD led to increasing pain (P <0.001). LA reduced ESWT-related pain (P <0.02) and prevented an ESWT-related drop in the pressure pain threshold (P <0.001).

Presently, ESWT is deemed an effective and safe method of treating a wide range of pathological, in particular musculoskeletal, conditions.[13,15,19] The list of indications for ESWT treatment is continuously evolving and adapting to different clinical fields, including chronic and acute soft tissue wounds.

Potential of ESWT mechanisms in animal wound healing. The potential of the therapeutic mechanisms and clinical efficacy and safety of ESWT in musculoskeletal disorders has been well investigated. Clinical investigations aimed at achieving a positive effect in accelerating wound healing are in the initial stages, but results are encouraging.

Animal model experiments[14] illustrate ESWT for soft tissue wound healing can promote positive molecular and immunochemical reactions focused on improving blood flow microcirculation, activating anti-inflammatory response, and enhancing the tissue regeneration process. In a randomized controlled study, Goertz et al[21] analyzed the biological

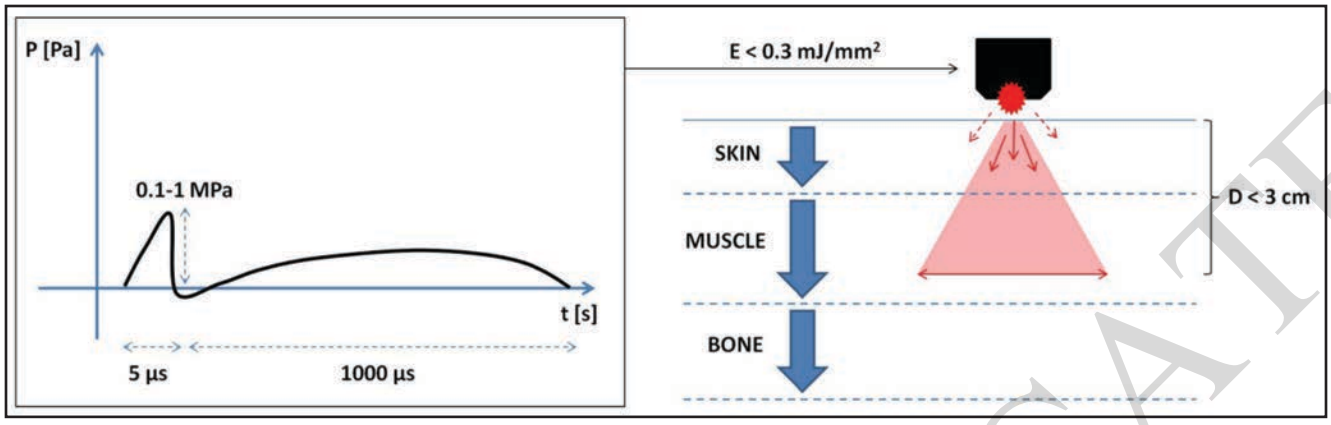

Figure 1. Schematic illustration of wave propagation with physical characteristics of radial extracorporeal shock wave therapy (ESWT).

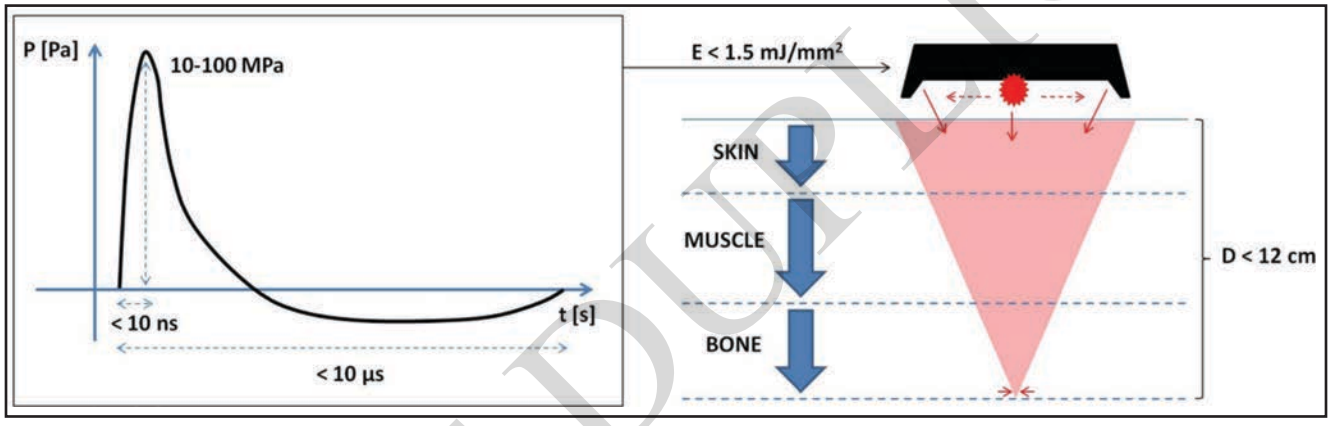

Figure 2. Schematic illustration of wave propagation with physical characteristics of focused ESWT.

mechanisms of ESWT in blood flow enhancement in mice with full-thickness burns (n = 51). The mice were randomized into five groups: burns but no ESWT (control group); low-energy ESWT after burn injury (0.04 mJ/mm^2); very low-energy shock waves after burn injury (0.015 mJ/mm^2); mice without burns exposed to low-energy ESWT; and mice without burns and with no ESWT application. ESWT was performed on days 1, 3, and 7 (500 pulses, 1 Hz). Groups receiving ESWT showed accelerated angiogenesis and an increased number of rolling and sticking leukocytes in the wound area ($P = 0.005$). The authors concluded shock waves have a positive effect on several parameters of wound healing after burns, especially with regard to angiogenesis and leukocyte behavior. Moreover, shock waves increased the number of rolling and sticking leukocytes as a part of an improved metabolism in the healing process. However, obtained results should be supported by clinical studies.

Results of a controlled experimental trial by Hayashi et al[22] determined that single low-energy ESWT (focused, 0.25 mJ/mm^2, 100 pulses, 4 Hz) in diabetic mice (n = 32) with skin wounds accelerated healing through the expression of endothelial nitric oxide synthase (eNOS) and generation of new vessels with the neovascularization process as an effect of vascular endothelial growth factor (VEGF) activation ($P < 0.05$). The authors concluded these results raised the possibility that eNOS may be involved in the beneficial effects of ESWT. In a controlled study, Kuo et al[23] investigated the effectiveness of ESWT in healing partial-thickness wounds in the presence of diabetes mellitus among male rats (n = 50) divided into five groups: nondiabetic control, diabetic control without ESWT, rats with one ESWT session on day 3 post-wounding, rats with two ESWT sessions on days 3 and 7, and rats with three ESWT sessions on days 3, 7, and 10. ESWT was performed using 800 pulses at 0.09 mJ/mm^2. The authors confirmed significant VEGF and eNOS expression and a determined promotion of proliferating cell nuclear antigen (PCNA) associated with increased revascularization and tissue regeneration in the ESWT-treated rats, especially in the diabetic control without ESWT and one ESWT session on day 3 post-wounding groups, as compared with the control ($P < 0.01$).

Moreover, several experimental model trials (total sample: 98 rats) suggest low-energy ESWT may promote cell proliferation, increase collagen deposition, enhance granulation

Table 1. Basic description of focused and radial extracorporeal shock wave therapy

Specification	fESWT	rESWT
Generator type (devices)	Electromagnetic, electrohydraulic, piezoelectric	Pneumatic
Shock wave subtype	Defocused (planar)	N/a
Energy flux density (level)	0.01 – 1.50 mJ/mm^2 (high)	0.01 – 0.50 mJ/mm^2 (low)
Peak pressure pulses (rise)	100 – 1000 bar (fast)	1 – 10 bar (slow)
Shock wave propagation (depth)	Concentrated (0 – 12 cm)	Diffused (0 – 5 cm)
Highest values (target area)	In focus zone (smaller)	At generator tip (larger)
Treatment sessions (effectiveness)	1 – 3 (higher)	3 – 5 (standard)
Overall effect (precision)	Cells and tissues (higher)	Tissues (lower)
Typical indications	Orthopedic , urologic, cardiologic, dermatologic (wounds)	Orthopedic (musculoskeletal)
Pain tolerance (local anesthesia)	Higher (justified)	Lower (n/a)
Risk of adverse effects	Higher	Lower
Administer level (price)	Easy and quick (higher)	Easy and quick (lower)
Size of device (loudness)	Bigger (lower)	Smaller (higher)

fESWT=focused extracorporeal shock wave therapy; rESWT=radial extracorporeal shock wave therapy.

tissue formation, and improve blood supply through neovascularization to the post-ischemic tissue zone of skin flaps.[24-27]

Another mechanism that may promote wound healing is anti-inflammatory action by a quick increase of the neuronal nitric oxide synthase (nNOS) activity and basal nitric oxide (NO) production. An experimental trial conducted by Ciampa et al[28] examined the effect of ESWT (focused, 500 to 1,500 pulses at 0.03 mJ/mm^2 and 0.11 mJ/mm^2) on the modulation of nNOS catalytic activity and NO production in rat glioma C6 cells taken as a cellular model. The authors reported ESWT rapidly increased NO production by enhancing catalytic activity of nNOS, with the maximum effect achieved by use of 500 pulses at 0.03 mJ/mm^2 (P <0.005).

It has been speculated that ESWT increased the levels of inflammatory cells — ie, pro-inflammatory cytokines and proteases. In their randomized, placebo-controlled trial, Davis et al[29] investigated the role of ESWT on the early pro-inflammatory response using a severe, full-thickness, highly inflammatory cutaneous burn wound in a murine model (n = 40). A single unfocused ESWT session was performed using 200 pulses at 0.01 mJ/mm^2 and 5 Hz. In this case, ESWT treatment significantly reduced the number of both infiltrating neutrophils and macrophages after injury. Furthermore, expression of proinflammatory cytokines, chemokines. and matrix metalloproteinases was globally suppressed (P <0.05).

In their controlled trial, Kuo et al[30] used a random pattern, extended dorsal skin flap rodent model that included male rats (n = 36) divided into three groups: control group without treatment (A), rats with one ESWT session immediately after surgery (B), and rats with two ESWT sessions immediately and the day after surgery (C). ESWT was performed using 500 pulses at 0.15 mJ/mm^2. Results indicated the necrotic area in the flaps in group B was significantly smaller compared with group A (P <0.01). The authors concluded the action mechanisms of ESWT involved modulation of oxygen radicals, attenuation of leukocyte infiltration, reduction of tissue apoptosis, and recruitment of skin fibroblasts, which results in increased flap tissue survival.

Some data suggest an ESWT source may be used to suppress the transforming growth factor-β1 (TGF-β1) and increase the production of tissue granulation. In their controlled experiment among 14 healthy horses with surgically

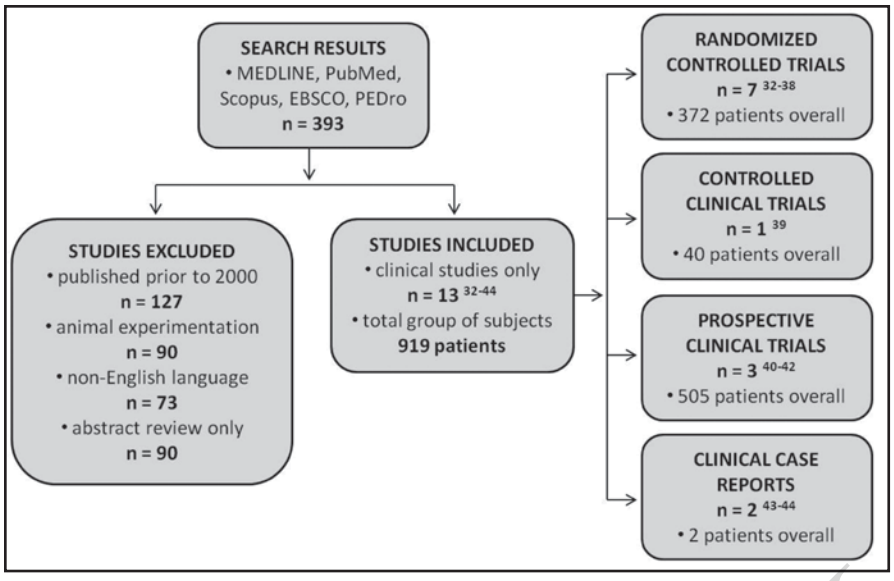

Figure 3. Literature search results.

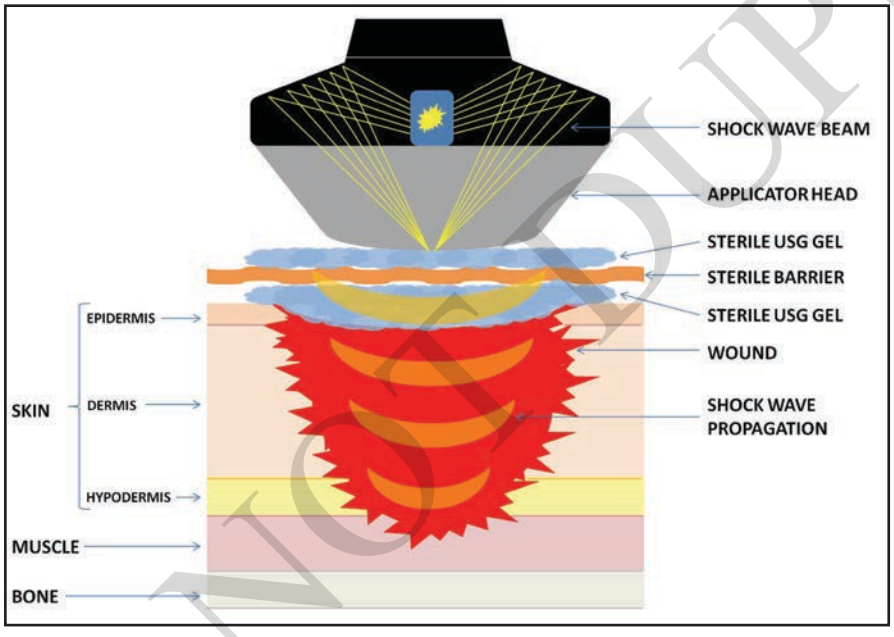

Figure 4. Diagram of typical methodology of extracorporeal shock wave therapy application in wound management.

created wounds, Link et al[31] found ESWT treatment was associated with reduced TGF-β1 expression during the entire study period compared to control wounds. Moreover, insulin-like growth factor-1 (IGF-1) expression was significantly increased for ESWT-treated and untreated wounds at 28 days following wound creation, compared with findings on days 7, 14, 21, and 35 (P <0.05).

Inspired by the lack of relevant literature regarding a clear and well-prepared algorithm, especially on wound therapy using shock waves, a systematic review of the literature was conducted to evaluate evidence of ESWT effectiveness in humans.

Methods

Computer research of the following databases was performed: MEDLINE, PubMed, Scopus, EBSCOhost, and PEDro. The main keywords used for selection purposes were: *wound healing, venous leg ulcer, diabetic foot ulcer, pressure ulcer, arterial insufficiency ulcer, burn wound, post-traumatic wound, postsurgical wound, chronic wound, extracorporeal shock wave therapy, shock wave treatment, focused shock wave* (fESWT), *radial shock wave* (rESWT), and *defocused shock wave* (dESWT). Only articles published between 2000 and 2013 that involved clinical trials on human subjects, written in English, and with full-version available were included. Articles published before 2000, based on animal experiments, written in languages other than English, and versions with only abstracts were excluded. After completing the first stage of selection based on the main keywords, the abstracts of identified articles were assessed according to the eligibility criteria.

For the purpose of evaluating study methodological quality and validity, all included publications were divided into two groups: the first consisted of well-designed randomized trials and the second of other clinical trials.

All articles were assessed with regard to study methodology (types of wounds, patient characteristics, type of treatment, parameters of ESWT), the level of evidence (methods of randomization, patient allocation, blind intervention, follow-up analysis), and the results of treatment with ESWT (initial wound size, duration of wound, results of ESWT sessions, side effects after ESWT).

The findings were coordinated by an European Pressure Advisory Panel (EPUAP) trustee. The research team was composed of physical therapists, a nurse, a dermatologist, and a vascular surgeon experienced in wound healing treatment. The risk of bias was independently assessed with accordance to the guidelines for systematic reviews presented by Cochrane Collaboration Group.

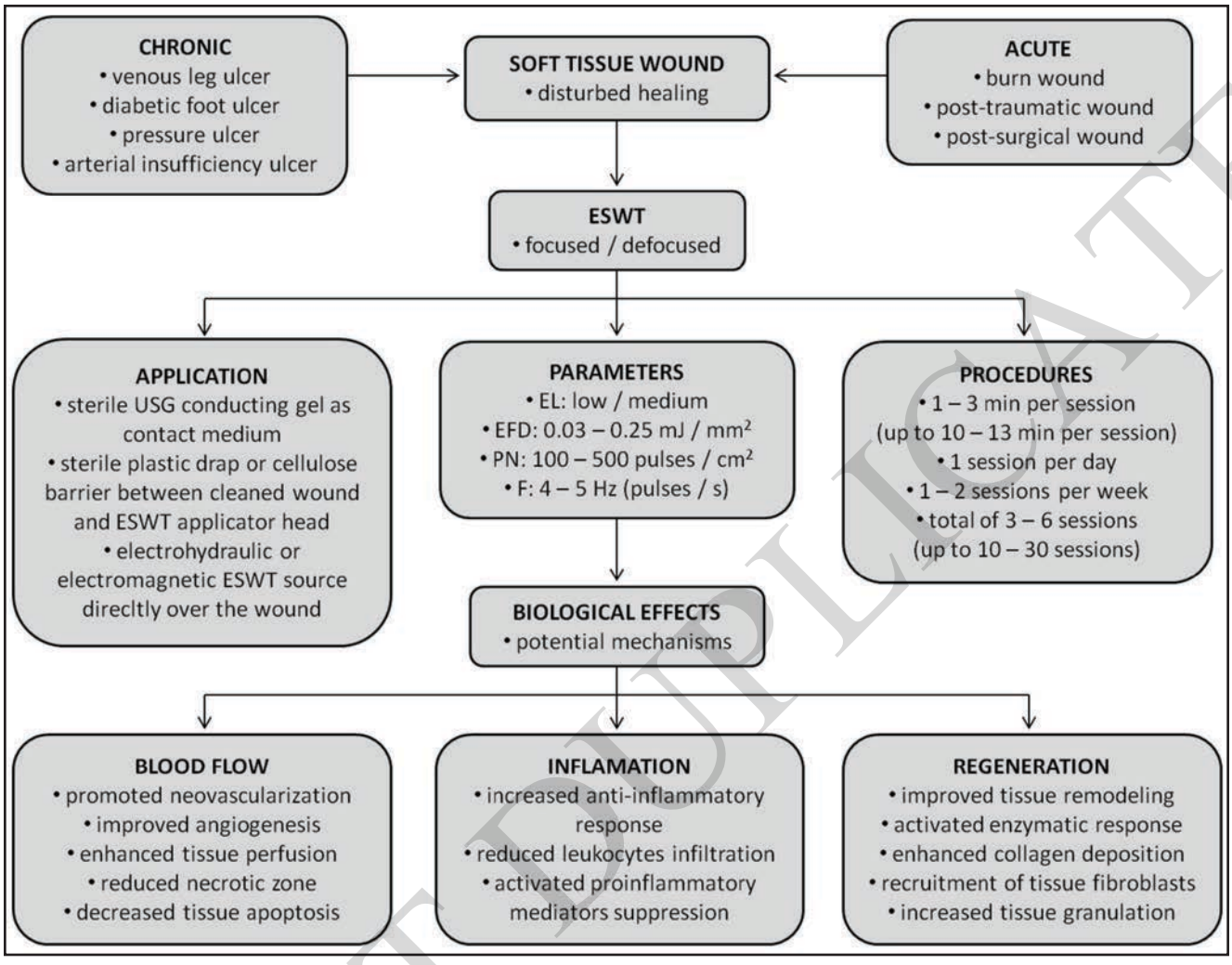

Figure 5. Example chart of extracorporeal shock wave therapy in wound healing.

Results

A total of 393 articles were found. Articles published before 2000 (n = 127), based on animal experiments (n = 90), written in languages other than English (n = 73), and abstract not available (n = 90) were excluded. No systematic reviews and meta-analyses were found. Thirteen clinical trials[32-44] were accepted for analysis and involved a total population of 919 patients. These studies included seven randomized controlled trials (RCTs),[32-38] one clinical controlled trial (CCT),[39] three prospective clinical trials (PCTs),[40-42] and two clinical case reports (CCRs)[43,44] (see Figure 3).

ESWT efficacy was evaluated in patients with chronic VLU,[39,40,42-44] DFU,[33,34,37,39] PU,[36,40,42] AIU,[40,44] and acute BW,[38,40-42] TW,[39,40,42] and SW in patients with coronary artery bypass grafting (CABG)[32] or split-thickness skin grafting (STSG).[35] The authors of the vast majority of analyzed studies designed them with control groups that received standard wound care (SWC) alone at a study facility,[32,34,35,38,39] consisting of nonocclusive surgical dressings and antibiotic treatment,[32] application of topical nonadherent silicone mesh and antiseptic gel,[35] and wound debridement and antiseptic silver dressing.[34,38,39] The other control groups received SWC including offloading the affected leg, wound cleansing with sterile normal saline solution, and application of silver sulfadiazine cream combined with hyperbaric oxygen therapy (HBOT)[33,37] or received inactive sham ESWT.[36] In all the studies, participants received ESWT plus SWC procedures supported by the administration of additional antibiotics at the discretion of the treating physician. In all studies, the pre-ESWT wound dressing regimen remained unchanged and was continued after each treatment session.[32-44]

The Cochrane-based methodological quality[45] of the reviewed, well-designed RCTs ranged between 8 and 15 points (11.1 ± 3.13; median 10.0) out of a total of 16 points (the more points, the higher quality of the study. See Table 2). The studies received best scores in having similar groups at baseline, regarding the most prognostic indicators (C),[32-38] describing dropout rate and its acceptability (I),[32-38] having

comparable timing of outcome assessment in all groups (J),[32-38] and including only one type of wound (M).[32-38] In almost all studies, the outcome assessor was blinded to the intervention (F),[32,33,35-38] and the duration of the study for at least 4 (O)[33-38] or 10 (N)[33-36,38] weeks was presented in seven and six reviewed studies, respectively. In six studies, the described treatment methods in the experimental and control groups were basically correspondent, with no co-interventions (G).[33-38]

On the other hand, the worst scores included lack of blinding of a patient to the intervention (D)[32-34,37] and care provider (E),[32-38] failure to include an intention-to-treat analysis (K),[32-34,37] and failure to achieve complete closure of all wounds (P).[32-34,36,37] Only three double-blind studies featured designs where patients (D)[35,36,38] and outcome assessors (F)[35,36,38] were blinded to the intervention.

In three of the studies, methodological issues concerning adequate methods of randomization (A)[33,34] and concealing the treatment allocation (B)[32-34] remained unclear. In two studied experiments, compliance to the intervention was acceptable in all groups (H).[33,34] In most studies, ESWT was applied to at least 10 participants (L).[32-35,37,38] Wounds completely closed in only two of the studies (P).[35,38]

Overall, four of the studies in this review were awarded high scores of at least 10 points[35,38] from the listed methodological quality criteria; three were of low quality, scoring 8[32,34] or 9 points.[33] Three of the high-scoring studies addressed SW, DFU, and BW, reporting complete epithelialization that led to wound closure after 9.6[38] or 13.9 days[35] of ESWT treatment. In the lowest scoring of the four, which discussed PU, the authors observed a healed area in 67.45% of the study participants after a total of 6 to 8 weeks of ESWT treatment.[36]

Two of the low-quality studies featured DFU; their results showed a range of 31.0% to 53.5% completely healed wounds in the ESWT groups, compared with 22.0% to 33.3% in the controls.[33,34] In the low-quality study that addressed SW, the authors noted an improvement of wound healing, indicated by better postoperative wound infection, including additional treatment, presence of serous discharge, erythema, purulent exudates, separation of deep tissue, isolation of bacteria, and duration of inpatient stay (ASEPSIS) scores and decreased necessity for antibiotic treatment.[32]

Evidence from well-designed RCTs (see Table 3 and Table 4). In Dumfarth et al's[32] controlled study, 100 patients were randomly assigned to prophylactic low-energy ESWT (n = 50) or control without ESWT (n = 50). All consecutive participants underwent CABG surgery and were receiving intraoperative antibiotic treatment. A single session of ESWT was performed at the site of vein harvesting immediately after the wound was closed under sterile conditions using absorbable subcutaneous sutures and staples. ESWT was generated by an electromagnetic wave focusing source using an EFD at 0.1 mJ/mm^2 at a frequency of 5 pulses per second (5 Hz), and 25 pulses per cm of wound length. Total ESWT treatment time was 10 minutes. Ultrasonic transmission gel (USG) was used as contact medium. The primary endpoint was to assess wound healing quantified by score points including ASEPSIS. Secondary endpoints were the need for surgical revisions of the vein graft harvesting site and need for antibiotic treatment of wound healing disturbances. Researchers noticed lower ASEPSIS scores, indicative of improved wound healing, in patients receiving ESWT (4.4 ± 5.3) compared with control group patients (11.6 ± 8.3) (P = 0.0001). Moreover, ESWT was characterized by a significantly lower incidence of wound healing disorders, with the necessity for antibiotic intervention of 4%, compared with control of 22% (P = 0.015). No significant differences in episodes of surgical revision of the leg wound and no adverse events were observed.

In a randomized, single-blind, controlled study, Wang et al[33] assessed ESWT efficacy in treating chronic DFU. Seventy-two (72) patients were randomized to receive either ESWT (n = 34 out of 36 with DFU) or HBOT (control; n = 36 DFU). ESWT was performed without anesthesia, and the DFU was covered with sterile cellulose barrier. USG sterile gel was applied to the area of skin in contact with the ESWT generator head. Focused ESWT was provided every 2 weeks for a total of three treatments over 6 weeks using an electrohydraulic shock wave device with an EFD at 0.11 mJ/mm^2 and 300 + 100 pulses/cm^2 of wound; the frequency was not documented. HBOT was performed once a day, five times a week, for a total of 20 treatments. All patients received the same local wound care regimen that included wound cleansing and silver sulfadiazine cream. At the end of the study (3 months), ESWT-treated wounds healed completely in 31% of cases, improved in 58%, and were unchanged in 11%, compared to 22% completely healed, 50% improved, and 28% unchanged after HBOT (P = 0.001). Significant improvement was noted in the local blood flow perfusion (P = 0.04) of persons in the ESWT group, compared with the results of the HBOT group (P = 0.30). Bacteriostatic effect was documented in both ESWT and HBOT patients. Histomorphological examination of the biopsy specimens showed lower cell concentration and less cell proliferation and activity after HBOT (P = 0.42) as compared to ESWT (P = 0.002). Immunohistochemical analysis showed a significant increase in eNOS (P <0.001), VEGF (P <0.001), and PCNA (P = 0.005), as well as a lower expression of transference-mediated digoxigen-in-deoxy-uridine-triphosphate nick end-labeling (TUNEL) (P <0.001) in the ESWT than in the HBOT group (P >0.05). Authors did not observe any adverse events and complications following ESWT.

In a prospective, randomized, controlled trial, Moretti et al[34] studied 30 persons with neuropathic DFU; 15 were treated with SWC and ESWT and 15 received SWC alone. No local anesthetic was used during ESWT treatment, which was generated by a focused electromagnetic ESWT applicator using an EFD at 0.03 mJ/mm^2 and 100 pulses/cm^2 of wound; the frequency was not described. ESWT protocol consisted of one session every 72 hours, resulting in a total of three treatments in 9 days. Each ESWT session

lasted <1 to 2 minutes. Researchers noted complete DFU closure in 53.33% of the ESWT-treated patients, compared with 33.33% patients in the control group; the healing time was also shorter for ESWT patients (60.8 ± 4.7 days) compared to controls (82.2 ± 4.7 days) (P <0.001). Significant improvement of the re-epithelialization index was observed among the ESWT group (2.97 ± 0.34 mm^2/die) and control patients (1.30 ± 0.26 mm^2/die) (P <0.001). Some adverse effects (eg, symptoms of local infection) were noted, and oral antibiotics were prescribed. Two patients, one in each group, developed complications that resolved within 5 to 7 days, and the patients were allowed to remain in the study.

In a randomized, prospective, double-blind trial, Ottomann et al[35] enrolled 28 patients with acute traumatic wounds and burns at a minimum size of 200 cm^2 that required STSG. All participants were blinded and randomized to either a group receiving (n = 13) or not receiving ESWT (n = 15). In both groups, graft donor sites were treated with SWC. A single session of ESWT was performed immediately after STSG harvest and delivered intraoperatively on the donor site of the anesthetized patient. ESWT was generated by a defocused electrohydraulic source using an EFD at 0.1 mJ/mm^2 and 100 pulses/cm^2 of donor site surface area; the frequency was not documented. The total average ESWT time was 13 minutes. Sterile USG-conducting gel applied onto a sterile plastic drape was used as a contact medium. The primary outcome was time to complete donor site healing, defined as >95% reepithelialization. Average hospitalization time was 15 days, with a follow-up period of 12 weeks after hospital discharge. All donor sites healed, but significantly faster reepithelialization was documented in the ESWT (13.9 ± 2.0 days) than in the control group (16.7 ± 2.0 days) (P = 0.0001). No post-ESWT related complications were noted in the control group.

Larking et al[36] conducted a double-blind, randomized, cross-over study, with a population of nine severely disabled patients with chronic PU. All study participants were randomly allocated by a blinded assessor to active or placebo ESWT. Three weeks of observation with weekly measurements was conducted before the start of the interventions. After 6 weeks, including a 2-week washout phase, the ESWT group and sham ESWT group were swapped. In both groups, SWC was continued. ESWT treatment was generated by a defocused electrohydraulic system using an EFD at 0.1 mJ/mm^2 and 200 + 100 pulses/cm^2 of PU area at a frequency of 5 Hz. ESWT protocol for both phases of active and sham ESWT consisted of one session every week, resulting in a total of four treatments during 4 weeks. Sterile USG gel was applied to the clean wound and the surface of the ESWT applicator head, and a sterile drape was placed on the wound site. Results indicated improved healing in all patients with chronic PU without any significant differences between groups, regardless of commencing the study with active (67.45% average healed area) or sham ESWT (64.25% average healed area). A statistically significant difference was observed between the period of PU improvement following the start of ESWT after 8 weeks in the ESWT-first study group and after 6 weeks in the sham-first study group (P <0.05). Authors described an enlargement of three PU during ESWT phase, two of which were previously classified for surgical debridement that was not necessary after ESWT. Authors hypothesized the ESWT seemed to heal wounds more rapidly by causing the tissue with poor viability to break down.

In a prospective, open-label, randomized, single-blinded study, Wang et al[37] randomized 77 patients with chronic DFUs into an ESWT (n = 39 out of 44 DFU) and an HBO treatment group (n = 38 out of 40 DFU). ESWT was performed without anesthesia, and the DFUs were covered with a sterile cellulose barrier. USG sterile gel was applied to the area of skin in contact with the ESWT generator head. ESWT was generated by a defocused electromagnetic applicator using an EFD at 0.23 mJ/mm^2 and 500 pulses/cm^2 of wound, with the frequency at 4 pulses per second (4 Hz). ESWT sessions were performed twice per week for a total of six treatments over 3 weeks. In the control group, HBOT was performed once a day, five sessions a week, resulting in a total of 40 treatments. All patients in both groups received basically the same local wound care protocol, which included wound cleansing and silver sulfadiazine cream application, with a possibility of administering antibiotic treatment. After 3 weeks, 57% of wounds in the ESWT and 25% of wounds in the HBOT groups were completely healed (P = 0.003). Wounds in 32% of ESWT and 15% of HBOT group were improved (P = 0.071). No significant differences in improvement of local blood flow perfusion were noted between groups (P = 0.245), but the change from baseline in the ESWT group was significant (P = 0.002). Histopathological examination of biopsy samples showed lower cell apoptosis and higher cell proliferation, concentration, and activity in the ESWT group, but no statistics were reported. No systemic or local neurovascular adverse events were noted.

A randomized, controlled, double-blind clinical study was conducted by Ottomann et al[38] among 44 burn patients with superficial second-degree BWs. The study participants were randomized to ESWT (n = 22) or no ESWT intervention (n = 22). All patients were blinded to treatment allocation and analyzed as intent-to-treat. Patient median total body surface area (TBSA) involved by thermal injury was 3% (range 1%–8%) in the ESWT and 4% (range 1%–50%) in the control group. Participants in the ESWT group were significantly older (average age 52.2 ± 16.6 years) than participants in the control group (average age 37.5 ± 13.3 years) (P = 0.002). A single session of ESWT was performed with a defocused electrohydraulic device using an EFD at 0.1 mJ/mm^2 and 100 pulses/cm^2 of BW area at a frequency of 5 Hz. Sterile USG gel was applied onto a sterile plastic drape placed over the wound, which also was covered with USG gel. The primary endpoint — reepithelialization >95% — was assessed by an

Table 2. Randomized, controlled clinical study criteria and assessment results[45]

		Dumfarth et al[32]	Wang et al[33]	Moretti et al[34]	Ottomann et al[35]	Larking et al[36]	Wang et al[37]	Ottomann et al[38]
A	Was the method of randomization adequate?	Yes	Unclear	Unclear	Yes	Yes	Yes	Yes
B	Was the treatment allocation concealed?	Unclear	Unclear	Unclear	Yes	Yes	No	Yes
C	Were the groups similar at the baseline regarding most prognostic indicators?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
D	Was the patient blinded to the intervention?	No	No	No	Yes	Yes	No	Yes
E	Was the care provider blinded to the intervention?	No	No	No	No	No	No	No
F	Was the outcome assessor blinded to the intervention?	Yes	Yes	No	Yes	Yes	Yes	Yes
G	Were co-interventions avoided or comparable?	No	Yes	Yes	Yes	Yes	Yes	Yes
H	Was the compliance acceptable in all groups?	Yes	No	No	Yes	Yes	Yes	Yes
I	Was the dropout rate described and acceptable?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
J	Was the timing of the outcome assessement in all groups similar?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
K	Did the analysis include an intention-to-treat analysis?	No	No	No	Yes	Yes	No	Yes
L	Were there at least 10 participants?	Yes	Yes	Yes	Yes	No	Yes	Yes
M	Was the only one type of wound?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
N	Was the duration of study at least 10 weeks?	No	Yes	Yes	Yes	Yes	No	Yes
O	Was the duration of study at least 4 weeks?	No	Yes	Yes	Yes	Yes	Yes	Yes
P	Was complete closure of all wounds achieved?	No	No	No	Yes	No	No	Yes
Total score		8 points	9 points	8 points	15 points	13 points	10 points	15 points

independent, blinded observer. All BWs were healed after an average 11.0 ± 2.4 days; 9.6 ± 1.7 days in the ESWT and 12.5 ± 2.2 days in the control group (P <0.0005). Infections were noted in 9% of ESWT and 14% of control group patients.

Evidence obtained from other clinical studies (see Table 5 and Table 6). Saggini et al[39] conducted a controlled clinical study among 40 patients with VLUs, DFUs, and TW. All study participants were allocated to either a SWC and ESWT group (n = 30 out of 32 wounds) or a SWC only control group (n = 10 out of 10 wounds). No general or local anesthesia or other injections were used during the ESWT treatment, which was performed with a focused electrohydraulic system using an EFD at 0.037 mJ/mm^2 and 100 pulses/cm^2 of each wound area at a frequency of 4 Hz. The ESWT protocol consisted of one session per 2 weeks, resulting in a total of four to 10 sessions. A single-layer sterile gauze was placed on the USG gel, which was applied to the wound surface and the ESWT applicator head. Researchers recorded the following results for the ESWT sessions and control procedures, respectively: complete wound closure 53.3% and 10.0%, reduced necrotic fibrin 30.7% and 12.5%, and post-treatment wound area decreased from 10.41 cm^2 to 2.03 cm^2 (P <0.01). Additionally, the authors determined greater improvement in granulation tissue among 30.7% of ESWT recipients compared to worsening among 7.5% of patients from the control group (P <0.01). Most improvements were noted following the first four to six ESWT sessions. No complications or side effects such as microtraumatic effect, bleeding, hematomas, sarcomas, or painful sensations were documented after ESWT sessions.

Schaden et al[40] prospectively enrolled 208 patients with etiologically different nonhealing wounds: SW (n = 82), TW (n = 67), VLU (n = 14), PU (n = 7), AIU (n = 6), and BW (n = 7). ESWT was applied via defocused electrohydraulic generator using an average dosage of EFD at 0.01 mJ/mm^2 and 100 pulses/cm^2 depending on the wound area at a frequency of 5 Hz. An ESWT session was performed once every 2 weeks, resulting in a total of one to 10 treatment sessions. A plastic drape covered with sterile USG coupling gel was used after necrotic tissue was removed. ESWT was the primary wound therapy performed with adjunctive SWC management. Of the 176 patients who completed the study, 156 (88.6%) had completely healed wounds. Mean period of ESWT stimulation needed for complete epithelialization was 43.5 days. Complete wound closure was significantly associated with the wound area in 81.0% and 61.8% of the patients with ≤10 cm^2 and >10 cm^2 wound area, respectively (P = 0.005). Also,

Table 3. Extracorporeal shock wave therapy methods used in randomized, controlled trials

	Dumfartht al[32]	Wang et al[33]	Moretti et al[34]	Ottomann et al[35]	Larking et al[36]	Wang et al[37]	Ottomann et al[38]
Type of wound	SW (CABG)	DFU	DFU	SW (STSG)	PU	DFU	BW
Total number of patients	100 patients	72 patients	30 patients	28 patients	9 patients	77 patients	44 patients
Number of groups receiving ESWT	1 group	1 group	1 group	1 group	2 group	1 group	1 group
Number of patients in the ESWT group	50 patients	36 patients	15 patients	13 patients	9 patients	39 patients	22 patients
Gender of patients in the ESWT group	12 female 38 male	Not specified	6 female 9 male	3 female 10 male	5 female 4 male	Not specified	8 female 14 male
Average patient age in the ESWT group	68.7 years	58.6 years	56.2 years	52.1 years	63.3 years	60.5 years	52.5 years
Treatment in the ESWT group	ESWT + SWC	ESWT + SWC	ESWT + SWC	ESWT + SWC	ESWT / sham ESWT	ESWT + SWC	ESWT + SWC
Treatment in the control group	SWC	HBO + SWC	SWC	SWC	Sham ESWT / ESWT	HBO + SWC	SWC
Type of ESWT source	Electromagnetic	Electrohydraulic	Electromagnetic	Electrohydraulic	Electrohydraulic	Electromagnetic	Electrohydraulic
Type of ESWT generator head	Focused	Focused	Focused	Defocused	Defocused	Defocused	Defocused
Specifications of ESWT	0.1 mj/mm^2, 5Hz	0.11 mj/mm^2, frequency unclear	0.03 mj/mm^2, frequency unclear	0.1 mj/mm^2, frequency unclear	0.1 mj/mm^2, 5 Hz	0.23 mj/mm^2, 4 Hz	0.1 mj/mm^2, 5 Hz
Number of ESWT pulses	25 pulses/cm	300+100 pulses/cm^2	100 pulses/cm^2	100 pulses/cm^2	200+100 pulses/cm^2	500 pulses/cm^2	100 pulses/cm^2
Period of ESWT treatment	Single application intraoperative	Once / 2 weeks Total of 3 treatments	Once / 3 days Total of 3 treatments	Single application intraoperative	Once / 1 week Total of 4 treatments	Twice / 1 week Total of 6 treatments	Single application

SW=postsurgical wound; CABG=coronary artery bypass grafting; STSG=split-thickness skin grafting; DFU=diabetic foot ulcer; PU=pressure ulcer; BW=burn wound; ESWT=extracorporeal shock wave therapy; SWC=standard wound care; HBO=hyperbaric oxygen therapy

complete tissue epithelialization was significantly associated with wound duration in 83.0% and 57.1% of completely healed participants with ≤1 month and >1 month duration, respectively (P <0.001). Wound epithelialization improved in 81.0% of acute and 56.3% of chronic wounds (P = 0.001). Researchers did not report any adverse events following ESWT.

In a clinical, observational, prospective pilot study by Arno et al[41] involving patients with acute BW <5% TBSA (N = 15), participants were provided ESWT on the third and fifth post-burn accident day. ESWT was performed with a defocused electrohydraulic machine using an EFD at 0.15 mJ/mm^2 and 500 pulses/cm^2 of BW area, with unspecified frequency values. ESWT sessions were provided twice a week, resulting in a total of two treatment sessions in sterile conditions, without anesthesia or antibiotics. Some potential adverse events — eg, bleeding, hematomas, petechiae, and painful sensations — were documented. Researchers documented 80% of patients completely healed after 3 weeks of ESWT treatment, but 15% required surgical debridement and grafting and 5% displayed hypertrophic scarring after burn healing. Additionally, blood perfusion levels in laser Doppler imaging were enhanced after a single session of ESWT (P value not reported). Authors did not describe any side effects or adverse events, and the patients tolerated ESWT well.

Wolf et al[42] performed an open, prospective clinical study among 282 patients with various chronic soft tissue wounds who received ESWT stimulation in conjunction with SWC procedures. Participants included 93 SW (36.1%), 83 TW (33.3%), 38 VLU (14.7%), 13 DFU (5%), 11 AIU (4.3%), nine PU (3.5%), and eight BW (3.1%) patients. ESWT was performed with a defocused electrohydraulic device using an EFD at 0.1 mJ/mm^2 and median number of 167 pulses/cm^2 at a frequency of 5 Hz. ESWT sessions were performed one to two times every 2 weeks, resulting in a total of <10 treatment sessions. To improve skin contact, the USG sterile gel was placed on the wound surface and covered with a surgical drape. SWC was systematically continued in all patients after each ESWT session. Authors reported 24 participants lost to follow-up. The majority of patients (74.03%) demonstrated complete wound closure after SWC plus ESWT after a median time of 31.8 months and two treatment sessions. No side effects or tissue damage following ESWT were documented.

Fioramonti et al,[43] who published the first clinical case report, saw positive results of ESWT in the treatment of a VLU in a 63-year-old patient with chronic venous insufficiency (CVI) and two ulcers on the right leg (3 cm^2 on the external malleolar region and 8 cm^2 on the medial pretibial region)

Table 4. Summary of randomized, controlled clinical studies

	Level of evidence	Type of wound	Groups	Number of patients	Duration of wound	Initial size of wound	Results of ESWT intervention	Adverse events after ESWT
Dumfarth et al[32]	RCT SB	SW (CABG)	ESWT + SWC SWC	50 50	N/a	39.0 cm 37.0 cm	4.4 in ASEPSIS score indicating improved wound healing (11.6 score in control); 4% patients antibiotics treatment necessity (22% patients in control)	Not observed
Wang et al[33]	RCT SB	DFU	ESWT + SWC HBO + SWC	34 36	22.7 mo 19.0 mo	12.2 cm^2 10.5 cm^2	31% completly healed (22% in control); 58% improved (50% in control); 11% unchanged (28% % in control); 11% improved blood flow perfusion (8% improved in control)	Not reported
Moretti et al[34]	RTC	DFU	ESWT + SWC SWC	15 15	> 6 mo > 6 mo	2.97 cm^2 2.45 cm^2	53.55% patients complete wound closure (33.33% in control); 2.97 mm^2/die in re-epithelization index (1.30 mm^2/die in control)	Local signs of infection of 1 patient
Ottomann et al[35]	RCT DB	SW (STSG)	ESWT + SWC SWC	13 15	N/a	Min 200 cm^2 Min 200 cm^2	13.9 days to complete epithelialization; (16.7 days in control)	Not observed
Larking et al[36]	RCT DB CO	PU	ESWT first sham ESWT first	4 5	13.5 mo 13.5 mo	1.79 cm^2 1.23 cm^2	67.45% healed area (64.25% in control)	Enlarged of 3 ulcers with ischaemic edges
Wang et al[37]	RCT SB	DFU	ESWT + SWC HBO + SWC	39 38	6 mo 6 mo	4.0 cm^2 7.0 cm^2	57% completly healed (25% in control); 32% improved (15% in control); 11% unchanged (60% % in control); 13% improved blood flow perfusion (9% worsened in control)	Not observed
Ottomann et al[38]	RCT DB	BW	ESWT + SWC SWC	22 22	6.5 h 6.8 h	3.0% TBSA 4.0% TBSA	9.6 days to complete epithelialization (12.5 days in control); 100% patients healed completely prior 13 days (68% patients in control)	Infections in 9% of ESWT and 14% of control

RCT=randomized controlled trial; SB=single-blind; DB=double-blind; SW-postsurgical wound; CABG=coronary artery bypass grafting; STSG-split-thickness skin grafting; DFU=diabetic foot ulcer; PU=pressure ulcer; BW=burn wound; ESWT=extracorporeal shock wave therapy; SWC=standard wound care; HBO=hyperbaric oxygen therapy

and one on the left leg (6 cm^2 on the medial pretibial region). Only the VLUs on the right leg were treated with ESWT; the left leg was designated the control and managed with SWC. ESWT was performed with a focused electrohydraulic source using an EFD at 0.037 mJ/mm^2 and median number of 100 pulses/cm^2 at a frequency of 4 Hz. ESWT sessions were provided once a week, amounting to a total of six treatment sessions. Complete VLU healing of the right extremity wound was reported after six ESWT treatment sessions and compared with a 6-week period of SWC on the left VLU, where healing was still incomplete. Researchers did not document any complications and adverse events after ESWT sessions.

The case report by Stieger et al[44] evaluated the efficiency of ESWT in a case of a 56-year-old patient with secondary lymphedema, class III morbid obesity, and a VLU of at least 6-years' duration characterized by a severely fibrotic, partially fibrin-coated ulcer of 150 cm^2 total wound area exhibiting minimal granulation, severe perifocal reddening, and maceration that extended from the pretibial part of the right lower leg to the lateral calf. Various treatments had been provided, including surgical procedures, compression therapy, negative pressure therapy, and wound dressings. Sterile USG conducting gel was applied to a cleaned wound and covered with polyurethane film. To improve ESWT transmission, USG gel was applied on that film again. ESWT was performed with a defocused electromagnetic generator using an EFD at 0.25 mJ/mm^2 and 10 pulses/cm^2 at a frequency of 4 Hz to a total area of 200 cm^2 (150 cm^2 of VLU area plus the wound margins). ESWT sessions were performed once a week as an adjuvant therapy; SWC procedures remained unchanged for the duration. After five ESWT sessions, wound granulation and reepithelialization improved, and complete wound closure was observed after a total of 30 ESWT sessions. No adverse events or pain were reported during ESWT.

Discussion

The purpose of this study was to evaluate evidence of ESWT effectiveness in humans. Results of the systematic literature review suggest there is substantial published evidence documenting that ESWT application is safe and effective for the treatment of different etiologically soft tissue wounds.

In the analyzed studies, ESWT was used to facilitate healing of chronic DFU,[33,34,37,39] PU,[36,40,42] VLU,[39,40,42-44] and AIU wounds,[40,42] as well as acute wounds involving BW,[38,40-42] TW,[39,40,42] and SW resulting from CABG[32] or STSG procedures.[35] ESWT applied to soft tissue wounds produced a wide

Table 5. Extracorporeal shock wave therapy methods used in non-randomized clinical studies

	Saggini et al[39]	Schaden et al[40]	Arnó et al[41]	Wolf et al[42]	Fioramonti et al[43]	Stieger et al[44]
Type of wound	VLU, TW, DFU	DHW, TW, VLU, PU, AIU, BW	BW	SW, TW, VLU, PU, AIU, BW	VLU	VLU
Total number of patients	40 patients	208 patients	15 patients	258 patients	1 patient	1 patient
Number of groups receiving ESWT	1 group	1 group	1 group	1 group	N/a	N/a
Number of patients in the ESWT group	30 patients	208 patients	15 patients	258 patients	1 patient	1 patient
Gender of patients in the ESWT group	12 female 18 male	99 female 109 male	5 female 10 male	142 female 140 male	1 female	1 female
Average patient age in the ESWT group	58.5 years	61.0 years	35.7 years	63.5 years	63.0 years	56.0 years
Treatment in the ESWT group	ESWT + SWC	ESWT + SWC	ESWT + SWC	ESWT + SWC	ESWT	ESWT + SWC
Treatment in the control group	SWC	N/a	N/a	N/a	SWC	N/a
Type of ESWT source	Electrohydraulic	Electrohydraulic	Electrohydraulic	Electrohydraulic	Electrohydraulic	Electromagnetic
Type of ESWT generator head	Docused	Defocused	Defocused	Defocused	Focused	Defocused
Specifications of ESWT	0.037 mJ/mm^2, 4 Hz	0.1 mJ/mm^2, 5 Hz	0.15 mJ/mm^2 frequency unclear	0.1 mJ/mm^2, 5Hz	0.037 mJ/mm^2, 4 Hz	0.25 mJ/mm^2, 4 Hz
Number of ESWT pulses	100 pulses/cm^2	100 pulses/cm^2	500 pulses/cm^2	167 pulses/cm^2	100 pulses/cm^2	10 pulses/cm^2
Period of ESWT treatment	Once / 2 weeks Total of 4-10 treatments	Once / 2 weeks Total of 1-10 treatments	Twice / 1 week Total of 2 treatments	1 – 2 / 2 weeks Total of < 10 treatments	Once / 1 week Total of 6 treatments	Once / 1 week Total of 30 treatments

VLU=venous leg ulcer; TW=post-traumatic wound; DFU=diabetic foot ulcer; DHW=disturbed healing wound; PU=pressure ulcer; AIU=arterial insufficiency ulcer; BW=burn wound; SW=postsurgical wound; ESWT=extracorporeal shock wave therapy; SWC=standard wound care

variety of positive results, including complete wound closure and reepithelialization,[33-35,36-44] improvement of blood flow perfusion,[33,37,41] enhancement of tissue granulation, reduction of necrotic fibrin tissue,[39,44] shortened period of wound treatment,[35,38,43] and decreased necessity for antibiotic treatment.[32]

Better results were reported for patients who received additional ESWT treatment sessions in contrast to SWC alone,[32,34,35,38,39,43] HBOT concomitant to adjunctive SWC,[33,37] or sham ESWT sessions.[38] Most studies reported no or few adverse events or complications.[32,33,35,37-44] Adverse events and side effects documented following ESWT included signs of ulcer infections[34,38] and enlarged wounds with ischemic edges.[36]

In most of the studies reviewed, ESWT treatment sessions were performed without hospitalization and without anesthesia.[33,37,39,41,43] Methodological similarities included ensuring sterile conditions and use of a sterile ultrasonic gel as contact medium and the use of a sterile barrier: a sterile USG gel was applied to a cleaned wound to improve transmission of acoustic ESWT waves and/or the wound was covered with sterile barrier in the form of cellulose[33,37,39] or plastic drape.[32,34,35,38-40,44] Also, the same USG gel was applied onto the drape as a medium to provide full skin contact. In many studies, the ESWT applicator head was placed directly over the surface of the wound[32-44] (see Figure 4).

All of the reviewed studies used low- and medium-energy ESWT treatment, with the shock waves generated with electrohydraulic[33,35,36,38-43] or electromagnetic sources.[32,34,37,44] Two types of ESWT generator heads were generally used: defocused[35-38,40-42,44] or focused.[32-34,39,43] The EFD in the studied cases was characterized by a range from 0.03 to 0.25 mJ/mm^2 (0.11 ± 0.07 mJ/mm^2)[34,44] but the most regular value of EFD was 0.1 mJ/mm^2.[32,33,35,36,38,40,42]

The frequency was set at 4[36,39,43,44] or 5 pulses per second (Hz)[32,37,38,40,42]; however, a few of the studies did not describe that parameter.[33-35,42] In most studies, the number of pulses in a single ESWT session ranged from 10 to 500 pulses/cm^2 (206.4 ± 172.3 pulses/cm^2),[41,44] but the most frequent value was 100 pulses/cm^2 of wound area.[34,35,38-41,43]

Table 6. Summary of non-controlled clinical studies

	Level of evidence	Type of wound	Groups	Number of patients	Duration of wound	Initial size of wound	Results of ESWT intervention	Adverse events after ESWT
Saggini et al[39]	CCT	VLU, TW, DFU	ESWT + SWC SWC	30 10	5.3 mo 5.2 mo	5.64 cm^2 6.13 cm^2	53.33% patients complete wound closure (10% in control); 2.03 cm^2 post-treatment wound area (4.63 cm^2 in control); 30.7% improved granulation tissue (7.5% worsened in control); 30.7% reduced necrotic fibrin tissue (12.5% reduced in control)	Not observed
Schaden et al[40]	PCT	DHW, TW, VLU, PU, AIF, BW	ESWT + SWC	208	79% ≤ 1 mo 4% > 1 < 12 mo 14% > 12 mo	8.76 cm^2	43.5 days to complete epithelialization; 75% patients completely healed; 81% healed patients with ≤ 10 cm^2 vs. 61.8% participants with > 10 cm^2 wound area; 83% treated subjects with ≤ 1 month vs. 57.1% with > 1 month old wound	Not observed
Arnó et al[41]	PCT	BW	ESWT + SWC	15	< 24 h	1.4% TBSA	80% patients healed prior 3 weeks; 15% patients required surgical debridement and grafting; 5% patients had hypertrophic scarring	Not observed
Wolf et al[42]	PCT	SW, TW, VLU, PU, AIU, BW	ESWT + SWC	258	76.36% < 3 mo 12.79% > 4 < 12 mo 10.85% > 12 mo	5.0 cm^2	74.03% patients complete wound closure; 2 total treatment sessions in 2 weeks duration of therapy to wound closure	Not observed
Fioramonti et al[43]	CCR	VLU	ESWT SWC	1	Unclear	11.0 cm^2 6.0 cm^2	6 total ESWT sessions in 6 weeks duration of therapy to wound closure; Incomplete healing after 6 weeks duration of SWC procedures	Not observed
Stieger et al[44]	CCR	VLU	ESWT + SWC	1	> 6 yrs	150.0 cm^2	5 treatments to progressive wound granulation and reepithelialization; 30 total sessions in 2.5 years duration of therapy to wound closure	Not observed

CCT=controlled clinical trial; PCT=prospective clinical trial; CCR,=clinical case report; VLU=venous leg ulcer; TW=post-traumatic wound; DFU=diabetic foot ulcer; DHW=disturbed healing wound; PU=pressure ulcer; AIU=arterial insufficiency ulcer; BW=burn wound; SW=postsurgical wound; ESWT=extracorporeal shock wave therapy; SWC=standard wound care; TBSA=total body surface area

According to the review of clinical research studies, in the case of chronic wounds ESWT sessions were typically once[36,42-44] or twice per week,[34,37,41] as well as once every 2 weeks.[33,39,40,42] The total number of treatment sessions ranged between three[33,34] and six.[37,43] However, in some studies ESWT therapy was continued for a longer period (10[39,40,42] to 30 sessions[44]). In studies that included patients who had presented with acute SWs, a single intraoperative session of ESWT treatment was applied.[32,35]

The average time of a single ESWT session was 1 to 3 minutes, depending on the size of the wound.[34,36,39-42] The duration of a single intraoperative ESWT session in the case of acute wounds ranged between 10[32] to 13 minutes.[35] An outline of ESWT application for wound treatment with regard to the methodological and practical issues, as well as biological effects and potential therapeutic properties, is presented in Figure 5.

Conclusions

The results of this literature review suggest ESWT can be used as an adjunct therapy for healing chronic and acute soft tissue wounds. Substantial supporting clinical evidence confirms ESWT utility and the range of positive results, such as completed wound closure and reepithelialization, enhanced tissue granulation, reduced necrotic fibrin tissue, improved blood flow perfusion and angiogenesis, reduced period of total wound treatment, and decreased necessity of antibiotic treatment.

Nevertheless, additional well-designed clinical studies and meta-analyses are necessary to investigate ESWT safety, efficacy, and cost-effectiveness in patients suffering from wide range of skin wounds. Despite the results obtained from well-designed studies showing positive wound healing outcomes, further studies should address methodological study shortcomings such as adequate methods of randomization, concealment of treatment allocation, and clear information about blinding, as well as inclusion of intent-to-treat and follow-up analysis.

Sham-controlled, randomized, multicenter, blinded clinical trials with the highest methodological quality and scientific data reliability are needed to ascertain ESWT efficacy and develop explicit evidence-based guidelines and recommendations. The results of this study show ESWT can be characterized as a noninvasive, painless, and safe physical treatment modality that seems beneficial in healing soft tis-

sue wounds. In the future, ESWT may play an important role in wound care; however, evidence-based practical guidelines should be developed first. ■

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