Electrical Stimulation in the Treatment of Pressure Injuries: A Systematic Review of Clinical Trials

Bogna Szołtys-Brzezowska, PT, Physical Therapist and Doctoral Student, Doctoral School, Academy of Physical Education, Katowice, Poland
Alicja Bańkowska, PT, Physical Therapist and Assistant, Department of Physical Therapy, Academy of Physical Education
Laura Piejko, PhD, PT, Physical Therapist and Assistant Professor, Department of Physical Therapy, Institute of Physiotherapy and Health Sciences, Academy of Physical Education
Ryszard Zarzeczny, PhD, Associate Professor, Institute of Health Sciences, The Jan Kochanowski University, Kielce, Poland
Agnieszka Nawrat-Szołtysik, PhD, PT, Physical Therapist and Assistant Professor, Department of Physical Therapy, Institute of Physiotherapy and Health Sciences, Academy of Physical Education
Luther C. Kloth, PhD, PT, Professor Emeritus of Physical Therapy, Department of Physical Therapy, Marquette University, Milwaukee, Wisconsin, and Licensed Physical Therapist and Certified Wound Specialist, American Academy of Wound Management
Anna Polak, PhD, PT, Physical Therapist and Associate Professor, Department of Physical Therapy, Institute of Physiotherapy and Health Sciences, Academy of Physical Education

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ANCC 3.5 Contact Hours

GENERAL PURPOSE: To provide information on evidence-based practice regarding the use of electrical stimulation for pressure injury management.

TARGET AUDIENCE: This continuing education activity is intended for physicians, physician assistants, nurse practitioners, and nurses with an interest in skin and wound care.

LEARNING OBJECTIVES/OUTCOMES: After participating in this educational activity, the participant will:

1. Apply clinical practice recommendations related to the use of electrical stimulation in the treatment of pressure injuries.
2. Identify issues related to the use of electrical stimulation to treat pressure injuries.

ABSTRACT

OBJECTIVE: To summarize evidence regarding the use of electrical stimulation for pressure injury (PI) management with a systematic review of randomized clinical trials.

DATA SOURCES: The authors searched scientific databases (PubMed, EBSCO, Medline, and Elsevier) and the online resources of gray publications for studies published between January 1, 1980, and June 20, 2021, using the keywords "electrostimulation," "electrical stimulation," "pressure ulcer," "pressure injury," "bedsore," and "decubitus ulcer."

STUDY SELECTION: The search procedure generated 342 articles. Of these, 241 were disqualified after title screening, 52 after abstract screening, and 33 after full-text review; 16 articles were included in the review. Included articles were full-text reports of randomized clinical trials involving patients with PIs that had at least two patient groups, detailed how wounds healed, and were written in English.

DATA EXTRACTION: The authors extracted information about the purpose and design of each trial, patient inclusion and exclusion criteria, research methods, statistical analysis, findings, and conclusions.

DATA SYNTHESIS: Researchers applied high-voltage monophasic pulsed current (HVMPC) in 10 trials, two trials used low-voltage monophasic pulsed current, three trials tested a low-voltage biphasic pulsed current, and one trial used low-intensity direct current.

CONCLUSIONS: The effect of HVMPC in the treatment of PIs has been most thoroughly investigated in clinical trials. The results are consistent and indicate that HVMPC (twin-peak impulse, 50–154 μs, 100 pps, 45–60 min/d) is effective in PI treatment.

KEYWORDS: biphasic pulsed current, direct current, electrical stimulation, monophasic pulsed current, physical therapy, pressure injury, wound healing

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INTRODUCTION

Chronic wounds affect millions of people globally. Epidemiologic reports from various countries estimate that pressure injuries (PIs) develop in as many as 31% to 52% of patients with central nervous system injuries,[1,2] 4.1% to 32.2% of older adults in residential care facilities,[3–5] and 13.1% to 45.5% of patients in intensive care wards.[6,7] Further, PIs are diagnosed in 5% to 53% of patients who underwent surgery lasting longer than 2 hours, and this rate increases with the length of the procedure.[7,8]

Treatment of PIs and other chronic wounds is time-consuming and costly. Consequently, researchers continue to search for inexpensive therapies that can be administered safely and effectively in patients' homes. In recent years, an increasing number of studies have investigated the influence of physical modalities such as electrical stimulation (ES) on wound healing. An increasing body of evidence from preclinical studies (in vitro[9–17] and in vivo animal trials[18–21] and studies of experimental wounds in healthy individuals[22,23]) indicates that electrical currents promote wound healing.

Damaged tissue and the epidermis surrounding it have different electrical charges (positive and negative, respectively), which causes the flow of an endogenous electrical current that stimulates natural healing processes.[17,24,25] This current needs a moist wound environment to flow; however, chronic wounds not only tend to dry out but also are treated with nonconductive agents. Research indicates that current flow can be induced in such cases by external ES.[25] Electrical stimulation increases protein and DNA synthesis in cultures of human fibroblasts[11] and induces electrotaxis (the movement of healing cells toward damaged tissue). Blood vessel epithelial cells,[15] fibroblasts,[10,12] and keratinocytes[13] migrate to the cathode, whereas macrophages,[9] fibroblasts, and vascular smooth muscle cells[15] are attracted by the anode.

Electrical stimulation also reduces the expression of proinflammatory cytokines (eg, interleukin 1β [IL-1β], tumor necrosis factor α, IL-6);[20] increases the ratio of proinflammatory IL-10 to proinflammatory cytokine tumor necrosis factor α;[26] and stimulates the production of factors participating in the proliferative phase of wound healing, including angiogenic factors (IL-8, vascular endothelial growth factor, fibroblast growth factor 1 and 2, transforming growth factor β1, and platelet-derived growth factor).[16–19,22,23,27,28] Further, ES increases the activity of α-smooth muscle actin and the production of type 1 collagen, which accelerate scar maturation and remodeling[21] and cause the superficial skin vascular endothelium to release nitric oxide that dilates blood vessels, thus improving circulation.[29,30]

The most recent clinical guidelines (2019 and 2020) recommend ES for treating stage 2 through 4 PIs,[7,31] but they do not delineate how to apply ES in the clinical setting most effectively. To address this question, the authors undertook a systematic review of clinical trials that treated patients' PIs with ES to determine the state of evidence-based knowledge in this field and derive practical implications for the use of electric currents.

METHODS

Search Strategy

Three authors searched scientific databases (PubMed, EBSCO, Medline, and Elsevier) and the online resources of gray publications for relevant studies published between January 1, 1980 and June 30, 2021 using the following keywords: "electrostimulation," "electrical stimulation," "pressure ulcer," "pressure injury," "bedsore," and "decubitus ulcer."

Study Selection

Three authors examined the titles and content of identified studies. Publications were considered eligible for review if they were full-text articles, written in English, reported randomized clinical trials (RCTs) involving patients with PIs, included at least two groups of patients (eg, an experimental group [EG] treated with ES and a control group [CG] receiving standard wound care [SWC] alone or SWC in conjunction with sham ES), and detailed how wounds healed (eg, wound area reduction, wound healing rates, etc).

Methodological Quality

Two authors independently rated the methodological quality of the included RCTs using the 10-item Physiotherapy Evidence Database (PEDro) scale.[32] The following scoring criteria were adopted: 3 to 4 points, low quality; 5 to 7 points, medium quality; 8 to 9 points, high quality. Differences in opinions were resolved by a third author.

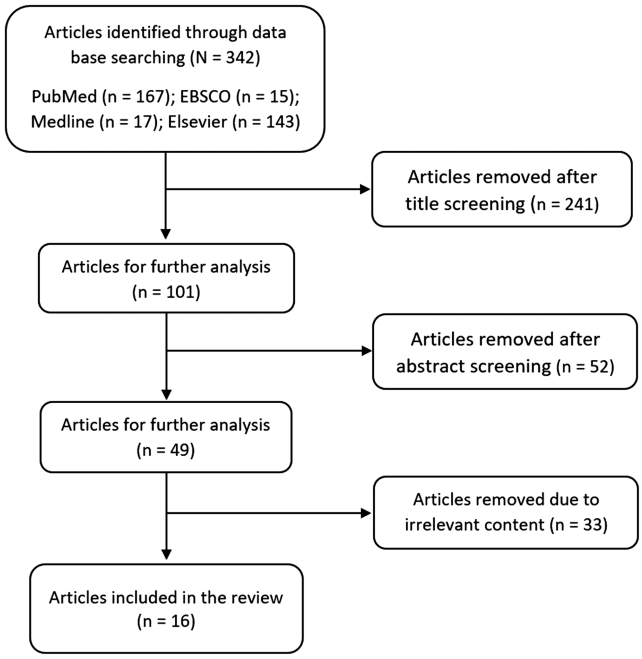
Data Extraction

Three authors independently scrutinized the selected articles to extract information about the purpose and design of the trial, patient inclusion and exclusion criteria, research methods (randomization and blinding, patient assessment and treatment, ES protocol), statistical analysis, findings, and conclusions. Extracted data were saved in Excel (Microsoft Inc) and checked for accuracy by a third author.

RESULTS

The search procedure generated 342 articles, of which 241 were excluded after title screening. Of the remaining 101 articles, 52 were excluded following examination of their abstracts, and 33 were excluded after full-text screening for irrelevance. Ultimately, 16 articles were included in the review and subject to quality assessment (Figure 1).

Figure 1. STUDY SCHEME



Methods of ES and Patient Characteristics

Investigators treated a total of 890 PIs in 793 patients aged 10 to 95 years. For 457 EG participants, PIs were treated with ES, and for 299 CG participants, wounds were treated using only SWC or SWC plus sham ES. An additional 37 participants received ultasound (US) therapy, and its effects were compared with treatment results in the ES groups.

The RCTs used a variety of electric currents. Ten trials applied a high-voltage monophasic pulsed current (HVMPC),[33–42] two trials used low-voltage monophasic pulsed current (LVMPC),[43,44] and three trials tested a low-voltage biphasic pulsed current (LVBPC).[45–47] In one trial, PIs were treated with a low-intensity direct current (DC).[48]

Patients' PIs ranged in severity from stage 2 to 4. Altogether, 243 stage 2 PIs, 259 stage 3 PIs, and 67 stage 4 PIs were treated in 12 trials.[33–43,48] In four trials, the authors did not specify the severity of PIs, only the size of their surface area.[44–47]

The majority of the authors graded patients' PIs using the scale developed by the National Pressure Injury Advisory Panel;[7,36–43,48] the DeLisa Classification System[34] and the Yarkony-Kirk Classification[35] were used in one trial each. The authors of several reports did not state how PIs were graded.[33,44–47]

The patients were predominantly adult men and women.[33,35,36,38–45,48] However, three trials[34,37,47] also treated patients younger than 18 years. In these trials, participants' ages ranged from 10 to 70 years,[34] 14 to 87 years,[37] and 17 to 76 years.[47] In the trial by Karba et al,[46] all patients were adult men.

The causes of PIs were diverse and included central nervous system injuries,[34,36,40,42,45–48] advanced age-related conditions,[38,39,41,48] and immobilization after orthopedic interventions.[37] In one trial, PIs were caused by diabetes, cardiovascular diseases, or cerebrovascular accidents.[33] Three trials did not indicate PI etiologies.[35,43,44]

In all trials, wound healing progress was measured as changes in wound surface area (WSA). Several trials also measured characteristics such as wound depth,[37,45] healing rate,[33,43,45–48] the degree of wound tissue granulation,[37,45] and capillary blood flow in wound edges.[42] The authors of two trials used the Gilman parameter, which enables comparisons of healing among PIs with different initial shapes and sizes.[37,38]

Quality Assessment

Based on the PEDro scale, six trials[33–35,40,45,46] were of low quality, eight trials[36–39,43,44,47,48] were of medium quality, and two trials[41,42] were of high quality (Table).

High-Voltage Monophasic Pulsed Current

Of the 10 HVMPC trials, four RCTs had low methodological quality,[33–35,40] four were medium quality,[36–39] and two were high quality.[41,42] The RCT methodologies and treatment results are summarized in Supplemental Table 1 (http://links.lww.com/NSW/A137).

The RCTs involved 454 patients aged 10 to 95 years with 485 stage 2, 3, and 4 PIs, of which 275 were treated with HVMPC. Eight trials treated stage 2 to 4 PIs[34,36,39–42] or stage 2 to 3 PIs.[37,38] The majority of PIs in four of the eight trials were stage 3 to 4 (55.1%–85.24%). In the remaining two trials, all PIs were either stage 4[33] or stage 2.[35]

A frequent cause of PIs in these trials was neurologic problems. In two trials,[34,36] all patients had spinal cord injury (SCI), and in two others,[40,42] patients had various central nervous system disorders. The authors of four studies treated PIs that developed in older adults[38,39,41] or patients with orthopedic injuries.[37] The patients in the study by Kloth and Feedar[33] developed PIs as a result of cerebrovascular traumas, peripheral vascular diseases, lower extremity fractures, diabetic fractures, above-knee amputations, or pilonidal cysts. Ahmad[35] did not denote the causes of PIs in their patients.

The EGs were treated with SWC and HVMPC, whereas the CGs received SWC[36,37,39] alone or SWC and sham HVMPC.[33–35,38,41,42] In two trials,[39,40] the results of ES with HVMPC and high-frequency US (1 and 3 MHz) were compared between the treated groups.

In all RCTs, WSA decreased more in the EGs treated with HVMPC than in the CGs.[33–39,41,42] Electrical stimulation also accelerated PI healing,[33,41,42] stimulated granulation tissue growth,[37] and improved periwound skin blood flow.[42]

Table. METHODOLOGICAL QUALITY ASSESSMENT OF RCTS BASED ON THE PEDRO SCALE

		PEDro Scale Criteria (1 = Yes, 0 = No)										
Current Type	**Author, Year**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**Total**
HVMPC	Kloth and Feedar,[33] 1988	1	0	1	0	0	0	1	0	0	1	4
	Griffin et al,[34] 1991	1	1	0	1	1	0	0	0	0	0	4
	Ahmad,[35] 2008	1	0	1	0	0	0	0	0	1	1	4
	Houghton et al,[36] 2010	1	1	1	1	0	0	0	1	1	1	7
	Franek et al,[37] 2012	1	1	1	1	0	0	0	0	1	1	6
	Polak et al,[38] 2016	1	1	1	1	1	0	0	0	1	1	7
	Polak et al,[39] 2016	1	1	1	1	0	0	1	0	0	1	6
	Karsli et al,[40] 2017	1	1	0	1	0	0	0	0	0	1	4
	Polak et al,[41] 2017	1	1	1	1	1	0	1	1	1	1	9
	Polak et al,[42] 2018	1	1	1	1	0	1	1	1	1	1	8
LVMPC	Gentzkow et al,[43] 1991	1	1	1	1	1	1	0	0	1	0	7
	Wood et al,[44] 1993	1	0	1	1	1	0	1	0	1	1	7
LVBPC	Jerčinović et al,[45] 1994	1	1	0	0	0	0	0	0	0	1	3
	Karba et al,[46] 1995	1	1	0	0	0	0	0	1	0	1	4
	Baker et al,[47] 1996	1	0	1	0	0	1	0	0	1	1	5
DC	Adunsky and Ohry,[48] 2005	1	1	0	1	1	1	0	0	1	1	7

Abbreviations: DC, direct current; HVMPC, high-voltage monophasic pulsed current; LVBPC, low-voltage biphasic pulsed current; LVMPC, low-voltage monophasic pulsed current; PEDro, Physiotherapy Evidence Database; RCTs, randomized clinical trials.
Criteria: (1) participants were randomly allocated to groups; (2) allocation was concealed; (3) the groups were similar at baseline regarding the most important prognostic indicators; (4) there was blinding of all participants; (5) there was blinding of all therapists who administered the therapy; (6) there was blinding of all assessors who measured at least one key outcome; (7) measures of at least one key outcome were obtained from more than 85% of the participants initially allocated to groups; (8) all participants for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome were analyzed by "intention to treat;" (9) the results of between-group statistical comparisons are reported for at least one key outcome; (10) the study provided both point measures and measures of variability for at least one key outcome.

In the earliest of the RCTs, conducted by Kloth and Feedar[33] in 1988 (PEDro score of 4), nine older adult patients with stage 4 PIs were treated with HVMPC (twin-peak pulses, 100 μs, 105 pps, 342 μC/s) during 45-minute sessions performed 5 d/wk (until wounds healed completely). Five patients were given anodal stimulation for the length of the treatment period; in the remaining four patients, the polarity of the treatment electrode was changed to cathodal when wound healing stalled. The treatment electrode was placed on a moist gauze pad separating it from the surface of the wound, and the return electrode was attached to intact skin a minimum of 15 cm from the treatment electrode. Wounds treated with HVMPC closed in a mean of 7.3 weeks at 45% per week. In seven control participants who received SWC and sham HVMPC, the mean WSA increased by 29% over a mean of 7.4 weeks.

In 1991, Griffin et al[34] treated eight stage 2 to 4 PIs in patients with SCI for 20 days using SWC and cathodal HVMPC (twin-peak pulses, 100 pps, 200 V, 500 μC/s). The cathode (treatment electrode) was placed on the wound, and the anode (return electrode) was strapped over the patient's medial thigh. In the EG, WSA decreased by a mean of 80% compared with 52% obtained for nine PIs in the CG, which was administered SWC and sham HVMPC ($P < .05$). The main weakness of this trial and that conducted by Kloth and Feedar[33] was a small sample size.

However, the results of these two trials[33,34] were later supported by the findings of six other RCTs,[35–38,41,42] conducted between 2008 and 2018, four of which were blinded. The number of patients in the trials ranged from 6 to 34. The smallest of the EGs (all of which were treated with SWC and HVMPC) had 15 patients, and the largest included 26 patients. In four trials, the treatment results in the EGs were compared with the CGs treated with SWC and sham HVMPC.[35,38,41,42] In two trials,[36,37] SWC was the only therapy in the CGs.

Houghton et al[36] carried out a single-blind RCT with patients with SCI in community care facilities. After 12 weeks of treatment, the mean percentage area reduction (PAR) of 16 stage 2 to 4 PIs in the group treated with HVMPC (twin-peak pulses, 50 μs) and SWC was greater than that of the 16 PIs in the CG, which received SWC and sham HVMPC (70% vs 38%, $P = .048$). Electrical stimulation sessions were performed at night while the patients slept. During a 1-hour session, 20 minutes of stimulation with HVMPC at 100 pps was followed by 20 minutes of rest, and 20 minutes of HVMPC at 10 pps. The total duration of ES was 5.35 h/d. The polarity

of the treatment electrode was negative in the first week and then alternated weekly thereafter. The treatment electrode was placed on the PI, and the dispersive electrode was attached to healthy skin at least 20 cm from the PI. The trial[36] demonstrated that ES was both feasible and effective for use in community care facilities. However, because the patients were treated in different facilities, the HVMPC protocol may not have been consistently applied. Further, the physiotherapists in charge of ES procedures were unblinded to group assignment and the treatment period was too short for wounds to heal completely, failing to assess long-term efficacy.

In the RCT conducted by Franek et al,[37] the EG consisting of orthopedic patients with a total of 26 stage 2 and 3 PIs was treated with SWC and HVMPC (twin-peak pulses, 100 μs, 100 pps). The treatment sessions lasted for 50 minutes and were performed once daily, 5 d/wk, for 6 weeks. For the first 1 to 2 weeks, cathodal stimulation was applied to promote granulation tissue growth, and then anodal stimulation was introduced for the remainder of treatment. The treatment electrode was placed on the PI, and the dispersive electrode was attached to healthy skin at least 20 cm from the PI. The authors reported an increase in the granulation tissue area over the 6 weeks of treatment in both the EG and the CG (SWC alone); statistical significance was reached only in the first group (P = .0006 and P = .845, respectively). The mean PARs of the groups were 88.9% and 44.4% (P = .00003). The trial's findings have limited validity, however, because patients were treated for as long as 4 years, and new wound prevention and treatment methods became available in the meantime. Further, the trial was not blinded, sham ES in the CG discontinued treatment before wounds healed completely, and the authors did not evaluate the long-term efficacy of ES.

In the blinded RCT by Polak et al,[38] older adults with a total of 25 stage 2 and 3 PIs received cathodal HVMPC (twin-peak pulses, 154 μs, 100 pps, 250 μC/s) and SWC. The treatment electrode was placed on the PI, and the dispersive electrode was attached to healthy skin at least 20 cm from the PI. The treatment sessions lasted for 50 minutes and were performed once daily, 5 d/wk, for a period of 6 weeks. The WSA reduced over the treatment period by 80.31% in the EG and 54.65% in the CG treated with SWC and sham HVMPC (24 PIs; P = .046). The Gilman parameter values in the groups were 0.95 and 0.57, respectively (P = .015). This study was not blinded, the CG did not receive sham ES, treatment duration was too short for wounds to heal, and the therapeutic efficacy of HVMPC was not monitored after treatment.

The authors of the five cited trials[33,34,36–38] used different polarity of the treatment electrode. In two trials, wounds were stimulated with the cathode;[34,38] in one trial, only anodal stimulation was used,[33] and in two trials, the polarity of the treatment electrode was changed between positive and negative.[36,37]

In two RCTs conducted in 2017 and 2018, Polak and colleagues[41,42] investigated the relationship between PI healing and the polarity of the treatment electrode. The first RCT lasted 6 weeks and involved 63 older adults with stage 2 and 3 PIs divided into two EGs (1 and 2) and one CG (3).[41] The patients in group 1 (23 PIs) received cathodal HVMPC (twin-peak pulses, 154 μs, 100 pps, 250–360 μC/s; 50 min/d, 5 d/wk) for the whole treatment period, those in group 2 (20 PIs) received cathodal HVMPC in the first week and anodal HVMPC in the remaining 5 weeks, and participants in the CG (20 PIs) were treated with SWC and sham HVMPC. In both EGs, the treatment electrode was placed on the PI, and the dispersive electrode was attached to healthy skin at least 20 cm from the PI. After 6 weeks of treatment, the mean WSA in groups 1 and 2 decreased by 82.34% and 70.77%, respectively (not significant; P = .99). Both of these outcomes were significantly better than group 3, in which the mean WSA only decreased by 40.53% (P = .0006 and P = .0124). Polak et al[41] estimated that cathodal HVMPC would reduce WSA in group 1 by 50% over a mean of 1.92 weeks (95% CI, 1.62–2.23 weeks), and the combination of cathodal and anodal HVPC in group 2 would need 2.6 weeks (95% CI, 2.08–3.13 weeks) to produce the same effect. The difference between the two periods is not statistically significant (P > .05), and both are significantly shorter than the 10.6 weeks required in group 3 (95% CI, 7.25–13.95 weeks). Kaplan-Meier analysis showed that the probability of wounds treated with cathodal or cathodal and anodal HVMPC not healing was significantly lower (P < .01) than that of CG wounds (P < .01).

In the second RCT, Polak et al[42] randomly divided 61 patients with stage 2 to 4 PIs following neurologic spinal cord and brain injuries into two EGs, anodal HVMPC (n = 20) and cathodal HVMPC (n = 21), and a CG that received SWC and sham ES (n = 20). The HVMPC parameters were the same as in the previous trial,[41] but the treatment duration was extended to 8 weeks. The investigators aimed to determine whether there was a relationship between wound healing and the polarity of the treatment electrode. In both EGs, the treatment electrode was placed on the PI and the dispersive electrode was attached to healthy skin at least 20 cm from the PI. The measurements of WSA at week 8 showed it decreased by 64.10% and 74.06% in the EGs, respectively (not significant, P = .99). Both EGs' WSA reduction values were significantly greater than the CG WSA reduction (41.42%; P = .0391 and P = .0024). According to study authors, the WSA of PIs stimulated with anodal HVMPC would need a mean of 4.3 weeks (95% CI, 0.20–0.26 weeks) to decrease by 50%; in the case of cathodal HVMPC, 3.86 weeks (95% CI, 0.23–0.28 weeks) would be necessary.

The trial thus established no difference in efficacy between cathodal versus anodal stimulation ($P > .05$), but ES was significantly better than SWC and placebo (9.86 weeks; 95% CI, 0.08-0.11 weeks; $P < .05$). Polak et al[42] also observed that after 2 weeks periwound cutaneous blood flow increased significantly more in both EGs than in the CG (109.52% in the anodal ES group, 131.54% in the cathodal ES group, and 35.83% in the CG). The difference between EGs and the CG was statistically significant ($P = 0.047$ and $P = 0.0152$, respectively). In both studies, treatment was discontinued before patients' wounds could heal completely, and its effects were not monitored afterward.[41,42]

Ahmad[35] randomly divided 60 patients aged 30 to 50 years with stage 2 PIs of unreported etiology into 4 groups of 15 (3 EGs and a CG). Each of the EGs received SWC and ES with HVMPC (twin-peak pulses, 120 pps, an interphase interval of 50 μs, 100–175 V). The CG was administered SWC and sham HVMPC. The ES sessions lasted for 45, 60, or 120 minutes depending on the group and were performed every day for 5 weeks. The researchers applied cathodal stimulation for the first 3 days, after which anodal stimulation was introduced and continued until wounds healed. If a healing plateau was reached, cathodal stimulation was reintroduced for another 3 days. The treatment electrode was placed on the PI, and the dispersive electrode attached to the patient's medial thigh. After 5 weeks' treatment, there was a significant reduction in WSA in the 45-minute ES group (7.12 vs 5.10 cm^2), in the 60-minute ES group (7.12 vs 0.60 cm^2), and in the 120-minute ES group (7.14 vs 0.64 cm^2) compared with the CG (7.21 vs 5.39 cm^2; $P < .001$ in all cases). There was also a significant reduction in WSA in the 60-minute ES group and in the 120-minute ES group compared with the 45-minute ES group ($P < .001$ in both cases). The 60- and 120-minute ES groups did not differ in WSA reduction ($P > .05$). As a result, Ahmad concluded that HVMPC applied every day during 60- or 120-minute sessions was optimal to enhance chronic PI healing. However, treatment ended before wounds could heal completely, and the author did not describe patient comorbidities, wound location and duration, or blinding.

The authors of the next two RCTs[39,40] compared the efficacy of ES with HVMPC and high-frequency US (1 and 3 MHz) in the treatment of stage 2 through 4 PIs. Polak et al[39] treated 77 older adults who were randomly divided into two EGs and a CG. One EG received SWC and HVMPC (twin-peak pulses, 154 μs, 100 pps, 250 μC/s, 50 min/d), and the other received SWC and US (1 MHz, 0.5 W/cm^2, 20%, 1-3 min/cm^2); the CG received SWC. The treatment sessions were performed 5 d/wk for a period of 6 weeks. After 5 days of cathodal stimulation, anodal stimulation was introduced and continued until the end of the treatment period. The treatment electrode was placed on the PI, and the dispersive electrode was attached to healthy skin at least 20 cm from the PI.

Although statistically significant reductions in the mean WSA were recorded for all three groups (P's < .0001), the US group and the ES group had significantly greater PAR compared with the CG (77.48%, 76.19%, and 48.97%; $P = .024$ and .030). The reduction in WSA did not significantly differ between the EGs ($P = .990$). Thus, Polak et al[39] concluded that HVMPC and 1-MHz US had a similar potential to reduce the area of stage 2 through 4 PIs. The weaknesses of this RCT include a very long period over which data were collected and a lack of placebo and blinding. Also, patients' wounds were not treated until complete healing, and the long-term effects of the intervention were not monitored.

Karsli et al[40] divided 27 patients (mean age, 32.63 [SD, 15.96] years) with neurologic conditions (SCI, traumatic brain injury, stroke, myelitis) into two groups of 15 and 12 patients. The larger group received SWC and HVMPC (twin-peak pulses, 160 μs, 100 pps, 60 min). The first pulse of 10 μs was followed by a 50-μs interval and then a 100-μs pulse. Stimulation intensity was set at a sensory level (50–150 V) and caused muscle contractions. The authors did not report the location and polarity of the treatment and dispersive electrodes. The smaller group of patients received US therapy. Wound beds were treated with US for 1 to 2 min/cm^2 (3 MHz, 0.3 W/cm^2, 20% duty cycle) and wound edges were treated for 2 to 3 min/cm^2 (1 MHz, 1–1.5 W/cm^2, 100% duty cycle, continuous mode). Both groups were treated three times per week for 4 to 12 weeks. In the ES group, WSA decreased by a mean of 43%, and in the US group, WSA decreased by 63%; mean wound volume decreased by 16 and 12 cm^3, respectively. Because the treatment results were not significantly different between groups, the authors concluded that HVMPC and US (1–3 MHz) had a similar ability to enhance the healing of PIs, a finding consistent with Polak et al.[39] The main weakness of the study is that the PIs of patients in the ES group were more severe and had greater WSA at baseline than those of patients in the US group.[40] Moreover, neither therapy was continued until wounds healed completely, and the authors did not assess their long-term effects.

Low-Voltage Monophasic Pulsed Current

The authors of two RCTs from 1991[43] and 1993[44] applied LVMPC to adults (age range, 31–90 years) with 114 stage 2 through 4 PIs located on the pelvic girdle and the lower extremities.[43,44] Unfortunately, only one of the trials specified the numbers of stage 2, 3, and 4 PIs; most wounds (39 of 40 [97.5%]) were described as stage 3 or 4 PIs.[43] The causes of the PIs were not reported. The therapeutic effects of the trials and the ES protocols used by their

authors are summarized in Supplemental Table 2 (http://links.lww.com/NSW/A138).

Gentzkow et al[43] carried out a placebo-controlled RCT with 37 patients (age range, 31–90 years) who had a total of 40 stage 2 through 4 PIs (primarily stage 3; n = 30). The patients were divided into an ES group (SWC and LVMPC) with 16 stage 3 PIs and 5 stage 4 PIs and a CG (SWC and sham LVMPC) with 1 stage 2 PI, 14 stage 3 PIs, and 4 stage 4 PIs. A rectangular-pulse LVMPC was generated using a Varipulse device by Staodyn Inc, Logmont (later known as Dermapulse and, recently, as WoundEL [GerroMed GMbH]). Electrical stimulation was applied at a sensory threshold without causing muscle contractions for 30 minutes twice a day every day for 4 weeks. An accumulated pulse charge (0.89 C per 30 minutes of treatment [1.78 C per day]) was delivered via a single-use treatment electrode attached to the wound surface (stage 2 PIs) or the wound bed (stage 3 and 4 PIs). The return electrode was placed on intact skin 15 to 30 cm from the wound edge. The treatment electrode polarity was initially set as negative and remained that way until the PI was debrided and a serosanguinous drainage appeared. Thereafter, the polarity was alternated between positive and negative every 3 days. In the first phase of treatment, researchers used 140-μs electrical pulses at 128 pps; as wounds progressed to a stage 2 classification, researchers instead used 132-μs pulses at 64 pps. Over 4 weeks of treatment, twice as many PIs in the ES group healed as in the CG (49.8% vs 23.4%; P = .042). The healing rates were 12.5% and 5.8%, respectively.

Wood et al[44] carried out a double-blind RCT involving 74 patients with stage 2 and 3 PIs (PIs by stage not reported). The researchers allocated 43 patients (mean age, 75.6 years) to an ES group (SWC and LVMPC of 600 μA and 0.8 pps) and 31 patients (mean age, 74.9 years) to a CG (SWC and sham LVMPC). Over 8 weeks, ES sessions (active or sham) were performed three times per week. The LVMPC was delivered via anode and cathode electrodes attached opposite each other, 2 cm away from the wound edges. Compared with 25 PIs (58%) that healed completely in the ES group, only 1 PI (3%) closed in the CG. Whereas 10 PIs in the CG increased in size, no PIs increased in size in the ES group. The authors did not state the length of an ES session or pulse waveform and duration; they mentioned, however, that the current intensity was only 600 μA, which suggests that it was below the threshold of excitability of sensory axons.

Low-Voltage Biphasic Pulsed Current

The authors of three RCTs[45–47] treated PIs of patients with SCI using LVBPC (Supplemental Table 2, http://links.lww.com/NSW/A138). The initial stage of the PIs was not specified in any of the trials, but two reports provided their baseline WSA,[45,47] and one stated the depth of the wounds.[45]

Jerčinović et al[45] treated 73 patients (age range, 18–68 years) with a total of 109 PIs. Researchers allocated 42 patients (61 PIs) to the ES group to receive SWC and ES (biphasic, asymmetric, charge-balanced pulses; 250-μs pulses at 40 pps, a 4-s pulse train with a 50:50 s on-off-ratio) and 31 patients (48 PIs) to the CG (SWC only). The mean wound area and depth at baseline were 10.6 (SD, 13.3) cm^2 and 3.0 (SD, 8.5) mm in the ES, and 17.2 (SD, 20.0) cm^2 and 4.0 (SD, 8.2) mm in the CG. The depth of 36 PIs (75%) in the ES and 51 PIs (83%) in the CG exceeded 5 mm. The electrodes were placed on the opposite wound edges. The LVBPC was delivered at an intensity eliciting visible muscle contractions. Patients underwent 2-hour-long treatment sessions 5 d/wk for 4 weeks. The authors reported that the mean daily healing rate was not significantly different between the ES and the CG (5.7% vs 2.7%; P > .05). In this trial, wounds were not treated long enough to heal completely, and neither sham ES nor blinding was used. Information about the stages of patients' PIs was not provided.

Karba et al[46] carried out a trial with 12 adult men equally divided between the ES and the CG, who had a total of 12 PIs. The PI stages and dimensions at baseline were not reported. In the CG, the treatment started with semiocclusive foam gel dressings. Because measurements at days 14 and 56 showed that such treated wounds did not heal but, in fact, had increased from baseline by a mean of −0.06% per day, the dressings were replaced, in conformity with ethical standards, with a therapy combining standard gauze dressings and ES with LVBPC. As a result, all PIs in the CG started to heal at a mean of 2.93% per day (a statistically significant improvement compared with the previous period; P < .05). Patients in the ES group were treated throughout with semiocclusive foam dressings and ES with LVBPC. The ES parameters and location of the electrodes were the same as those used by Jerčinović et al,[45] but Karba et al[46] performed ES sessions 7 d/wk until patients' wounds closed, which took from 35 to 98 days. The authors reported that the mean wound healing rate in the EG was statistically significantly greater than in the CG (7.13%; P < .05). The main shortcomings of this RCT were a relatively small group of patients and a lack of information about the stages and dimensions of PIs before treatment.

Baker et al[47] treated a group of 80 patients (age range, 17–76 years) who had 192 PIs altogether. Researchers randomly allocated patients to a CG (19 patients with 25 PIs; SWC plus sham ES) and three ES groups (ES1, ES2, and ES3; 61 patients with 167 PIs). The only information the authors provided about patients' wounds was their baseline surface areas. The ES1 group (20 patients with 67 PIs) and the ES2 group (21 patients with

58 PIs) received ES with LVBPC (ES1: rectangular asymmetrical pulses, 100 μs, 50 pps, 7 seconds on and 7 seconds off; ES2: rectangular symmetrical pulses, 300 μs, 50 pps, 7 seconds on and 7 seconds off) at a sensory threshold (ie, without causing muscle contractions). The ES3 group (20 patients with 42 PIs) received subsensory LVBPC (4 mA, 10 μs, 1 pps, 7 seconds on and 7 seconds off). In all ES groups, the current was delivered via electrodes placed opposite each other on the wound edges during 30-minute sessions performed three times daily, 5 d/wk, until the wounds healed completely. The mean weekly rates of PI area reduction calculated for all wounds in EG1, EG2, EG3, and CG were 36.4%, 29.7%, 23.3%, and 32.7%, respectively, and the differences between the groups were not statistically significant ($P > .05$ in all cases). The authors note that this finding was likely related to the wide variety of data. The wounds in each group were then divided into those that showed signs of healing ("good response") and those that did not heal ("no response"). For PIs showing good response to treatment, the average weekly rates of WSA reduction in EG1, EG2, EG3, and CG were 63.7%, 50.6%, 38.5%, and 29.2%, respectively. The results in EG3 and CG were statistically significantly worse than those in EG1 ($P < .05$ in both cases). These results indicate that ES performed at the sensory level with LVBPC using rectangular asymmetrical pulses accelerates the healing of PIs and is more effective than ES with LVBPC performed at a level below the excitability threshold of sensory nerves. The limitations of this trial include a short treatment period (4 weeks) and a lack of evaluation of the long-term effects of ES.

Low-Intensity DC

In 2005, Adunsky and Ohry[48] conducted the only high-quality trial where PIs were treated with low-intensity DC (Supplemental Table 3, http://links.lww.com/NSW/A139). The participants were 54 older adults and 9 patients with SCI, all of whom had stage 3 PIs. Low-intensity DC combined with SWC was administered to 35 participants in the ES group (mean age, 71.8 [SD, 18.9] years). The CG consisted of 28 participants (mean age, 71.4 [SD, 19.5] years) who received SWC and sham DC. The trial ended after 28 weeks, but its results were monitored for another 3 months. The anode and cathode electrodes were placed on the opposite wound edges. The authors of the trial did not specify the duration of an ES session or current amplitude; they only mentioned that the latter was similar to that of an endogenous wound current (likely subsensory) and that ES could be safely administered for 24 h/d. Measurements performed after 28 weeks and at the end of the follow-up period did differentiate the ES from the CG in terms of the number of wounds that healed/closed completely ($P = .28$ and $P = .39$, respectively). An absolute wound area reduction and a relative wound area reduction (percentage change in wound area from baseline) obtained after 6 weeks of treatment (45 days) favored the ES group: mean wound area decreased by 44% compared with 14% in the CG. Thereafter, the groups' healing rates were similar. A logistic regression analysis determined that the probability of all wounds healing was greater for the ES than for the CG (odds ratio, 1.6; 95% CI, 0.4–4.73). A per-protocol analysis found that the CG's PIs would need 52% more time to heal completely compared with the PIs of patients in the ES group ($P = .03$). The trial authors reported that a combination of SWC and ES with DC was effective in accelerating the healing of stage 3 PIs in the first 6.5 weeks of treatment.

DISCUSSION

Application of HVMPC

In 10 RCTs, HVMPC reduced the WSA of stage 2 to 4 PIs, accelerated wound healing, facilitated granulation tissue growth, and increased periwound blood flow. The similarity of ES protocols used by all authors (Figure 2) provides a firm basis for formulating some recommendations regarding the clinical use of HVMPC.

Providers can deliver HVMPC to the wound via adhesive or carbon rubber electrodes. The electrodes (especially those made of carbon rubber) and wound tissue should be separated by a sterile gauze pad moistened with 0.9% sodium chloride solution, which improves electrical conductivity and prevents the wound from drying out.

Providers should place the treatment electrode directly on a debrided wound bed and the dispersive electrode on intact periwound skin at least 15 to 20 cm from the wound edge. The preferred treatment electrode is the anode when it is necessary to stimulate autolysis in wounds that are partially or completely covered with fibrous material or slough or to stimulate lymphocytes and macrophages (in the inflammation phase) in infected wounds. Anodal stimulation also increases blood perfusion to wound and periwound tissues. It can be applied until the end of the treatment period if it is accompanied by granulation and epithelialization processes; however, if weekly measurements indicate these processes are slowing down, introduce cathodal stimulation instead.

Cathodal stimulation increases blood perfusion to wound and periwound tissues and is particularly useful when granulation and epithelialization processes need to be accelerated. If wounds continue to heal, cathodal stimulation can be used until they close completely. Otherwise, alternate between cathodal and anodal stimulation every 3 days or weekly, depending on healing progress.

Apply HVMPC (twin-peak pulses, 50–154 μs, 100 pps, 250–500 μC/s, 0.89–1.78 μC/d) at a sensory threshold; that is, without causing visible muscle contractions. Perform 45- to 60-minute treatment sessions once daily, three to seven times per week (ie, 2.25–7 hours of treatment per week), until wounds heal completely.

Application of LVMPC

In two RCTs, researchers used LVMPC to treat patients with PIs. The authors of both trials reported that it was effective in accelerating the healing of stage 2 to 4 PIs. According to the ES protocol provided in one of the trials,[43] LVMPC (rectangular pulses, 140 and 132 μs; 128 and 64 pps) promotes PI healing when the intensity is set to a sensory level and 30-minute treatment sessions are performed twice daily, 7 d/wk. Treatment should start with cathodal stimulation, alternating with anodal stimulation every 3 days.

Application of LVBPC

In three RCTs, researchers treated PIs with LVBPC (biphasic, asymmetric, charge-balanced pulses) that evoked either weak muscle contractions[45,46] or sensory responses[47] only. According to the trials' results, LVBPC (100 or 250 μs,[45] 40–50 pps,[45] on and off times of 4 and 4 seconds[45,46] or 7 and 7 seconds[47]) is especially effective when applied at an intensity that induces muscle contractions. Place the treatment and inactive electrode opposite each other on the wound edges.[45–47] Perform treatment sessions lasting 1.5 to 2 hours 5 to 7 d/wk.

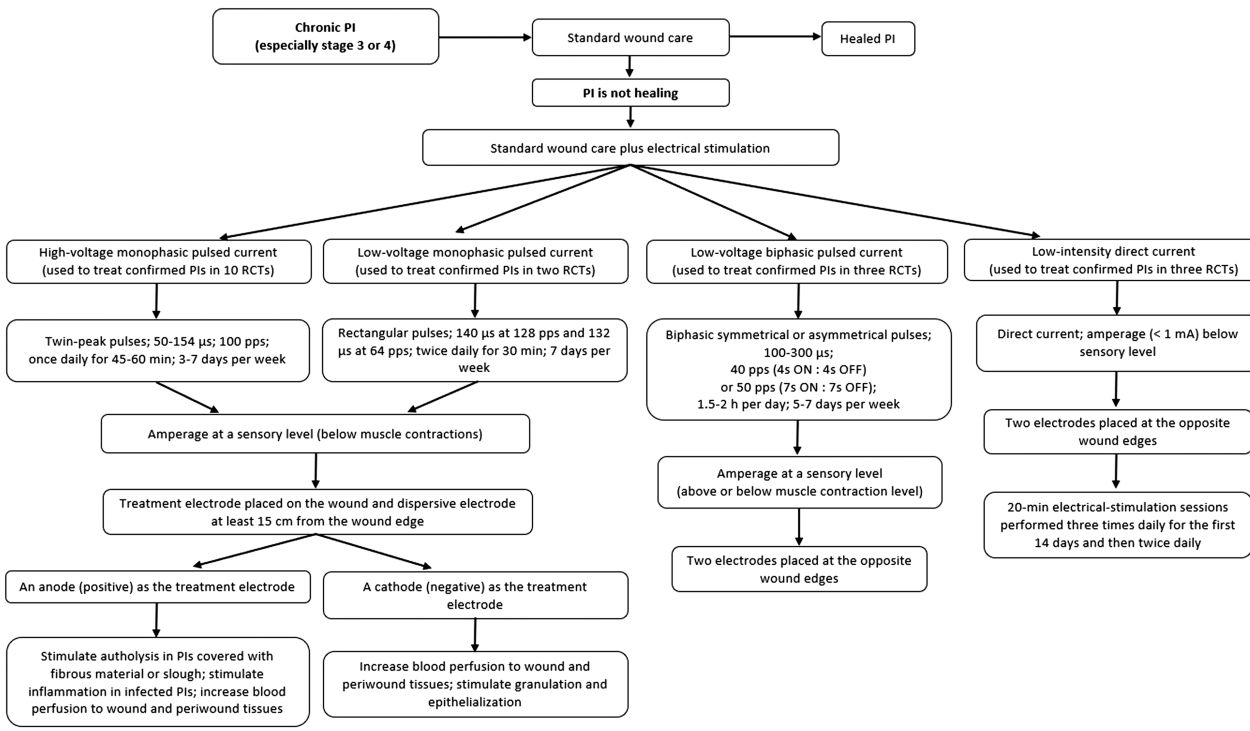
Application of Low-Intensity DC

Only one RCT found that low-intensity DC enhances the healing of stage 3 PIs, which is insufficient to develop wider recommendations on its use. The current intensity was described by the authors as similar to that of a "current of injury" (<1 mA), so it was likely below the sensory response threshold. The researchers delivered ES via electrodes placed opposite each other on the wound edges during 20-minute sessions performed three times daily for the first 14 days and then twice daily thereafter. The authors did not state the total treatment duration.

Adverse Effects and Contraindications of ES

In the 16 RCTs reviewed, ES had no adverse effects on the patients treated. However, the patients did not have acutely inflamed, necrotic wounds; wounds with

Figure 2. ELECTRICAL STIMULATION IN THE TREATMENT OF PIs



Abbreviations: PI, pressure injury; RCT, randomized clinical trial.

osteomyelitis; or wounds overlying malignant tumors or electronic implants.

Cost and Availability of ES for PI Treatment

The results of the trials conducted by Clegg and Guest[49] in the UK and Mittmann et al[50] in Canada show that adding ES to SWC can reduce the cost of treating PIs. Clegg and Guest[49] used the Markov model to compare the cost of treating PIs and venous leg ulcers with SWC versus bioelectric dressings delivering a current of less than 1 mA. The authors concluded that using bioelectric stimulation instead of SWC could reduce healthcare costs per patient by £366 over 16 weeks (from £2,287 to £1,921). Mittmann et al[50] used a decision analytic model and the results of clinical trials to estimate the cost of treating stage 3 and 4 PIs in a cohort of patients with SCI. They reported that 16.4% more PIs healed with ES plus SWC versus SWC alone, offering a cost savings of CAD $224 after a year.

Providers can perform ES sessions in medical or rehabilitation centers[33–35,37–48] or in patients' homes.[36,43,47] The ES devices meant for home use are easy to operate and can be programmed by a physiotherapist or by the patient's caregiver after training.

Although the use of ES in PI treatment is recommended by international guidelines,[7] and clinical trials provide ample evidence in support of its effectiveness, ES procedures are not yet paid for by national health funds. However, miniature electrostimulators for home use typically range in price from €200 to €500, so they are still affordable for many patients or caregivers. The ES of PIs can also be performed with devices that are used in physiotherapy for other purposes, such as in anesthetic therapy. These devices have the functionality of selecting current parameters, including those that are recommended in PI treatment. Jünger et al[51] found that most of the cost involved in treating the venous ulcers of at-home patients was related to the purchase of self-adhesive disposable electrodes. This cost can be significantly reduced by using carbon rubber electrodes, which are reusable and require only standard disinfection after each use.

CONCLUSIONS

In this review of RCTs, the authors evaluated the evidence accumulated in the past 30 years regarding the use of electrical currents in the treatment of PIs. Most of the RCTs provided evidence recommending the use of HVMPC. The usefulness of LVMPC, LVMBC, and low-intensity DC was confirmed by only a few trials. The ES sessions in the trials were mostly performed by medical staff at medical and rehabilitation centers, but the authors of three RCTs[36,43,47] demonstrated that ES is also feasible at patients' homes. ●

PRACTICE PEARLS

- According to international recommendations based on the results of RCTs, healthcare providers should use ES in the treatment of stage 2 through 4 PIs.
- Researchers have investigated HVMPC most thoroughly in RCTs, confirming it is effective in treating PIs.
- Healthcare providers should treat PIs with HVMPC (twin-peak pulses, 50–154 μs, 100 pps, at a sensory threshold) for 45 to 60 minutes a day, 3 to 7 days a week.
- The cathode as a treatment electrode should primarily be used to stimulate granulation and epithelialization of wounds, and the anode to treat infected wounds and stimulate angiogenesis.
- In addition to HVMPC, stage 2 through 4 PIs can also be treated with LVMPC (rectangular pulses, 140 μs and 132 μs, 128 and 64 pps; at sensory level, for 60 minutes a day, 7 days a week) and LVBPC (100 or 250 μs, 40–50 pps, on:off times = 4:4 or 7:7 s, at muscle contraction level, 1.5–2 h/d, 5–7 d/wk).

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