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● *Original Contribution*

THE INFLUENCE OF COMORBIDITIES AND ETIOLOGIES ON THE SUCCESS OF EXTRACORPOREAL SHOCK WAVE THERAPY FOR CHRONIC SOFT TISSUE WOUNDS: MIDTERM RESULTS

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Abstract—Possible effects of comorbidities and of different wound etiologies on the success of extracorporeal shock wave therapy (ESWT) of chronic soft tissue wounds were investigated. From September 2003 until February 2007, 282 patients, being previously treated unsuccessfully were enrolled. Treatment consisted of ESWT occurring at defined intervals. At each treatment session a wound bed score was recorded, also at initial presentation a detailed patient history and wound etiology. Observed comorbidities were pooled according to the chapters of the ICD-10 system. Two hundered fifty-eight patients were analyzed (91.49%) and underwent follow-up for a median of 31.8 months. Wound closure occurred in 191 patients (74.03%) by a median of two treatment sessions. No wound reappeared at the same location. A multivariate logistic regression model showed that pooled comorbidities and wound etiologies did not have a significant influence on success. Comorbidities and wound etiologies have surprisingly no significant influence on the success of ESWT. (E-mail: klaus.s.wolff@meduniwien.ac.at) © 2011 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Extracorporeal shock-wave therapy, Chronic soft tissue wounds, Comorbidities, Wound etiology, Wound bed score.**

INTRODUCTION

Chronic soft tissue wounds represent a difficult problem for patients and physicians alike. Chronic wounds are found in almost all medical specialties ranging from dermatology (Panuncialman and Falanga 2009), internal medicine (Sanchez-Vazquez et al. 2008), surgery (Golinko et al. 2009), vascular surgery (Pappas et al. 2009), trauma (Wright and Khan 2009) and war surgery (Wolff et al. 2007). The primary goal in the treatment of chronic soft tissue wounds is to achieve wound closure. Usually necrotic tissue is debrided (surgically removed) to assess the full extent of the tissue damage, to detect underlying abscesses or other pathologies responsible for the disturbed wound healing. Wet-to-wet dressings are primarily applied to induce a healing process. As second line attempts for obtaining closure special dressings like semi permeable films, hydro gels, hydrocolloids and calcium alginates are administered. These dressings are associated with extended time periods of conservative treatment and the development of an allergic state after a certain period of application of these dressings (Davey et al. 2000). An additional treatment option is vacuum-assisted wound closure therapy or the application of skin grafts or tissue flaps after failure of nonoperative treatment. Unfortunately, for a limited number of patients, all three lines of treatment fail.

The use of extracorporeal shock waves for clinical applications was introduced more than two decades ago (Demling et al. 1982). Extracorporeal shock wave therapy (ESWT) is nowadays applied in the fields of urology, orthopaedic surgery (Metzner et al. 2010) and trauma surgery (Biedermann et al. 2003). Extracorporeal shock waves are associated with the induction of neovascularisation and with mechanical stimuli causing proliferation of a large number of cells including osteoblasts (Martini

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et al. 2006). The biologic effects of extracorporeal shock waves on human cells are currently studied in several centres worldwide (Martini et al. 2006; Nishida et al. 2004; Wang et al. 2002). Pioneers in ultrasound research showing its possibilities and bioeffects over the decades were Dunn and others (Dunn et al. 1975; Ter Haar and Robertson 1993; Fry et al. 1995; Dalecki et al. 1997; Nyborg 2006; Miller et al. 2009). Our research group's experience with ESWT in trauma surgery and the unanticipated observation that not only the traumatic condition *i.e.*, fracture non-union (Schaden et al. 2001), but also the surrounding tissue, showed favourable tissue healing after ESWT lead us to undertake more research to appraise the effects of this treatment option on soft tissue wounds. First, results showing significant influence of age, wound size/surface and duration as positive predictors of complete healing were published earlier (Schaden et al. 2007). In this present retrospective study, we identified existing comorbidities and the wound aetiology of each patient and observed over time, if these factors had an influence on the outcome of the healing of chronic soft tissue wounds treated by extracorporeal shock waves.

MATERIALS AND METHODS

From September 2003 through February 2007, 282 patients were enrolled in this retrospective analysis of our ESWT study (Clinical Trials.gov number, NCT00545896). Patients of both sexes older than 18 years were included if presenting with a chronic soft tissue wound persisting for longer than 30 days at the time of first presentation. During these 30 days before initial presentation, established treatment concepts, especially surgical debridement and wet-to-wet dressings, hydrocolloids, calcium alginates or negative pressure, wound therapy had to be applied unsuccessfully on the patient applying to be included into this study. All causes of chronic wounds except circumferential second or higher degree burn wounds of the upper or lower extremity were included.

The study used a single group assignment (one-armed, open, prospective study) to examine the effects of extracorporeal shock wave treatment on chronic wounds. Defined primary outcomes were all cause mortality (30 days mortality after last ESWT session). Secondary outcomes originally defined were the rate of complete wound closure and the number of ESWT sessions needed. Another secondary outcome formulated from the beginning was the rate of nonhealing wounds and the number of ESWT sessions until drop-out. The influence of patient comorbidity and wound aetiology on treatment success was retrospectively analyzed.

The properties of each wound were assessed by a wound bed score (WBS) at every treatment session and at the end of treatment; photo documentation was also carried out at each session. ESWT occurred once a week after the initial session. After the second ESWT, the interval between visits was usually extended to 2 weeks. If no progress was observed after 10 sessions (*i.e.,* approximately after 105 to 120 days) ESWT was stopped. Each treatment session was conducted in the outpatient clinic of the trauma centre. Before the first extracorporeal shock wave was applied, a thorough debridement of the wound was carried out. At each treatment session, the patients were monitored for side effects during and shortly thereafter. Beginning with the final visit after the last ESWT application, patients were followed for at least 1 year to determine the midterm healing properties of ESWT. Follow-up was carried out by the investigators through telephone interviews with the patient or with persons of the patient's household (*i.e.*, 24-hour home nurses, spouses, children).

This study was initiated by the investigators. The data of this study were gathered, analyzed and verified by the investigators. The manuscript was at all stages written and supervised by the authors/investigators. The providers of the extracorporeal shock wave apparatus orthowave 180 C™ (Tissue Regeneration Technologies [TRT], Atlanta, GA, USA) had no influence on the study, did not have access to the gathered data of this study and did not see the manuscript for reviewing in any stage before submission. Informed consent was obtained from all patients. The study was carried out in accordance with the decision of the AUVA Institutional Review Board at the AUVA Unfallkrankenhaus Meidling - Trauma Center Meidling.

Extracorporeal shock wave technology, applied apparatus and settings

A special shock wave applicator orthowave 180 C™ (Tissue Regeneration Technologies) delivering unfocused planar shock waves was used in this study (Schaden et al. 2007). After careful wound debridement, sterile ultrasound gel was applied on the wound surface followed by placing a surgical drape over the wound to avoid air bubbles and to improve coupling conditions. After calibration of the orthowave 180 C™ (Tissue Regeneration Technologies) and setting the energy to 0.1 mJ/mm^2 and the frequency to 5 pulses/s, the parabolic reflector (*i.e.*, shock wave head) was placed on the wound. A median number of 167 $impulses/cm^2$ wound-surface (interquartile range Q1–Q3: 100–300; range 2.7–2400) was delivered, depending on wound size. Pre-ESWT wound dressing therapy remained unchanged and was continued after each treatment session.

Wound bed score

To apply a uniform and reproducible scoring system of the chronic soft tissue wounds, we used the wound bed

Fig 1. Venous ulcer of the left leg at first presentation (wound bed score - WBS 3), after 2 weeks (WBS 10, after two sessions) and at the final visit (WBS 16).

score (WBS) (Falanga et al. 2006). The advantage of this wound bed classification was that it also allegedly offered a predictive factor with regards to wound healing success. The scoring system incorporates the following parameters: healing edges, presence of eschar, greatest wound depth/granulation tissue, amount of exudate, oedema, peri-wound dermatitis, peri-wound callus/fibrosis and pink/red wound bed. Each parameter is scored between 0 and 2. All single parameter scores are added. Each wound could, thus, have a score ranging from 16 (best score) to 0 (worst possible score). The chronic wound was assessed with the WBS every time before a treatment session began (Fig. 1).

Comorbidities and wound aetiology

At the initial evaluation session, each patient's medical history was documented and the possible cause for the chronic soft tissue wound was investigated. As expected, a considerable number of patients presented with one or more comorbidities.The multifactorial component of chronic wounds, the difficulty to objectively weigh the severity of comorbidities (*e.g.*, cancer with chemotherapy vs. cachexia vs. congestive heart failure) and the number of different pathologies (documented with the ICD-10 code) made it necessary to combine them into the given 21 chapters of the ICD-10 system to enable statistical analysis.

Wounds were divided into seven subgroups regarding their aetiology: post-surgical wounds (partial or complete failure to heal after primary closure of a surgical wound), post-traumatic wounds (chronic soft tissue wounds resulting from direct penetrating or blunt trauma associated with necrosis of epithelial and nonepithelial extra-skeletal structures), venous stasis ulcers, decubitus ulcers, cast pressure sores, arterial insufficiency ulcer and burn wounds (noncircumferential deep second or third degree burns). Patients presenting with these burn wounds were included in the study disregarding the 30-day rule on chronicity of wounds.

Monitoring of adverse events and follow-up

Sporadic reports associated ultrasound shock waves with possible haemorrhage (Pastor Navarro et al. 2009; Uemura et al. 2008) after kidney stone treatment as well as generally with microvascular damage (Samuel et al. 2009). As a consequence, patients were kept at the outpatient clinic for at least 60 min under close supervision after each ESWT. Patient complaints about pain during treatment were immediately heeded by reduction of frequency but not recorded. After each treatment session, patients were questioned about a swelling sensation, pain, and "heaviness" of an extremity or shortness of breath. If these symptoms were affirmed, they were recorded and respective diagnostic and curative measures initiated. In the follow-up process by telephone possible, haemorrhage, thrombosis or pulmonary emboli were specifically asked for.

Statistical analysis

SAS software, version 9.1 (SAS Institute Inc., Cary, NC, USA) was used for data analysis. Cut-off for patient data acquisition for analysis in this ongoing trial was February 27, 2007 so that a theoretic follow-up period of at least 1 year could be obtained. Patients not showing up to scheduled ESWT sessions or refusing to cooperate during the follow-up period were excluded. A multivariate logistic regression model was employed to identify possible positive or negative factors influencing ESWT success on wound closure. Significance level to enter and to stay in the logistic regression model was $p < 0.01$, respectively. Success was defined as full wound closure or at least a final WBS of 14 or higher. All cause death and ESWT related deaths within 30 days after last treatment session were analyzed. All p values were two-sided. Odds ratios were calculated. P-values less than 0.01 were considered statistically significant.

RESULTS

Twenty-four (8.51%) of 282 enrolled patients were lost to follow-up. The remaining 258 patients presented with a median age of 63.5 years (interquartile range Q1–Q3: 46.1–79.5 years) were analyzed, median follow-up lasted 31.8 months (interquartile range Q1–Q3: 24.0–38.0 months). No patient died within 30 days after ESWT of possible treatment related causes (hemorrhagic shock, pulmonary embolism, ischemic cerebral infarction), whereas seven unrelated deaths (2.71%) were observed. Further analysis of baseline data is shown in Table 1. An overview of wound characteristics and treatment details is depicted in Table 2.

Successful treatment could be achieved in 191 patients (74.03%) by a median of two ESWT sessions. A multivariate logistic regression model analyzing the influence of comorbidities, wound aetiology, initial WBS, sex and the already identified factors age, duration of wound and wound surface on success was employed. Table 3 offers an overview of the three parameters being statistically significant in this model: initial WBS ($p < 0.001$), duration of wound ($p < 0.001$) and wound

Table 1. Characteristics of the study group (n = 258)

Age – year	
Median	63.5
Interquartile range Q1–Q3	46.1–79.5
Range	13.0–100.4
Male sex – no. of patients (%)	140 (54.3)
Wound aetiology – no. (%)	
Postsurgical	93 (36.1)
Traumatic	86 (33.3)
Venous ulcer	38 (14.7)
Decubital ulcer	13 (5.0)
Arterial ulcer	11 (4.3)
Cast pressure	9 (3.5)
Burn/combustion	8 (3.1)
Comorbidities – no. (%)	
0	110 (42.6)
1	80 (31.0)
2	30 (11.6)
≥3	38 (14.7)
Comorbidities (encoded by ICD–10) – no. (%)	
I A00-B99 Certain infectious and parasitic diseases	12 (4.7)
II C00-D48 Neoplasms	10 (3.9)
III D50-D89 Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	2 (0.8)
IV E00-E90 Endocrine, nutritional and metabolic diseases	34 (13.2)
V F00-F99 Mental and behavioural disorders	14 (5.4)
VI G00-G99 Diseases of the nervous system with health services	17 (6.6)
VII H00-H59 Diseases of the eye and adnexa	9 (3.5)
VIII H60-H95 Diseases of the ear and mastoid process	0
IX I00-I99 Diseases of the circulatory system	59 (22.9)
X J00-J99 Diseases of the respiratory system	6 (2.3)
XI K00-K93 Diseases of the digestive system	8 (3.1)
XII L00-L99 Diseases of the skin and subcutaneous tissue	0
XIII M00-M99 Diseases of the musculoskeletal system and connective tissue	9 (3.5)
XIV N00-N99 Diseases of the genitourinary system	7 (2.7)
XV O00-O99 Pregnancy, childbirth and the puerperium	0
XVI P00-P96 Certain conditions originating in the perinatal period	0
XVII Q00-Q99 Congenital malformations, deformations and chromosomal abnormalities	0
XVIII R00-R99 Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	0
XIX S00-T98 Injury, poisoning and certain other consequences of external causes	17 (6.6)
XX V01-Y98 External causes of morbidity and mortality	0
XXI Z00-Z99 Factors influencing health status and contact	0
XXII U00-U99 Codes for special purposes	0

Table 2. Characteristics of wounds and their treatment

Duration of wound	
4–12 weeks	197 (76.36%)
4–12 months	33 (12.79%)
> 1 year	28 (10.85%)
Surface of wound (cm^2)	
Median	5.0
Interquartile range Q1–Q3	2.0–14.0
Range	0.5–300
Wound localization – no. (%)	
Head and trunk	11 (4.3)
Upper extremity	35 (13.6)
Thigh and knee	23 (8.9)
Lower leg	119 (46.1)
Ankle and foot	70 (27.1)
Wound bed score	
Initial	
Median	9
Interquartile range Q1–Q3	7–12
Range	2–15
Last	
Median	14
Interquartile range Q1–Q3	14–15
Range	3–16
Difference	
Median	4
Interquartile range Q1–Q3	0–7
Range	−4–13
Total treatment sessions	
Median	2
Interquartile range Q1–Q3	1–4
Range	1–10
Duration of therapy (days)	
Median	14
Interquartile range Q1–Q3	1–40
Range	1–288
Successful treatment – no. (%)	191 (74.03)

surface in cm^2 ($p < 0.001$), as well as information concerning wound aetiology and comorbidities. Chronic wounds lasting for weeks (4–12 weeks) before initial presentation showed a success rate of 82.23%. Wounds having lasted for months (4–12 months) showed treatment success in 63.64% and those lasting for years (>1 year) in 28.57%. Figure 2 shows the predictive value of the initial WBS at the time of the first presentation of the patient.

Table 3. Results of logistic regression analysis with stepwise selection of parameters influencing the probability of ESWT-success

Parameter	Odds ratio (95% confidence interval)	*p* value
Duration of wound	0.314 (0.198–0.499)	0.0001
Surface of wound	0.959 (0.938–0.981)	0.0003
Initial wound bed score	1.223 (1.087–1.377)	0.0008

All other investigated parameters (*i.e.*, age, sex, wound localization, wound aetiologies, comorbidities classified by the ICD-10 code) failed to meet the significance level ($p < 0.01$) to enter the logistic regression model.

ESWT = extracorporeal shock wave therapy.

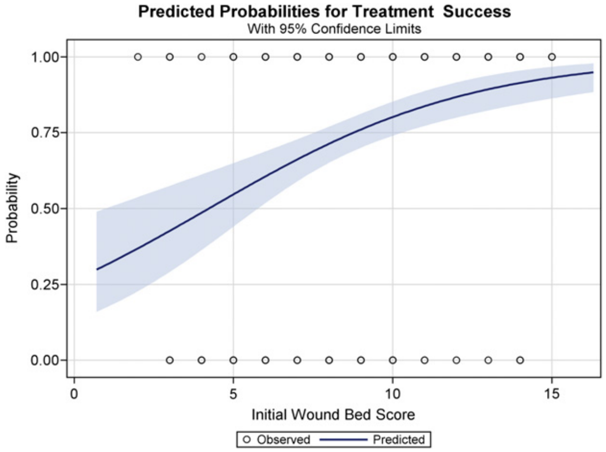


Fig 2. Initial wound bed score and the probability of ESWT success. Probabilities were calculated by logistic regression.

A median positive difference between the initial WBS and the final WBS of +4 was observed (Q1:0, Q3:+7, range –4 to +13). Paired profiles for the initial and final WBS as well as the distribution of the difference between initial and final WBS are shown in Figure 3.

A significant correlation ($p = 0.005$) existed between the initial WBS and the wound surface. The larger the wound surface was, the higher was the initial WBS (Fig. 4). Figure 4 also provides information about the relation between the initial WBS and wound duration as well as between wound surface and wound duration. No statistic significance could be detected.

DISCUSSION

Chronic soft tissue wounds pose a treatment challenge for doctors in a large number of medical specialties. The problems arise from a bouquet of reasons, the three most prominent being outpatient setting, treatment cost and duration and, finally, patient/nursing staff compliance with dressing systems. The outpatient problem cannot be solved by the involved doctor alone but is a product of the chronicity of the wound and the resulting extraneous decision making factors (reduction of hospital beds, per die costs of hospitalization and insurance coverage policies) leading to the patient's discharge after attempted primary treatment. Thus, the focus in the management of chronic soft tissue wounds is directed towards reduction of costs and of duration and towards simplification of treatment modalities in the outpatient/extramural setting. By achieving better compliance through the last measure, costs are held at bay again. Methods devised in the last decade were vacuum-assisted wound closure (Mullner et al. 1997), topical application of recombinant human platelet-derived growth factor-BB (Robson et al. 1992)

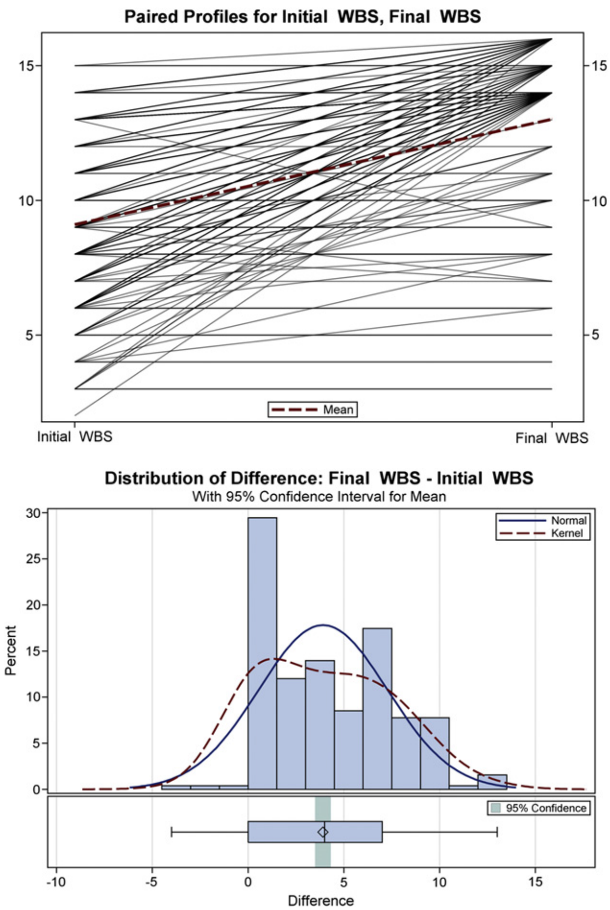
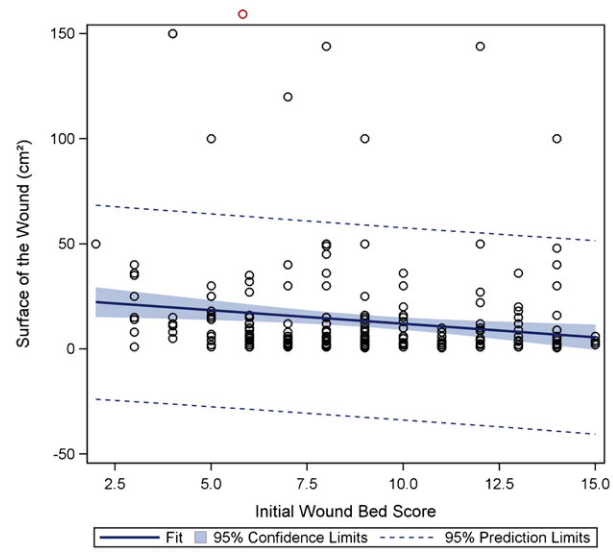


Fig. 3. Paired profiles and distribution of the difference of initial vs. final wound bed score (WBS).

and the use of an acellular matrix as human skin equivalent (Brigido et al. 2004). All these systems showed significant wound size reduction and accelerated healing properties but lacked complete epithelialisation. Another therapy introduced for soft tissue wounds in the last 10 years is hyperbaric oxygen therapy. It showed significant healing properties compared with conventional dressing regimes but was only applied to defined patient subgroups and its successes were not always reproducible (Bouachour et al. 1996; Wang et al. 2003).

In a recently published work, we were able to show that extracorporeal shock wave had the properties to achieve wound closure and complete epithelialisation, albeit the healing mechanism is not understood so far (Schaden et al. 2007). Our assumption was that through the local application of energy a neovascularisation could be achieved. This theoretic model gained more support by four research articles published lately (Stojadinovic et al. 2008; Davis et al. 2009; Kuo et al. 2009a). Interesting are the findings of Kuo (Kuo et al. 2009b) when they analyzed the effect of ESWT on wounds in diabetic rats. Increased vascular endothelial



Duration of Wound	Initial WBS (interquartile range)	Wound Surface (cm²) (interquartile range)
4-12 Weeks	9 (7-12)	5.0 (2.0-14.0)
4-12 Months	9 (6-11)	6.0 (2.0-11.0)
>1 Year	8 (5-10)	5.5 (3.8-27.5)
	p=0.070	p=0.402

Fig. 4. Correlations between initial wound bed score (WBS) and surface of the wound ($p = 0.005$) and the influence of wound duration on the two factors. The red circle represents an outlier (wound surface: 300 cm^2, initial WBS: 6).

growth factor (VEGF), endothelial nitric oxide synthesis (eNOS), and proliferating cell nuclear antigen (PCNA) expression were observed and, thus, a neo-angionetic property of ESWT could be postulated. Specifically, this last publication supports our present research that even over midterm observation periods, comorbidities do not influence the local wound healing processes induced through ESWT. It seems legitimate to announce that by the local application of pulsed energy, a local neoangiogenesis is achieved that overrides the negative generalized aspects of for example nutritional and metabolic diseases.

None of the adverse side effects described after the application of extracorporeal shock waves like organ perforation (Rodrigues Netto et al. 2003), hemorrhagic shock (Uemura et al. 2005) and tissue damage through gas body activation and inertial cavitation (Matlaga et al. 2008; Miller 2007) were observed in our patients. Destruction of nervous tissue (Hausdorf 2008) could not be ascertained, but gross clinical examination and follow-up did not open room for this assumption. Other publications (Malay 2006) support our results. Even our concern of activating a thrombotic process through platelet and vascular-wall destruction

Table 4. Estimated costs of treatment to obtain closure of an ulcus cruris venosum (6 cm × 3cm) by different advanced treatment systems

	Special dressings (~30 days)	Vacuum assisted wound closure (~14 days)	ESWT (~ 14 days)
1a	Antimicrobial calcium alginate dressing with nanocristaline silver for 7 days (3 dressing changes) 42.00 Euros	Mobile therapeutic vacuum pump • Installation fee 105.00 Euros	Orthowave 180C ESWT apparatus (200 sessions in 3 years as basic calculation until amortization) • 2 ESWT sessions 63.58 Euros
1b	Hydrogel, sterile 3.40 Euros/tube	Rent for 14 days 546.00 Euros	Ultrasound coupling gel, 1 tube (60 mL) 15.70 Euros
1c	Waterproof polyurethane foil for fixation of wound dressings, (3 changes) 10.35 Euros		
2a	Non-adhesive polyurethane foam dressing for 21 days (7 dressing changes) 42.00 Euros	Small granulation foam- dressing kit (3 dressing changes) 159.00 Euros	Non-adhesive polyurethane foam dressing for 14 days (4 dressing changes) 24.00 Euros
2b	Waterproof polyurethane foil for fixation of wound dressings, sterile (7 dressing changes) 24.15 Euros	Vacuum pump canister – 300 mL 31.00 Euros	Waterproof polyurethane foil for fixation of wound dressings, sterile (4 dressing changes) 20.70 Euros
3a	0.5 billing h for home-nursing/dressing change. 10 sessions 5 h	1 billing h for home-nursing/dressing change. 3 sessions 3 h	0.5 billing hours for home-nursing/dressing change. 4 sessions 2 h
3b	4 billing visits to surgeon/general practioner for debridement and weekly control	2 billing visits to surgeon/general practioner for debridement and control	2 billing visits to surgeon/general practioner for debridement, ESWT and control
Total	122 Euros/163 USD 5 nursing billing h 4 billing visits	841 Euros/1125 USD 3 nursing billing h 2 billing visits	124 Euros/166 USD 2 nursing billing h 2 billing visits

Prices are calculated according to suppliers in Europe, exchange rate 1 USD = 0.748 Euros, taxes and duties are not included.

with subsequent activation of the clotting agents could not be observed.

Success of ESWT seems to be independent of existing comorbidities because none of the observed comorbidities had a statistical influence on the probability of treatment success.

Furthermore, treatment success obviously does not depend on wound aetiology. Chronic soft tissue wounds resulting from post-traumatic wounds or from postsurgical wounds represented the majority in our study. ESWT of venous and of arterial ulcers as well as other aetiologies did not influence the rate of wound closure in the multivariate analysis. Comparing the three major groups of the ICD10 system (diseases of the circulatory system; mental disorders and diseases of the nervous system; endocrine, nutritional and metabolic diseases) with the three wound aetiologies (venous-, decubital- and arterial ulcers), one would expect that the comorbidities would have an influence when 47.1% of the patients (n = 70) with comorbidities suffer from these three mentioned entities and also show a hypothetic correlation with the three types of ulcers (*i.e.* 24% of the patients analysed for wound aetiology [n = 62]). That the influence of comorbidities and of wound aetiology on success of ESWT, anticipated by our team, could not be proven rests to a large extent on the not as yet understood healing mechanisms of ESWT. The above-mentioned research articles tend to support the notion that an ESWT overrides systemic effects locally, comparable to a femoro-popliteal bypass operation alleviating the local circulatory problem while the patient still suffers from arterial occlusive disease.

ESWT in combination with a wound bed scoring system represents an economically feasible treatment option (Table 4). Since success is significantly influenced by wound duration and the initial WBS, a timely beginning of ESWT and documentation of the initial WBS is recommended. If after an early treatment start and a median of two ESWT sessions, an increase in the WBS could not be observed, one could conclude that the ESWT could be considered unsuccessful and the search for other therapeutic options might be warranted. By applying this combination of ESWT and a wound bed scoring system, unnecessary outpatient clinic visits, hospital/clinic capacities and working hours of medical staff can be reduced. If a positive trend of the wound bed score could be observed on the other hand, wound closure could be achieved in a relatively short time (median duration of ESWT in successfully treated patients: 14 days or two ESWT sessions, Table 1) compared with the duration of the chronic wound before ESWT.

Limitations of our study were the one-armed, nonrandomized, nonblinded study design, but the aim of this work was to treat and to analyze subsequently all cases of chronic soft tissue wounds that were, prior to the individual ESWT, treated unsuccessfully with conservative and surgical methods. We, thus, offered ESWT to patients as a last line of treatment method, where established treatment options had already failed for more than a month.

In the near future, more phase 2 research will be needed to investigate the ESWT healing mechanisms on human tissue. Parallel to that, single or multicenter studies focussing on a defined single group of comorbidities or on one aetiology and its influence on ESWT success (employing large numbers of patient volunteers) will be needed. Prime candidates for investigation would be metabolic diseases and diseases of the circulatory system.

CONCLUSION

Comorbidities and wound aetiology have surprisingly no significant influence on the success of ESWT. Only the local wound properties, as represented by the WBS, matter when it comes to healing.

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