Prophylactic Low-Energy Shock Wave Therapy Improves Wound Healing After Vein Harvesting for Coronary Artery Bypass Graft Surgery: A Prospective, Randomized Trial

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Background. **Wound healing disorders after vein harvesting for coronary artery bypass graft surgery increase morbidity and lower patient satisfaction. Low-energy shock wave therapy (SWT) reportedly improves healing of diabetic and vascular ulcers by overexpression of vascular endothelial growth fractor and downregulation of necrosis factor κB. In this study, we investigate whether prophylactic low-energy SWT improves wound healing after vein harvesting for coronary artery bypass graft surgery.**

Methods. **One hundred consecutive patients undergoing coronary artery bypass graft surgery were randomly assigned to either prophylactic low-energy SWT (n = 50) or control (n = 50). Low-energy SWT was applied to the site of vein harvesting after wound closure under sterile conditions using a commercially available SWT system (Dermagold; Tissue Regeneration Technologies, Woodstock, GA). A total of 25 impulses (0.1 mJ/mm^2; 5 Hz) were applied per centimeter wound length. Wound healing was evaluated and quantified using the ASEPSIS score. (ASEPSIS stands for Additional treatment, presence of Serous discharge, Erythema, Purulent exudate, Separation of the deep tissue, Isolation of bacteria, and duration of inpatient Stay). Patient demographics, operative data, and postoperative adverse events were monitored.**

Results. **Patient characteristics and operative data including wound length (SWT 39 ± 13 cm versus control 37 ± 11 cm, $p = 0.342$) were comparable between the two groups. We observed lower ASEPSIS scores indicating improved wound healing in the SWT group (4.4 ± 5.3) compared with the control group (11.6 ± 8.3, $p = 0.0001$). Interestingly, we observed a higher incidence of wound healing disorders necessitating antibiotic treatment in the control group (22%) as compared with the SWT group (4%, $p = 0.015$). No SWT-associated adverse events were observed in the treatment group.**

Conclusions. **As shown in this prospective randomized study, prophylactic application of low-energy SWT improves wound healing after vein harvesting for coronary artery bypass graft surgery.**

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Wound healing disturbances after vein graft harvesting for coronary artery bypass graft surgery (CABG) reportedly occur in 1% to 24% of patients [1, 2]. Wound healing disturbances increase morbidity, prolong in-hopsital stay, increase treatment costs, and decrease patient satisfaction [1, 3]. Besides surgical accuracy and the best postoperative care, there are no prophylactic measures for the prevention of wound healing disturbances after vein graft harvesting for CABG.

Shock waves have been used to disintegrate kidney stones for the past 20 years [4]. Low-energy shock waves possess tissue regenerative potential and are routinely being used for the treatment of nonunions, plantar fasciitis, diabetic and vascular ulcers, burns, posttraumatic necroses, and disturbed wound healing [5–9]. One of the potential mechanisms behind the tissue regenerative potential of low-energy shock waves is their ability to upregulate expression of vascular endothelial growth factor (VEGF) and Flt-1, both in vivo and in vitro [10–14].

In this prospective randomized trial, we investigated, firstly, if low-energy shock wave therapy (SWT) improves wound healing, quantified using the ASEPSIS score (ASEPSIS stands for Additional treatment, presence of Serous discharge, Erythema, Purulent exudate, Separation of the deep tissue, Isolation of bacteria, and duration of inpatient Stay); and secondly, if low-energy SWT

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Fig 1. Low-energy shock wave therapy. (Use of illustration approved by MTS Europe GmbH, Konstanz, Germany, and Tissue Regeneration Technologies, Woodstock, GA.)

impacts the need for surgical revisions or use of antibiotics after vein graft harvesting for CABG.

Material and Methods

Patients

After approval was obtained by the Ethics Committee of the Medical University of Vienna, 100 consecutive patients undergoing elective CABG (with or without concomitant valve procedures) at our department gave their written informed consent and were enrolled in this prospective randomized study. Patients were randomly allocated to the SWT group and control group in a 1:1 ratio stratified according to age, sex, and body mass index. Emergency cases as well as patients tested positive for hepatitis C and human immunodeficiency virus were excluded from the study.

Shock Wave Therapy and Vein Graft Harvesting

After randomization, patients were assigned to undergo CABG with prophylactic low-energy SWT (SWT group, n = 50) or without it (control group, n = 50). Vein graft harvesting as well as wound closure in both groups was performed according to institutional standards using absorbable subcutaneous sutures (Vicryl; Ethicon Inc, Somerville, NJ) and staples for skin closure. Subcutaneous drains were placed if necessary. All patients received intraoperative antibiotic treatment (Cefazolin 2 × 2 g; AstroPharma, Vienna, Austria) before skin incision and before skin closure. In the treatment group, low-energy SWT was applied after wound closure at the end of the operation under sterile conditions. Shock waves were generated using a Dermagold system (Tissue Regeneration Technologies, Woodstock, GA, manufactured by MTS Europe GmbH, Konstanz, Germany [Fig 1]). Ultrasound transmission gel (Aquasonic; Parker Laboratories, Fairfield, NJ) was used as contact medium. A total of 25 impulses (0.1 mJ/mm^2; 5 Hz) per centimeter wound length were applied to the vein harvesting area. The

Table 1. ASEPSIS Score

	Proportion of Wound Affected (%)					
Wound characteristics	0	<20	20–39	40–59	60–79	>80
Serous exudate	0	1	2	3	4	5
Erythema	0	1	2	3	4	5
Purulent exudate	0	2	4	6	8	10
Separation of deep tissues	0	2	4	6	8	10

Criteria	Points
Additional treatment:	
Antibiotics	10
Drainage of pus under local anesthesia	5
Debridement of wound (general anesthesia)	10
Serous exudate	daily 0–5
Erythema	daily 0–5
Purulent exudate	daily 0–10
Separation of deep tissues	daily 0–10
Isolation of bacteria	10
Stay as inpatient prolonged over 14 days	5

Category of infection	Total Score
Satisfactory healing	0–10
Disturbance of healing	11–20
Minor wound infection	21–30
Moderate wound infection	31–40
Severe wound infection	>40

ASEPSIS = Additional treatment, presence of Serous discharge, Erythema, Purulent exudate, Separation of the deep tissue, Isolation of bacteria, and duration of inpatient Stay.

total duration of the low-energy SWT depended on the wound length and lasted as long as 10 minutes. Patients in the control group underwent routine vein graft harvesting without low-energy SWT. Wounds were closed with non-occlusive surgical dressing under sterile conditions at the end of the operation; drains were removed 48 hours postoperatively.

Wound Healing Assessment

ASEPSIS SCORE. The primary study endpoint was wound healing assessed and quantified using the ASEPSIS score [15], which is a scoring method for postoperative wound infections. Based on the ASEPSIS score, wound healing was quantified by a blinded investigator from postoperative days 3 to 7. The principles of the ASEPSIS score are given in Table 1.

SURGICAL REVISIONS AND ANTIBIOTIC TREATMENT. Secondary endpoints were (1) need for surgical revisions of the vein graft harvesting site and (2) need for antibiotics defined as any new antibiotic treatment initiated for wound healing disturbances of the vein graft harvesting site.

Statistics

Statistical analysis was performed using SPSS 14.0 (SPSS, Chicago, IL). Categorical variables are expressed as frequency distributions and percentages, continuous variables are expressed as mean ± SD. Categorical variables were compared by means of χ^2 or Fisher's exact test, as appropriate. Continuous variables were compared using two-way analysis of variance after testing for normality of distribution. A Bonferoni-Holm correction for multiple testing was performed. A power analysis was performed before the study initiation, based on a power of 0.8 and an alpha of.05. All p values less than 0.05 were considered significant, two-sided.

Results

Patients

Patients randomly assigned to the SWT group and control group were comparable according to age, sex, body mass index, risk factors for wound healing disorders, and history of impaired wound healing. Detailed patient characteristics are given in Table 2.

Table 2. Patient Demographics

	SWT Group (n = 50)	Control Group (n = 50)	*p* Value
Age (years)	68 ± 7	70 ± 8	0.255
Male (%)	76.0	70.0	0.499
BMI (kg/m^2)	29 ± 5	28 ± 4	0.313
Diabetes mellitus (%)	32.0	38.0	0.675
Hypertension (%)	84.0	90.0	0.372
Hyperlipidemia (%)	86.0	78.0	0.436
LVEF (%)	54 ± 16	53 ± 14	0.648
Caucasian (%)	100.0	100.0	1.000
History of impaired wound healing (%)	14.0	4.0	0.160

BMI = body mass index; LVEF = left ventricular ejection fraction; SWT = shock wave therapy.

Table 3. Intraoperative and Postoperative Data

	SWT Group (n = 50)	Control Group (n = 50)	*p* Value
Number of grafts	2.7 ± 1	2.7 ± 0.8	0.833
CPB time (min)	110 ± 35	112 ± 32	0.800
Aortic cross-clamp time (min)	66 ± 21	65 ± 24	0.784
Duration of operation (min)	246 ± 59	239 ± 41	0.488
Leg wound length (cm)	39 ± 13	37 ± 11	0.342
In-hospital stay (days)	15 ± 11	16 ± 19	0.759
In-hospital death (%)	2	4	0.242
Surgical revision leg wound (%)[a]	2	10	0.092
Antibiotics for leg wound (%)[b]	4	22	0.015
Total ASEPSIS score (points)	4.4 ± 5.3	11.6 ± 8.3	0.0001

[a] Surgical revision of the vein graft harvesting site. [b] Antibiotic treatment initiated because of wound healing disturbance of the vein graft harvesting site.

CPB = cardiopulmonary bypass; SWT = shock wave therapy; other abbreviation as in Table 1.

Operative and Postoperative Data

Veins were harvested by conventional open harvest technique according to our institutional standards. Intraoperative data, including length of vein harvesting site and total operation time, were comparable between the two groups (Table 2). Interestingly, we observed a higher incidence of wound healing disorders necessitating antibiotic treatment in the control group (22%) as compared with the SWT group (4%, $p = 0.015$). Furthermore, we observed a strong trend toward more need for surgical revisions in the control group (control group 10%, versus SWT group 2%; $p = 0.092$). We observed a total of 3

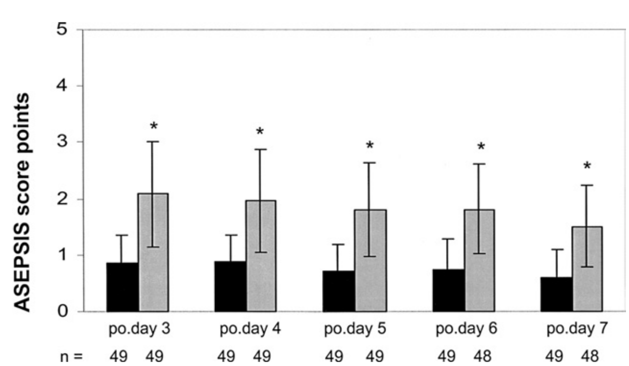

*Fig 2. Mean ASEPSIS score points from postoperative day (po.day) 3 to 7 for shock wave therapy group (black bars) and control group (gray bars). Results are expressed as mean ± SD. *p < 0.05 versus shock wave therapy group. (ASEPSIS = Additional treatment, presence of Serous discharge, Erythema, Purulent exudate, Separation of the deep tissue, Isolation of bacteria, and duration of inpatient Stay.)*

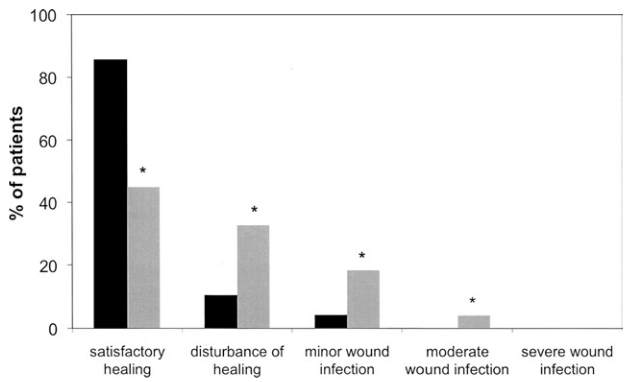

*Fig 3. Wound healing classes according to the ASEPSIS score for shock wave therapy group (black bars) and control group (gray bars). *$p < 0.05$ versus shock wave therapy group. (ASEPSIS = Additional treatment, presence of Serous discharge, Erythema, Purulent exudate, Separation of the deep tissue, Isolation of bacteria, and duration of inpatient Stay.)*

in-hospital deaths (3% of the study population), 2 in the control and 1 in the treatment group. Causes of death were multiorgan failure in 1 patient, hemorrhagic stroke in 1 patient, and pulmonary embolism in 1 patient. Detailed operative and postoperative data are given in Table 3.

ASEPSIS Score

The ASEPSIS score was analyzed by two methods. First, we compared the ASEPSIS score on postoperative days 3 to 7 between the two groups. We found significantly lower ASEPSIS scores in the SWT group on postoperative days 3 through 7 as compared with the control group. Results of ASEPSIS score from postoperative days 3 to 7 are given in Figure 2. Second, we grouped the overall ASEPSIS score into five descriptive classes (satisfactory healing, 0 to 10 points; disturbance of healing, 11 to 20 points; minor wound infection, 21 to 30 points; moderate wound infection, 31 to 40 points; and severe wound infection, more than 40 points). By this method, we found more satisfactory healing in the SWT group. Furthermore, we found significantly more disturbances of healing and minor as well as moderate wound infections in the control group (Fig 3). According to the ASEPSIS score, we observed no severe wound infection during the study period in the whole study population.

Comment

Despite the increased use of endoscopic techniques, conventionally harvested greater saphenous veins remain the most commonly used conduits for CABG. Wound healing disturbances after conventional open vein harvesting affect as many as 24% of patients, increase morbidity and treatment costs, and decrease patient satisfaction [1–3]. Besides surgical accuracy and best care, no accepted prophylactic treatment that improves wound healing exists. Here, we demonstrate that prophylactic low-energy SWT improves wound healing after conventional open vein harvesting for CABG.

Although SWT-mediated tissue regeneration in orthopedic diseases and ulcers is not yet fully clarified, two potential mechanisms have been described in the past. Low-energy SWT induces overexpression of VEGF and Flt-1 and angiogenesis in different animal models [10–14]. This activation of the endogenous angiogenic system may be the result of SWT-induced hyperpolarization and Ras activation [16] and nonenzymatic nitric oxide synthesis [17]. Although enhanced blood supply plays an important role for wound healing, shock waves also possess an anti-inflammatory action. Low-energy SWT efficiently downregulates necrosis factor κB activation, which normally is a key event in the induction of numerous inflammatory cytokines in vitro [18]. Importantly, as yet, no low-energy SWT–associated serious adverse events have been reported. Therefore, prophylactic low-energy SWT may improve wound healing after vein harvesting for CABG.

Low-energy SWT was used as prophylactic treatment in the present study. Wound healing of the vein harvesting site was assessed and quantified using a well-established scoring system, the ASEPSIS score [15]. Using this scoring system, we observed lower ASEPSIS scores, indicating improved wound healing in the SWT group. The APEPSIS score furthermore revealed a higher percentage of satisfactory healing in the SWT group and a higher percentage of minor and moderate wound healing disturbances in the control group. Moreover, we observed a higher incidence of wound healing disturbances necessitating antibiotic treatment and a strong trend toward more surgical revisions of the vein harvest site in the control group. Interestingly, in-hospital stay was not prolonged in the control group. The explanation for that could be that patients with wound healing disturbances are treated on an outpatient basis at our department. Low-energy SWT did not prolong the overall operative time, and we did not observe any adverse events (hematoma formation, skin lacerations, postoperative pain) after low-energy SWT. Prophylactic low-energy SWT treatment impressively improved healing of the vein harvest site in the present study.

Limitations to the study are that we performed no analysis on the cost effectiveness of low-energy SWT in the present study, nor did we analyze patient satisfaction.

As shown in this prospective randomized study, prophylactic low-energy SWT improves wound healing after vein harvesting for CABG. Therefore, low-energy SWT may develop into an efficient and easily applicable prophylaxis for wound healing disorders after vein harvesting.

The shock wave therapy system (Dermagold; Tissue Regeneration Technologies, Woodstock, GA, manufactured by MTS Europe GmbH, Konstanz, Germany) as well as the needed disposables were provided by MTS Europe GmbH, Konstanz, Germany.

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The Society of Thoracic Surgeons: Forty-Fifth Annual Meeting

Please mark your calendars for the Forty-Fifth Annual Meeting of The Society of Thoracic Surgeons, to be held in San Francisco, California, from January 26–28, 2009. The program will provide in-depth coverage of surgical topics selected to enhance and broaden the knowledge of cardiothoracic surgeons. Attendees will benefit from traditional Abstract Presentations, as well as Surgical Forums, Breakfast Sessions, and Surgical Motion Pictures. Parallel sessions will focus on specific subspecialty interests.

Advance registration forms, hotel reservation forms, and details regarding transportation arrangements, as well as the complete meeting program, were mailed to Society members this fall. Also, complete meeting information is available on the Society's Web site at www.sts.org. Nonmembers who wish to receive information on the Annual Meeting may contact the Society's secretary, Douglas E. Wood.

The abstract submission deadline was June 23, 2008, at 11:59 PM CDT. Please direct any questions regarding your submission to the Society's headquarters.

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