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ORIGINAL ARTICLE

Electrical Myostimulation (EMS) Improves Glucose Metabolism and Oxygen Uptake in Type 2 Diabetes Mellitus Patients—Results from the EMS Study

Frank van Buuren, MD, MBA,[1] Dieter Horstkotte, MD, PhD,[1] Klaus Peter Mellwig, MD,[1] Andreas Fründ,[1] Marios Vlachojannis, MD,[1] Nicola Bogunovic, MSc,[1] Zisis Dimitriadis, MD,[1] Jürgen Vortherms, MD,[1] Reed Humphrey, PhD,[2] and Josef Niebauer, MD, PhD, MBA[3]

Abstract

Aims: In patients with type 2 diabetes mellitus (T2DM) exercise training is recommended to improve glycemic control. Electrical myostimulation (EMS) of skeletal muscles is a new method to increase exercise capacity in patients with chronic heart failure. The aim of this study was to investigate the effects of EMS in T2DM on glucose metabolism, body composition, and exercise performance using a newly designed stimulation suit that involves trunk, leg, and arm muscles.

Subjects and Methods: Fifteen individuals (nine males; 61.7 ± 14.8 years old) were trained for 10 weeks twice weekly for 20 min with EMS. Effects on glucose, glycosylated hemoglobin (HbA_{1c}), oxygen consumption, and body composition were evaluated.

Results: There was a significant increase of oxygen uptake at the aerobic threshold from 12.3 ± 0.8 to 13.3 ± 0.7 mL/kg/min ($P = 0.003$) and of maximal work capacity from 96.9 ± 6.4 to 101.4 ± 7.9 W ($P = 0.046$), with a concomitant trend for improved maximal oxygen uptake (from 14.5 ± 0.9 to 14.7 ± 0.9 mL/kg/min [$P = 0.059$]). Fasting blood glucose level decreased from 164.0 ± 12.5 to 133.4 ± 9.9 mg/dL ($P = 0.001$), and HbA_{1c} level decreased from 7.7 ± 0.3% to 7.2 ± 0.3% ($P = 0.041$), whereas mean total weight (from 101.5 ± 4.0 to 103.1 ± 4.3 kg) and proportion of body fat (from 38.8 ± 3.2% to 40.3 ± 3.4%) remained statistically unchanged.

Conclusions: EMS can improve glucose metabolism and functional performance in T2DM patients. These data suggest that EMS might emerge as a novel additional therapeutic mode of exercise training and might help patients to overcome their sedentary lifestyle.

Introduction

Exercise training in type 2 diabetes mellitus (T2DM) patients is recommended to improve glycemic control, obesity, and body composition.[1–4] Studies to date have investigated the effects of endurance and resistance training. It has been assumed that endurance training might act to improve glycemic control primarily by improving insulin resistance, whereas resistance training would augment the capacity for glucose uptake by increasing skeletal muscle mass.[5] The amelioration of insulin resistance caused by physical training may be due to changes in several potential factors, including, but not limited to, body fat mass, fat distribution, and maximal aerobic performance.[6]

It is well documented that exercise induces an improved muscle glucose transport, in an interaction independent of insulin levels. As the acute effect of physical activity on glucose diminishes, it is replaced by an increase in insulin sensitivity that leads to a decrease in the insulin concentration required to achieve a defined glucose transport.[7] Both physical activity and insulin trigger independently the redistribution of the glucose transporter protein 4 (GLUT4) from the cell interior to the cell surface membranes, where it transports glucose from the extracellular milieu into the cell.[8–10] Even a

[1]Heart and Diabetes Center North Rhine-Westphalia, Department of Cardiology, Ruhr University Bochum, Bad Oeynhausen, Germany.
[2]School of Physical Therapy & Rehabilitation Science, The University of Montana, Missoula, Montana.
[3]University Institute of Sports Medicine, Prevention and Rehabilitation, Paracelsus Medical University, Salzburg, Austria.

single exercise session can induce an increased insulin-stimulated glucose transport in the cell and improves whole-body insulin sensitivity for up to 2–72 h.[8,11]

Recent studies demonstrated that different GTPase activation proteins (TBC1D1 and TBC1D4) play different roles in the regulation of glucose transport stimulated by insulin and/or exercise.[8] The better understanding of their complex biological roles is subject of ongoing studies.

Previous studies have revealed a significant association between an improvement of aerobic fitness through aerobic training and glycosylated hemoglobin (HbA_{1c}) levels.[12] Oxygen consumption, maximal workload, and ventilatory threshold were significantly associated with changes in HbA_{1c} level when a combination of endurance and resistance training was performed.[12] Improving both upper and lower extremity muscle force and increasing exercise tolerance in low-functioning patients with diabetes might establish a baseline for conventional exercise training in this population and improve clinical outcomes.

Electrical myostimulation (EMS) of the skeletal muscles is a new therapeutic strategy with promising treatment effects in patients with chronic heart failure.[13–15] It is based on the electrical stimulation of large muscle groups resulting in a pulsed contraction of the muscles without any active movement of the individual. In the past EMS was performed in critical ill and bedridden patients with underlying diseases like muscular dystrophy, scoliosis, or paraplegia.[16] As some cardiac patients are not clinically suited for classic physical training, EMS has been shown to be an elegant alternative for physical training either as a primary intervention or as a baseline program bridging patients to more conventional exercise training. In fact, studies have shown that EMS can be effective in patients suffering from chronic heart failure to improve exercise capacity and avoid muscle atrophy due to advanced comorbidities or the severity of left ventricular dysfunction.[17,18]

EMS might provide a novel alternative for patients with diabetes who cannot or will not exercise at sufficiently therapeutic levels. This is of great relevance because T2DM patients often fail to meet the recommended amount of exercise training[19–22] and consequently miss the beneficial effects of both endurance[23,24] and strength[25] training. A case study with eight patients showed that after 2 months of EMS training of the thigh muscles, the HbA_{1c} level could be reduced significantly.[26] However, there are no data in the literature that describe the effects of an EMS training also including, in addition to the legs, muscle groups of the arms and trunk (extended EMS [exEMS]) to improve glycemic control, the objective of the present study. Furthermore, our aim was to measure the effects of EMS in T2DM patients on body composition and exercise performance.

Subjects and Methods

Subjects

The data of the presented EMS training program are an analysis of an ongoing longitudinal cohort study including 60 individuals. Fifteen of these patients were diagnosed as having T2DM, and we present the data of this subgroup analysis as a pilot study in this article. All patients received exEMS training. Their baseline characteristics are listed in Table 1. The hospital ethics committee approved the study (protocol number 27/2008, University of Bochum, Bad Oeynhausen, Germany), and written informed consent was obtained from all individuals.

Table 1. Baseline Characteristics of Patients with Diabetes

	Preintervention	*Postintervention*	P *value*
Age (years)	61.73 ± 3.82		
Body surface area (m^2)	2.20 ± 0.0	2.20 ± 0.00	0.512
Body mass index (kg/m^2)	34.6 ± 1.50	35.5 ± 1.6	0.451
Weight (kg)	101.5 ± 4.0	103.1 ± 4.3	0.470
Fat (%)	38.8 ± 3.2	40.3 ± 3.4	0.301
Water (%)	46.5 ± 1.9	46.7 ± 1.9	0.726

Nine men and six women with diabetes participated in the intervention. Data are mean ± SD values.

Inclusion and exclusion criteria

Patients were included if the duration of T2DM was more than 2 years. All individuals were on optimal drug therapy when entering the study. A change of medication during the EMS phase had to be reported by the patients. A written confirmation of a maintained habitual activity level during the EMS phase was obtained. None of the individuals involved in the study started a supplementary individual activity program. Medication and the level of activity remained unchanged during the EMS phase and in the preceding 8 weeks (written confirmation was obtained).

Patients with severe cardiac arrhythmias, New York Heart Association Class IV, ejection fraction of <25%, hemodynamic relevant valve stenosis or regurgitation (i.e., > mild), active myocarditis, hypertrophic cardiomyopathy, pregnancy, and kidney dysfunction (creatinine level of >1.5 mg/dL) were not suitable for inclusion in the study. Because an interference of EMS with internal cardioverter defibrillators or permanent pacemakers could not be ruled out, these patients were not included. Severe dermatologic disorders made the application of EMS impossible.

Medication

At baseline and at the end of the study medication was recorded. In order to avoid hypoglycemic events, physicians were allowed to adapt drug therapy throughout the study.

EMS therapy and stimulation protocol

EMS is a technique of causing contraction of muscles by electrical stimulation. Energy is applied transcutaneously to the skin overlying the muscles via electrodes. Electrodes were fixed in the inside surface of a dedicated suit and connected via electrical cords to the application unit (Fig. 1). EMS simultaneously activated eight major muscle groups, including muscles of upper arm, chest, shoulder, upper and lower back, abdominal, gluteal, hip region including the pelvic floor, and upper legs.

Training was performed for 10 weeks, twice weekly for 20 min under controlled conditions, using the Miha-Bodytec stimulation system (Miha-Bodytec GmbH, Augsburg, Germany). Heart rate and blood pressure were measured at rest

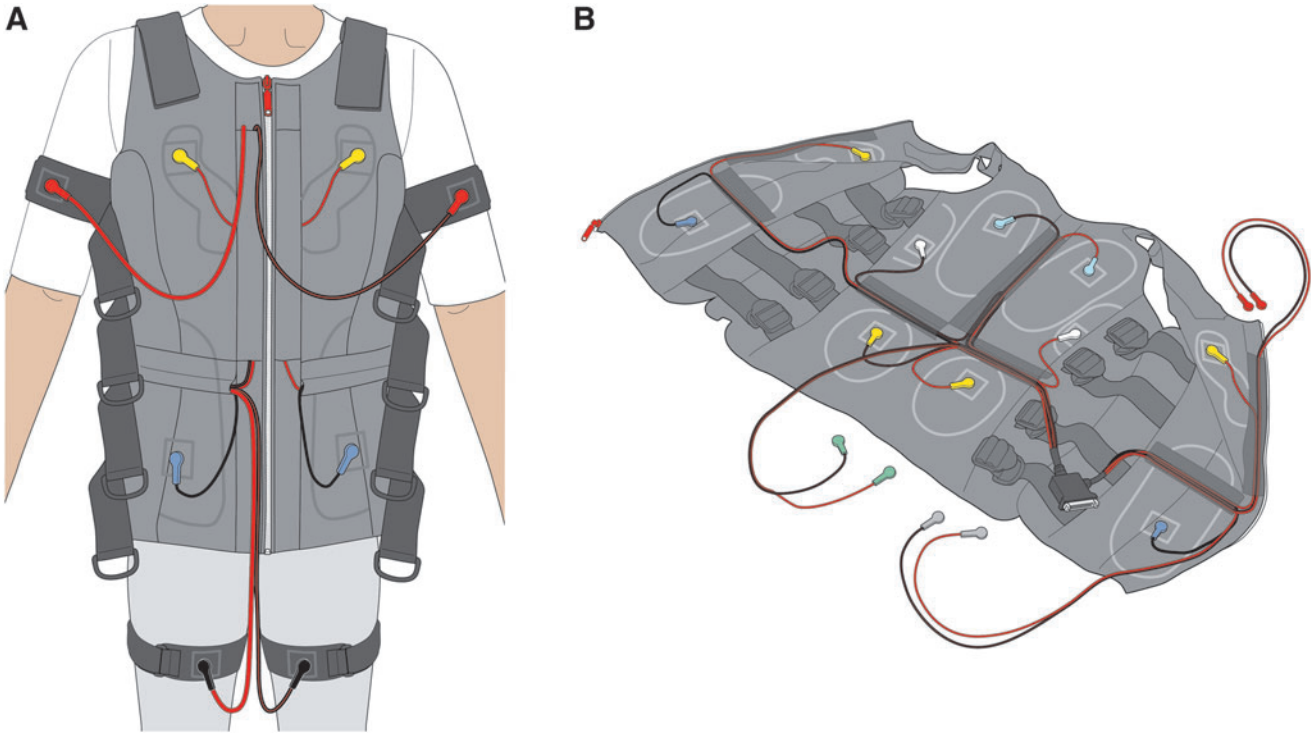

FIG. 1. **(A** and **B)** Stimulation vest of the dedicated suit. All electrodes are placed in the inside surface and are connected via electrical cords to the application unit. There are supplementary electrodes for the upper arm and the upper leg. Electrical cords connect also these electrodes to the vest. Reprinted with permission from Miha-Bodytech, Augsburg, Germany.

immediately before each EMS session. Muscle contraction initiated by a given energy depends on the composition of the body (fat, water, etc.) and the resistance of the skin. The aim of the training was a sufficient activation of the muscles without inducing pain due to ''overcontraction.'' Electrical stimulation of the muscles was performed under supervision for 4 s, followed by a 4-s recovery period (frequency of the impulse was 80 Hz). The intensity of the impulses was self-selected by the patient, with a maximum output of 350 mA.

Study protocol

All 15 individuals were examined immediately before entering the study and within 1 week after finishing EMS therapy. In addition to assessment of medical history and physical examination, all subjects had a 12-lead electrocardiogram performed. Height, weight, and body fat were measured with the subject barefoot on an impedance scale (TBF-410 MA body composition analyzer; Tanita, Tokyo, Japan). Body mass index and body surface area were calculated from these data. Fasting glucose and HbA_{1c} levels were measured before and after the exEMS training phase during the morning.

Conventional echocardiography was performed according to the guidelines of the American Society of Echocardiography[27] (Vingmed Seven; GE Healthcare, Horten, Norway). Left ventricular end-diastolic index and left atrial end-systolic diameter index were calculated using body surface area. Measurement of cavity size and wall thickness (interventricular septum end-diastolic and posterior wall end-diastolic) was derived from M-mode recording. Left ventricular function was determined by means of Simpson's rule. Biplane measurements were applied using paired apical four- and two-chamber views. Endocardial borders were outlined off-line in end-diastole and end-systole by two independent physicians accredited in echocardiography.

Cardiopulmonary exercise testing was performed as recommended by the recommended standards of the European Association for Cardiovascular Prevention and Rehabilitation.[14] The cardiopulmonary exercise testing was done with spiroergometry (ZAN 600 USB CPX, h/p/cosmos quasar; nSpire Health GmbH, Oberthulba, Germany). The exercise protocol was selected based on the subject's initial level of fitness, starting with 10 W and increasing by 10 W every 2 min for lower-fitness subjects or starting with 25 W and increasing by 25 W every 2 min. Each participant performed the same individual stress test protocol before and after EMS therapy. Subjects were encouraged to achieve a respiratory exchange ratio of ≥ 1.0. Oxygen consumption at anaerobic threshold (VO_2AT) and oxygen consumption at peak exercise capacity ($peakVO_2$) were measured using the v-slope method. Reasons for terminating the test were shortness of breath, muscular exhaustion, severe arrhythmia, blood pressure dysregulation, or dizziness.

Statistical analyses

The statistical analyses were performed using SPSS for Windows software (version 18.0; (SPSS Inc., Chicago, IL). The continuous variables were presented as means and medians, whereas SD was chosen as the measure of dispersion.

Regarding their normal distribution, the continuous variables were tested by means of the Kolmogorov–Smirnov test. Although some of the tested variables did not feature any

normal distribution ($P < 0.05$), a normal distribution could be calculated for other variables ($P \geq 0.05$). Thus, for the comparison of the samples, tests for normally distributed samples and nonparametric tests for non-normally distributed samples were used.

For the comparison of two independent, normally distributed samples, we applied the *t* test. Homogeneity of the variances was tested by means of the Levene test. Because of the proven homogeneity of the variances, Student's *t* test was carried out. However, for non-normally distributed samples, the Mann–Whitney U test was applied as a nonparametric procedure. For the comparison of more than two independent, normally distributed samples, the analysis of variance test was performed, but in the case of non-normal distribution, the Kruskal–Wallis test was used. The correlation between two variables was analyzed by Spearman's ρ.

A value of $P < 0.05$ was considered to be statistically significant for all statistical tests.

Results

Biometric data, blood pressure, and heart rate

The baseline characteristics of patients are reported in Table 1. None of the individuals had to interrupt or terminate EMS therapy. None of the enrolled individuals was without EMS for more than 6 days, and all completed 20 sessions in 10 weeks.

Of the 15 patients, four were on β-blockers, four were on AT1-blockers, five were on angiotensin-converting enzyme inhibitors, one was on diuretics, and five were on calcium channel blockers. T2DM therapy consisted of diet alone ($n = 2$ patients), metformin ($n = 9$), sulfonylureas ($n = 2$), incretins ($n = 3$), and insulin ($n = 10$). Five patients had to reduce their insulin intake; all other antidiabetes medications during the EMS phase were not changed. In all patients weight and proportion of fat did not change significantly (Table 1).

Systolic blood pressure at rest before each exEMS unit was 142.1 ± 3.4 mm Hg versus 139.7 ± 3.3 mm Hg after 10 weeks of (diastolic blood pressure went from 74.4 ± 2.7 to 73.9 ± 2.7 mm Hg). Resting heart rate pre- and posttraining was 82.3 ± 3.0 and 83.8 ± 3.4 beats/min, respectively.

Exercise capacity

After 10 weeks of exEMS training there was a significant increase of VO_2AT by 8.1%, from 12.3 ± 0.8 to 13.3 ± 0.7 mL/kg/min ($P = 0.003$) (Table 2), and a trend for an increase of $PeakVO_2$ (from 14.5 ± 0.9 to 14.7 ± 0.9 mL/kg/min [+1.4%; $P = 0.059$]). $PeakVO_2$ normalized to fat free mass increased from 22.3 ± 5.82 to 24.55 ± 6.29 mL/kg/min.

The maximum workload at the end of the stress test improved from 96.9 ± 6.4 to 101.4 ± 7.9 W (+4.6%; $P = 0.046$) (Table 2), whereas the improvement of workload at the aerobic threshold failed statistical significance (from 82.6 ± 5.0 to 88.2 W [+6.8%; $P = 0.142$]). Each patient reached a heart rate above 90% of the predicted maximum heart rate for his or her age. Respiratory exchange ratio at $PeakVO_2$ was 1.05 ± 0.02 when entering the study and 1.05 ± 0.03 at follow-up.

Echocardiographic data

The increase of left ventricular ejection fraction from 51.0 ± 1.7 to 53.2 ± 1.2 was not significant. Also, the other echocardiographic parameters like left ventricular diameter and wall thickness did not change significantly (Table 2).

Glucose metabolism

The fasting glucose level decreased by 18.6%, from 164.0 ± 12.5 to 133.4 ± 9.9 mg/dL ($P = 0.001$). The HbA_{1c} level dropped by 6.5%, from 7.7 ± 0.3% to 7.2 ± 0.3%, after the EMS phase ($P = 0.041$).

Discussion

Physical performance

EMS as a training modality as an alternative to classic exercise training yields mixed results in patients with T2DM

Table 2. Laboratory, Spiroergometry, and Echocardiography of diabetes Patients Before and After Extended Electrical Myostimulation

	Diabetes patients (n = 15) receiving extended EMS			
	Preintervention	*Postintervention*	*Change (%)*	P *value*
Work (W)				
At threshold	82.6 ± 5.0	88.2 ± 7.8	+6.8	0.142
Maximum	96.9 ± 6.4	101.4 ± 7.9	+4.6	0.046
VO_2AT (mL/kg of body weight/min)	12.3 ± 0.8	13.3 ± 0.7	+8.1	0.003
$PeakVO_2$ (mL/kg of body weight/min)	14.5 ± 0.9	14.7 ± 0.9	+1.4	0.059
LV EDD (mm)	51.1 ± 1.6	48.5 ± 1.0	−5.1	0.191
LA ESD (mm)	40.7 ± 2.1	41.2 ± 1.5	+1.2	0.966
LV IVS ED (mm)	11.3 ± 0.4	11.2 ± 0.6	−0.9	0.785
LV PW ED (mm)	11.8 ± 0.6	10.8 ± 0.7	−8.5	0.134
LV EF (%)	51.9 ± 1.7	53.2 ± 1.2	+2.5	1.0
Glucose (mg/dL)	164.0 ± 12.5	133.4 ± 9.9	−18.6	0.001
HbA_{1c} (%)	7.7 ± 0.3	7.2 ± 0.3	−6.5	0.041

Data are mean ± SD values.

EMS, electrical myostimulation; HbA_{1c}, glycosylated hemoglobin; LA ESD = left atrium end-systolic diameter; LV EDD, left ventricular end-diastolic diameter; LV EF, left ventricular ejection fraction; LV IVS ED, left ventricular interventricular septum end-diastolic; LV PW ED, left ventricular posterior wall end-diastolic; $PeakVO_2$, oxygen consumption at peak exercise; VO_2AT, oxygen consumption at aerobic threshold.

and low functional status. Both peak power output and VO_2AT improved, suggesting a modest degree of physiological adaptation that should translate to improved functional status and ability to engage in activities of daily living with less cardiovascular and physical stress. There was also a trend for an increase in $PeakVO_2$, which was rather modest.

The anaerobic threshold is often used as an indicator of performance. However, its correct measuring is in continuous debate as it has to be seen in the light of lactate kinetics.[28] The lactate threshold can be interpreted as the inflection point to indicate a significant increase in anaerobiosis, whereas others interpret the lactate threshold to reflect an imbalance among lactate production, disposal, and removal. Regular training can increase the metabolic clearance rate of lactate in healthy individuals by up to 97%.[28] Hence, the concentration of lactate in blood does not provide sufficient information about the lactate produced in the muscle through glycolysis.[29] The accumulation of lactate beyond the lactate threshold represents more that the lactate removal from the blood fails to keep pace with the lactate production. Lactate is used continuously under fully aerobic conditions, and it is produced and used by the muscle at the same time. This process does not fully depend on the presence of oxygen.[30–32] Lactate exchange between muscle and blood is a dynamic process consisting of continuous muscle uptake and release, depending on rest and physical activity.[31] It is of note that, because of their large mass and metabolic capacity, skeletal muscles are the major component of this so-called lactate shuttle.

In contrast to the lactate threshold, the concept of measurement of oxygen consumption is another accepted method to evaluate aerobic endurance capacity. There are still concerns regarding the validity of maximum oxygen uptake as it is difficult to discriminate in the presence of potential comorbidities and, of course, motivation.[33] Therefore, attempts have been made to establish submaximal parameters. In the 1960s Wasserman and McIlroy[34] plotted ventilation versus oxygen uptake and termed it anaerobic threshold. The visual assessment of the point where the rate of elimination of carbon dioxide increases nonlinearly with respect to oxygen uptake to determine the anaerobic threshold is referred to as the v-slope method.[35] Although recent studies have demonstrated relevant inter- and intra-observer variation, this remains one of the most accepted methods. In the presented study we also used the v-slope method to determine the anaerobic threshold. Lactate determination from blood samples can provide additional insight regarding the anaerobic threshold but were not collected in this particular study.

In a nonrandomized trial of EMS that included 34 patients with chronic heart failure, oxygen uptake improved by 28% in the EMS group after 10 weeks of training.[14] Twenty-six sedentary healthy patients with no underlying cardiac disease improved their VO_2AT by 13% in that study. These data correspond to the findings in the presented trial as in our group VO_2AT improved by 8%, whereas $PeakVO_2$ did not change fundamentally. However, we found a relevant but not significant increase of $PeakVO_2$ normalized to fat free mass.

The changes in muscle performance and functional status without changes in $PeakVO_2$ are consistent with the findings of Harris et al.,[17] but not those of Maillefert et al.,[18] who showed a significant increase in $PeakVO_2$ in patients with chronic heart failure. It is relevant to note that these two studies used significantly higher training volumes; the similar findings of Harris et al.[17] were accomplished by 30 min of EMS, 5 days per week, whereas the training by Maillefert et al.[18] was substantially more extensive, at 1 h daily, 5 days per week, suggesting a dose–response relationship for training may exist between 30 and 60 min. It is also important to note that in these studies significant findings could be obtained with 5 or 6 weeks of training, compared with 10 weeks in the present study. It is unknown if subjects in our study achieved significant physiological adaptation by the midpoint of training, but it would appear feasible. It does suggest that subsequent investigations of patients with T2DM might well benefit from increased volume of EMS for a shorter training period.

Glucose metabolism

It is known that EMS can enhance energy consumption and carbohydrate oxidation even at a rather low intensity.[36] It is of interest that even 7 days of exercise training can attenuate postprandial glucose levels as well as the frequency, magnitude, and duration of glycemic excursions.[37] Furthermore, 2 days per week of EMS training over 10 weeks at 20 min per session appears to have been sufficient to facilitate glucose uptake, which is suggestive of improved insulin resistance in the patients studied. Conventional advice for patients with T2DM is 3–5 days of exercise per week, accumulating 150 min.[25,38] In the present study, at least with respect to glucose management, a 2 day per week regimen of EMS appears to have been dose-responsive.

The full extent of the metabolic improvement may not be captured by HbA_{1c} as the period of training was only 10 weeks in duration. However, HbA_{1c} levels did change significantly in the present study. This is in line with other studies that showed an HbA_{1c} reduction from 7.4 to 6.6 mg/dL after 8 weeks of EMS training of the thighs in T2DM patients.[26] In that study EMS was applied six times per week for 1 h each. We saw similar effects in our study, but we used EMS twice a week for 20 min and involved more muscle groups, suggesting that our stimulation unit, which allows EMS of muscles other than the lower extremities, might neutralize the shorter time of therapy. This improved convenience could result in a better acceptance of this method.

It is well known that metformin, like exercise, increases whole-body insulin sensitivity by 10–30% in individuals with and without T2DM. Sharoff et al.[11] demonstrated, in contrast to other studies, that the combination of exercise and metformin intake does not further increase whole-body insulin sensitivity.[39,40] Sharoff et al.[11] confirmed these findings also in muscle biopsy specimens, where they found that the molecular energy sensor AMP-activated protein kinase, an accepted mediator of postexercise insulin sensitivity, was elevated in activity threefold after exercise, but there was no difference when compared with the individuals who received supplementary metformin. However, this was a rather small cohort, including only 16 individuals.

Of the 15 patients in our study, nine were taking metformin. Although the dosage has not been changed, there is still a small uncertainty to what extent the improved glucose metabolism is due to EMS therapy.

The effects of conventional resistance training on glucose metabolism (HbA_{1c}) were shown to be rather small after 12 weeks.[41] There was also no significant effect on serum

glucose level in that study in contrast to our data, suggesting that EMS might have a favorable impact on this parameter. Sufficient information from the standardized mixed-meal test or oral glucose tolerance test was not obtained in our study. Hence, the potential effects of EMS on these parameters are not properly addressed and should be included in future studies.[42]

Body composition

Changes in measures of body mass and composition were not significant in the present study, although in consideration of the likely low caloric cost of EMS and the overall modest training parameters of 40 min weekly, significant changes were not expected. Duclos et al.[43] described in a meta-analysis similar findings, as in most studies there was no significant weight loss in T2DM patients after at least 12 weeks of either resistance or endurance training.

Hemodynamic and echocardiographic measures did not change over the course of the study, but changes of this nature, although gratifying, would not be expected given the type and volume of exercise intervention in a study population with already normal measurements at baseline.

Conclusions

EMS as a training modality as an alternative to classic exercise training improved power output and VO_2AT, suggesting overall improved functional status in patients with T2DM and low exercise capacity. It is important that insulin resistance, as inferred by fasting blood glucose and HbA_{1c} measures, improved significantly with a modest training intervention. The new designed stimulation suit stimulates more muscles than conventional EMS. This might allow less time of training and still have the beneficial effects on glucose metabolism.

EMS training, at a minimum of just 20 min twice weekly, also appears to provide for maintenance of body mass and composition and hemodynamic measures as a bridge to classic exercise training when appropriate. Further research is warranted to determine the optimal length of treatment and the effects of greater training parameters. It also would be of interest to assess the effects of combining low-intensity and low-volume aerobic training to the EMS protocol in comparison with controls.

Limitation of the study

It is instructive to note that over the course of 10 weeks, modest EMS training appears to have prevented any further decline in functional status or deleterious changes in body mass or composition, although a limitation of this study is that no control group was studied to validate these findings.

Acknowledgments

Figure 1 is published by permission of Miha-Bodytec, Augsburg, Germany. The stimulation unit was also provided by this company. We did not receive any financial support from Miha Bodytec or any other company.

Author Disclosure Statement

No competing financial interests exist.

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Address correspondence to:
Frank van Buuren, MD, MBA
Heart and Diabetes Center North Rhine-Westphalia
Department of Cardiology
Ruhr University Bochum
Georgstrasse 11
32545 Bad Oeynhausen, Germany

E-mail: fvbuuren@hdz-nrw.de