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Article *in* Journal of Cachexia, Sarcopenia and Muscle · June 2021

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Journal of Cachexia, Sarcopenia and Muscle (2021)
Published online in Wiley Online Library (wileyonlinelibrary.com) **DOI:** 10.1002/jcsm.12717

Four weeks of electromyostimulation improves muscle function and strength in sarcopenic patients: a three-arm parallel randomized trial

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Abstract

Background Sarcopenia, defined as loss of muscle mass, quality, and function, is associated with reduced quality of life and adverse health outcomes including disability and mortality. Electromyostimulation (EMS) has been suggested to attenuate the loss of muscle mass and function in elderly, sedentary individuals. This study aimed to investigate the effects of EMS on muscle strength and function during 4 weeks of inpatient medical rehabilitation.

Methods Patients receiving 4 weeks of inpatient medical rehabilitation diagnosed with sarcopenia using bioimpedance analysis were eligible to participate. One hundred and thirty-four patients (55.7 ± 7.9 years, 25.4% female) were randomly assigned to three groups: whole-body (WB) EMS (n = 48): stimulation of major muscle groups (pectoral muscles, latissimus, trapezius, abdominals, upper arm and leg, lower back muscles, gluteal muscles, and thighs); part-body (PB) EMS (n = 42): stimulation of leg muscles including gluteal muscles and thighs; and control group (CG, n = 44). All participants performed six 20 min training sessions including dynamic movements (squats, lunges, biceps curl, chest press, butterfly reverse, reverse lunges, standing diagonal crunches, etc.) with superimposed (WB-, PB-) EMS or without EMS (CG) in addition to the standard rehabilitation programme. Primary outcome variables included muscle function assessed by chair rise test and 6 min walking test as well as muscle strength (isometric grip strength, leg, arm, and back extension).

Results Primary outcome variables chair rise test and leg extension improved significantly (P = 0.001, η^2 = 0.06 and P = 0.008, η^2 = 0.06; EMS vs. CG) in that chair rise test results increased in WB-EMS from 5 (4; 7) to 7 (5; 9), in PB-EMS from 5 (5; 7) to 7 (6; 8), and in CG from 6 (4; 7) to 7 (5; 8) repetitions. Knee extension increased in WB-EMS from 692.3 ± 248.6 to 831.7 ± 298.7 N, in PB-EMS from 682.8 ± 257.8 to 790.2 ± 270.2 N, and in CG from 638.5 ± 236.9 to 703.2 ± 218.6 N. No adverse events or side effects occurred.

Conclusions We conclude that EMS might be an additional training option to improve muscle function and strength in sarcopenic patients during a 4 week rehabilitation programme. EMS provides greater functional and strength improvements compared with standard treatment with additional potential health benefits for sarcopenic cardiac and orthopaedic patients.

Keywords Rehabilitation; Cardiology; Orthopedy; Exercise; Strength; Prevention

Received: 10 February 2021; Revised: 24 April 2021; Accepted: 30 April 2021
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Introduction

The age-related loss of muscle mass (sarcopenia) is commonly observed in patients referred to medical rehabilitation.[1] Sarcopenia is a muscle disease (ICD-10-MC M.62.84), characterized by low muscle mass and low physical strength, reduced muscle function or performance, which is aggravated by previous immobilization or inactivity leading to muscular atrophy.[2] Sarcopenia is associated with increased mortality, a higher likelihood of disability, and loss of independence as well as reduced quality of life.[3,4] The concept of primary (age-related) sarcopenia has recently been extended to secondary (disease-related) sarcopenia evoked by causal factors like systemic diseases.[4] Chronic obesity-induced systemic inflammation combined with reduced muscle mass, loss of mobility, and decreased energy metabolism may intensify the downward spiral. This is of relevance because the worldwide prevalence of obesity and metabolic syndrome including associated pro-inflammatory conditions is constantly increasing. Reduced lean body mass (LBM) as seen in obesity (i.e. sarcopenic obesity) is also commonly observed in patients referred to medical rehabilitation and affects cardiovascular[5] and orthopaedic disease outcomes.[6]

Physical exercise is a cornerstone of medical rehabilitation, and sarcopenia has to be considered as a therapy-limiting condition because it may reduce participation in exercise programmes and prevent overall rehabilitation success.[2] While varying prevalence of sarcopenia in clinical or rehabilitation settings has been reported,[1] sarcopenic patients are especially challenging in therapy because muscular deconditioning and functional limitations prevent patients from reaching prescribed exercise intensities or frequencies to improve their clinical condition.[7]

To overcome these limitations, electromyostimulation (EMS) might represent a promising training option. EMS uses external current impulses to maintain or build muscles, and established EMS systems provide the possibility to stimulate individual bilateral muscle groups such as leg muscles including gluteal muscles and thighs [i.e. part-body EMS (PB-EMS)] or larger muscle area by stimulating pectoral muscles, latissimus, trapezius, abdominals, upper arm, and leg as well as lower back muscles including gluteal muscles and thighs [i.e. whole-body EMS (WB-EMS)]. EMS is described as a time-efficient, non-invasive, and joint-friendly training modality, and several studies in healthy individuals provided evidence that WB-EMS may reduce body fat and increase muscle mass as well as strength and performance.[8–10] These effects appear independent of age or sex and have been shown to induce beneficial adaptations also in the elderly.[9,11,12] Of note, a recent study reported that superimposed submaximal WB-EMS improved strength and power already after 8 weeks of training (two sessions per week) in young healthy individuals.[13] Thus, similar short-term effects might be achieved in sarcopenic patients because physiological adaptations are pronounced in unfit or sedentary subjects starting a training programme.

This study is the first to evaluate the applicability and effectivity of EMS during 4 weeks of inpatient rehabilitation of sarcopenic patients with cardiologic and/or orthopaedic indications. The aim of this study was to determine the effects of superimposed EMS on muscle function and strength as well as clinical variables compared with an active control group (CG). Our primary hypothesis was that EMS used as additional treatment during a conventional 4 week rehabilitation programme leads to significantly greater improvements in muscle function and strength in sarcopenic patients compared with active CG. Furthermore, we expected that WB-EMS is more effective than PB-EMS in improving muscle function and strength in sarcopenic patients, because PB-EMS stimulates fewer muscles than WB-EMS.

Methods

Trial design and participants

The investigation was designed as a three-arm parallel randomized single-centre study with three different training groups: (i) active WB-EMS training, (ii) active PB-EMS training, and (iii) active CG. All participants received a German standard inpatient medical rehabilitation (phase II rehabilitation, usually 3 weeks extended by 1 week on doctor's order), during which EMS was delivered as additional superimposed treatment. During the intervention, patients performed a dynamic movement programme in a standing position (described below). Each subject underwent six controlled EMS training sessions during the 4 week inpatient rehabilitation stay (one training session during the first and last week and two training sessions during the second and third week). The study was conducted between April 2018 and June 2020 at the medical rehabilitation centre Klinik Königsfeld, Ennepetal, Germany, and complied with the Helsinki Declaration 'Ethical Principles for Medical Research Involving Human Subjects' and was approved by the ethics committee of University Witten/Herdecke (#91/2018). The study was registered at ClinicalTrials.gov (NCT03767088). All participants gave their written informed consent before participating in the study. The study was prematurely terminated as consequence of the COVID-19 pandemic for safety reasons.

Eligibility criteria

As part of the clinical admission process, all new arrivals underwent a bioimpedance analysis (BIA) during initial examination. BIA results were used to diagnose sarcopenia according to the Foundation for the National Institutes of Health (FNIH), and patients met eligibility when their skeletal muscle index (SMI) was <0.789 for men and <0.512 for women.[13] The SMI represents the ratio of appendicular skeletal muscle

DOI: 10.1002/jcsm.12717

mass (sum of absolute LBM of the extremities) and body mass index (BMI). Further inclusion criteria were age 18 years and older, a present cardiologic or orthopaedic indication, and a signed written informed consent. Patients sent after coronary artery bypass surgery within the last 3 months and patients with a diagnosis of chronic kidney disease stage IIIa, cardiac pacemaker/defibrillator, or event recorder, epilepsy, and acute infectious diseases were not eligible to participate. Patients after hip replacement within the last 3 months were also not eligible as their reduced range of motion would not allow to perform the motions included in the intervention programme. Exclusion criteria were injury and illness during the study programme. The study flow chart is presented in *Figure* 1.

Randomization procedure

One hundred and thirty-four eligible participants were randomly assigned to the three study arms (WB-EMS vs. PB-EMS vs. CG). We used lots enclosed in identical sealed plastic tubes. Each participant drew their lot themselves under supervision of an investigator (M. T. or M. H.). Neither participant nor researcher knew the allocation before. After allocation to one of the groups, the researcher (M. T. or M. H.) instructed the participant about the study procedures.

Blinding

We did not attempt to blind participants to their exercise status. However, test assistants and outcome assessors were kept unaware of the participants' group status and were not allowed to ask, either.

Interventions

Electromyostimulation equipment and stimulated muscles

The CE-certified medical EMS equipment miha bodytec II (miha bodytec, Gersthofen, Germany) was used according to the manufacturer's instructions to simultaneously stimulate muscle groups with up to 2600 cm^2 total area of the electrodes. The system consists of a control station with an integrated display and control options for the individual muscle groups. Participants were equipped with functional underwear (water absorbing cotton/elastane mix) recommended by the manufacturer, on which a vest (upper body) and belts (arms, legs, and gluteal muscles) were individually tightly adjusted before each training session. An example of EMS equipment is shown in Supporting Information, *Figure* S1. To ensure optimal stimulation and transmission of electrical impulses to the muscles, the training gear was wet with water as recommended. For WB-EMS, current was applied

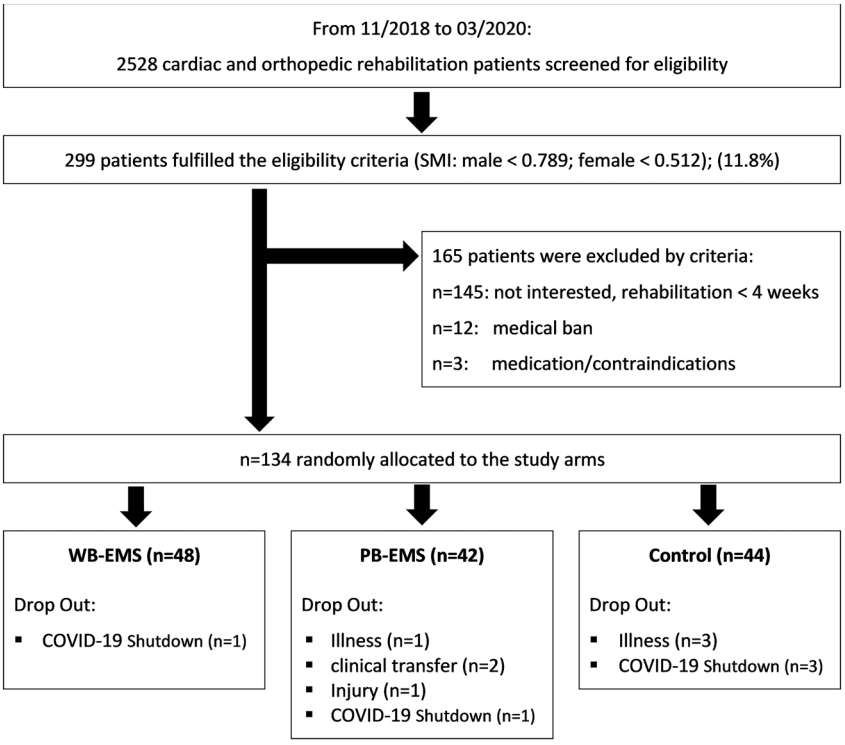

Figure 1 CONSORT flow chart. PB-EMS, part-body electromyostimulation; SMI, skeletal muscle index; WB-EMS, whole-body electromyostimulation.

DOI: 10.1002/jcsm.12717

with the electrode vest to the upper body integrating two bilateral paired surface electrodes for pectoral muscles, latissimus, trapezius, lower back, and the abdominals as well as a belt system for arms and legs, including the muscles of the gluteal muscles and thighs. In contrast, PB-EMS focused on the legs, as only the gluteal muscles and thighs were stimulated. The active CG trained without any EMS equipment to evaluate only the additional effect of the EMS application.

Training

A maximum of two subjects trained in parallel for 20 min [total of six training sessions; one training session during the first and last week and two training sessions during the second and third week; (Mon./Thu. or Tue./Fri.)] under supervision of a qualified trainer (M. T. or M. H.). Participants from each of the three groups performed two equal sets of eight exercises with eight repetitions each in a standing position. Exercises included variations of squatting with additional biceps curl or arm extension, chest press and butterfly reverse, reverse lunges, standing diagonal crunches, single-legged stand with hip flexion, and standing trunk flexion (all without additional weights). The training was supported by a standardized animated training video (miha bodytec), which allowed the trainer to concentrate on a clean movement execution of all participants.

During EMS, biphasic rectangular wave pulsed currents (85 Hz) with an impulse width of 350 μs and impulse ramp of 0.4 s were applied as described.[8,14] The training intensity for each muscle group was adjusted individually during the initial familiarization session (Session 1) using patients' perception of muscle contraction stimulation intensity in combination with the 6–20 Borg Scale for Rating of Perceived Exertion (RPE).[15] This was done because no valid objective load specifications for EMS exist and individual variables such as local body fat, skin thickness, and muscle mass affect EMS stimulation. As too intense muscle stimulation should be avoided during initial training sessions, training load was continuously increased from RPE 11/12 (light+) to RPE 17/18 (very hard) in the final session. For load control and progression, RPE was asked at time intervals of 3 to 4 min to adjust the training load individually. The final EMS settings of each session were individually recorded on a personalized chip card and served as orientation for upcoming training session. To avoid overstraining of the participants, we chose an established load ratio of 4 s of current followed by 4 s of rest (ratio 1:1). The current phase was used to perform the slow eccentric part of the respective movement (e.g. during the downward movement of the squat), the rest interval to return to the starting position. Especially for the CG, where tactile feedback of the EMS gear is missing, the visualization by synchronized training video and an active support by the trainer were used to standardize the sessions.

Outcomes

Primary study outcome was defined as improvement in muscle function assessed by chair rise test and 6 min walking test (6MWT) as well as muscle strength assessed by isometric grip strength and isometric leg, arm, and back extension. All six primary outcome measures were assessed at baseline and 4 weeks after inclusion (see below).

Secondary study outcomes included changes of body composition assessed as total body fat mass (BFM) and LBM; metabolic variables including serum levels of triglycerides, high-density lipoprotein (HDL), low-density lipoprotein (LDL), glutamic-oxaloacetic transaminase (GOT), glutamic-pyruvate transaminase (GPT), gamma-glutamyl transferase (GGT), estimated glomerular filtration rate (eGFR), creatine kinase (CK), myoglobin, sodium, and potassium; and quality of life, self-efficacy, and function/disability assessed by questionnaires SF-36, *Allgemeine Selbstwirksamkeit Kurzskala* (ASKU score), and late-life function and disability index. All 16 secondary outcome measures were assessed at baseline and 4 weeks after inclusion (see below).

Changes in trial design

Due to the COVID-19 lock down, the study was terminated prematurely, as usual recruitment was no longer possible and standard medical rehabilitation changed fundamentally.

Adverse events

Standard case report forms (CRF) were used for documentation of (severe) adverse events. Adverse events of clinical interest for EMS were kidney damage/acute kidney failure defined as significantly decreased or absent urine production and a serum creatinine $\geq$ 0.3 mg/dL within 48 h as well as rhabdomyolysis defined by muscle pain, weakness and swelling, nausea, vomiting, and confusion and/or darkening of urine due to presence of myoglobin. Patients were interviewed on a regular basis after each training session, and standard CRFs were used to document adverse events.

Measuring, testing, and assessment

All tests were performed with the same material and methods on calibrated devices by the same researchers (M. T. and M. H.) in a fixed sequence and time schedule (±2 h). Tests were conducted not later than the third day after arrival and 1 day before departure with at least 2 days rest before/after the first and last training session. All procedures took place at the same time of day. Emphasis was put

DOI: 10.1002/jcsm.12717

on the standardization of the tests by using consistent verbal test prescriptions.

Anthropometric data

Anthropometric data were collected during the initial examination, using standard medical equipment for height (seca 216, seca, Hamburg, Germany). Weight, LBM, TBF mass, and visceral fat (VF, cm^2) were measured via direct-segmental multi-frequency bioelectrical impedance analysis (Inbody720, Biospace, Seoul, Korea). Using an eight-point tactile electrode system, the procedure allows a separate analysis for the extremities and trunk.

Diagnostics of muscle strength and function

Isometric strength tests A test battery was used to assess muscle force and function. First, patients underwent isometric strength tests (DIERs myoline professional, DIERs Biomedical Solutions, Schlangenbad, Germany) measuring bilateral leg, arm, and trunk strength in this exact order, determining maximal voluntary strength by conducting three maximal voluntary repetitions with a break of 30 s between each repetition. The best peak value was considered for analysis. During all measurements, the participants received motivational biofeedback providing visual information of each ongoing repetition. To standardize the measurements and to reproduce identical lever ratios and angles at follow-up, all individual settings and results were recorded using the DiCAM software Version 3.9 (DIERs Biomedical Solutions). All assessments were performed in an individually adjusted upright sitting position (hip flexion 90°) with fixation by a hip strap. For leg strength, knees were flexed 45° and the lower legs fixed to the footrest with hands folded in front of the chest. Arm strength was assessed with the shoulder flexed by 45° and a 90° flexion of the elbow joint. Pelvis and legs were fixed by straps, upper arms rested on the corresponding arm pads. The extension was performed with hands inside; flexion was performed with hands outside. For trunk strength, participants were fixed to the corresponding front and side pads as described by the manufacturer with hands folded in front of the chest.

Chair rise test Muscle function (i.e. strength and coordination) of the leg muscles was tested using the 10 s chair rise test as described.[16] In brief, a digital stopwatch was used for timing the 10 s that subjects performed as many sit-to-stand-to-sit repetitions as possible, starting from an upright sitting position (front of the seat, 90° angle of ankles, knees, and hips) with parallel feet and arms folded across the chest. Patients were advised to completely extend the knees and hips to reach a full upright stand and without delay sit down again. Before commencing the test, the procedure was demonstrated. The test was performed from a standard 46 cm height chair that was slightly padded without adjustment of the seat height as described.[17] Only full sit-to-stand-to-sit repetitions were accepted and considered for analysis.

Six-minute walking test Diagnostics involved the aerobic 6MWT as it is known as long-term predictor for functional limitations, cardiovascular mortality, and (re-)hospitalization.[18] Because the 6MWT was performed at the end of the test battery, no additional warm up was performed. The walks were standardized on a pre-measured 48 m indoor square path (4 × 12 m) with flat and even surface in an area not accessible to other patients. Participants were instructed to walk as many metres as possible in 6 min without any verbal encouragement. If necessary, they could slow down or stop and resume the walk as soon as possible. The test ended with a 'stop' call at exactly 6 min. Completed laps and the distance covered during the last lap were considered, and total distance (metres) was included in the analysis. Two participants were not able to complete the test, and their results were not considered for analysis.

Ergometry As part of the clinical routine, standard ergometer testing was performed with an electrocardiogram according to World Health Organization stage protocol starting at 25 W with an increase of 25 W every 2 min until individual exhaustion. Testing was conducted using the GE eBike, KISS electrocardiogram with associated software CardioSoft (GE Healthcare Technology, Illinois, USA) to assess total exercise duration (seconds), peak values for power output (watts), heart rate, and arterial blood pressure. Patients were instructed to perform the test to exhaustion, defined as peripheral fatigue or, if required, termination due to electrocardiographic abnormalities. Data were used to calculate peak metabolic equivalent (MET) according to Ainsworth *et al*.[19]

Blood samplings

Under fasting condition, blood was sampled from an antecubital vein in sitting position between 7:00 and 7:30 on the second day of rehabilitation, as well as on the day of departure. All blood samples were analysed at SYNLAB MVZ Laboratory GmbH (Leverkusen, Germany) including glucose, uric acid, triglycerides, total cholesterol, HDL, LDL, GOT, GPT, GGT, CK, creatinine (for eGFR using Chronic Kidney Disease Epidemiology Collaboration), myoglobin, sodium, and potassium. Co-morbidity index was determined as described according to D'Hoore.[20] To safeguard and control especially the initial load of WB-EMS training, participants of the WB-EMS group were tested 3 days after their first training session for deviations of markers of muscle damage (e.g. CK).

Questionnaires

The German version of the Short Form (36) Health Survey (SF-36; 4 week version) was used to assess quality of life. The SF-36 physical and mental component subscores were calculated according to Ware *et al*.[21] Self-efficacy was assessed using ASKU score. Late-life function and disability

DOI: 10.1002/jcsm.12717

index was used to assess self-reported function and physical disability.

Statistical analyses

Statistical analyses are performed using SPSSv23 software (IBM, Armonk, NY, USA). Data are presented as mean ± standard deviation or median and interquartile range as indicated. Normal distribution was statistically and graphically tested via the Kolmogorov–Smirnov test. Between-group differences at baseline were assessed using one-way analysis of variance. Baseline to follow-up between-group differences were analysed using change scores (post-measurements minus pre-measurements) adjusted for baseline values using analysis of covariance. To account for multiple testing (six primary outcome variables), Bonferroni's correction was used, and significance was declared at $P < 0.0083$ for primary analysis. Following a prioritized sequence of tests, differences between the two EMS groups (WB-EMS vs. PB-EMS) were only assessed if the comparison EMS vs. CG was significant. *P*-values < 0.05 for differences in secondary outcome variables or exploratory analyses were considered as hypothesis generating. Subgroup analyses for women and men as well as cardiologic and orthopaedic patients were performed using change scores and analysis of covariance with baseline values as covariate and sex or indication for rehabilitation as additional factors. Within-group changes from baseline to follow-up were analysed using two-sided paired *t*-test. Overall effects on strength development were calculated using the sum of individual component relative changes divided by the number of components tested. Homogeneity of variances was asserted using Levene's test assuming equal variances for $P > 0.05$. Eta squared (η^2) was used to calculate effect size (ES) with <0.06 indicating a small, 0.06 to 0.14 a medium, and >0.14 a strong effect. Sample size was estimated using G*Power 3.1.9.7 based on changes in knee extension with a reported ES of 0.601[22] suggesting a total sample size of 138 for a power of 0.9 (1-beta) at $\alpha = 0.05$.

Results

Of the 134 randomly assigned subjects included in the study, 12 participants (WB-EMS: $n = 2$; PB-EMS: $n = 5$; CG: $n = 5$) did not complete the intervention for various reasons including six participants who could not complete the programme due to the COVID-19 shutdown (*Figure* 1). Patients' characteristics are presented in *Table* 1; a detailed characterization by indication for rehabilitation including diagnosis, co-morbidities, and medication is shown in *Table* S1. Compared with the general patient population referred to medical (cardiac) rehabilitation, patients included in our study were slightly younger (55.7 vs. ~63.7 years) and had a higher BMI (35.8 vs. ~28 kg/m^2).[23] Training attendance was high with ~98% for all three groups. Except for BMI (WB-EMS vs. PB-EMS), there were no significant differences between the three groups for any variable at baseline (all $P > 0.15$). We did not observe any adverse events that could be referred to the EMS application during the intervention period.

Primary outcomes

Change in knee extension showed a significantly ($P = 0.008$, $\eta^2 = 0.06$) stronger increase in the EMS group than in the CG with a difference between means of 10.4% (95% confidence interval, 1.5–19.3%) (*Table* 2, *Figure* 2). Chair rise test improved significantly ($P = 0.001$, $\eta^2 = 0.09$) better in the EMS group compared with the CG with a difference between means of 0.8 (95% confidence interval, 0.3–1.2) repetitions

Table 1 Participants' baseline characteristics

Variable	WB-EMS ($n = 47$)	PB-EMS ($n = 37$)	Control ($n = 38$)	*P*-value
Age (years)	53.9 ± 7.2	57.9 ± 6.3	55.6 ± 9.4	0.063
Height (cm)	164.9 ± 7.4	165.0 ± 7.5	164.8 ± 7.0	0.994
Weight (kg)	101.6 ± 19.8	92.5 ± 18.4	98.6 ± 24.8	0.148
Waist-to-hip ratio[a]	1.05 ± 0.08	1.02 ± 0.08	1.04 ± 0.1	0.210
SMM (kg)[a]	31.7 ± 6.8	31.3 ± 5.7	32.0 ± 6.5	0.879
Skeletal muscle index (SMI)	0.643 ± 0.124	0.695 ± 0.107	0.697 ± 0.192	0.153
HR (rest) (1/min)	82.8 ± 13.5	76.2 ± 16.0	80.3 ± 12.0	0.107
Systolic blood pressure (mmHg)	120.2 ± 19.7	117.4 ± 17.0	113.6 ± 18.4	0.289
Diastolic blood pressure (mmHg)	77.3 ± 13.6	75.4 ± 12.3	73.3 ± 12.2	0.386
Co-morbidity index (CMI)[b]	2.2 ± 1.5	2.1 ± 1.3	2.1 ± 1.7	0.978
Sex ratio (female/male)	17/30	6/31	8/30	0.087
Indication (orthopaedic/cardiologic)	22/25	10/27	16/22	0.171

HR, heart rate (determined before stress electrocardiogram and sitting); PB-EMS, part-body electromyostimulation; SMM, skeletal muscle mass; WB-EMS, whole-body electromyostimulation.
Data are presented as mean ± standard deviation or *n*. Between-group differences were assessed using one-way analysis of variance.
[a]Via bioelectrical impedance analysis.
[b]CMI: according to the modified D'Hoore co-morbidity index (Zoghbi *et al.*[20]).

DOI: 10.1002/jcsm.12717

Table 2 Primary outcome variables and relative changes by study group

Variable		WB-EMS (n = 47)	PB-EMS (n = 37)	Control (n = 38)	3-group comparison (P)	EMS vs. control (P)
Grip strength (kg)	Pre	37.7 ± 12.9	37.8 ± 11.7	36.6 ± 10.8		
	Post	38.5 ± 12.5	38.8 ± 12.0	38.6 ± 10.6**	0.506	0.251
	(%)	4.0 ± 13.6	3.7 ± 16.2	7.3 ± 15.9		
Knee extension (N)	Pre	692.3 ± 248.6	682.8 ± 257.8	638.5 ± 236.9		
	Post	831.7 ± 298.7***	790.2 ± 270.2***	703.2 ± 218.6***	0.013	0.008
	(%)	22.1 ± 19.3	22.2 ± 35.7	13.9 ± 19.1		
Arm extension (N)	Pre	477.8 ± 207.5	471.4 ± 185.2	455.7 ± 156.5		
	Post	593.4 ± 341.6**	508.2 ± 187.9**	519.6 ± 169.3***	0.064	0.609
	(%)	24.3 ± 33.2	10.7 ± 23.9	17.8 ± 27.6		
Trunk extension (N)	Pre	416.5 ± 199.8	453.2 ± 211.0	398.9 ± 162.2		
	Post	518.7 ± 223.7***	515.3 ± 206.5**	454.3 ± 147.4**	0.101	0.103
	(%)	32.7 ± 42.3	20.9 ± 33.0	18.9 ± 27.2		
Chair rise test (repetitions, n)	Pre	5 (4; 7)	5 (5; 7)	6 (4; 7)		
	Post	7 (5; 9)***	7 (6; 8)***	7 (5; 8)*	0.004	0.001
	(%)	27.2 ± 23.0	29.1 ± 29.9	12.9 ± 22.7		
6MWT (m)	Pre	504.7 ± 90.6	504.1 ± 111.8	499.2 ± 94.2		
	Post	553.8 ± 81.6***	552.6 ± 112.5***	529.4 ± 88.1***	0.062	0.018
	(%)	11.0 ± 10.3	10.3 ± 9.9	7.1 ± 9.5		

6MWT, 6 min walking test; EMS, electromyostimulation; PB-EMS, part-body electromyostimulation; WB-EMS, whole-body electromyostimulation.
Data are presented as mean ± standard deviation or median (interquartile range) and per cent change; P-values were calculated using change scores and analysis of covariance with baseline values as covariate for between-group comparison or by paired t-test for within-group comparison.
***$P < 0.001$.
**$P < 0.01$.
*$P < 0.05$.

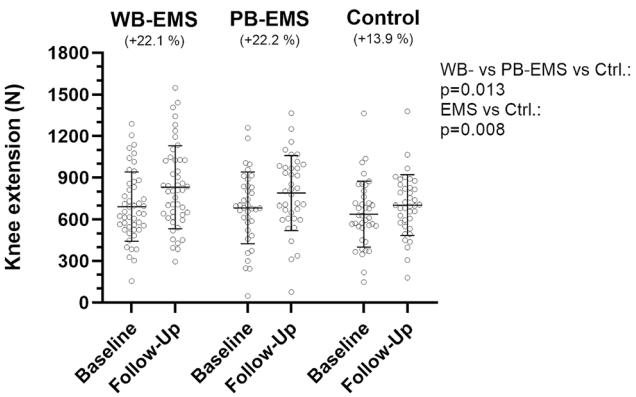

Figure 2 Active electromyostimulation (EMS) training improves muscle strength. Scatter plot of knee extension strength (Newton, N) showing individual performance at baseline and follow-up. Error bars indicate mean and standard deviation. In the WB-EMS group, improvement was 22.1 ± 19.3%, in the PB-EMS group 22.2 ± 35.7%, and in the Ctrl. group 13.9 ± 19.1%. Ctrl., control group; PB-EMS, part-body EMS; WB-EMS, whole-body EMS. P-values indicate baseline to follow-up between-group comparison using change scores adjusted for baseline values by analysis of covariance. EMS vs. Ctrl. indicates comparison of both EMS groups combined vs. Ctrl.

(*Table* 2, *Figure* 3). For both tests, no difference between the response to WB-EMS or PB-EMS was detected. All other primary outcome variables did not change differently between groups during the intervention.

Secondary outcomes

None of the secondary outcome variables including body composition, metabolic variables, and questionnaire tools showed a significantly different change in response to the intervention (*Table* 3). CK serum levels, a known indicator of muscle damage in general and for EMS application in particular, were elevated in the EMS group compared with the CG (P = 0.032) (*Table* 3). The Day-3 CK monitoring after initial WB-EMS, used as safety parameter to indicate excessive training load, showed an average increase of up to 1270 U/L, with one peak outlier of ~16 000 U/L.

Exploratory and subgroup analyses

An exploratory analysis of overall mean strength increase suggested a higher strength improvement in the WB-EMS group (28.7%) compared with the PB-EMS group (17.9%) and the CG (18.4%; P = 0.011), potentially associated to the higher number of muscles stimulated by WB-EMS (*Table* S2). LDL levels in the WB-EMS group were not reduced to the same extend as in the PB-EMS and CG (WB-EMS: −11.5 ± 20.9 mg/dL vs. PB-EMS: −26.8 ± 27.5 mg/dL vs. CG: −14.5 ± 18.9 mg/dL; P = 0.020) (*Table* 3). Comparable changes were observed for total cholesterol levels (*Table* S2). A detailed analysis of the SF-36 subscores did not reveal any differences between the intervention groups (*Table* S3). Subgroup analyses were performed to investigate if the

DOI: 10.1002/jcsm.12717

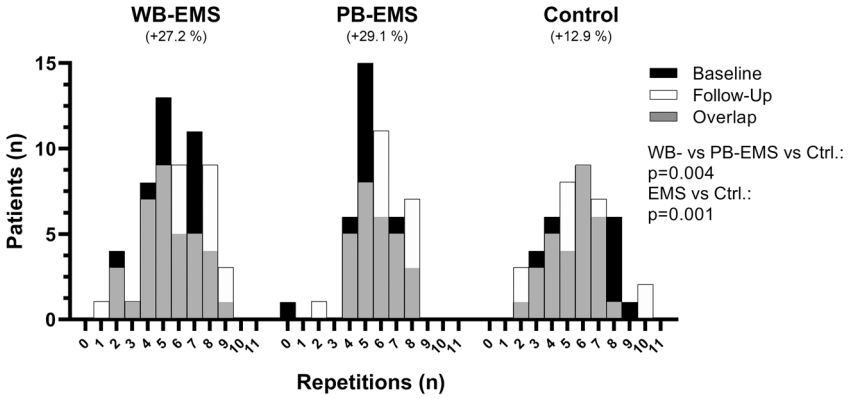

Figure 3 Active electromyostimulation (EMS) training improves muscle function. Overlapping histogram of the 10 s chair rise test (completed sit-to-stand-to-sit repetitions) showing number of repetitions achieved by number of patients per group. Black bars represent baseline data, white bars follow-up data, and grey bars the overlap. In the WB-EMS group, improvement was 27.2 ± 23.0%, in the PB-EMS group 29.1 ± 29.9%, and in the Ctrl. group 12.9 ± 22.7%. Ctrl., control group; PB-EMS, part-body EMS; WB-EMS, whole-body EMS. *P*-values indicate baseline to follow-up between-group comparison using change scores adjusted for baseline values by analysis of covariance. EMS vs. Ctrl. indicates comparison of both EMS groups combined vs. Ctrl.

detected differences on improvements in chair rise test, knee extension strength, and potentially, 6MWT were affected by sex or the indication for rehabilitation, that is, by a cardiologic or orthopaedic indication. Results suggested that neither sex nor the indication for rehabilitation affected the outcome (*Table* S4).

Discussion

This study is the first to evaluate the effects of a short-term active EMS protocol in a 4 week inpatient rehabilitation setting. We found that EMS, applied as supporting exercise therapy in rehabilitation patients with sarcopenia, led to significant improvements of muscle function in terms of improved chair rise test performance and leg muscle strength in terms of knee extension. The detected changes are of prognostic relevance because further improvement of health and physical functioning might help patients to return to work and to participate in their usual social interactions.

So far, only few studies have addressed effects of EMS in patients with the indication of sarcopenia.[9,12,24] These studies were based on an intervention period of 6 to 12 months including 1 to 1.5 applications per week. The improvements achieved within the current study using EMS in addition to a standard rehabilitation programme are comparable with those described after long-term WB-EMS interventions. The detected ES of η^2 = 0.06 for improvement of primary outcome variable knee extension strength by 10.4% over CG indicated an intermediate ES, suggesting a likely meaningful difference. The within-group effect was comparable with values reported after 6 months training in sarcopenic elderly women.[25] Correspondingly, the improved leg strength after EMS training translated into a significant increase in chair rise test results in the EMS group by ~28% with only 13% observed in the CG, exceeding previous findings reported by Kemmler et al. (~6.5%).[25] Of note, further analysis did not suggest a significant difference between WB-EMS or PB-EMS training on the primary outcome variables knee extension strength and chair rise test.

In terms of aerobic performance, only one study reported on the effect of WB-EMS on 6MWT performance,[26] suggesting that acute cancer patients (60.3 ± 13.1 years) performing WB-EMS over a 12 week period twice a week improved their 6MWT walking distance by 10.6%. This improvement is comparable with a ~10.5% improvement after EMS-supported rehabilitation in our series. However, EMS training did not stimulate significantly greater improvement compared with CG. Subsequent exploratory comparison of ergometry results also suggested no significant between-group differences even though within-group improvement of test duration (by 42.5 ± 73.2 s; 8.1%) and power output (by 8.3 ± 15.1 W; 7.6%) were only observed in the WB-EMS group but not in the PB-EMS group (both 2.5%) and the CG (2.9% and 4.3%). The observed improvement with WB-EMS equals an improvement of 0.3 METs, which is of relevance, as a 1-MET increase is associated with a 12% reduced mortality in coronary heart disease.[27]

The observed findings induced by EMS application might be explained by different aspects. Besides the diagnosis of sarcopenia in our patients, comparison of baseline test results to published data indicates that our patients showed severe signs of deconditioning. With respect to the chair rise test, patients before and after kidney transplantation have been reported to perform 5.9 and 5.1 cycles, respectively.[17] Our patients were able to perform a mean of 5.6 repetitions before the intervention. During the 6MWT, our patients

DOI: 10.1002/jcsm.12717

Table 3 Secondary outcome variables and changes by study group

Variable		WB-EMS (n = 47)	PB-EMS (n = 37)	Control (n = 38)	3-group comparison (P)	EMS vs. control (P)
Body composition						
Total BFM (kg)	Pre	44.7 ± 12.4	36.4 ± 12.0	41.2 ± 16.3		
	Post	43.1 ± 11.8***	35.4 ± 11.8**	41.2 ± 15.3**	0.711	0.440
	(%)	−3.4 ± 3.8	−2.5 ± 5.2	−1.9 ± 6.2		
Total LBM (kg)	Pre	50.9 ± 10.7	49.8 ± 9.0	50.7 ± 10.9		
	Post	50.2 ± 10.2**	49.4 ± 8.6	50.6 ± 10.1*	0.799	0.933
	(%)	−1.2 ± 2.4	−0.6 ± 3.3	−1.1 ± 2.9		
Metabolic variables						
Triglycerides (mg/dL)	Pre	174.5 ± 143.7	156.7 ± 60.9	146.4 ± 71.7		
	Post	151.9 ± 81.8	135.0 ± 42.5**	125.1 ± 58.6*	0.485	0.299
	(d)	−22.6 ± 126.7	−21.7 ± 35.2	−21.2 ± 48.5		
HDL (mg/dL)	Pre	44.0 ± 8.0	42.7 ± 8.5	44.1 ± 12.5		
	Post	41.5 ± 7.2**	39.1 ± 6.9**	42.5 ± 12.3*	0.121	0.099
	(d)	−2.5 ± 4.0	−3.6 ± 4.9	−1.6 ± 3.9		
LDL (mg/dL)	Pre	129.6 ± 41.5	126.5 ± 36.1	118.3 ± 42.4		
	Post	118.2 ± 42.4**	99.8 ± 23.5***	103.8 ± 37.6***	0.020	0.757
	(d)	−11.5 ± 20.9	−26.8 ± 27.5	−14.5 ± 18.9		
GOT (U/L)	Pre	29.0 ± 15.5	33.5 ± 22.3	32.2 ± 12.6		
	Post	31.8 ± 13.5	40.1 ± 32.9	31.6 ± 11.8	0.167	0.149
	(d)	2.8 ± 16.6	7.2 ± 18.5	−0.6 ± 10.0		
GPT (U/L)	Pre	36.4 ± 21.5	41.7 ± 31.1	42.1 ± 18.8		
	Post	39.5 ± 16.0	43.3 ± 21.9	45.2 ± 33.3	0.920	0.684
	(d)	3.1 ± 14.9	1.6 ± 14.0	3.1 ± 28.6		
GGT (U/L)	Pre	58.8 ± 116.1	57.1 ± 45.9	52.6 ± 36.0		
	Post	37.8 ± 24.2	44.6 ± 38.1*	44.9 ± 30.9*	0.387	0.361
	(d)	−21.0 ± 102.1	−12.5 ± 28.7	−7.7 ± 18.7		
CK (U/L)	Pre	130.1 ± 90.1	134.5 ± 116.8	169.4 ± 159.6		
	Post	297.6 ± 384.3**	286.6 ± 403.5	158.8 ± 96.1	0.099	0.032
	(d)	167.5 ± 365.0	152.0 ± 409.5	−10.7 ± 106.2		
Myoglobin (U/L)	Pre	45.3 ± 20.6	49.7 ± 16.8	73.2 ± 85.1		
	Post	60.5 ± 45.3	70.1 ± 58.5	61.0 ± 49.6	0.619	0.424
	(d)	15.3 ± 41.4	20.5 ± 59.7	−12.2 ± 80.3		
eGFR (mL/min/1.73 m^2)	Pre	93.1 ± 16.1	91.9 ± 9.8	89.7 ± 22.3		
	Post	92.8 ± 15.8	91.5 ± 18.0	91.0 ± 18.6	0.862	0.592
	(d)	−0.33 ± 6.1	−0.39 ± 16.1	1.3 ± 9.1		
Sodium (mmol/L)	Pre	141.7 ± 1.9	142.2 ± 2.0	142.0 ± 2.3		
	Post	142.1 ± 1.6	142.2 ± 2.5	141.8 ± 2.2	0.623	0.378
	(d)	0.3 ± 1.4	0.0 ± 2.2	−0.1 ± 2.0		
Potassium (mmol/L)	Pre	4.3 ± 0.4	4.4 ± 0.5	4.5 ± 0.5		
	Post	4.6 ± 0.4***	4.5 ± 0.4	4.6 ± 0.4	0.173	0.691
	(d)	0.3 ± 0.4	0.1 ± 0.5	0.1 ± 0.4		
Questionnaires						
SF-36						
Physical component score	Pre	32.7 ± 10.9	32.1 ± 10.1	31.9 ± 10.7		
	Post	39.0 ± 11.4***	36.6 ± 10.5**	36.0 ± 12.6**	0.424	0.378
	(d)	6.3 ± 9.5	4.6 ± 7.7	4.2 ± 9.2		
Mental component score	Pre	38.0 ± 9.2	38.7 ± 11.1	36.7 ± 10.5		
	Post	41.7 ± 7.5**	41.0 ± 8.8	40.7 ± 9.7*	0.822	0.977
	(d)	3.7 ± 7.9	2.3 ± 8.9	4.0 ± 10.4		
ASKU score	Pre	6.4 ± 2.3	7.5 ± 2.7	6.8 ± 2.2		
	Post	6.3 ± 2.4	6.9 ± 2.9	6.9 ± 3.0	0.750	0.456
	(d)	−0.04 ± 2.1	−0.60 ± 2.7	0.07 ± 2.9		
LLFDI score	Pre	62.9 ± 8.4	59.1 ± 10.0	57.0 ± 11.9		
	Post	62.4 ± 11.7	59.4 ± 11.0	58.2 ± 12.3	0.933	0.784
	(d)	−0.5 ± 10.0	0.3 ± 10.1	1.3 ± 6.8		

ASKU, *Allgemeine Selbstwirksamkeit Kurzskala* (self-efficacy); BFM, body fat mass; CK, creatine kinase; eGFR, estimated glomerular filtration rate (Chronic Kidney Disease Epidemiology Collaboration); EMS, electromyostimulation; GGT, gamma-glutamyl transferase; GOT, glutamic-oxaloacetic transaminase; GPT, glutamic-pyruvate transaminase; HDL, high-density lipoprotein; LBM, lean body mass; LDL, low-density lipoprotein; LLFDI, late-life function and disability index; PB-EMS, part-body electromyostimulation; WB-EMS, whole-body electromyostimulation.

Data are presented as mean ± standard deviation and per cent or absolute change (d); P-values were calculated using change scores and analysis of covariance with baseline values as covariate for between-group comparison or by paired t-test for within-group comparison.

***$P < 0.001$.

**$P < 0.01$.

*$P < 0.05$.

DOI: 10.1002/jcsm.12717

(age ~55 years) reached a mean distance of 503 m before the intervention, a result identical to the reported value of healthy (i.e. community-dwelling) individuals in the age group of 80–89 years (503 m) and slightly above that of low-active individuals at a mean age of ~78 years (469 m).[28] Increase in strength in initially untrained or deconditioned subjects is primarily provoked by functional adaptations in the neuromuscular system, leading to large functional improvements in short periods of time.[29,30] Here, EMS seems to provide significant additional support, as documented by positive effects on overall strength in our study, which likely depends on a larger stimulated muscular area.[31] Moreover, strength development is not necessarily linked to a high propensity or increase in muscle mass as muscle size contributes to only 3–5% of muscle strength.[32,33] This has also been observed after prolonged EMS, in that independently from increases in LBM ranging from 0.8%[9] up to 3.3% in elderly,[34] a superior effect on strength outcome has been reported. At the molecular level, EMS has been reported to stimulate muscle regeneration by enhanced fusion of satellite cell with mature skeletal fibres in elderly subjects.[35] The improved regenerative capacity of satellite cells was associated with elevated leg muscle strength and subjects' mobility. In addition, myogenic precursor cells showed increased cytoplasmic Ca^{2+} levels and gene expression of myogenic transcription factor D and G. EMS has also been reported to reduce the production of reactive oxygen species[35] and to stimulate overall skeletal muscle protein synthesis rates already after a single EMS session.[36]

In general, WB-EMS has been suggested to exert strong effects on body fat reduction,[10,12,34,37,38] a circumstance based on the observation that one single session of WB-EMS may increase the resting metabolic rate and therefore fat metabolism for several hours, at least in healthy individuals.[39] Long-term interventions in sarcopenic elderly reported reduction of up to 6.7% for BFM and 5.5% for VF[11] after 6 months of training. In our study, we found reduced BFM and VF for the WB-EMS group (BFM: −3.4%, VF: −3.4%), PB-EMS group (BFM: −2.5%, VF: −3.0%), and CG (BFM: −1.9%, VF: −0.7%) without significant between-group differences. These findings are of interest, as especially VF represents a strong and independent predictor of all-cause mortality due to the associated pro-inflammatory effects mainly deteriorating cardiovascular function.[5] With regard to the initially applied definition of sarcopenia, no difference between the three interventions on SMI was observed and seven subjects of the WB-EMS group (~15%), four subjects of the PB-EMS group (~11%), and one person in the CG (3%) no longer fell within the range of defined sarcopenia at the end of the intervention. In terms of metabolic adaptations, exploratory analyses suggested a stronger reduction of total cholesterol and LDL cholesterol levels in the PB-EMS group compared with the WB-EMS group and CG. As statin therapy was generally frequent in all three groups and did not change during intervention, already lower LDL cholesterol levels in the CG at baseline might have prevented a potential effect in the CG. Nevertheless, LDL reductions within all groups approached or reached the recommended therapeutic level of $<$100 mg/dL.[40]

It is important to note that, since applied in a rehabilitation setting, increased awareness towards safety was mandatory in this study. Thus, a reduced load/rest ratio of 4 s vs. 4 s (1:1)[38] was chosen while other studies on sarcopenia used higher load/rest ratios (6 s vs. 4 s).[9,24] Furthermore, to avoid recently reported initial overload after too intense WB-EMS sessions with (possible) subsequent muscle damage and associated rhabdomyolysis,[41–43] we strictly followed corresponding training guidelines that have been developed to rule out severe contraindication.[44] Of note, no adverse events were observed during the study, rendering the reported protocol safe also for patients during medical rehabilitation. The monitoring of CK deviations 3 days after the initial WB-EMS load showed a seven-fold increase, commonly observed in strength training protocols and well below the definition of mild rhabdomyolysis (~1700 U/L).[45]

The current study might have several limitations. It can be assumed that higher EMS intensity might have resulted in greater improvements and could have induced differences between the two EMS groups. However, a progression in RPE from initially 13.5 ('somewhat hard') up to 15 ['hard (heavy)'] seems to be sufficient to induce additional physiological and clinical benefits by either EMS variant. Moreover, the unequal sex distribution between the groups may have affected study outcomes, but subgroup analyses revealed that neither sex nor clinical indication appeared to have a significant effect for any of the selected primary outcome variables (*Table* S4). The observed between-group differences in chair rise test performance results may have been affected by higher baseline values in the CG, which might have limited the potential improvement in this specific test. The short time span of 4 weeks might be a limiting factor, although this period was chosen deliberately. On the one hand, it corresponds with a regular standard medical rehabilitation in Germany. On the other hand, short-term effects in a deconditioned cohort during rehabilitation have not yet been evaluated. In addition, a good integration into the clinical routine provides ideal conditions for effective training in this 4 week rehabilitation setting. With a fixed time schedule, standardized training programme supported by video animation, and the highly personalized trainer support (care key of 2:1), the patient can benefit from a safe, time-efficient, and effective training tool. The presented findings were achieved in a selected group of sarcopenic patients in a controlled environment of inpatient medical rehabilitation in one single rehabilitation centre. Even though results are quite promising, great care should be taken when adopting the described protocol to other rehabilitation settings including outpatient rehabilitation. Due to the COVID-19

DOI: 10.1002/jcsm.12717

pandemic, the planned number of patients was not reached. It will thus be necessary to confirm the findings by other adequately power studies.

Conclusion

The described EMS protocol was well tolerated, safe, and effective to improve leg muscle function and strength in sarcopenic patients with orthopaedic and/or cardiologic indication. Effects were comparable between female and male patients. Due to the standardized medical rehabilitation and training programme applied to all three groups during the intervention, the detected improvements most likely depend on the additional muscle stimulation by EMS. No differences between WB-EMS and PB-EMS were seen. Thus, short-term EMS, applied as either WB-EMS or PB-EMS, may represent a promising training option for deconditioned subjects in clinical settings for the improvement of muscular and functional abilities and may support standard rehabilitation to improve health outcomes. Further research should address the cellular and molecular mechanisms underlying the observed EMS effects including potential neuromuscular adaptations.

Acknowledgements

The authors acknowledge the support of clinicians and assistants at Klinik Königsfeld (Ennepetal, Germany), and miha bodytec (Gersthofen, Germany) for technical assistance, without whom this study would not have been possible. The translation of SF-36 is based on the 36-Item Short Form Survey developed and owned by the RAND Corporation, copyright © RAND. Although permission to translate the survey was granted by RAND, the translation itself has not been approved or reviewed by RAND. RAND's permission to reproduce the survey is not an endorsement of the products, services, or other uses in which the survey appears or is applied.

Conflict of interest

The authors report no conflicts of interest in this work.

Funding

We thank the Institute for Rehabilitation Science at VFR e.V., Norderney, for funding. VFR had no role in the study design, collection, analysis, or interpretation of the data, writing of the manuscript, or the decision to submit the paper for publication.

Online supplementary material

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1: Baseline characteristics by cardiac and orthopedic diagnosis.
Table S2: Additional variables and changes by study group.
Table S3: Pre- to post-intervention changes of individual SF-36 categories.
Table S4: Baseline and intervention differences by sex and indication for rehabilitation.
Figure S1: EMS equipment (miha bodytec); electrode vest and cuffs used in EMS training.

References

1. Churilov I, Churilov L, MacIsaac RJ, Ekinci EI. Systematic review and meta-analysis of prevalence of sarcopenia in post acute inpatient rehabilitation. *Osteoporos Int* 2018;**29**:805–812.
2. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing* 2019;**48**:601–601.
3. Delmonico MJ, Harris TB, Lee JS, Visser M, Nevitt M, Kritchevsky SB, et al. Alternative definitions of sarcopenia, lower extremity performance, and functional impairment with aging in older men and women. *J Am Geriatr Soc* 2007;**55**:769–774.
4. Goodpaster BH, Park SW, Harris TB, Kritchevsky SB, Nevitt M, Schwartz AV, et al. The loss of skeletal muscle strength, mass, and quality in older adults: the health, aging and body composition study. *J Gerontol A Biol Sci Med Sci* 2006;**61**:1059–1064.
5. Rodríguez-Hernández H, Simental-Mendía LE, Rodríguez-Ramírez G, Reyes-Romero MA. Obesity and inflammation: Epidemiology, risk factors, and markers of inflammation. *Int J Endocrinol* 2013;**2013**:1–11.
6. Sabharwal S, Root MZ. Impact of Obesity on Orthopaedics. *J Bone Joint Surg Am* 2012;**94**:1045–1052.
7. Chodzko-Zajko WJ, Proctor DN, Fiatarone Singh MA. Exercise and physical activity for older adults. *Med Sci Sports Exerc* 2009;**41**:1510–1530.
8. Filipovic A, Kleinöder H, Dörmann U, Mester J. Electromyostimulation—a systematic review of the effects of different electromyostimulation methods on selected strength parameters in trained and elite athletes. *J Strength Cond Res* 2012;**26**:2600–2614.
9. Kemmler W, Bebenek M, Engelke K, von Stengel S. Impact of whole-body electromyostimulation on body composition in elderly women at risk for sarcopenia: the Training and ElectroStimulation Trial (TEST-III). *AGE* 2014;**36**:395–406.
10. Kemmler W, Teschler M, Weißenfels A, Bebenek M, Fröhlich M, Kohl M. Effects of whole-body electromyostimulation versus high-intensity resistance exercise on body composition and strength: a randomized controlled study. *Evid Based Complement Alternat Med* 2016;**2016**:1–9.
11. Kemmler W, Kohl M, Freiberger E, Sieber C, von Stengel S. Effect of whole-body electromyostimulation and / or protein supplementation on obesity and cardiometabolic risk in older men with

sarcopenic obesity: the randomized controlled FranSO trial. *BMC Geriatr* 2018;**18**:70. https://doi.org/10.1186/s12877-018-0759-6
12. Kemmler W, Teschler M, Weissenfels A, et al. Whole-body electromyostimulation to fight sarcopenic obesity in community-dwelling older women at risk. Results of the randomized controlled FORMOsA-sarcopenic obesity study. *Osteoporos Int* 2016;**27**:3261–3270.
13. Studenski SA, Peters KW, Alley DE, Cawthon PM, McLean RR, Harris TB, et al. The FNIH sarcopenia project: rationale, study description, conference recommendations, and final estimates. *J Gerontol A Biol Sci Med Sci* 2014;**69**:547–558.
14. Kemmler W, Weissenfels A, Willert S, et al. Efficacy and safety of low frequency whole-body electromyostimulation (WB-EMS) to improve health-related outcomes in non-athletic adults. A systematic review. *Front Physiol* 2018;**9**:573.
15. Borg E, Kaijser L. A comparison between three rating scales for perceived exertion and two different work tests. *Scand J Med Sci Sports* 2006;**16**:57–69.
16. Bohannon RW. Measurement of sit-to-stand among older adults. *Top Geriatri Rehabil* 2012;**28**:11–16.
17. Bohannon RW, Smith J, Hull D, Palmeri D, Barnard R. Strength, balance and gait before and after kidney transplantation. *Int J Rehabil Res* 1997;**20**:199–204. https://doi.org/10.1097/00004356-199706000-00010
18. Faggiano P, D'Aloia A, Gualeni A, Brentana L, Cas LD. The 6 minute walking test in chronic heart failure: indications, interpretation and limitations from a review of the literature. *Eur J Heart Fail* 2004;**6**:687–691.
19. Ainsworth BE, Haskell WL, Hermann SD, Meckes N, Bassett DR, Tudor-Locke C, et al. 2011 Compendium of Physical Activities. *Med Sci Sports Exerc* 2011;**43**:1575–1581.
20. Zoghbi GJ, Sanderson B, Breland J, Adams C, Schumann C, Bittner V. Optimizing risk stratification in cardiac rehabilitation with inclusion of a comorbidity index. *J Cardiopulm Rehabil* 2004;**24**:8–13.
21. Ware JE, Kosinski M, Keller S. SF-36 physical and mental health summary scales. A user's manual. Boston: Health Institute, New England Medical Center; 1994.
22. Micke F, Kleinoder H, Dormann U, Wirtz N, Donath L. Effects of an eight-week superimposed submaximal dynamic whole-body electromyostimulation training on strength and power parameters of the leg muscles: a randomized controlled intervention study. *Front Physiol* 2018;**9**:1719.
23. Bestehorn K, Jannowitz C, Horack M, Karmann B, Halle M, Voeller H. Current state of cardiac rehabilitation in Germany: patient characteristics, risk factor management and control status, by education level. *Vasc Health Risk Manag* 2011;**7**:639–647.
24. Kemmler W, Grimm A, Bebenek M, Kohl M, von Stengel S. Effects of combined whole-body electromyostimulation and protein supplementation on local and overall muscle/fat distribution in older men with sarcopenic obesity: the randomized controlled Franconia Sarcopenic Obesity (FranSO) study. *Calcif Tissue Int* 2018;**103**:266–277.
25. Kemmler W, von Stengel S, Teschler M, Weissenfels A, Bebenek M, Kohl M, et al. Ganzkörper-Elektromyostimulation und Sarcopenic Obesity. *Osteologie* 2016;**25**:204–211.
26. Schink K, Herrmann HJ, Schwappacher R, Meyer J, Orlemann T, Waldmann E, et al. Effects of whole-body electromyostimulation combined with individualized nutritional support on body composition in patients with advanced cancer: a controlled pilot trial. *BMC Cancer* 2018;**18**:886. https://doi.org/10.1186/s12885-018-4790-y
27. Myers J, Prakash M, Froelicher V, Do D, Partington S, Atwood JE. Exercise capacity and mortality among men referred for exercise testing. *N Engl J Med* 2002;**346**:793–801.
28. Rikli RE, Jones CJ. Development and validation of criterion-referenced clinically relevant fitness standards for maintaining physical independence in later years. *Gerontologist* 2013;**53**:255–267.
29. Ahtiainen JP, Pakarinen A, Alen M, Kraemer WJ, Hakkinen K. Muscle hypertrophy, hormonal adaptations and strength development during strength training in strength-trained and untrained men. *Eur J Appl Physiol* 2003;**89**:555–563.
30. Del Vecchio A, Casolo A, Negro F, Scorcelletti M, Bazzucchi I, Enoka R, et al. The increase in muscle force after 4 weeks of strength training is mediated by adaptations in motor unit recruitment and rate coding. *J Physiol* 2019;**597**:1873–1887.
31. Hashida R, Takano Y, Matsuse H, Kudo M, Bekki M, Omoto M, et al. Electrical stimulation of the antagonist muscle during cycling exercise interval training improves oxygen uptake and muscle strength. *J Strength Cond Res* 2021;**35**:111–117.
32. Ahtiainen JP, Walker S, Peltonen H, Holviala J, Sillanpää E, Karavirta L, et al. Heterogeneity in resistance training-induced muscle strength and mass responses in men and women of different ages. *AGE* 2016;**38**:10. https://doi.org/10.1007/s11357-015-9870-1
33. Buckner SL, Dankel SJ, Mattocks KT, Jessee MB, Mouser JG, Counts BR, et al. The problem of muscle hypertrophy: revisited. *Muscle Nerve* 2016 ;**54**:1012–1014.
34. Kemmler W, Weissenfels A, Teschler M, Willert S, Bebenek M, Shojaa M, et al. Whole-body electromyostimulation and protein supplementation favorably affect sarcopenic obesity in community-dwelling older men at risk: the randomized controlled FranSO study. *Clin Interv Aging* 2017;**12**:1503–1513.
35. Di Filippo ES, Mancinelli R, Marrone M, Doria C, Verratti V, Toniolo L, et al. Neuromuscular electrical stimulation improves skeletal muscle regeneration through satellite cell fusion with myofibers in healthy elderly subjects. *J Appl Physiol* 2017;**123**:501–512.
36. Wall BT, Dirks ML, Verdijk LB, Snijders T, Hansen D, Vranckx P, et al. Neuromuscular electrical stimulation increases muscle protein synthesis in elderly type 2 diabetic men. *Am J Physiol Endocrinol Metab* 2012;**303**:E614–E623.
37. Fritzsche D, Fruend A, Schenk S, Mellwig KP, Kleinöder H, Gummert J, et al. Elek tromyostimulation (EMS) bei kardiolo gischen Patienten. *Herz* 2010;**35**:34–40.
38. Kemmler W, Teschler M, von Stengel S. Effekt von Ganzkörper-Elektromyostimulation – "A series of studies". *Osteologie* 2015;**24**:20–29.
39. Teschler M, Wassermann A, Weissenfels A, et al. Short time effect of a single session of intense whole-body electromyostimulation on energy expenditure. A contribution to fat reduction? *Appl Physiol Nutr Metab* 2018;**43**:528–530.
40. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). *JAMA* 2001;**285**:2486–2497.
41. Finsterer J, Stollberger C. Severe rhabdomyolysis after MIHA-bodytec® electrostimulation with previous mild hyper-CK-emia and noncompaction. *Int J Cardiol* 2015;**180**:100–102.
42. Herzog A, Büchele F, Keller DI. Muskelschmerzen nach Elektromyostimula tionstraining. *Praxis* 2017;**106**:1121–1124.
43. Teschler M, Weissenfels A, Fröhlich M, et al. (Very) High creatine kinase (CK) levels after whole-body electromyostimulation. Are there implications for health? *Int J Clin Exp Med* 2016;**9**:22841–22850.
44. Kemmler W, Fröhlich M, von Stengel S, Kleinöder H. Whole-body electromyostimulation—the need for common sense! Rational and guideline for a safe and effective training. *Dtsch Z Sportmed* 2016;**67**:218–221.
45. Visweswaran P, Guntupalli J. Rhabdomyolysis. *Crit Care Clin* 1999;**15**:415–428.