The Impact of Training with Whole Body EMS

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The Impact of Training with Whole Body-EMS

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Aims and Objectives

This study will be undertaken in healthy adults who are employees at Mayo Clinic, Rochester MN

Primary Aim:

To assess the impact of training with whole body-EMS for a 16-week period of time, involving 1.0 x 20 minute training sessions per week, on peripheral endothelial function as measured using EndoPAT.

Secondary Aims:

To assess the impact of training with whole body-EMS for a 16-week period of time, involving 1.0 x 20 minute training sessions per week, on:

i) Body mass index, waist circumference, percentage body fat and distribution, and blood pressure

ii) Serum lipid profile, blood glucose and HbA1c, blood inflammatory markers including high sensitivity-CRP and uric acid, and novel cardiovascular markers in the blood such as fibrinogen, homocysteine and lipoprotein

iii) VO2 maximum (Cardiopulmonary exercise testing parameters)

iv) Maximum strength and maximum power in chest press and leg press

v) Symptoms of angina as measured by the Rose Questionnaire

vi) Quality of life as measured by the LASA Questionnaire, symptoms of depression as measured by the PHQ-9 Questionnaire, and symptoms of stress as measured on the Perceived Stress Scale

vii) Temporal changes in blood levels of creatinine kinase

Sensorimotor characteristics (visual-motor reaction time, peak knee muscular force, muscular force steadiness, and balance/posture

Hypotheses

We hypothesize that healthy adults who are employees at Mayo Clinic, Rochester MN who undergo whole body-EMS training for a 16-week period of time, involving 1.0 x 20 minute training sessions per week, will experience:

i) A significant improvement in peripheral endothelial function measured using EndoPAT

ii) A significant improvement in body mass index, waist circumference, percentage body fat and distribution, and blood pressure

iii) A significant improvement in lipid profile, blood glucose and HbA1c, blood inflammatory markers including high sensitivity-CRP and uric acid, and novel cardiovascular markers in the blood such as fibrinogen, homocysteine and lipoprotein

iv) A significant improvement in VO2 maximum and cardiopulmonary exercise testing parameters

v) A significant improvement in maximum strength and maximum power in chest press and leg press

vi) A significant improvement in symptoms of angina as measured by the Rose Questionnaire

vii) A significant improvement in quality of life as measured by the LASA Questionnaire, symptoms of depression as measured by the PHQ-9 Questionnaire, and symptoms of stress as measured on the Perceived Stress Scale

viii) No significant difference in blood levels of creatinine kinase across time

viii) A significant improvement in sensorimotor characteristics (visual-motor reaction time, peak knee muscular force, muscular force steadiness, standing balance, and overhead squatting posture)

ix)

Methods

Trial Design

This study will consist of a **blinded randomized controlled prospective study design**, and will include 80 healthy individuals who are employees at Mayo Clinic, Rochester MN.

Excluded subjects will consist of:

- Subjects under the age of 18
- Pregnancy/or suspected pregnacy
- Subjects with a history of liver or kidney disease, acute illness, taking medications (such as glucocorticoids)
- Subjects who have conditions (such as chronic inflammatory muscular diseases or Cushing's syndrome) that affect muscle mass

- Individuals with pacemakers and implantable cardiac defibrillators
- Individuals who conduct any other type of resistance training (> 45 minutes/week)
- Individuals who have regular "high" alcohol consumption (> 80g/day on 5 days a week), or are under acute influence of alcohol, drugs narcotics, and/or painkillers
- Subjects unable to consent to or participate in the 16-week EMS intervention or be available for follow up (1).
- Subjects who report recent surgeries
- Cardiac arrhythmias
- Active medical implants
- Epilepsy
- Seizures
- Severe circulatory disorders
- Arterial circulatory disorders
- Strong bleeding tendencies (hemophilia)
- Bleeding
- Abdominal wall hernia
- Inguinal hernia
- Tuberculosis
- Tumor diseases
- Arteriosclerosis in advanced stage
- Severe neurological disorders
- Diabetes mellitus
- Febrile diseases
- Acute bacterial or viral infections
- Liver diseases
- Kidney diseases
- Cardiovascular diseases
- Coronary heart diseases
- Infected or wounded areas of the skin
- Skin cancer
- Rhabdomyolysis

All subjects in both groups who enroll into this study will undergo an assessment of peripheral endothelial function with reactive hyperemia-peripheral arterial tonometry (RH-PAT) testing using EndoPAT; an assessment of vital signs including heart rate, blood pressure, weight, height and body mass index; laboratory blood work; cardiorespiratory testing using treadmill testing to determine VO2 max and maximal tolerated heart rate; maximal strength and maximal power

testing on chest press and leg press testing; and ultrasound-based percent body fat and fat distribution testing at baseline, and at 16-weeks follow-up (immediately after completing a 16-week training program using whole body-EMS) **(Figure 1)**. Baseline cardiovascular risk factors will be assessed by subject questionnaire and verified by chart review. In addition, subjects will complete an angina/chest pain symptom questionnaire (Rose Questionnaire), quality of life questionnaire (LASA Questionnaire), depression questionnaire (Patient Health Questionaire-9) and perceived stress questionnaire (Perceived Stress Scale) to assess for psychosocial wellness at each point in the study. Women of childbearing potential will have a urine pregnancy test to rule out pregnancy prior to enrollment. Sensorimotor characteristics such as visual-motor reaction time, Other sensorimotor characteristics (standing balance and posture) will be examined using a force plate and 2D camera with a commercially available app. .. . . Standing balance will be assessed by subjects standing on two legs for 30 seconds eyes-open and –closed. . Overhead squatting posture will be examined by analyzing static pictures of performing subjects with ipad-based postural assessment application (Posture Co, Inc, Trinity, FL, USA).

Intervention

Individuals who enroll in this study will be randomized to two groups, in a 1:1 ratio: intervention group and control group. In the intervention group we will apply 16-weeks of conventional whole body-EMS training 1.0 time a week for a maximum of 20 minutes per session, with no intermittent breaks. Individuals will undertake routine exercise maneuvers (including squatting, lunging, forward flexion etc.) under the guidance of certified trainers while simultaneously having percutaneous electrical stimulation applied to their bodies while exercising through the

whole body-EMS machine. Individuals will be trained in a ratio of 2 subjects to 2 machines and one trainer. Subjects in the control group will undergo training with a similar physical exercise program as those in the interventional group undertaking routine exercise maneuvers (including squatting, lunging, forward flexion etc.), and will use the same equipment and will be 'dressed' as if they were undergoing whole body-EMS, but will have no/subthreshold electricity signals applied to their body vest. The EMS machine will be switched on and show normal wave patterns suggesting that it is working normally, but study participants will be blinded to whether or not they are receiving percutaneous electrical stimulation while doing the routine exercise maneuvers. This will be applied for a 16-week training program 1.0 time a week for a maximum of 20 minutes per session, with no intermittent breaks. Individuals will be trained in a ratio of 2 subjects to 2 machines and one trainer. Individuals will be randomized to each group, and they and the study investigators will be blinded to the intervention. Otherwise, individuals in both groups will be asked to maintain their normal lifestyles.

In order to generate a safe, individualized, joint-friendly, and time-efficient exercise protocol which will be potentially effective and feasible for a cohort that may have physical limitations, we plan to implement the same previously utilized whole body-EMS training protocol successfully applied in other whole body-EMS trials undertaken in Germany that have focused on body composition and functional parameters (1-4). Briefly, with the whole body-EMS equipment (miha bodytec®, Gersthofen, Germany) we will apply a simultaneous but region specific stimulation of all the main muscle groups with an overall area of up to 2750 cm^2. We will consistently run an guided whole body-EMS program in groups who will always supervised

and guided by two certified instructor (i.e., two applicants coached by one instructor). Whole body-EMS will be conducted on approximately the same day, once a week (i.e., 1.0 × week) for 20 minutes. The device will apply a bipolar electric current; we will select an impulse frequency of 85 Hz, an impulse width of 350 μs, and will apply an interval approach with 4 seconds of stimulation alternating with 4 seconds of rest. Gentle slight dynamic exercises will be performed during the 4-second stimulation phase. Each session will consist of 10–14 dynamic exercises structured in one to two sets of eight repetitions performed without any additional weights in a standing position. Most exercises will be based on a low amplitude squat exercise (< 35° leg flexion) with full amplitude movements of the arms (such as rowing, lat pulley, or butterfly). The emphasis of the protocol however will not be the effect on muscles induced by voluntary activation but by the application of whole body-EMS with high current intensity during functional movements. During the course of the study, the instructor will progressively increase the volume of stimulation by extending the length of the session from 14 up to 20 minutes after 4 weeks of training. The intensity of the stimulation will be regulated using a rate of perceived exertion (RPE) scale to generate a sufficient, but tolerable, intensity of EMS application to all stimulated areas. For each of the muscle groups stimulated, participants will be encouraged to exercise at a RPE of "6–7 out of 10" (i.e., "hard+ to very hard") on the Borg CR10 Scale (5). This specification will be achieved in close interaction between the participant and instructor. Based on initial start settings determined after 4, 8, and 12 weeks, the impulse intensity will be increased slightly every 3 minutes to maintain/slightly increase the prescribed RPE during each session **(refer to Supplemental Video).**

Schedule of events

	Baseline Day 0	Weeks 1-7	Week 8 follow-up (+/- 7 days)	Weeks 9-15	Week 16 follow-up (+/-7 days)
Informed Consent	X				
Brief review of medical history	X				
Exercise with EMS device	X	X	X	X	X
Blood draw and laboratory testing**	X				X
Creatinine Kinase	X		X		X
Physical Assessment*	X				X
Survey Questionnaires***	X				X
EndoPAT	X				X
Ultrasound-Based Body fat and fat distribution measurements (Sports Medicine Testing)	X				X
Urine pg test±	X				
Sensorimotor tests	X				X

*Physical assessment includes: body mass index, waist circumference, percentage body fat and distribution, blood pressure, maximum heart rate, VO2 maximum, maximum strength and maximum power in chest press and leg press

**Laboratory Testing includes: high-sensitivity CRP, uric acid, fasting glucose, HbA1c, lipid panel, lipoprotein A, homocysteine fibrinogen.

***Rose, LASA, PHQ-9, PSS Questionnaire

±Women of childbearing potential only

Outcomes and Measurements

Research assistants will perform all baseline, and follow-up tests at 16-weeks based on availability of subjects schedule and tests equipment.

Peripheral Endothelial Function: Endothelial function will be measured via the RH-PAT index as previously described (6-9). The studies will be performed in a designated quiet, temperature controlled and uniformly lit room. Individuals in the interventional and control groups will be tested at baseline, and will undergo re-testing after completing 16-weeks of training within their assigned arm (within 2 weeks of completion). Subjects will be fasting for 4 hours before the study and will abstain from coffee or tobacco use on the day of the examination. Subjects taking any vasoactive medications, including calcium channel blockers, nitrates, ACE-inhibitors or beta blockers, will discontinue these for 24 hours prior to testing. The study will be conducted in the sitting position in a comfortable chair with armrests. A fitted blood pressure cuff will be placed on one arm, and the finger cuffs of the Endo-PAT 2000 device (Itamar Medical Inc. Ltd., Caesarea, Israel) will be placed on one finger of each hand (10). Subjects will relax for 10 minutes before initiation of the protocol. Baseline blood pressure and heart rate will be obtained via a digital automated blood pressure cuff (Omrom Healthcare, Inc., Vernon Hills, Illinois). The EndoPAT 2000 will be used specifically in this study because it is a Food and Drug Administration–approved noninvasive device, it allows continuous recording of the signal, and interpretation of the data is operator independent. The use of a control arm will allow the elimination of systemic interference of the test and independence from the participant's knowledge or conscious control of the signals (10-14). The finger probes consist of inflatable latex air cuffs connected by pneumatic tubes to an inflating device controlled through a computer algorithm. A constant counter pressure

(predetermined by baseline diastolic blood pressure) will be applied through the air cushions. This prevents venous pooling and thereby venoarteriolar reflex vasoconstriction while not occluding arterial blood flow. Pulsatile volume changes of the distal digit induce pressure alterations in the finger cuff, which are sensed by pressure transducers and transmitted to and recorded by the Endo-PAT device. A decrease in the arterial blood volume in the distal fingertip causes a decrease in pulsatile arterial column changes, reflected as a decrease in the measured PAT signal, and vice versa.

Previous studies have demonstrated dependence of the RH-PAT score on nitric oxide, confirming that reported RH-PAT scores indeed reflect changes in nitric oxide– dependent endothelial function, rather than neurohormonal activation (15). The reactive hyperemia protocol will consist of a 16-minute reactive hyperemia test, in the following sequence. A five-minute baseline measurement, after which a blood pressure cuff on the test arm will be inflated to 60 mmHg above baseline systolic blood pressure, or at least 200 mmHg for five minutes (occlusion of pulsatile arterial flow will be confirmed by the reduction of the PAT tracing to zero) after which, the cuff will be deflated, and the post-deflation PAT tracing will be recorded for an additional six minutes. The ratio of the PAT signal after cuff release compared to baseline will be calculated through a computer algorithm automatically normalizing for baseline signal, and indexed to the contralateral arm. The calculated ratio reflects the RH-PAT score (scores below 1.7 will be considered consistent with abnormal peripheral endothelial function). Although RH-PAT scores may not be the gold standard for endothelial function, several studies have shown good correlation between these methods and more widely accepted methods of

endothelial function testing, such as intra-arterial acetylcholine infusion and brachial artery Doppler ultrasound following reactive hyperemia (11, 13, 14).

Laboratory Testing: Laboratory testing will be undertaken in all participants at baseline, and at 16-weeks follow-up in both the intervention and control group. Venous blood will be drawn for high-sensitivity CRP, uric acid, fasting glucose, HbA1c, lipid panel, lipoprotein A, homocysteine and fibrinogen. For patients in both groups, venous blood will also be tested for creatinine kinase levels at baseline, 8-weeks (halfway into the training programs), and 16-weeks (after completing each respective training program for both groups). A blood sample of approximately 30 mL will be drawn and all samples will be sent to the Mayo Clinic central laboratory for analysis.

Body Weight, Height, and Waist Circumference: Body height, weight and waist circumference will be measured using calibrated devices. Body mass index will be calculated as mass (kg)/height (m^2).

VO2 MAX and Maximal Heart Rate: This will be tested using exercise treadmill testing in the conventional manner.

Questionnaires: Baseline clinical characteristics of all the participants will be carefully determined with validated baseline questionnaires (16). Completeness and accuracy of the questionnaires will be carefully checked by research assistants in close cooperation with the participants. In addition, all participants will complete four additional questionnaires at baseline, and 16-weeks follow-up in each of the intervention and non-intervention arms as follows:

i) Rose Questionnaire Is a validated questionnaire that has been used previously to assess for symptoms of angina (17)

ii) Linear Analog Self-Assessment (LASA) Mayo Clinic has developed a series of items that asks adults to rate their level of functioning on a scale from 0 (as bad as it can be) to 10 (as good as it can be). The six items to be used in this study inquire about overall quality of life, and then cover the five domains of quality of life: (1) mental well-being, (2) physical well-being, (3) emotional well-being, (4) social well-being, and (5) spiritual well-being.(18, 19)

iii) Patient Health Questionnaire-9 (PHQ-9) This is a questionnaire commonly used in clinical practice to assist in the assessment of patients who are suspected to have features consistent with a diagnosis of depression

iv) Perceived Stress Scale (PSS) This is a 14-item self-report tool that provides a global measure of perceived stress.(20) Responses range on a 5-point scale from "never" to "very often." A higher score indicates greater stress. The PSS correlates well with

life-events stress measures and social anxiety, and has adequate reliability (α= .84, .85, .86) in three different samples.

i)

ii) **Standing Balance:** For standing balance test, participants will first stand on a portable force plate (Model6090-06, Bertec, Columbus, OH) with two feet as steady as possible for 30 seconds with eyes open. Then, the same procedures will be repeated with eyes closed. Next, the low back region will be strapped with a vibration device to stimulate the muscle spindles of the low back muscles during eyes-open and –closed balance. A total of three trials will be collected. Position and velocity data about the center of pressure (CoP) of the body will be calculated and used for analysis.

Statistical Analysis

This will be a randomized controlled trial in which there will be an interventional group and a control group into which individuals will be randomly assigned in a 1:1 ratio. We will match individuals, a priori, as best as possible on age (within 5 years) and sex. Baseline, demographic and risk factor distribution will be outlined in Table 1 of our analyses. The following parameters will be measured in all subjects at baseline, and at 16-weeks follow-up (immediately after completing training in either study protocol depending on which group the participant is in): peripheral endothelial function measured with RH-PAT using EndoPAT; body weight and body mass index; waist circumference; blood pressure; total cholesterol, low and high density

lipoprotein cholesterol and triglycerides, fasting blood glucose and HbA1c; high sensitivity-CRP, uric acid, fibrinogen, homocysteine and lipoprotein A; percentage body fat; maximum strength and maximum power in leg press; VO2 maximum, maximal heart rate, and scores measured on the Rose questionnaire, LASA questionnaire, PHQ-9 questionnaire and Perceived Stress Scale. In addition, serum creatinine kinase will be measured at baseline, 8 weeks and 16 weeks.

We will compare values of each parameter between groups at baseline and after 16-weeks using unmatched analyses (using Student's t-test when comparing the aforementioned measures as continuous variable and using Chi-squared test when characterizing variables in categories of normal vs. abnormal). We will also assess for differences in the value of each parameter within groups between baseline and 16-weeks follow-up using matched analyses (using Student's paired t-test when comparing the aforementioned measures as continuous variable and McNemar's test when characterizing variables in categories of normal vs. abnormal). Lastly, we will compare the differences between baseline and 16-weeks follow-up for each parameter between groups using unmatched analyses (using the student t-test when comparing the aforementioned measures as continuous variable and using Chi-squared test when characterizing variables in categories of normal vs. abnormal).

Clinical Significance

Cardiovascular disease (CVD) is the primary cause for morbidity, mortality, and the associated rising health care costs in the world (21). According to 2012 statistics, poor diet, smoking, and

lack of physical activity continue to account for an overwhelming majority of CVD and death (22). Recent data demonstrate that nearly one million people in the US have suffered an acute coronary syndrome (21) and recent reports highlight the increasing burden of CVD in the developing world (23). Despite these figures, the medical community has been unable to translate our current understanding of conventional cardiovascular risk factors and existing preventative strategies into a reduction in CVD morbidity and mortality (24).

Strategies to Manage Risk of Cardiovascular Disease

Major modifiable risk factors for CVD include hyperlipidemia, smoking (current or former), hypertension, abdominal obesity and diabetes mellitus, which are responsible for approximately 80% of the population attributable risk for acute myocardial infarction in men and women (25). Identification of at-risk groups and appropriately addressing risk factors forms the cornerstone of successful management of CVD. This is often achieved using multi-variable risk-prediction algorithms (26-29), of which the most widely used in clinical practice are the Framingham based models. These scores assign weights to different levels of traditional risk factors such as age, total cholesterol and systolic blood pressure, which are combined to generate an absolute probability of developing CVD within a specified time frame. Framingham based risk prediction models are well-established, practical and easy to use, supported by large amounts of data and in most cohorts discriminate risk well, after calibration where necessary (30). Nevertheless, Framingham based scores are limited by incorporating only a limited number of risk factors, which have been identified from historically based population studies (31). Further these conventional cardiovascular risk factors only account for between 58% and 72% of all incident

cases of coronary heart disease (CHD) (32). Alternative nonconventional risk factors may account for some of this gap and are becoming increasingly important particularly as the effects of previously implemented attempts at managing conventional risk factors are being seen. For example, one time trend analysis showed that patients presenting to the catheterization laboratory with CHD had better blood pressure and lipid profiles between 2006-2010, compared with 1994-1999 (33), which may reflect improved uptake of primary and secondary preventative strategies such as smoking cessation (34) as well as a higher proportion of patients taking risk modifying cardiovascular medication (35). Furthermore, in one study of young adults hospitalized with their first myocardial infarction, less than 25% would have qualified for lipid-lowering therapy. This is based on guidelines available at the time (36), and further demonstrates the limitation of current risk-based algorithms. Thus, there is a need to identify, account for and manage novel risk factors not currently accounted for in traditional risk prevention models. An example of such a factor is physical (in)activity and exercise.

Physical Activity and Primary Prevention

From 2006–2011, physical inactivity was associated with 11.1% of the aggregate healthcare spending in the USA, with inactive adults accounting for a 30% difference in mean annual US expenditure per capita compared with active adults ($1437 vs $713) (37). Recent evidence has also indicated that time spent in sedentary behaviors is an independent risk factor for a number of adverse health consequences including obesity, metabolic syndrome, type 2 diabetes, some cancers, CVD-related mortality and all-cause mortality (38). Physical inactivity has also been

shown to be associated with approximately 6% of CHD cases and a 0.68-year reduction in life expectancy (39). Moderate-to-high levels of physical activity have clearly been shown to be protective against CVD (40, 41). A dose response relationship between physical activity and cardioprotection has been shown, such that even small amounts of physical activity can have a beneficial effect on CVD risk (42). Studies have shown that adults who maintain an active lifestyle as measured by accumulating more steps, and not necessarily through exercise *per se*, are likely to have a lower prevalence of metabolic syndrome (43) and regardless of exercising regularly or not, better cardiovascular health and longevity (44, 45). A further study showed that postmenopausal women who either walk or vigorously exercise have substantial reductions in the incidence of CVD events (46). Other large population-based studies have also shown a relationship between regular physical activity and reduced rates of CVD-related morbidity and mortality as well as favorable changes in risk factors for CVD such as systolic and diastolic blood pressure and lipid profile (47-50). Physical activity also improves cardiorespiratory fitness, which also independently improves CVD risk profile (51).

Physical Activity and Secondary Prevention

Amongst patients with established CHD, exercise-based cardiac rehabilitation (CR) is the cornerstone of secondary prevention. CR consists of several core components including baseline patient assessment, nutritional and psychosocial counselling, risk factor management, as well as physical activity counselling and exercise training (52). In patients with CHD, CR is associated with a 13% and 26% lower all-cause and CVD mortality, respectively, in addition to a 31% reduction in hospital admissions at 12 months (53). CR participation is also associated with

improvements in CHD risk factors, reduced angina symptoms and depression, improved exercise capacity and enhanced health-related quality of life (54-56). In patients with heart failure who are receiving optimal therapy, exercise-based CR programs confer an additional 11% reduction in all-cause mortality and hospitalization, a 15% reduction in CVD death and heart failure hospitalization, and improved quality of life (57-59). In light of these significant benefits, most contemporary guidelines provide a Class I-level recommendation for referral to CR for eligible patients including those with stable angina, myocardial infarction within the past 12 months, cardiac surgery (coronary artery bypass grafting, valve repair/replacement or heart or lung transplant), percutaneous coronary intervention and systolic heart failure. A careful history and physical examination are important to ensure that patients with CHD do not have residual ischemic symptoms, uncontrolled heart failure or threatening arrhythmias that may be triggered by vigorous exertion. The risks for these adverse events decrease significantly after the index cardiac event, allowing patients to safely enroll in CR as early as 1–2 weeks after hospital discharge (60). Prior to prescribing physical activity for patients with CHD, patients' exercise tolerance should be assessed by undertaking peak or symptom limited exercise testing to establish a baseline fitness level, and to evaluate for exercise-induced myocardial ischemia or arrhythmias that may alter ongoing medical management (60). Patients should be continued on their usual medications during exercise testing to simulate the anticipated hemodynamic responses during exercise training. The safety of contemporary exercise based CR programs is well established, with a reported incidence of cardiac arrest and death of approximately 1 in 115,000 and 1 in 750,000 patient hours of participation, respectively (53, 56, 60). The general recommendation for patients is 30–60 minutes daily of moderate-intensity physical activity for at

least 5 days of the week and performed at an intensity of 40–80% of the peak heart rate (60). For patients with ischemic signs or symptoms during exercise, the intensity of exercise should be prescribed at a heart rate at least 10 beats per minute below the ischemic or angina threshold (60). While adverse CVD events are rare, increased medical supervision is necessary for those patients with moderate to high risk of complications. A stable patient, however, can start CR as early as 1 week after discharge. Due to the significant cardiovascular benefits of exercise, patients unable to attend supervised exercise sessions should continue to exercise independently. The recommended exercise intensity may be reduced to approximately 60% to 75% of the peak heart rate to decrease the risk of myocardial infarction or life-threatening arrhythmias (61).

Lack of Uptake of Physical Activity

In a recent study of 58,269 patients with acute myocardial infarction who were eligible for CR only 62.4% were referred to CR at the time of hospital discharge, and only 23.4% of all patients actually attended one or more CR sessions in the year following discharge, suggesting significant CR underutilization (62). In addition, with regards to the primary prevention setting, though studies have shown a slight increase in physical activity amongst adults living in the United States between 1988 and 2000, 25% of American adults report no participation in leisure-time physical activity (63). Further, most older people are unable or unwilling (64) to undertake the exercise doses recommended to favorably impact body composition and CVD risk (65). Despite this the American Heart Association (AHA) and American College of Sports Medicine (ACSM) recommend at least 30 minutes of moderate-intensity physical activity 5 days a week, 20 minutes

of vigorous aerobic exercise 3 days a week or a combination thereof, in addition to 2-3 days/week of resistance, flexibility and neuromotor exercises (66).

Anecdotally, lack of time is a commonly cited reason for lack of widespread and consistent uptake of physical activity amongst healthy subjects as well as those with established CHD or heart failure. A further reason may include lack of awareness and education in the potential benefits of engaging in frequent exercise as well as the harms of living a sedentary life. Additional reasons may include injury or fear of injury and indeed the most common risk associated with physical activity is musculoskeletal injury. Unaccustomed vigorous physical activity may also trigger adverse cardiovascular responses including myocardial infarction and malignant arrhythmia. Nevertheless, while musculoskeletal and cardiovascular complications from exercise increase with physical activity of increasing intensity, regular exercise and enhanced cardiorespiratory function unequivocally confer partial protection (67, 68). Finally a lack of direction and monitoring as well as awareness in what type of exercise to do, how often to do it, and for how long further inhibits the widespread uptake of this habit whose integration into a day-to-day routine has proved challenging even for the most motivated of individuals.

Existing Tools to Increase Uptake of Physical Activity

To help improve the uptake of regular physical activity at the population level the US Preventative Service Task Force emphasizes the effectiveness of clinician counselling and specifically recommends that overweight adults with risk factors for CVD receive intense behavioral counselling (Grade B recommendation) (69). When counselling patients, the AHA

recommends that clinicians use the following strategies: setting specific and short-term goals, providing feedback on progress, advocating strategies for self-monitoring, establishing a plan for frequency and duration of follow-up, using individually tailored interventions based on readiness to change, and motivational interviewing and enhancing patient self-efficacy (70). Health coaching, in which dedication towards one's health is fostered via professional support and motivational interviewing, is generally well received and offers additional support in promoting lifestyle changes (71). In an attempt to ensure physical activity is addressed frequently in the outpatient clinical setting, the American College of Sports Medicine and American Medical Association launched the initiative 'Exercise is Medicine' in 2007 (72). The campaign calls for promoting physical activity as part of routine practice in healthcare, encouraging clinicians to evaluate their patients' physical activity at every visit, 'prescribing' exercise at appropriate 'dosages,' and where appropriate, referring patients to credentialed exercise professionals and to use technology to track participation (72). This novel philosophy sees physical activity as a multi-disease targeting pharmaceutical equivalent that should be monitored, re-dosed and modified on an ongoing basis cultivating the mindset that exercise is indeed medicine. Clearly, effectively enhancing the uptake of regular physical activity to improve population health requires a significant commitment in time and human capital, which are ever-present barriers encountered by patients and clinicians alike. Rapidly evolving technology has helped to create adjunctive tools that assist in the promotion of physical activity by overcoming these barriers and upholding the key aforementioned strategies that help ensure lifestyle changes endure over time.

Electronic Muscle Stimulation

These technological tools have included pedometers/accelerometers, mobile applications and social media, all of which have provided motivation and monitoring of progress (73). Whole body electronic muscle stimulation (EMS), a method that primarily focusses on muscular dimensions, is a further development of local EMS application that enables all main muscle groups to be stimulated simultaneously with customizable intensity. Whole body EMS provides a time efficient, joint friendly, highly adaptable training technology that forms a promising option to enhance the widespread and frequent uptake of physical activity, at least in middle-aged and older people (2, 4) **(see Figures 2 and 3)**. While conventional exercise protocols may comprehensively influence cardiovascular risk factors and disease, as well as physical functioning amongst the elderly, decades of promoting physical activity has failed to enhance its widespread uptake such that only 30% of the European Union population aged 55 years and older exercise regularly (1). This situation indicates the need for low-threshold interventions, which could at least offer the potential for improving some important health and functional parameters of advanced age.

Furthermore, sarcopenic obesity (SO), defined as the combination of low muscle and high fat mass (74), is reported to be a frequent condition in elderly people, and is present in up to 94% of people aged $\geq$ 60 years (75). SO is predominately caused by a decrease of physical activity in combination with stable caloric intake, malnutrition, and hormonal changes (76). Older people with SO have demonstrated poor health, reduced functional capacity, and quality of life right up to loss of independence and institutionalization (74). Besides the problems associated with progressive loss of muscle mass, the concurrent accumulation of (intra-)abdominal fat induces a

higher risk for cardio-metabolic diseases (77, 78). Regular exercise favorably affect a number of cardiovascular risk factors and diseases in old age (79). Indeed, resistance training is becoming an increasingly popular method of conditioning for recreational purposes and in competitive athletes. In addition to recreation, resistance training is also increasingly being used in rehabilitation (80). The benefits of resistance training on the skeletal muscle are well established (81), and may extend to the prevention and treatment of cardiovascular risk factors (82). However, the effect of resistance training on cardiac morphology and function remain equivocal. A cross-sectional cardiovascular MRI study by Fleck et al (83) showed concentric left ventricular myocardial adaption in individuals undergoing resistance training. A further longitudinal cardiovascular MRI study showed that a relatively short period of high intensity resistance training in previously untrained men was associated with physiologically significant changes in cardiac atrial and ventricular morphology and function (84). Apart from its potential use in endurance training, EMS could be of use in individuals who are not able to undertake physical training due to comorbidities or the underlying cardiac disease. EMS has demonstrated positive effects on muscle and fat mass, and a gain of functional capacity in older sedentary people (85) (see below). However, even though there is some evidence that EMS may induce changes in body composition and could favorably decreased the metabolic syndrome amongst elderly patients (77), studies evaluating the potential role of EMS training on cardiac function and cardiovascular risk are lacking.

Previous Studies Evaluating Electronic Muscle Stimulation

STUDY TITLE	AIMS	SAMPLE	STUDY DESIGN	MAIN RESULTS	ADVERSE EFFECTS
Kemmler et al. Evid Based Complement Alternat Med 2016 Effects of Whole-Body Electromyostimulation versus High-Intensity Resistance Exercise on Body Composition and Strength: A Randomized Controlled Trial (3)	To determine the effectiveness of WB-EMS compared with the gold standard reference HIT, for improving body composition and muscle strength in middle-aged men	Healthy untrained men, ages 30-50 years N=48	Randomized controlled trial: healthy untrained men aged 30-50 years were randomly allocated to either HIT (2 sessions/week) or a WB-EMS group (3 sessions/2 weeks) that exercised for 16 weeks HIT was applied as "single-set-to-failure protocol," while WB-EMS was conducted with	Lean body mass changes of both groups (HIT 1.25 ± 1.44% versus WB-EMS 0.93 ± 1.15%) were significant (p = .001); however, no significant group differences were detected (p = .395) Leg-extensor strength also increased in both groups (HIT 12.7 ± 14.7%, p = .002, versus WB-EMS 7.3 ± 10.3%, p =	Nil reported

			intermittent stimulation (6 s WB-EMS, 4 s rest; 85 Hz, 350 ms) over 20 minutes	.012) with no significant (p = .215) between-group difference Corresponding changes were also determined for body fat and back-extensor strength	
Kemmler, W. et al. Calcified Tissue International 2018 Effects of combined whole body electromyostimulation and protein supplementation on local and overall muscle/fat distribution in older men with sarcopenic obesity: the Franso Study (1)	To determine the combined effect of WB-EMS and protein supplements on local and overall muscle/fat distribution in older man	Community dwelling men ≥ 70 years with sarcopneic obesity N = 67	Randomized controlled trial: WB-EMS and protein supplementation (n = 33) vs. a non-intervention control group (n = 34) WB-EMS was conducted 1.5 sessions of 20	Thigh lean muscle volume increased significantly in the WB-EMS&P ($p < 0.001$) and increased slightly in the CG ($p = 0.435$) Fat volume increased significantly in the CG ($p <$	3 participants in each of the WB-EMS&P and control group were lost to follow-up: 1 gave "discomfort during WB-EMS application" as a reason

	with sarcopenic obesity		min/week for 16 weeks. Whey protein supplementation aimed to ensure a daily intake of 1.8 g/kg body mass	0.001) and was maintained in the WB-EMS&P group (p = 0.728) Group differences for both parameters were significant (p = 0.033 and p = 0.002) Appendicular muscle mass and trunk fat also differed significantly (p < 0.001) between WB-EMS and controls, with significant positive	0 participants of the WB-EMS&P group reported serious problems; and no injuries or adverse effects were observed or reported by the participants

				changes in the WB-EMS&P ($p < 0.001$) and no relevant changes in controls Changes of gait velocity, leg-extensor strength, and advanced lower extremity function of the WB-EMS&P group differed significantly from controls ($p \leq 0.002$)	
Van Buuren et al. Rehabilitation 2014 Electrical Myostimulation:	To compare the effects of extended EMS to limited EMS	Stable CHF patients (NYHA class II–III) were evaluate	Randomized controlled trial: Extended EMS (n=18) vs.	QoL was found to be improved in all	No safety concerns or adverse effects were described

Improvement of Quality of Life, Oxygen Uptake and Left Ventricular Function in Chronic Heart Failure (86)	on physical performance, left ventricular ejection function, and quality of life in congestive heart failure patients	N=31	limited EMS (n=13) Training was performed for 10 weeks twice weekly for 20 minutes	domains of the SF-36 questionnaire In the extended EMS group there was a significant improvement in the domain physical functioning and emotional role Limited EMS group showed significant improvement in the domain vitality There was a significant increase in oxygen uptake	Patients with pacemakers or implantable cardiac devices had been excluded from this study

				at aerobic threshold in all groups (exEMS: + 29.6 %, p < 0.001; limEMS + 17.5 %, p < 0.001) EF increased from 36.94 ± 8.6 to 42.36 ± 9.1 % (+ 14.7 %, p = 0.003) in the extended EMS group and 37.7 ± 3.6 to 40.3 ± 5.9 % [+ 6.9 %, p = 0.18] in the limited EMS group	
Wittman et al. Clinical Interventions in Aging 2016	To determine the combined	Community dwelling women ≥ 70 years with	Randomized controlled trial: 6 months of WB-EMS with	Metabolic syndrome Z-score decreased in both groups;	No safety concerns or adverse effects were described

Impact of whole body electromyostimulation on cardiometabolic risk factors in older women with sarcopenic obesity: the randomized controlled FORMOsA-sarcopenic obesity study (87)	effect of WB-EMS and protein supplements on the metabolic syndrome in elderly community dwelling women with sarcopenic obesity	sarcopneic obesity N = 75	or without protein supplementation (150 kcal/day, 56% protein) vs. a non-intervention control group (n=25 in each group) WB-EMS included one session of 20 minutes (85 Hz, 350 μs, 4 s of strain–4 s of rest) per week with moderate-to-high intensity	however, changes compared with the control group were significant (P=0.001) in the WB-EMS&P group only On analyzing the components of the metabolic syndrome, significant positive effects for both WB-EMS groups were identified for mean arterial pressure, while the WB-EMS group significantly differed for	

				waist circumference, and the WB-EMS&P group significantly differed for HDL-cholesterol (P=0.006) from the control group No significant differences were observed between the WB-EMS groups	

Efficacy and Safety Considerations

In voluntary strength training, the resistance of additional weight regulates the training intensity due to the maximum voluntary contraction (MVC), which is defined as one repetition maximum. In contrary to voluntary exercise, EMS activates muscle contraction artificially without using a resistance load. For this reason, it is not possible to simply transfer conventional training

regimens into strength training with EMS. Several studies have shown that electrical stimulus can be more intense than voluntary stimulus activated by the central nervous system (88). In contrast to voluntary strength training, the MVC in EMS strength training is regulated according to the level of stimulation parameters. In turn, these parameters depend on the individual condition of the muscular system and on individual pain perception. Under voluntary conditions, it is difficult to reach the absolute maximum level of contraction because accomplishing this depends on the individual's level of strength and motivation. Some studies revealed that elite athletes with a high level of maximal strength are able to reach levels of MVC close to the absolute maximum, while average subjects only reach their maximum in extreme situations. For this reason, EMS could enable strength training at intensities that are otherwise difficult to reach because of personal motivation levels (88).

In a previous study, Hortobagyi et al showed the effectiveness of different EMS methods for enhancing maximal strength, speed strength, jumping and sprinting ability, and power in trained and elite athletes (89). In another review, the authors showed that EMS is effective for developing physical performance. Specifically, after a stimulation period of 3–6 weeks, significant gains were shown in maximal isometric and dynamic strength; eccentric isokinetic speed and concentric isokinetic speed strength; rate of force development; and power. Developing these parameters increased vertical jump height by up to 25% (squat jump +21.4%, countermovement jump +19.2%, drop jump + 12%) and improved sprint times by as much as -4.8% in trained and elite athletes. With regards to the level of fitness, the authors showed that trained and elite athletes, despite their already high level of fitness, were able to significantly

enhance their level of strength to the same extent as is possible with untrained subjects (90). Thus, EMS offers a promising alternative to traditional strength training. However, compared to traditional voluntary strength training, several EMS parameters have to be considered in addition to parameters for common training regimens when undertaking strength training with EMS. This complexity of different combinations of training regimens and stimulation parameters makes it difficult to systematically implement EMS.

In a review comparing different training regimens using EMS and their training effectiveness, Filipovic et al. highlighted a number of preconditions necessary for producing a stimulus above the training threshold using EMS to promote strength adaptations. In doing so, they provided guidelines for implementing EMS effectively and safely in strength training (88). They showed a significant relationship between applying a stimulation intensity of ≥ 50% MCV and significant strength gains. To generate this level of MVC, they recommended training regimens that featured 4.4 +/- 1.5 weeks of training; 3.2 +/- 0.9 sessions per week for 17.7 +/- 10.9 minutes per session. They also recommended 6.0 +/- 2.4 seconds per contraction with 20.3 +/- 9.0% duty cycle, with stimulation parameters as follows: impulse width 306.9 +/- 105.1 microseconds; impulse frequency 76.4 +/- 20.9 Hz; and impulse intensity 63.7 +/- 15.9 mA to optimize training to systematically enhance abilities such as maximal strength, speed strength, jumping and sprinting ability, and power (88). These formed acceptable training parameters that did not overstress the subjects' muscular system that could in turn potentially hamper strength adaptations.

An important issue that has arisen with EMS training is the potential risk of elevation in blood creatinine kinase levels. Studies investigating the effects of EMS on creatinine kinase levels have shown that the electrical stimulus from EMS can cause significantly more stress to the muscular system and therefore could lead to higher creatinine kinase levels compared to voluntary muscle contraction exercise (88, 91). Indeed, due to the ability to innervate large muscle areas simultaneously with dedicated individual intensity to each muscle group, EMS can be associated with potential muscle injury. One study showed that, compared to traditional strength training, the stress on the muscular system is about 40% higher after intensive EMS (88). The authors arrived at the conclusion that the level of stimulation intensity is responsible for the elevation in creatinine kinase, while the duration of stimulation had no influence. The authors also showed that subjects still exhibited high values after long periods ranging from 24 hours to 4 days. Further stimulation within this time of decomposition would result in a cumulative rise in creatinine kinase levels (88), which in turn could overstress the muscular system further. Further, one study in which whole body EMS was implemented to the point of exhaustion in healthy novices confirmed very high elevations in creatinine-kinase levels. Although this study did not detect any of the reported clinical consequences of this “severe” rhabdomyolysis, in less fit subjects who are neither optimally prepared nor supervised, initial whole body EMS to exertion may have more far-reaching consequences. Consequently, EMS requires a greater interval between training sessions to prevent overstressing the muscular system and to ensure strength adaptations compared to conventional training. Of note, a subsequent whole body EMS conditioning phase of 10 weeks completed by a second EMS test application to exhaustion demonstrated creatinine-kinase peaks in the range of conventional resistance exercise

(92). Studies have also shown that the muscular system acclimatizes to the electrical stimulus in as little as 3 weeks, which in turn results in reduced creatinine kinase activity (88). These results indicate that a short period of careful whole body EMS conditioning should be mandatorily implemented in order to realize a safe application. Introducing the electrical stimulus to subjects before starting with the actual stimulation period as part of an acclimatization period might prevent a cumulative rise in creatinine kinase levels while helping to mitigate muscle soreness. **Figure 4** highlights additional safety considerations.

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Regarding the stimulation intensity, the aforementioned review showed that intensities of ≥ 50% MVC were mostly produced with biphasic impulses (88). Monophasic current flows from one electrode to the other in a fixed direction and can create an ionic current within the tissue. This can result in unpleasant side effects such as electrolysis and risk of chemical burning. Conversely, biphasic currents flow between both electrodes and thus have a zero net current. Accordingly, biphasic currents are perceived as more pleasant for the subjects' muscles and thus subjects are able to tolerate biphasic currents better, which means that the impulses can be more intensive. Consequently, biphasic currents offer advantages for applying high stimulation intensities and therefore have a positive influence on the enhancement of strength abilities.

In regards to the influence of the impulse intensity (mA) on stimulation intensity (MVC), muscle contraction force can be regulated by varying the level of amperage (mA). Accordingly, a higher impulse intensity (mA) results in a higher % MVC. However, the impulse intensity depends on the resistance of different tissue structures, a major proportion of which is due to resistance of

the skin. Therefore, it is not possible to precisely determine the impulse intensity (mA) that ultimately reaches the muscle. Consequently, most studies used the maximum pain threshold (maximum tolerated amperage) to regulate the maximum impulse intensity (88). Nevertheless, the pain threshold depends on the subject's individual pain perception on the particular muscle. Studies have shown that subjects quickly experience pain acclimatization with EMS, and thus in order to maintain a certain level of stimulation intensity the impulse intensity (mA) has to be continuously enhanced to adapt to the changing situation. However, studies have also shown that when increasing the impulse intensity, a maximal level of muscle contraction force is achieved with intensities over 100 mA, above which no further positive effects result. Furthermore, maximal impulse intensities and thus high levels of muscle tension will limit dynamic movements, which are important when training with EMS. Thus the impulse intensity (mA) has to be regulated to ensure unlimited and free movement. This is an important consideration also when considering stimulation frequency. While using 2–15 Hz stimulates mostly slow-twitch fibers (type 1), fast-twitch fibers (type 2), which are responsible for the development of high forces, may not contract below 35 Hz. Any further increase in frequency can lead to a complete tetanus of the stimulated muscle. There are different opinions about the maximum/ideal level of stimulation frequency and the authors of the aforementioned review have suggested a target range of 60 and 100 Hz as most effective. Finally, studies have shown that a minimum impulse width of 500 microseconds is needed to develop high forces, and that lowering the impulse width significantly reduces the MVC. Impulse widths of > 500 microseconds should not be used as they would be unpleasant or even painful for the subject. Thus the authors of the aforementioned review concluded that an impulse width in a range

between 200 and 400 microseconds would be sufficient for generating the target stimulation intensities of ≥ 50% MVC. Furthermore, this would also activate the deeper motor units without being unpleasant for the subject, and would still be intense enough to influence strength adaptations.

Thus, EMS has to be applied intelligently and carefully, especially in untrained subjects who have to be trained with caution because of their lower resistance to intensive loads. Overloading the subjects' muscular system by for example applying EMS with high stimulation intensity in combination with not enough regeneration time between sessions could inhibit or delay strength adaptations. This must be balanced against the fact that employing a load that is too low can result in a rapid decrease (within 2–4 weeks) in achieved strength gains, or to a lack of any significant enhancements in post-testing (88). Nevertheless, significant strength gains have been demonstrated in individuals training appropriately with EMS after a period of only 2–6 weeks (88). Several trials have also shown that when EMS is applied with optimal loads, the achieved strength gains can be kept at a constant level, amongst untrained and trained subjects, for up to 4 weeks after post-testing without doing any exercise (88).

Guidelines for safe and effective WB-EMS
In general:

1. Safe and effective Whole-Body-EMS Training must always be accompanied by a trained and licensed WB-EMS trainer or scientifically trained personnel familiar with this field of application.
2. Before the first training session of every beginner, an anamnesis of possible contraindications based on a list of questions must be taken and then documented in

writing, confirmed by the client's signature and archived. Where relevant anomalies are found, a doctor is to be consulted and training only be commenced if clearance has been given.

Preparing for training:

1. As with any kind of intensive training, Whole-Body EMS training must only be carried out in a good physical condition and free of pain. This includes abstaining from alcohol, drugs, stimulants/muscle relaxants or stress ahead of the training session. Training must never be carried out by anybody suffering from an illness with fever.

2. Whole-Body EMS training leads to very high metabolic stress of the organism because of very high volume of muscle mass addressed. This factor has to be taken into account through sufficient food intake that is as high in carbohydrates as possible. If this is not possible, then at least a high carbohydrate, but light snack (≈250 kcal) should be eaten, ideally about 2 hours before training.

3. So as to avoid possible renal stress (especially with undiagnosed problems) through intensive WB-EMS, additional fluids should be consumed before/during and after training (500 ml each).

4. Generally, medical – ideally sport-medicinal – consultation and clarification is advisable in the case of any discomfort, physical restrictions, infections or other internal, cardiological or orthopedic illnesses.

Training:

1. Regardless of physical status, sport experience and the user's wishes to that effect, under no circumstances may WB-EMS training to exhaustion take place during the first training session or trial training. This has led in the past to undesired side effects and negative health consequences and so must be avoided at all costs.
2. After moderate initial WB-EMS, the stimulation level or current must be successively increased and adapted to the individual goals. The highest level is to be reached only after 8-10 weeks of systematic training at the earliest (user's subjective effort impression: hard-hard+). Training to complete exhaustion, especially in the sense of painful, continuous tetanus during the current phase, must generally be avoided.
3. In addition, the initial training should be conducted with a reduced effective training period. Advisable is 5 min impulse familiarization and a curtailed training session with moderate stimulus intensity (user's subjective effort impression: a bit hard) and 12 min intermittent load with short impulse phase (□). Only then should the training duration be cautiously increased and never exceed 20 minutes.

4. To ensure sufficient conditioning and to minimize or rule out possible health impairments, training frequency may not exceed one training unit per week during the first 8-10 weeks.
5. Even after this conditioning phase, an interval of ≥4 days must be maintained between training units in order to avoid accumulation of muscle breakdown products, permit regeneration and adaptation and thus ensure a successful training outcome.

Safety aspects during and after training

1. During the training session, the trainer or the trained and qualified personnel should concentrate exclusively on the interests of the user(s). Before, during and after training the trainer verbally and visually checks the user's condition so as to rule out health risks and ensure effective training. Training is to be stopped immediately if there are any contraindications. A trainer can train a maximum of 2 people at the same time with EMS.

2. During training, the equipment's operating controls must be directly in reach of the trainer and the user at all times. Operation/adjustment must be simple, quick and precise.

Exercise and Endothelial Dysfunction

Greater than > 40% of the risk reduction associated with exercise cannot be explained by changes in conventional risk factors. This suggests a cardioprotective vascular conditioning effect of exercise that is characterized by enhanced nitric oxide vasodilator function, altered vascular structure and improved vascular reactivity (93, 94). Sedentary behavior has also been shown to impair endothelial function (95-98). Endothelial dysfunction is the unique yet almost universal "response to injury" of the vasculature under various clinical circumstances (99, 100). It represents the first stage of atherosclerosis, and in fact, relates to plaque progression and vulnerability as well as a several fold increased risk of ischemic cardiac events and stroke (101-106). In clinical practice it is most often recognized by an abnormal vasodilatory response to increased flow (shear stress) or endothelial-dependent vasodilating agents such as acetylcholine

(103, 107-109). In the coronary vasculature, an attenuated increase or decrease in coronary blood flow (110-114) to acetylcholine marks the presence of microvascular endothelial dysfunction, whereas an angiographically evident vasoconstrictive response of the coronary arteries is indicative of epicardial endothelial dysfunction (103, 113, 115, 116). Endothelial function can be assessed noninvasively, peripherally by the measurement of digital (finger) reactive hyperemia using peripheral arterial tonometry (RH-PAT) (117-119) (see below). Peripheral endothelial dysfunction (120) measured using RH-PAT correlates well with invasively measured coronary endothelial dysfunction and has been shown to be a strong independent predictor of adverse CVD outcomes (121, 122). Observational data has demonstrated that people with minimal traditional risk factors for CVD but who have peripheral endothelial dysfunction have a higher incidence of heart disease, hospitalization, and death at follow-up compared to those without peripheral endothelial dysfunction (123-125). Few clinical trials have evaluated the impact of physical activity and/or exercise on endothelial function as measured peripherally using RH-PAT. One small trial demonstrated that when breaking prolonged sitting with very light activity, deterioration of endothelial function was avoided (97). Another study showed a strong relationship between lifetime physical activity level and reactive hyperemia index (RHI), but also showed higher levels of endothelial dysfunction in the group undergoing only low-moderate levels of activity, suggesting little beneficial effect (126). A further study randomized patients with stable post-infarction heart failure to either moderate continuous training (70% of peak heart rate) or high intensity aerobic interval training (95% of peak heart rate) three times per week for 12 weeks or to a control group that received standard advice regarding physical activity. The authors showed greater improvements in not only

cardiorespiratory function but also left ventricular remodeling and brachial artery flow-mediated dilation, an index of peripheral endothelial function, in the high-intensity aerobic interval training group compared to the moderate continuous training group (127). High intensity training offers greater time efficiency in addition to superior cardiovascular effects, but the challenging nature of this form of training limits its widespread uptake. An assessment of vascular health and endothelial function could provide an individualized and integrated index of cardiovascular risk, accounting for the cumulative effects of both harmful and protective factors, as the terminal pathway which precedes overt CVD. Consequently, evaluating the link between exercise, and in particular, EMS as a novel tool in promoting time efficient, and highly individualizable physical training, and endothelial function forms an unique and interesting question that offers potential benefits to patients in the primary and secondary prevention setting alike.

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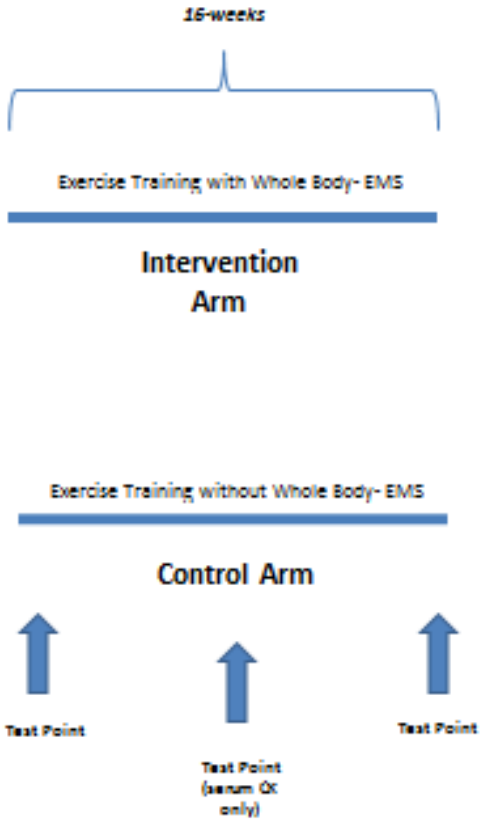
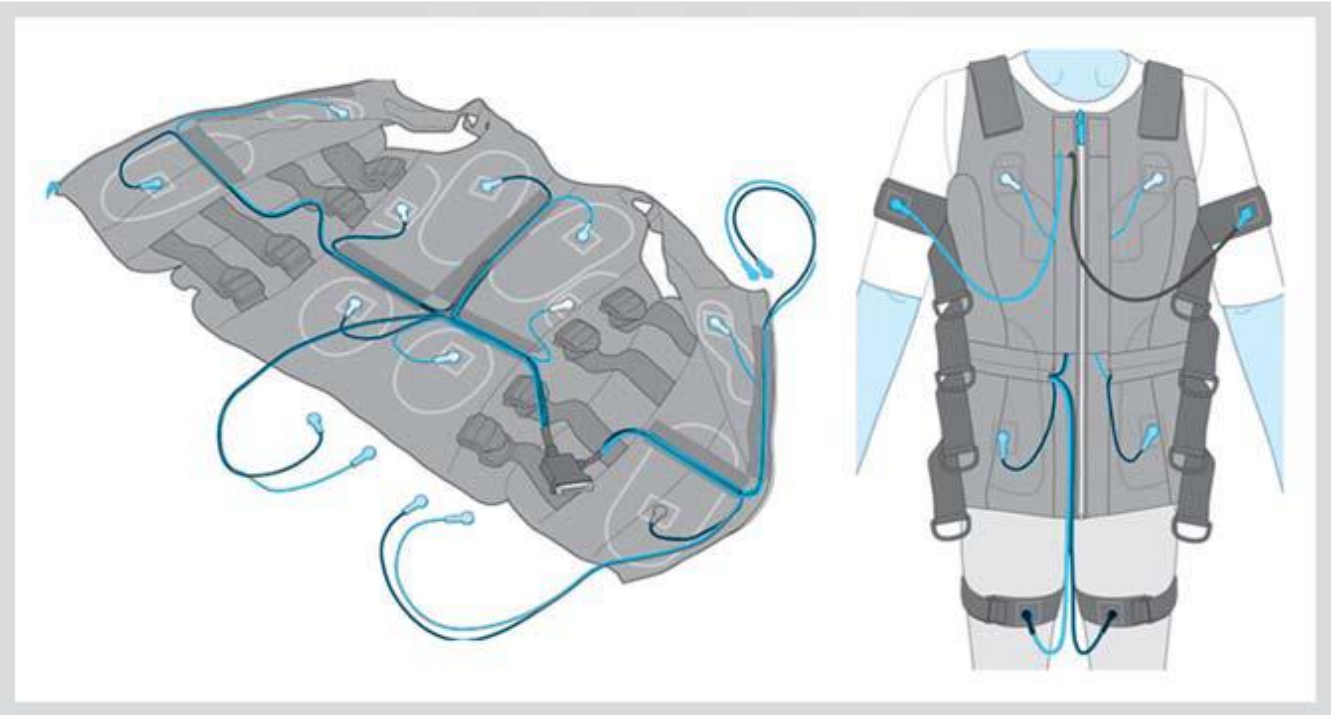
FIGURE 1



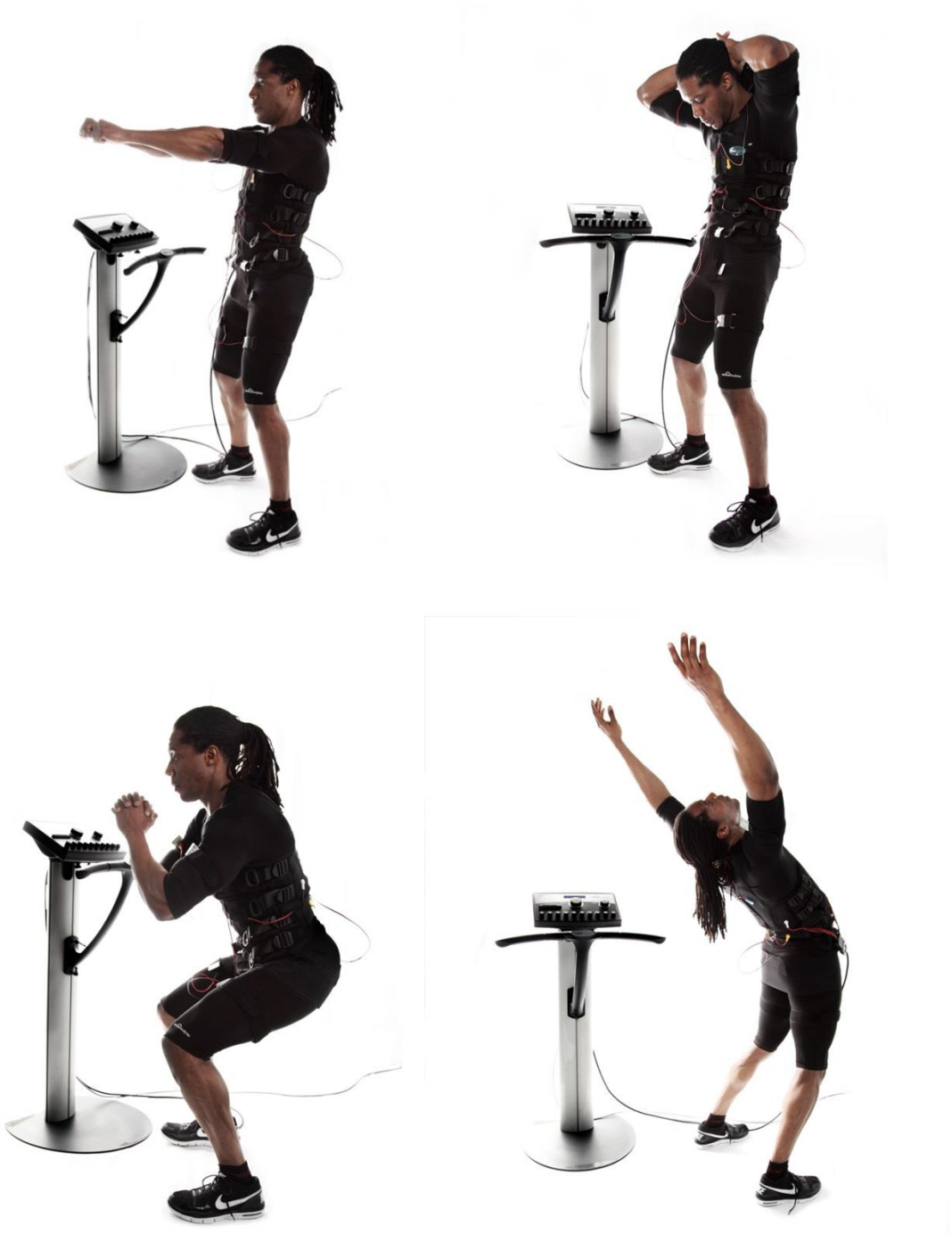
Schematic outlining study flow

FIGURE 2



The stimulation unit for the extended electronic muscle stimulation (vest with stimulation module for the legs) (courtesy of MihaBodytech Augsburg)

FIGURE 3



Demonstration of potential physical exercises that can be undertaken while applying whole body electronic muscle stimulation using the MihaBodyTec (Gersthofen, Germany) device

FIGURE 4

Guideline for Safe and Effective WB-EMS

In General

1. Safe and effective Whole-Body-EMS Training must be advised and accompanied by a trained and licensed WB-EMS trainer or scientifically trained personnel familiar with this field of application.
2. Before the first training session of every beginner, an anamnesis of possible contraindications based on a list of questions must be taken and then documented in writing, confirmed by the client's signature and archived. Where relevant anomalies are found, a doctor is to be consulted and training only be commenced if clearance has been given.

Preparing for Training

1. As with any kind of intensive training, Whole-Body EMS training must only be carried out in a good physical condition and free of pain. This includes abstaining from alcohol, drugs, stimulants/muscle relaxants or stress ahead of the training session. Training must never be carried out by anybody suffering from an illness with fever.
2. Whole-Body-EMS training leads to very high metabolic stress of the organism because of very high volume of muscle mass addressed. This factor has to be taken into account through sufficient food intake that is as high in carbohydrates as possible. If this is not possible, then at least a high carbohydrate, but light snack (≈250kcal) should be eaten, ideally about 2 hours before training.
3. So as to avoid possible renal stress (especially with undiagnosed problems) through intensive WB-EMS, additional fluids should be consumed before/during and after training (500ml each).
4. Generally, medical – ideally sport-medicinal – consultation and clarification is advisable in the case of any discomfort, physical restrictions, infections or other internal, cardiological or orthopedic illnesses.

Training

1. Regardless of physical status, sport experience and the user's wishes to that effect, under no circumstances may WB-EMS training to exhaustion take place during the first training session or trial training. In the past, this has led to undesired side effects and negative health consequences and must be avoided at all costs.
2. After moderate initial WB-EMS, the stimulation level or current must be successively increased and adapted to the individual goals. The highest level is to be reached only after 8-10 weeks of systematic training at the earliest (user's subjective effort impression: hard-hard+). Training to complete exhaustion, especially in the sense of painful, continuous tetanus during the current phase, must generally be avoided.
3. In addition, the initial training should be conducted with a reduced effective training period. Advisable is 5min impulse familiarization and a curtailed training session with moderate stimulus intensity (user's subjective effort impression: a bit hard) and 12min intermittent load with short impulse phase (~4s). Only then should the training duration be cautiously increased and never exceed 20min.
4. To ensure sufficient conditioning and to minimize or rule out possible health impairments, training frequency may not exceed one training unit per week during the first 8-10 weeks.
5. Even after this conditioning phase, an interval of ≥4 days must be maintained between training units in order to avoid accumulation of muscle breakdown products, permit regeneration and adaptation and thus ensure a successful training outcome.

Safety Aspects During and After Training

1. During the training session, the trainer or the trained and qualified personnel should concentrate exclusively on the interests of the user(s). Before, during and after training the trainer verbally and visually checks the user's condition so as to rule out health risks and ensure effective training. Training is to be stopped immediately if there are any contraindications.
2. During training, the equipment's operating controls must be directly in reach of the trainer and the user at all times. Operation/adjustment must be simple, quick and precise.
3. Actually, we generally advise against private use of technology without support of a qualified and licensed trainer/instructor or correspondingly scientifically trained personnel.

Safety recommendations put forward by a German consensus conference in December 2015, consisting of whole body-EMS manufacturers (miha-bodytec, Gersthofen, Germany), educational institutions (GluckerKolleg, Kornwestheim, Germany), Licensees (PT Lounge Koln, Cologne, Germany) and publishing researchers. In April 2016, the scientific part of the consortium (Frohlich, M.; Kemmler, W.; Kleinoder, H. v. Stengel, S.) formulated these general safety guidelines