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ORIGINAL PAPER

Electrical myostimulation improves left ventricular function and peak oxygen consumption in patients with chronic heart failure: results from the exEMS study comparing different stimulation strategies

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Abstract

Aims Electromyostimulation (EMS) of thigh and gluteal muscles is a strategy to increase exercise capacity in patients with chronic heart failure (CHF). The aim of this non-randomised pilot study was to investigate the effects of different stimulation strategies in CHF patients using a newly developed stimulation suit also involving trunk and arm muscles [extended electromyostimulation (exEMS)] in comparison with EMS therapy limited to gluteal and leg muscles (limEMS).

Methods 60 individuals joined the EMS training programme. Stable CHF patients (NYHA class II–III) received either exEMS (22 patients, 15 males, mean age 59.95 ± 13.16 years) or limEMS (12 patients, 9 males, 62.75 ± 8.77 years). 26 participants served as healthy control group (CG) receiving exEMS. Training was performed for 10 weeks twice weekly for 20 min, and the level of daily activity remained unchanged. Effects on exercise capacity, oxygen uptake, left ventricular function (EF) and biomarkers were evaluated.

Results There was a significant increase of oxygen uptake at aerobic threshold in all groups (exEMS: 13.7 ± 3.9–17.6 ± 5.1 ml/kg/min (+28.46 %, $p < 0.001$); limEMS 13.6 ± 3.0–16.0 ± 3.8 ml/kg/min (+17.6 %, $p = 0.003$); CG 15.0 ± 4.9–17.0 ± 6.4 ml/kg/min (+13.3 %, $p = 0.005$). LVEF increased from 38.3 ± 8.4 to 43.4 ± 8.8 % (+13.3 %, $p = 0.001$) (limEMS 37.1 ± 3.0–39.5 ± 5.3 % (+6.5 %, $p = 0.27$); CG 53.9 ± 6.7–53.7 ± 3.9 % (−0.4 %, $p = 0.18$). In CHF patients changes in oxygen consumption and LVEF were higher in the exEMS group than in limEMS (not significant). Maximal workload improved in healthy controls ($p = 0.002$) but not in CHF patients.

Conclusion Extended EMS can improve oxygen uptake and EF in CHF. In patients with limited EMS and in control patients without heart failure but extended EMS, oxygen uptake can be improved but EF is unaltered. For all groups, NT proBNP is unaffected by EMS.

Keywords Physical performance · Chronic heart failure · Cardiac rehabilitation · Extended electromyostimulation (exEMS) · EMS training · Limited EMS (limEMS)

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Introduction

Electrical myostimulation (EMS) of the skeletal muscles is a new therapeutic strategy with promising treatment effects in patients with chronic heart failure (CHF) [1]. It is based on the electrical stimulation of large muscle groups resulting in a pulsed contraction of the muscles without any active movement of the individual. In the past EMS was performed in critical ill and bedridden patients with underlying diseases like muscular dystrophy, scoliosis or paraplegia [2]. Then it was found to be a possible

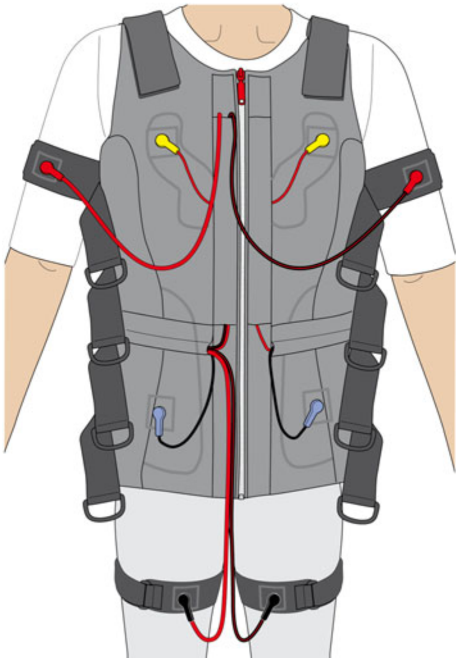

Fig. 1 Stimulation vest of the dedicated suit. All electrodes are placed in the inside surface and are connected via electrical cords to the application unit. There are supplementary electrodes for upper arm and upper leg. Electrical cords connect also these electrodes with the vest (with friendly permission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

supplement therapeutic tool also in patients suffering from CHF to avoid muscle atrophy due to advanced comorbidities or the severity of left ventricular dysfunction. As some cardiac patients are not in a position to get involved in classic physical training EMS is discussed as an elegant alternative for physical training.

Reduced left ventricular function in CHF initiates a series of changes that lead to a wasting of skeletal muscle and resultant abnormalities of muscular metabolism [3]. This skeletal myopathy alters vascular structure, catabolic alteration and autonomic tone and thus might aggravate LV dysfunction by increasing vasoconstriction.

The preservation of muscle mass in CHF patients is an accepted strategy to improve LV dysfunction [4–7]. Hence, physical training could be one tool to break through this vicious circle because of its significant beneficial effects on the neurohumoral, immunoreactive and functional status [8]. Recent trials could show that the relative effect of training on proteolytic processes in the skeletal muscle is even not attenuated by age [9].

Previous studies demonstrated that EMS provides similar improvements to exercise capacity like conventional exercise training (treadmill, bicycle, arm cycling) [10–12]. However, in these studies electrical stimulation was restricted to gluteal, quadriceps and calf muscles [limited EMS (limEMS)].

These promising findings in EMS studies stimulated us to develop a fitting suit with embedded electrodes that additionally stimulate the muscles of the upper extremity and the trunk [extended EMS training (exEMS)] (Fig. 1). As far as we know this stimulation protocol that includes also the muscles of the upper extremities has never been applied in patients with CHF.

The aim of the present longitudinal cohort study was to evaluate the beneficial effects of different stimulation strategies (exEMS and limEMS) on exercise capacity, oxygen uptake and left ventricular function in patients with stable CHF. Furthermore, the impact of exEMS in healthy controls was evaluated. Our hypothesis was that oxygen uptake could be influenced to a higher extent in patients with an impaired LV function.

Methods

Subjects

Sixty individuals undergoing our EMS training programme were included in a non-randomised pilot study. 34 of them with stable CHF and New York Heart Association symptoms (NYHA) Class II–III were subsequently recruited from our heart failure outpatient clinic. 22 patients received exEMS training (15 males, mean age 59.95 ± 13.16 years) and 12 patients limEMS (9 males, 62.75 ± 8.77 years).

Data were analysed in comparison with 26 sedentary healthy controls with similar baseline characteristics (Table 1) who also received exEMS (matched controls). None of these had performed sports for the last 12 months on a regular basis before entering the study. Five of them suffered from non-insulin-dependent diabetes mellitus, nine from sufficiently drug-controlled arterial hypertension, two had undergone aortic valve replacement. Three suffered from chronic back pain; two were sedentary due to a severe knee injury.

The hospital ethics committee approved the study (Ref. Nr. 27/2008, University of Bochum, Germany), and written, informed consent was obtained from all individuals.

Definitions

Inclusion criteria for CHF patients was CHF which was defined as symptoms of shortness of breath on a low level of physical exertion in the presence of an impaired left ventricular function on echocardiography (EF 25–45 %, Simpson method) with no other cause of breathlessness. All individuals were on optimal drug therapy when entering the study. None of the patients suffered from an ongoing clinically obvious infection. A written confirmation of a maintained habitual activity level during the EMS

Table 1 Baseline characteristics of CHF patients with extended EMS (exEMS), limited EMS (limEMS) and control group (exEMS)

	CHF exEMS ($n = 22$–women $n = 7$)			CHF limEMS ($n = 12$–women $n = 3$)			Control group exEMS ($n = 26$–women $n = 11$)		
	Mean ± SD		*p* value	Mean ± SD		*p* value	Mean ± SD		*p* value
	Pre	Post		Pre	Post		Pre	Post	
Demographic characteristics									
Age (years)	59.95 ± 13.16			62.75 ± 8.77			57.04 ± 16.08		
Body surface area (BSA) (m^2)	2.10 ± 0.20	2.10 ± 0.20	0.668	2.09 ± 0.19	2.08 ± 0.18	0.293	2.09 ± 0.22	2.09 ± 0.23	0.630
Body mass index (BMI) (kg/m^2)	28.9 ± 6.60	28.5 ± 5.8	0.576	28.9 ± 3.75	28.3 ± 3.4	0.264	30.8 ± 6.57	30.9 ± 6.9	0.531
Fat (%)	25.8 ± 11.4	26.0 ± 11.4	0.666	34.5 ± 12.4	33.5 ± 11.7	0.366	33.1 ± 12.0	34.1 ± 13.7	0.545
Cardiac parameters									
HR at rest (beats/min)	66.96 ± 10.83	73.96 ± 12.67	<0.01	70.80 ± 5.51	79.16 ± 7.63	<0.05	77.20 ± 3.6	85.1 ± 4.3	0.21
SBP (mmHg)	129.04 ± 15.75	128.97 ± 15.01	0.963	131.94 ± 13.79	133.10 ± 10.33	0.578	129.6 ± 3.0	120.22 ± 11.1	0.339
DBP (mmHg)	72.48 ± 9.41	73.23 ± 11.14	0.132	79.09 ± 6.91	80.77 ± 3.57	0.191	78.5 ± 8.5	78.8 ± 9.2	0.792
Medical history									
CAD cause for CHF	16 (73 %)			8 (67 %)			0		
DCM	6 (27 %)			4 (33 %)			0		
Art. hypertension	7 (32 %)			2 (17 %)			9 (35 %)		
Diab. mellitus	11 (50 %)			2 (17 %)			9 (35 %)		
Medical treatment of CHF									
β-blocker	20 (91 %)			12 (100 %)			0		
AT1-blocker	4 (18 %)			2 (17 %)			1		
ACE inhibitor	18 (82 %)			9 (75 %)			7		
Diuretics	17 (77 %)			11 (92 %)			0		
Digoxin	2 (9 %)			1 (8 %)			0		
Ca chan. blocker	3 (14 %)			4 (33 %)			0		

HR heart rate, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *CAD* coronary artery disease, *CHF* congestive heart failure, *DCM* dilated cardiomyopathy; (used tests: *t* test, Mann–Whitney *U* test)

phase was obtained. None of the individuals involved in the study started a supplement individual activity programme.

Patients with severe cardiac arrhythmias, cardiac decompensation in the past 3 months, NYHA Class IV, EF <25 %, hemodynamic relevant valve stenosis or regurgitation (degree > mild), active myocarditis, hypertrophic cardiomyopathy, pregnancy, and kidney dysfunction (creatinine >1.5 mg/dl) were not suitable for inclusion in the study. Because an interference of EMS with internal cardioverter defibrillators (ICD) or permanent pacemaker could not be ruled out these patients were not included. Severe dermatologic disorders made the application of EMS impossible. Medication and the level of activity remained unchanged during the EMS phase and in the preceding 8 weeks (written confirmation was obtained).

The control group consisted of healthy volunteers with a sedentary lifestyle, normal left ventricular function, and reduced oxygen uptake. Oxygen uptake at aerobic threshold (VO_2AT) of more than 20 ml/kg/min was an exclusion criterion.

EMS therapy and stimulation protocol

Electromyostimulation is a technique causing contraction of muscles by electrical stimulation. Energy is applied transcutaneously to the skin overlying the muscles via electrodes.

Electrodes were fixed in the inside surface of a dedicated suit and connected via electrical cords to the application unit (Fig. 1). exEMS activated eight major muscle groups simultaneously including muscles of upper arm, chest, shoulder, upper and lower back, abdominal, gluteal, hip region including the pelvic floor, and upper legs. In limEMS stimulation was restricted to gluteal and thigh muscles.

Electrical stimulation of the muscles was performed under supervision for 4 s followed by a 4-s recovery period (frequency of the impulse 80 Hz). Maximum output of the EMS unit is 350 mA. The intensity of the impulses (mA) was chosen by the patient himself because muscle contraction initiated by a given energy depends on the composition of the body (fat, water, etc.) and the resistance of the skin. The aim of the training was a sufficient activation of the muscles without feeling of pain due to "overcontraction". The training was performed for 10 weeks twice a week for 20 min under controlled conditions using the Miha-Bodytec stimulation system (Miha-Bodytec GmbH, Augsburg, Germany). Heart rate and blood pressure were measured at rest immediately before each exEMS session. Rate pressure product (RPP) (heart rate at rest x systolic blood pressure), a predictor of myocardial oxygen uptake, was calculated from data at rest before and at the end of the EMS phase.

Study protocol

All 60 individuals were examined immediately before entering the study and within 1 week after finishing EMS therapy.

Beside history taking and physical examination all individuals had a 12-lead ECG. Height, weight and body fat were measured barefooted on an impedance scale (TANITA, body composition analyzer, TBF-410 MA, Japan). Body mass index (BMI) and body surface area (BSA) were calculated from this data. B-type natriuretic peptide (BNP) and its amino-terminal co-metabolite (NT-proBNP) are the most widely used biomarkers in CHF and are considered to be the most appropriate markers for follow-up studies [13]. These markers were measured before and after the exEMS training phase during morning time.

Conventional echocardiography was performed according to the ASE guidelines (GE Vingmed Seven) [14]. Left ventricular enddiastolic index (LVEDDi) and left atrial endsystolic diameter index (LAESDi) were calculated using BSA. Measurement of cavity size and wall thickness [interventricular septum enddiastolic (IVS ED) and posterior wall enddiastolic (PW ED)] was derived from M-mode recording. Left ventricular function was determined by means of Simpson's rule. Biplane measurements were applied using paired apical four- and two-chamber views. Endocardial borders were outlined offline in end-diastole and end-systole by two independent accredited sonographers. Diastolic dysfunction was defined as an E/A ratio less than 1. Left ventricular mass (LVM) was calculated using the Penn-cube formula ($LVM = 1.04 \times (LVEDD + PWED + IVSED)^3 - LVEDD^3 - 13.6$ g) [15].

Stress test was done by spiroergometry (ZAN 600 USB CPX, h/p/cosmos quasar, Oberthulba, Germany). All individuals performed this test according to their personal skills either starting with 10 W increased by 10 W every 2 min or starting with 25 W increased by 25 W every 2 min. Each participant performed the same individual stress test protocol before and after EMS therapy. Subjects were encouraged to achieve a respiratory exchange level of 1.0 or more. VO_2AT and peak exercise capacity ($peakVO_2$) were measured using the v-slope method. Reasons for terminating the test were shortness of breath, muscular exhaustion, severe arrhythmia, blood pressure dysregulation or dizziness. Cardiopulmonary exercise testing was performed under consideration of the recommended standards of the European Association for Cardiovascular Prevention and Rehabilitation [16].

Statistical analysis

Regarding their normal distribution, the continuous variables were tested by means of the Shapiro–Wilk test because of the small sample size. While some of the tested variables did not feature any normal distribution ($p < 0.05$), a normal distribution could be calculated for other variables ($p \geq 0.05$). For the comparison of two independent, normally distributed samples, we applied the *t* test. Before that the Levine test was performed to confirm homogeneity of the variances.

For non-normally distributed samples we used the non-parametric Mann–Whitney *U* test. The correlation between two non-normally distributed variables was evaluated by Spearman Rho test.

A p value of <0.05 was considered to be statistically significant for all statistical tests.For the diagrams boxplots were chosen to visualise the medians and quartile-distances. While the median as well as the 25th–75th percentile are displayed in the boxes, the t-bars represent the smallest and largest value, provided there are no outliers or extreme values. In this context, outliers are considered values which lie between 1½ and 3 box lengths outside of the box; they are represented by circles in the diagram. Extreme values were measured to be more than 3 box lengths outside of the box and are represented by crosses. The categorised data were displayed graphically by means of bar diagrams.

Results

Biometric data, blood pressure and heart rate

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

Exercise capacity

After 10 weeks of exEMS training we observed a significant increase of the VO_2AT from 13.7 ± 3.9 to 17.6 ± 5.1 ml/kg/min ($p < 0.001$) in the CHF exEMS group [CHF limEMS: 13.6 ± 3.0 to 16.0 ± 3.8 ml/kg/min ($p = 0.003$); control group: 15.0 ± 4.9 to 17.0 ± 6.4 ml/kg/min ($p = 0.005$)] (Table 2).

PeakVO_2 increased from 17.6 ± 4.8 to 21.6 ± 7.1 ml/kg/min ($p < 0.001$) in the CHF exEMS group [limEMS 19.6 ± 4.3 to 21.7 ± 5.3 ml/kg/min ($p = 0.024$); CG 18.5 ± 6.7 to 19.3 ± 7.4 ml/kg/min ($p = 0.048$) (Fig. 2a–c)].

The maximum workload at the end of the stress test ($Watt_{max}$) improved in the CHF exEMS group from 115.0 ± 48.6 to 122.5 ± 46.9 W ($p = 0.200$), [limEMS 121.6 ± 49.3–135.5 ± 46.3 W ($p = 0.064$); CG 115.5 ± 43.6–130.1 ± 48.9 W ($p = 0.002$) (Table 2)].

In CHF patients effects on VO_2AT and peakVO_2 were higher in the exEMS groups in comparison with limEMS. The difference was not significant (VO_2AT $p = 0.517$, peakVO_2 $p = 0.719$).

Echocardiographic data

The increase of LVEF in the CHF exEMS group was highly significant [from 38.3 ± 8.4 to 43.4 ± 8.8 % ($p = 0.001$)], whereas EF in control group did not change significantly [53.9 ± 6.7–53.7 ± 3.9 % ($p = 0.180$) (Table 2; Fig. 2d–f). EF in the limEMS group improved from 37.1 ± 3.0 to 39.5 ± 5.3 ($p = 0.27$). In CHF patients there was no significant difference between the two groups ($p = 0.105$). LVEDD and diastolic function did not change significantly in all groups (Table 2).

Biomarkers

NT-proBNP levels were non-normally distributed (Table 2). CRP levels decreased from 0.57 ± 0.95 to 0.39 ± 0.52 mg/dl in the CHF exEMS group (limEMS 0.31 ± 021–0.37 ± 0.43 mg/dl; control group 0.15 ± 0.09–0.15 ± 0.11 mg/dl, not significant).

Discussion

Exercise training is recommended in all stable chronic CHF patients (level of evidence I A) and is considered complementary to pharmacological and resynchronisation treatment [17–21]- Furthermore, an adequate treatment of sleep-disordered breathing in CHF patients has shown to be an alternative non-invasive method of major prognostic impact [22]. There are only few studies testing the hypothesis that training should not be conducted in certain patients (aetiology, NYHA class, LVEF, or medication) [17]. However, the type of training, endurance, static or a combination of both is still up for discussion.

Some trials showed that EMS has significant positive effects on oxygen uptake in patients with reduced left ventricular function. Banerjee [23] reported on an increase of peakVO_2 of about 9 % in a collective of individuals with CHF (left ventricular ejection fraction ≤35 %). In his trial the electrical stimulation was limited to gluteal, quadriceps, hamstrings and calf muscles.

In normal men, peakVO_2 is predominantly determined by cardiac output, but also respiratory, skeletal muscle, metabolic, vascular and hematologic factors have a relevant impact on exercise performance [8, 24]. There is a close relationship between oxygen uptake, respiratory exchange ratio and the level of exercise intensity [25].

It has been demonstrated that in elderly stable CHF patients with preserved left ventricular function (HFPEF) decreased peakVO_2 is due to reduced cardiac output secondary to blunted chronotropic, inotropic and vasodilator reserve [26]. Some authors also discussed the role of an impaired skeletal muscle oxidative metabolism resulting in a reduced peak arterial-venous oxygen difference (peak A-VO_2 Dif). It could be shown that peak A-VO_2 Dif (calculated by using the Fick equation) in HFPEF patients was higher after exercise training in comparison with sedentary HFPEF controls. As peak A-VO_2 Dif was the primary contributor to improved peakVO_2, peripheral mechanisms like microvascular and skeletal muscle function have turned out to be the reasons for enhanced exercise capacity in these patients.

The effect of physical training in CHF patients on oxygen consumption is well studied. However, there is only scanty data about EMS effects on left ventricular function and physical performance in healthy individuals.

Several studies described the importance of dynamic exercise in the treatment of CHF [27–31]. Hambrecht et al. showed that 20-min ergometer exercise training per day for 6 months at a work level of 70 % of peakVO_2 resulted in a reduction of cardiomegaly, an improved exercise capacity and a small but significant improvement of left ventricular stroke volume [28]. Some trials even demonstrated that peakVO_2 strongly predicts prognosis in CHF [32].

Enhanced external counterpulsation (EECP), a system with pneumatic compression cuffs applied to each of the patient's legs, is considered to be a safe non-invasive treatment option in patients with angina and, for some years, in CHF patients as well. The cuffs inflate (onset of diastole) and deflate (onset of systole) based on the electrocardiogram causing an increase of venous return

Table 2 Spiroergometry and echocardiography of CHF patients with extended EMS, limited EMS and control group (exEMS)

	CHF (n = 22)—extended EMS				CHF (n = 12)—limited EMS				Control group extended EMS (n = 26)			
	Mean ± SD		Change (%)	p value	Mean ± SD		Change (%)	p value	Mean ± SD		Change (%)	p value
	Pre	Post			Pre	Pos			Pre	Post		
Watt AT (W)	89.2 ± 37.5	96.6 ± 34.4	+8.3	0.117	86.9 ± 30.2	110.4 ± 29.9	+27.0	0.002	96.1 ± 34.2	110.4 ± 40.8	+14.9	0.019
Watt max (W)	115.0 ± 48.6	122.5 ± 46.9	+6.5	0.200	121.6 ± 49.3	135.5 ± 46.3	+11.4	0.064	115.5 ± 43.6	130.1 ± 48.9	+12.6	0.002
VO_2 AT (ml/kg bw/min)	13.7 ± 3.9	17.6 ± 5.1	+28.5	<0.001	13.6 ± 3.0	16.0 ± 3.8	+17.6	0.003	15.0 ± 4.9	17.0 ± 6.4	+13.3	0.005
Peak VO_2 (ml/kg bw/min)	17.6 ± 4.8	21.6 ± 7.1	+22.8	<0.001	19.6 ± 4.3	21.7 ± 5.3	+10.7	0.024	18.5 ± 6.7	19.3 ± 7.4	+4.3	0.048
RER max	1.04 ± 0.05	1.05 ± 0.05	–	0.701	1.06 ± 0.04	1.04 ± 0.05	–	0.822	1.03 ± 0.04	1.03 ± 0.07	–	0.691
LV EDD (mm)	59.4 ± 11.9	56.5 ± 9.6	−4.9	0.58	59.2 ± 4.7	59.3 ± 3.8	+0.2	0.878	49.5 ± 5.2	48.8 ± 3.4	−1.4	0.753
LV EDDi (mm/m^2)	29.2 ± 6.4	27.7 ± 5.7	−5.1	0.095	28.4 ± 3.2	28.5 ± 3.1	+0.3	0.889	23.9 ± 3.4	20.6 ± 7.5	−13.8	0.234
LV IVS ED (mm)	10.6 ± 2.1	10.6 ± 1.7	0	1.0	11.5 ± 1.9	10.5 ± 1.0	−8.7	0.46	10.7 ± 2.0	10.7 ± 1.9	−0.6	0.527
LV PW ED (mm)	10.7 ± 2.3	10.5 ± 1.9	−1.9	0.696	11.25 ± 1.29	11.0 ± 1.54	−1.8	0.623	10.85 ± 2.6	10.12 ± 2.23	−6.7	0.072
LV mass index (g/m^2)	143.6 ± 43.5	130.1 ± 37.3	−9.4	0.46	153.6 ± 23.6	143.0 ± 18.9	−6.9	0.176	94.9 ± 17.0	94.3 ± 14.1	−0.7	0.52
LV EF (%)	38.3 ± 8.4	43.4 ± 8.8	+13.3	0.001	37.1 ± 3.0	39.5 ± 5.3	+6.5	0.27	53.9 ± 6.7	53.7 ± 3.9	−0.4	0.180
NT-pro BNP (pg/ml)	465 ± 979	309 ± 388	−33.5	0.551	501 ± 480	443 ± 484	−11.6	0.308	64 ± 52	53 ± 53	−17.2	0.424
RPP (mmHg bpm)$^{-1}$/1,000)	9.96 ± 2.04	10.88 ± 2.30	+9.24	0.024	9.36 ± 1.36	10.53 ± 1.21	+12.5	0.091	10.95 ± 1.85	11.38 ± 1.99	+3.93	0.016

VO_2 AT oxygen consumption at aerobic threshold, *Peak VO_2* oxygen consumption at peak exercise, *RER max* respiratory exchange ratio maximum, *LV EDD* left ventricular enddiastolic diameter, *LV EDDi* left ventricular enddiastolic index, *LV IVS ED* interventricular septum enddiastolic, *LV PW ED* posterior wall enddiastolic, *LV EF* left ventricular ejection fraction, *RPP* rate pressure product (heart rate at rest × systolic blood pressure); (used tests: *t* test, Mann–Whitney *U* test)

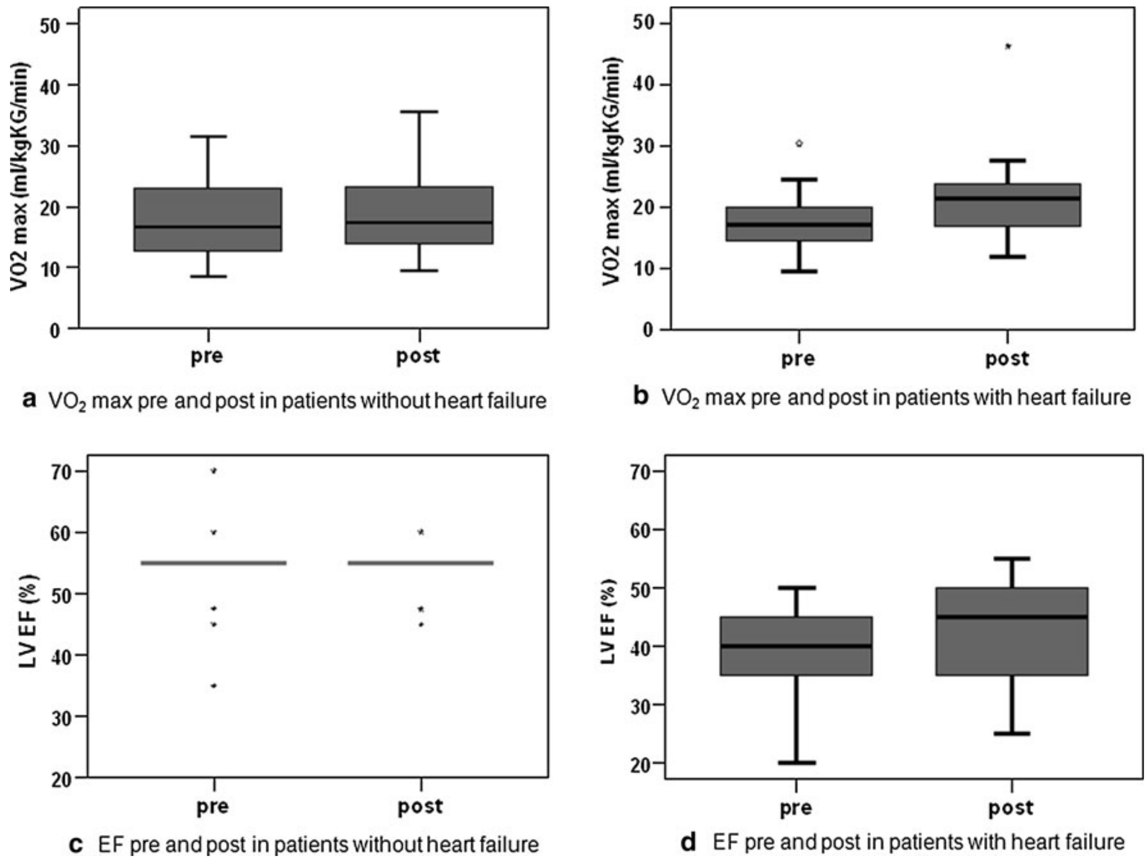

Fig. 2 Results on physical capacity (oxygen consumption) and left ventricular ejection fraction in the three groups

enhancing cardiac output [33–35]. Because of the increased diastolic filling pressure afterload is decreased and the left ventricular contractility is improved. The EECP effects are considered to be analogous to the peripheral vascular conditioning effect seen with exercise [33]. However, one primary concern in EECP is that the increased venous return could provoke pulmonary oedema in CHF patients. Furthermore, EECP could not improve left ventricular function as assessed by two-dimensional and Doppler echocardiography [33, 34].

In EMS the venous return to the heart, one main underlying cause of EECP efficacy, is supposed to be unaffected and, therefore, the risk of pulmonary oedema might be not increased.

Our study revealed positive effects of exEMS training in CHF patients in comparison with healthy controls. EMS was well tolerated by all subjects with a good level of compliance underlining the comfortable application of the stimulation suit. None of the subjects interrupted or discontinued therapy. Weight, BMI and proportion of fat did not change significantly in both groups suggesting that exEMS does not influence the proportion on muscle mass. However, the findings in the presented pilot study need to be evaluated in larger and randomised trials with a longer observation period and an appropriate control group.

Furthermore, financial aspects of EMS and the reduced opportunity of social contacts in comparison with conventional training in groups should be assessed.

BNP levels

An increased left ventricular wall tension, mainly induced by pressure and volume overload, initiates elevated levels of BNP and, due to the longer half-time, even more its amino-terminal co-metabolite NT-proBNP [13]. However, BNP only indicates ventricular loading conditions and does not reveal other important mechanisms of CHF [36, 37]. Concomitantly increased levels of serum soluble E-selectin, an indicator of inflammatory endothelial activation, have additive predictive power to evaluate the long-term outcome of CHF patients as endothelial dysfunction may aggravate heart failure [38, 39]. Galectin-3 could also add relevant information about structural changes in the heart, including inflammation, fibrosis and remodelling [36]. However, the role of soluble E-selectin and Galectin-3 needs to be evaluated in further trials and, in contrast to

BNP, has not been introduced to daily routine in the treatment of CHF patients.

The accepted biomarker BNP and NT-proBNP in CHF were, in contrast to the CG, significantly elevated in the CHF groups and did show a reduction after applying EMS therapy. However, this was not significant and NT proBNP levels were non-normally distributed.

In contrast, other trials demonstrated that BNP levels could be significantly reduced in CHF patients after initiating training therapy [40]. It is of clinical importance to bear in mind that BNP levels could be within normal range in fully compensated CHF individuals. Furthermore, there is a stoichiometric relationship between BNP and NT proBNP leading to the conclusion that these parameters might be of limited value in this context. However, it is of interest that other studies could show that serial measurements of BNP levels may have a less predictive value than single measurements in cases of stable clinical conditions [41].

Exercise test

We observed a statistically significant increase in both VO_2AT and peakVO_2 in all individuals. However, the change was much more accentuated in the CHF patients than in healthy controls. Banerjee reported an improvement of about 10 % of oxygen consumption in healthy sedentary adults after EMS training [42] fitting to our findings in the limEMS group. In his trial he limited, in contrast to our scheme of exEMS (also involving muscles groups of the upper extremity and the trunk), the proportion of the stimulated muscles to quadriceps, hamstrings, gluteal and culf muscles. An improvement from 19.5 ± 3.5 to 21.2 ± 5.1 ml/kg/min (+8.7 %) could be observed in his study after 8 weeks of training [1]. An increase of more than 28 % of VO_2AT in our exEMS group brings up a possible dose–response-relationship with a hypothesis of "the more muscles are stimulated the more intensive is the effect on oxygen uptake". However, this might be too simple and needs to be proven in larger sample sizes as this observation could be based on the lack of randomisation.

In addition, the dynamics of the modification of muscle structure and function as well as the metabolic changes due to training in different patient group are still not well understood. Interestingly, the maximum exercise capacity in CHF patients did not improve significantly in both groups in contrast to the healthy controls teaching that muscle myopathy in CHF is a complicated and multifactorial process influenced by immunological and neurohumoral effects. Its comprehension is one challenge to future projects.

The marked improvement of physical performance of CHF patients in our study is most likely due to the beneficial changes in peripheral hemodynamics and counteracting the vicious cycle of activated neurohumoral and inflammatory pathways common in sendentary CHF patients [3, 9, 43].

The reduction of local expression of inflammatory markers has been described previously in a small group of CHF patients ($n = 10$) who received muscle biopsy after 6 months of ergometer training [29]. Plasma levels of TNF-alpha, interleukin-1-beta and interleukin 6 remained unchanged but declined locally in biopsies obtained from the Musculus vastus lateralis. These reductions of local inflammatory processes may attenuate the catabolic wasting process associated with the progression of CHF. The skeletal myopathy induced by local inflammation provokes physical deconditioning and, hence, modification of vascular and muscular structure. Data from the same group showed that MuRF-1, a component of the ubiquitin–proteasome system involved in muscle proteolysis, is increased in the skeletal muscle of CHF patients. MuRF-1 levels could be reduced significantly after 4 weeks of endurance training suggesting that physical activity might block the muscle wasting process in CHF patients [9].

Also the presented data underlines this thesis as we observed a non-significant reduction of CRP level after initiating exEMS. However, this parameter is quite unspecific as it reflects the general inflammatory status, and not the situation in the muscle. The more precise evaluation of this issue is left to further trials that should include muscle biopsies.

Vagal withdrawal and vasoconstriction aggravates LV dysfunction. Activity and exercise training improves autonomic control by enhancing vagal tone and reducing sympathetic activation. Thus, exercise training, either resistance or endurance type, received class I recommendation in the ESC guidelines on CHF [17]. In the present study blood pressure at rest did not change significantly before and after the exEMS phase. Hence, signs of a possible sympathetic withdrawal could not be seen in this regard. However, there was a significant increase in heart rate at rest in both CHF groups. Bearing in mind the results of the SHIFT study [44, 45] this might be an objectionable effect as it was demonstrated that drug-induced (ivabradine) heart rate reduction dramatically improves the outcome in CHF patients with a left ventricular ejection fraction of ≤35 %. It could be demonstrated that, beginning from a resting heart rate of >70 beats per minute, 5-bpm heart rate increments progressively increased the risk for cardiovascular death of CHF-induced hospital admission by 16 % [45]. The control of resting heart rate also leads to a reduction of CHF-associated symptoms and improves health-related quality of life [46–49]. To what extent EMS-induced influences of resting heart rate might contribute to increase the incidence of major cardiovascular events is unknown. One possible aspect in this could be that especially EMS patients might benefit from a strict heart rate control with ß-blockers or I_f inhibitors (ivabradine).

RPP is a non-invasive method of estimating of myocardial oxygen consumption. The hemodynamic components of this product, HR and systolic blood pressure, are modulated by both branches (sympathetic and parasympathetic) of the autonomic nervous system. In all investigated groups RPP increased but was more accentuated in the exEMS group. This could serve as a supplement sign of improved haemodynamics after EMS. However, this needs to be evaluated further in a larger patient group.

The fact that maximum workload capacity ($Watt_{max}$) did not increase significantly (+6.5 %) in CHF patients could be explained by the high influence of motivation on this parameter and goes along with other studies investigating the effects of training on physical performance [28]. However, RER did not differ significantly in both CHF groups suggesting that the workload achieved might also be influenced essentially by other factors like muscle strength, etc.

Left ventricular function

An important finding of the present study is that left ventricular function at rest improved significantly from an EF of 38.3–43.3 % in the exEMS group. Similar effects were described by Hambrecht and others [28, 30, 50] after 6 months of ergometer exercise training in a cohort of CHF patients with an EF of 27 %. This effect was due to a reduction of total peripheral resistance during peak exercise that was measured by a Swan Ganz catheter in his study. EF in the limEMS group also improved. However, this was not significant.

The potential role of a breakthrough of the skeletal muscle hypothesis in CHF patients with its ongoing deterioration and skeletal myopathy as an important factor in the dynamics of the underlying disease has been described by some authors [3]. Our findings of positive effects of EMS on LV function might be initiated by an enhanced muscle metabolism with less sympathic excitation and reduced vasoconstriction. However, we cannot really comment on EMS effects on skeletal muscle structure as we did not take any biopsies.

We showed that CHF patients undergoing exEMS had a significantly improved EF in contrast to healthy individuals, whereas in the controls maximal workload increased significantly and in CHF patients it did not. Hence, it is still debatable if exEMS might be a suitable tool to improve EF in CHF patients with preserved ejection fraction.

The recently described reduced proteolytic activity in the muscle after endurance training has to be investigated in EMS patients and should be subject of future trials [9]. Also patients' reports on subjective changes of EMS (sore or warm muscles, fatigue, etc.) in comparison with conventional endurance training (bicycle training, etc.) were not in the scope of the investigation.

Furthermore, we saw a small but not significant change in left ventricular dimensions inconsistent with Hambrecht's results who reported a reduction of LV diameter after 6 months of exercise training [28]. Recently published data showed similar effects in HFPEF patients. Four months of endurance training resulted in a significantly higher $peakVO_2$, whereas left ventricular systolic and diastolic volume remained unchanged [26].

The stable enddiastolic diameter of the left ventricle and an improved EF in the present study strongly suggest that morphological adaptions of the myocardium needs more time than the functional effects. This goes along with recent studies showing that decreases of left ventricular volume and mass occur secondary to the recovery of the myocardium at the cellular and molecular level [50]. However, little is known about the concrete period of time of this process and it can be assumed that there is a large interindividual variety. Also wall thicknesses remained stable in our study. Thus, LV mass index was not significantly reduced after exEMS therapy in the CHF group ($p = 0.046$). Mitral inflow Doppler parameters (*E/A* ratio) showed signs of diastolic dysfunction in the CHF group whereas parameters in the group of healthy controls were in normal range. Finally, the role of EMS in patients with severe CHF as well as the interaction between EMS and ICD or pacemakers needs to be investigated.

Conclusion

Extended EMS can improve oxygen uptake and EF in patients with heart failure. In patients with limited EMS and control patients without heart failure but extended EMS, oxygen uptake can be improved but EF remains unaltered. For all groups, NT proBNP is unaffected by EMS.

The increased heart rate at rest might lead to the assumption that stricter heart rate control by drugs could be indicated in these patients.Against this background EMS might be recognised as a helpful tool to prevent CHF patients from muscular atrophy and hence could contribute to reduce the burden of CHF. If the promising improvement of LV function is confirmed as a long-term effect, EMS could contribute to prevent ICD implantation in patients with a reduced ejection fraction.

Limitation of the study

In this pilot study we report, as far as we know, about the largest group of patients receiving EMS therapy. However, the study was not initiated as a randomised controlled trial and so we cannot rule out a selection bias.

Although the EMS effects in CHF patients are promising, a statement on its long-term effects is not yet possible. Especially the reduction of cardiac dimensions might become evident after a longer observation time.

As patients with implanted devices like ICD or pacemaker were excluded from the study because of unknown potential interference between EMS and the devices the studied population is inhomogenous. CHF patients with severely impaired LV function often have an ICD. Hence, the overall impairment of LV function in the CHF group was mild.

Analysing the effects of exEMS on muscle structure by biopsy could be one more interesting aspect to better understand the structural changes and the inflammatory activity in the muscle.

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

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