# Exercise training combined with electromyostimulation in the rehabilitation of patients with chronic heart failure: A randomized trial

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**Aim.** Both aerobic training (AT) and electromyostimulation (EMS) of leg muscles improve exercise tolerance in patients suffering from chronic heart failure (CHF). It was speculated that combination of both methods might have an additive effect. This study was performed to evaluate the effects of a combination of AT and EMS in rehabilitation (RHB) of CHF patients.

**Patients and Methods.** Patients (n=71; age  $59\pm10.2$  yrs, NYHA II/III, EF  $32\pm7.1\%$ ) were randomized into 3 groups: a) group AT, b) group EMS, and c) group AT+EMS. AT protocol included standard activity on bicycle 3x a week at the level of individual anaerobic threshold. EMS (10Hz, mode 20s "on"/20s "off") was applied to leg extensors for 2 h/day. Total time of given type of RHB was 12 weeks.

**Results.** Data analysis revealed statistically significant improvements of patients in all experimental groups (averaged difference after 12 weeks of exercise as related to initial value:  $\Delta VO_{2peak}$ : +12.9%,  $\Delta VO_{2AT}$ : +9.3%,  $\Delta W_{peak}$ : +22.7%). No statistically significant difference among experimental groups was found. Quality of life (Minnesota Living with Heart Failure – MLHF) global score was significantly improved in all 3 groups: AT ( $\Delta MLHF$ : –27.9%; P=0.001), AT+EMS ( $\Delta MLHF$ : –29.1%; P=0.002), and EMS ( $\Delta MLHF$ : –16.6%; P=0.008). MLHF score in EMS group showed the smallest time–related improvement compared to AT and AT+EMS groups, and this difference in improvement between the groups was statistically significant (P=0.021).

**Conclusion.** No significant difference was found between the two types of exercise training and nor did, their combination have any significant additional improvement.

Key words: exercise, electromyostimulation, heart failure, quality of life, combined training

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## INTRODUCTION

Congestive chronic heart failure (CHF) is a frequent, gradually progressing and life-threatening disease occurring in 2% of the adult population in developed countries. Its incidence increases to 6-10% for populations above 65 years of age1. General deconditioning and the functional limitations in CHF are the results of the increasing number of pathophysiological changes caused by ventricular dysfunction and peripheral changes<sup>2,3</sup>. These peripheral changes include extensive morphological and functional abnormalities of skeletal muscles, especially loss of muscle mass, decreased number of type I (slow fibers), and reduced terminal microcirculation density<sup>4,5</sup>. At the metabolic level, muscular abnormalities are characterized by a decrease in the number of mitochondria and decline in their oxidation capacity<sup>6-8</sup>. Current treatment of heart failure (CHF) encompasses not only appropriate pharmacotherapy but also meticulous education consisting in changing patient's life style and performing adequate physical activity9. These measures are inseparably related to cardiovascular rehabilitation (RHB), which effectively contributes to optimizing the entire treatment. Thus, RHB represents today the standard non-pharmacological strategy and aerobic exercise training (ET) is a generally accepted tool for improving exercise tolerance and CHF patients' prognosis 10-12. The first reports on the use of electromyostimulation (EMS) for RHB in CHF patients appeared almost 15 years ago<sup>13</sup>; at present, there are sufficient arguments for using EMS as an alternative to classical training, in particular in patients with advanced stages of CHF (ref. 14). EMS and voluntary muscular contractions (VMC) during bicycle training are two different methods of activating muscle fibers. They both cause a number of acute changes at the level of the neuromuscular system (exercise training on bicycle is a dynamic exercise, while EMS is a rather static exercise). Therefore, long-term application of either type of muscle activation causes various types of resulting muscular adaptation. It can be presumed that using the combination of

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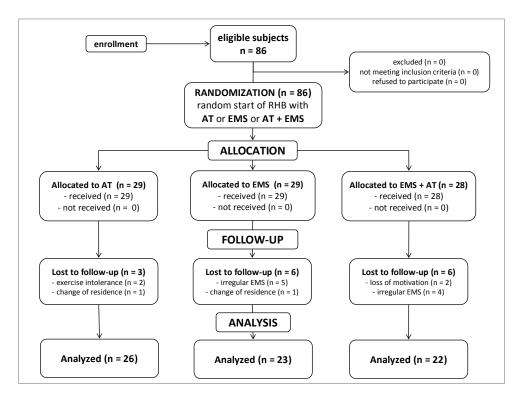
both types of exercise may lead to cumulative adaptation in the given muscle, as well as to higher overall efficiency. This presumption is confirmed by a few studies on the combination of EMS and VMC, in the area of muscle rehabilitation and regeneration after surgery <sup>15,16</sup>. From this perspective, achieving a higher training benefit for CHF patients would be of great importance, but to date the effects of ET + EMS combination in these patients have not been reported. The main purpose of this study was to evaluate the effects of the combination of standard aerobic training (AT) and the low-frequency EMS in the rehabilitation of patients with CHF of moderate grade.

## PATIENTS AND METHODS

Before inclusion into the study, all patients underwent a spiroergometric test to evaluate their cardiopulmonary performance. Peak oxygen consumption (VO<sub>2peak</sub>) was measured during gradually increasing load using a spiroergometric system (Power Cube, Ganshorn® Medizin Electronic, Niederlauer, Germany) with an integrated 12-lead ECG (AT-104 PC, Schiller®, Baar, Switzerland) and a bicycle ergometer (Ergoselect 200, Ergoline<sup>®</sup>, Bitz, Germany). Spiroergometric test was done up to the peak of individual functional capacity. A ramp protocol was used. Patients were instructed to maintain a stable RPM (60 rev.min<sup>-1</sup>) and the workload was automatically increased gradually from 0 to the tolerated maximum (W.min<sup>-1</sup>). HR was continuously and automatically recorded during the test, and BP was measured manually every 2 min. Standard ventilation and respiratory gas exchange parameters (VO2, VCO2, ventilation - VE) were measured using the "breath by breath" method, VO<sub>2peak</sub> was expressed as the highest value of O<sub>2</sub> reached in the last 30 s of exercise. Peak HR (HR  $_{\mbox{\tiny peak}})$  and peak workload (W  $_{\mbox{\tiny peak}})$ were determined in the same way. Anaerobic threshold (VO<sub>2AT</sub>) was determined by a standard method according to Wasserman<sup>17</sup>. The spiroergometer was calibrated individually for each patient. Each test was performed by a physician and a specially trained nurse. An identical protocol for the spiroergometric test was also used after completion of the RHB program. Eighty-six patients with moderate CHF were enrolled. After recruitment and initial testing, eligible patients signed the informed consent. Patients were randomly assigned to 3 groups: a) group with aerobic training (AT); b) group with electromyostimulation (EMS); and c) group with combination of aerobic training and electromyostimulation (AT+EMS). The experimental design including randomization plan was set up in statistical package SPSS (IBM Corporation, 2008). The final randomization procedure (3 arms, complete random selection of cases) was customized in a local table processor as random number generator. The study protocol was approved by the local Ethics Committee and conformed to the principles outlined in the Declaration of Helsinki (revised 2008 in Seoul) and to the GCP guidelines of the European Community.

Inclusion criteria: symptomatic stability, NYHA II-III, coronary stenosis identified by angiography, LVEF <40%, and optimized pharmacological treatment (unchanged for 2 months before and throughout the study). Exclusion criteria: unstable angina pectoris, cardiac pacemaker, evolutive ventricular dysrhythmia, intermittent claudication, diabetes mellitus, and chronic broncho-pulmonary disease.

Patients in the AT group (n=29) completed a standard AT on electromagnetically braked bicycle ergometers (REHA E900, Ergoline<sup>®</sup>, Bitz, Germany) controlled by computer program (ErgoSoft<sup>®</sup> AG, Switzerland). The



**Fig. 1.** Flow chart showing enrollment and the randomization procedure.

training protocol included an initial warm-up phase (10 min), interval AT (40 min) and a cool-down phase (10 min). Interval training alternate pedaling with the determined load (1 min) and pedaling without load (2 min). This training protocol was performed only during the initial 2 weeks. During the following 10 weeks, interval AT was shortened to 20 min and 20 min of resistance training (RT) were added. RT included 3 standard exercises: pulley lifting, leg extension and bench press. Load intensity for RT was always determined individually using 1-RM (one repetition maximum) test. Before RT, all patients completed a practice session to learn how to use correctly the exercise equipment and how to prevent Valsalva maneuver during the exercise. Initial RT intensity was set to 30% of 1-RM; then, it was gradually increased to the final 60% of 1-RM. Each of the RT exercises was always performed in three sets of 10 repetitions each (with 1 min pause between the series). AT was performed regularly three times per week (Monday - Wednesday - Friday) during the same time period from 10:00 to 12:00 AM for the entire period of 12 weeks.

Patients in the EMS group (n=29) underwent transcutaneous EMS of lower limb extensors at home. The quadriceps and calf muscles of both legs were stimulated using adhesive electrodes 80 x 130 mm (PALS® Platinum, Axelgaard, Denmark) and portable battery-powered stimulator (REHAB X-2, Cefar®, Malmö, Sweden). EMS was always performed 2 x 60 min per day, 7 day per week for the entire period of 12 weeks. Technical parameters of the stimulation were selected as follows: two-phase electric current with 10 Hz frequency, in "on-off" operation mode (20 s of contraction, 20 s of relaxation) and maximal amplitude of 60 mA. The first application of EMS was performed in hospital under medical supervision. After familiarization with the stimulation technique and the correct placement of electrodes, patients continued with the EMS at home. The intensity of stimulation was progressively increased to cause a visible contraction tolerable by the patient (the stimulation intensity during the first 2 weeks was 30-40 mA, and then it was increased to the target level of 60 mA which was not changed until the end of rehabilitation period). Patients regularly (1x/week) submitted the stimulators and electrodes for technical inspection at the clinic.

Patients in the AT + EMS group (n=28) performed standard bicycle AT according to a protocol identical to that of the AT group. In addition, these patients applied EMS using the technical equipment and stimulation protocol identical to that of the EMS group. EMS was performed at home only on the days without supervised aerobic training on bicycle (4 times a week) for the total period of 12 weeks.

The influence of the RHB program on the quality of life (QoL) was evaluated using a Czech version of the Minnesota Living with Heart Failure (MLHF) questionnaire (21 items). At the end of the rehabilitation period (12 weeks), a new evaluation of all functional parameters and the QoL identical to the initial assessment was carried out.

#### Statistical data analysis

The data were analyzed according to Eng<sup>18</sup>. Frequency analysis, estimates of arithmetic mean and standard error were used as summary statistics describing primary data. Prior to any parametric data processing, the normality of sample distribution (Shapiro-Wilk's test) and homogeneity of variance (Levene's test) was verified. Pearson's correlation coefficient was used as a measure of mutual correlation between original parameters as well as measure of correlation between the differences in values due to experimental exercise. ML-χ² test (categorical variables) and one-way ANOVA model (continuous variables) were applied for comparison of initial patient characteristics among experimental variants. Repeated measure ANOVA model was applied as principal method evaluating outcomes of experiments with model design including experimental groups (AT, EMS, AT+EMS as independent, effect component) and sampling in different time points (as dependent, pair-wise component). Statistical significance of differences among experimental groups was tested as independent component of rmANOVA model. Greenhouse-Geisser correction was applied to correct violation of sphericity assumption in case of testing repeated measures effect. For detailed mutual comparison of experimental variants with control group, Dunnet's post hoc test (independent comparisons) and pair-wise t-test (pair-wise comparisons) were used. Patients were considered as "responders" to exercise training if they reached > 10% increase in  $VO_{2peak}$ . Statistical analyses were computed using SPSS 19.0.1 (IBM Corporation, 2010). A value P<0.05 was accepted as boundary of statistical significance in all applied tests.

# **RESULTS**

A total of 86 patients were included in the study. Only 71 of them completed the 12-week rehabilitation training cycle. Evaluation was done for 26 patients in the AT group (3 did not complete), 23 in the EMS group (6 did not complete), and 22 in the AT + EMS group (6 did not complete). A total of 15 patients finished the training program prematurely. The reasons for not completing were: loss of motivation (7 cases), 6 patients admitted irregular EMS application for a period longer than 1 week, and 2 patients ended RHB due to a change of residence. Patients in the EMS group and those with the combination AT+EMS who completed the entire training program tolerated EMS very well. There were no reports of muscle pains, dyspnea, nausea or dermatological problems caused by the electrodes. There was no statistically significant difference between the three groups in any of the initial characteristics (Table 1).

## **Functional parameters**

The principal statistical analysis was based on repeated measures ANOVA model and on pair-wise comparison of changes within the experimental groups during 12 weeks of follow-up (Table 2).

**Table 1.** The initial characteristics of patients in compared experimental groups.

Parameter <sup>1</sup>	AT group $(N = 26)$	EMS group $(N = 23)$	AT + EMS group (N = 22)	$P^2$
Age (years)	63.5 (1.4)	57.3 (1.6)	60.8 (2.5)	0.079
Male sex	N=24 (92.3%)	N=15 (65.2%)	N=17 (77.3%)	0.227
Weight (kg)	88.8 (2.4)	85.4 (2.6)	87.9 (3.4)	0.675
Height (cm)	174.4 (1.5)	173.9 (1.6)	174.5 (2.1)	0.966
NYHA II/III	19/4	18/5	18/4	-
EF (%)	34.9 (1.4)	30.1 (1.3)	32.8 (1.9)	0.094
BMI	29.2 (0.7)	28.3 (0.9)	28.8 (0.8)	0.747
Exercise duration (min)	8:21 (0:25)	8:00 (0:28)	9:15 (0:32)	0.189
MLHF score	34.3 (3.5)	38.6 (4.9)	32.0 (4.0)	0.081
HR <sub>rest</sub> (beats/min)	68.5 (3)	66.6 (4)	65.8 (3)	0.214
Systolic BP <sub>rest</sub> (mmHg)	110.2 (5.2)	114.9 (4.8)	112.8 (4.4)	0.303
Diastolic BP <sub>rest</sub> (mmHg)	65.3 (4.1)	68.2 (2.2)	70.8 (5.3)	0.154
Pharmacotherapy				
ACE inhibitors	26	23	22	-
Beta-blockers	15	16	13	-
Diuretics	14	15	17	-
Digoxin	2	3	3	-
Statins	20	18	18	-
CHF etiology				
Coronary artery disease	21	16	16	-
Dilated cardiomyopathy	5	7	6	-

<sup>&</sup>lt;sup>1</sup> Categorical data are described by absolute number and percentage of patients in given category; continuous variables are described by mean (S.E.) <sup>2</sup> Statistical significance of differences among groups was tested by ML- $\chi^2$  test for categorical data and by one-way ANOVA model for continuous

Both dependent component (pair-wise changes in time due to exercise) and independent component (main effect of experimental treatment) of variability were tested. Comparing pair-wise reaction on exercise in key endpoints  $(VO_{2peak}, VO_{2AT} \text{ and } W_{peak})$  revealed statistically significant improvement of patients in all experimental groups. Changes over time in spiroergometric parameters were expressed as percentages of the initial absolute values (due to under- or overestimation of results) and interpreted on the basis of valid recommendations<sup>19</sup>. The changes induced by experimental training were quantitatively comparable in all three groups (averaged difference after 12 weeks of the exercise as related to the initial value:  $\Delta VO_{2neak}$ : +12.9%,  $\Delta VO_{2AT}$ : +9.3%, and  $\Delta W_{neak}$ : +22.7%). As a consequence, no statistically significant difference among experimental groups was found for the main effect component in the 0rmANOVA model. Similar statistically significant pair-wise changes due to all three modes of exercise were observed in the other examined parameters (VE/VCO<sub>2</sub> slope and HR<sub>peak</sub>), again without statistically significant differences among experimental groups. Furthermore, patients recruited in all three experimental groups significantly improved exercise duration, on average by +12.9% as related to the initial value (P=0.001).

parameters.

At the end of RHB period there were no significant changes in resting values of HR [group AT 68.2(4); group EMS 66.3(3); group AT + EMS 68.8(3) beats/min], systolic BP [group AT 116.2(4.5); group EMS 115.1(5.1); group AT + EMS 117.1(5.4) mmHg], and diastolic BP [group AT 69.7(4.3); group EMS 71.8(4.1); group AT a EMS 68.2(3.9) mmHg] compared to values at baseline. Although the mean changes in all key end-points due to experimental exercise regimes were statistically significant, the variability of responses to the training was increased due to occurrence of some proportion of non-responders. Non-responders in all three experimental groups were defined as patients with ≤10% change in parameter VO<sub>2neak</sub> of its initial value, calculated over the course of the experiment. There was no statistically significant difference in the occurrence of non-responders among the experimental groups. Table 3 summarizes proportion of non-responders in all examined combinations.

# Quality of life score

MLHF global score was significantly improved in the AT group ( $\Delta$ MLHF: -27.9% based on initial value, P=0.001), in the group with combined training AT + EMS ( $\Delta$ MLHF: -29.1% based on initial value, P=0.001), and

Table 2. The results of experimental testing for 12 weeks in three groups: AT (N = 28), EMS (N = 23) and AT/EMS (N = 22).

Parameter	Experimental results <sup>1</sup> Initial point (T0) 12th week (T12)		Differences: T12 - T0 <sup>2</sup>				
Group			Value	% of initial values	$P^4$		
VO <sub>2peak</sub> (ml.kg <sup>-1</sup> .min <sup>-1</sup> )							
AT	17.8 (0.9)	20.6 (0.9)	2.7 (0.7)	15.2%	0.001		
EMS	16.9 (1.0)	18.4 (0.9)	1.4 (0.3)	8.3%	0.001		
AT+EMS	17.8 (0.9)	20.5 (1.0)	2.7 (0.5)	15.3%	0.001		
$P^3$	0.405						
VO <sub>2AT</sub> (ml.kg <sup>-1</sup> .min <sup>-1</sup> )							
AT	11.4 (0.5)	12.5 (0.7)	1.1 (0.6)	9.6%	0.043		
EMS	10.9 (0.6)	11.6 (0.5)	0.7 (0.3)	6.4%	0.030		
AT+ EMS	10.9 (0.5)	12.1 (0.5)	1.3 (0.3)	11.9%	0.001		
$P^3$	0.568						
VE/VCO, slope							
AT	33.4 (1.2)	29.3 (0.9)	-4.1 (0.9)	-12.3%	0.013		
EMS	33.2 (1.4)	30.2 (0.8)	-3.0 (1.1)	-9.0%	0.012		
AT+EMS	31.4 (1.2)	28.5 (0.7)	-2.9 (1.1)	-9.2%	0.016		
$P^3$	0.314						
W <sub>peak</sub> (Watt.kg <sup>-1</sup> )							
AT	1.2 (0.1)	1.4 (0.1)	0.3 (0.0)	25.0%	0.001		
EMS	1.1 (0.1)	1.3 (0.1)	0.2 (0.0)	18.2%	0.001		
AT+ EMS	1.2 (0.1)	1.5 (0.1)	0.3 (0.1)	25.0%	0.001		
$P^3$	0.367						
HR <sub>peak</sub> (bpm)							
AT	116.9 (3.3)	128.6 (2.7)	11.7 (3.1)	10.0%	0.001		
EMS	120.0 (5.2)	125.9 (5.1)	5.9 (2.3)	4.9%	0.020		
AT+EMS	126.0 (4.7)	136.9 (4.2)	10.9 (1.9)	8.7%	0.001		
$P^3$	0.233						
Duration of exercise (min)							
AT	8:21 (0:25)	10:01 (0:26)	1:39 (0:24)	19.8%	0.001		
EMS	8:00 (0:28)	8:46 (0:30)	0:45 (0:16)	9.4%	0.013		
AT+EMS	9:15 (0:32)	10:15 (0:28)	1:00 (0:15)	10.7%	0.001		
$P^3$		0.1	19				
MLHF score							
AT	34.3 (3.5)	24.7 (3.0)	-9.6 (2.1)	-27.9%	0.001		
EMS	38.6 (4.9)	32.2 (4.9)	-6.4 (2.1)	-16.6%	0.008		
AT+ EMS	32.0 (4.0)	22.7 (3.5)	-9.3 (1.9)	-29.1%	0.002		
$P^3$	0.021						

<sup>&</sup>lt;sup>1</sup> Arithmetic mean and standard error (SE)

also in EMS group ( $\Delta$ MLHF: -16.6% based on initial value, P=0.008). Analyzing the final values after the exercise, the EMS group was significantly different from AT group (final MLHF score was 24.7) and AT + EMS (final MLHF score 22.7; P=0.021).

# **DISCUSSION**

Supervised ET performed in the context of a cardiovascular RHB program is traditionally considered to be an integral part of the overall therapeutic strategy for CHF management. Improvement in functional capacity and QoL, in particular, are the main positives<sup>20</sup>. The maintenance of physical fitness is a strong prognostic factor of CHF, whereas reduced functional capacity, loss of muscular strength and inactivity are (often underestimated) the main risk factors<sup>21</sup>. Combined interval training (aerobic + resistance elements) is generally recommended - its higher effectiveness in CHF patients has been proven, especially improving VO<sub>2peak</sub> and left ventricular function<sup>22,23</sup>. The results of this study do not deviate from the generally good experience with the positive influence of aerobic exercise training on the health status of CHF pa-

<sup>&</sup>lt;sup>2</sup> Pair-wise differences expressed as difference of arithmetic means (standard error) and as % of initial value

<sup>&</sup>lt;sup>3</sup> Significance level of independent component in rm ANOVA model

 $<sup>^4</sup>$  Significance level of pair-wise (time-related) component in rm ANOVA model

tients  $^{10,24}.$  The resulting improvement in  $\ensuremath{\mathrm{VO}_{_{2peak}}}\xspace$  peak values in the groups with bicycle training (AT and AT+EMS) averaged +15.2%, which corresponds with previously published experience from extensive clinical studies stating average improvement between +10% and +26% (ref.19) or +21% (ref.<sup>25</sup>). In the present study, a total of 38 (i.e. ca 54%) of the 71 patients who completed RHB program were evaluated as "responders", i.e. showing ≥10% improvement in VO<sub>2peak</sub>. Also this finding conforms to the data from the literature<sup>10</sup>. It is therefore evident that a majority of CHF patients reacted positively to the 12-week training by increasing values of  $VO_{2peak}$  as well as of  $VO_{2AT}$ and  $W_{peak}$ . The percentage occurrence of "non-responders" ( $VO_{2peak} \le 10\%$ ) in the groups with bicycle training (AT and AT + EMS) ranged around 41%, on average, while in the EMS group it was approx. 57%; this finding corresponds also to the rather modest increase in  $\Delta VO_{\gamma_{neak}}$ (only +8.3% in EMS group). The higher number of "nonresponders" in the EMS group might indicate lower effectiveness when using of EMS only. However, it is important that not in single case of a "non-responder" significant deterioration in  $VO_{2peak}$  output values was observed. The VE/VCO<sub>2</sub> slope parameter has been recently considered as a very important prognostic factor in CHF patients<sup>17,26,27</sup>. The relationship between VE and VCO, expresses ventilation effectiveness during exercise, i.e. records the amount of ventilated air which is necessary to evacuate 1 L of CO<sub>2</sub>. During exercise, VE and VCO<sub>2</sub> increase linearly until reaching RER, when the increase of VE sharply rises in comparison to VCO<sub>2</sub> (ref.<sup>28</sup>). In CHF patients, the VE/VCO<sub>2</sub> slope value increases - while normal values range between 20 and 30, in CHF patients they rise to as high as 80 (ref. 19). VE/VCO, can be positively affected by aerobic training and - as shown - it represents greater prognostic value than  $VO_{2peak}(\text{ref.}^{29\text{-}31})$ . In the present study, there was a significant decrease of VE/ VCO, slope in all three experimental groups, by -10.2% after RHB program. In absolute numbers there was a decrease in the VE/VCO, slope to below 30 in both groups with AT, while in the EMS group the final value was borderline<sup>30</sup>. Overall, this outcome can be considered a very positive shift from the perspective of prognosis for development of the disease; moreover, the influence of all three types of RHB protocol was comparable. The functional parameters improvement in the EMS group was fully comparable to those of the groups with aerobic training. This may seem surprising, if one considers the more or less local effects of EMS (only thigh and calf muscles). However, according to previously published findings, significant improvement of performance can be achieved even with local muscle exercise, and it is comparable to the traditional "full-body" training<sup>32,33</sup>. Therefore, EMS conforms to the criteria for achieving highly intensive muscle work in the stimulated muscles. Quality of life evaluation is among the primary indicators as to a training program's effectiveness and should be a part of any clinical study for CHF patients. The average decrease in the total MLHF score across all three groups was -24.6% (statistically significant in all groups). However, MLHF scoring was the only parameter where the rmANOVA

model recognized significant differences among experimental groups. The smallest, time-related improvement (and thus the highest level of the final MLHF score) after 12 weeks of exercise was observed in the EMS group (final score 32.2). Despite this, the overall result achieved can be considered a positive impact of regular muscle exercise on the QoL in CHF patients. This is in concordance with previously published experiences<sup>34,35</sup>. The physiological response to the increase of oxygen demand during contraction caused by EMS is similar to that caused by normal physical exercise. Banerjee et al.36 observed in a group of sedentary, healthy people that  $VO_{2peak}$ increased by a significant +10% and there was overall improvement in functional performance after 6-week EMS. In the present study, the improvement in  $VO_{2peak}EMS$ group was somewhat lower (+8.3%) but still statistically significant to that for the other groups. In the past decade, several studies focused on the EMS application in CHF. In a pilot study, Maillefert et al.<sup>37</sup> studied 14 patients with CHF. After 5 weeks of EMS (10 Hz), the authors observed an increase of  $VO_{2peak}(+14\%)$  and  $VO_{2AT}(+23.6\%)$ . In a randomized study, Nuhr et al. 38 compared the effects of EMS with a control group. The protocol included 4 h of direct stimulation of both quadriceps muscles daily (15 Hz); EMS was applied 7 days weekly for 10 weeks. The authors found a significant increase of  $VO_{2peak}$ ,  $VO_{2AT}$  and increase in walked distance during a 6-min walking test in stimulated group. Muscle biopsy in this study showed increased citrate synthase activity, decreased glyceraldehyde-phosphate dehydrogenase activity, and increase of myosin heavy chain isoforms. Another randomized study from 2005, 24 patients were divided into 2 groups - group with AT and EMS group<sup>39</sup>. The stimulation protocol included EMS (10 Hz) of quadriceps and triceps surae muscles. A nearly identical improvement in VO<sub>2peak</sub> (+11%) and VO<sub>2AT</sub> (+17%) was observed in both groups. Finally, in a study from 2009, Banerjee et al. 40 recorded a significant improvement of approx. +10% in VO<sub>2peak</sub> in CHF patients due to EMS. Muscle stimulation is accepted as one of the traditional methods of rehabilitation and physical medicine. There are several advantages in EMS and moreover its safety has been clinically proven. It can be used for patients for whom the standard physical activity cannot be prescribed due to the severity of disease and presence of comorbidities<sup>41</sup>. EMS causes no undesirable changes in hemodynamic parameters, its overall tolerance is good and patients do not complain of muscle pain, nausea or skin problems. EMS improves the functional characteristics of skeletal muscles not only in healthy volunteers<sup>42</sup> or post-injury situations<sup>43</sup> - its therapeutic effects have been already used for affecting several chronic diseases or for post-operative treatment in intensive care units<sup>44</sup>. From a physiological point of view, the final differentiation of mammalian muscle fibers into their individual subtypes is directly dependent on the electrical activity parameters of the driving motoneurons. EMS simulates the electrical activity of the driving motoneurons; setting up external electrical impulses at the appropriate frequency can substitute the original natural activity and as a result this promotes a number of functional and metabolic changes in the muscle fibers<sup>45,46</sup>. At first glance, muscular contractions evoked by EMS have similar acute effects on the neuromuscular system as voluntary muscular contractions (VMC), but during VMC motor units (MU) are activated synchronously in the direction from small to large depending on the intensity of physical workload<sup>47</sup>. EMS, however, by-passes the physiological hierarchy and the external electrical impulses activate all MU at the same time. Thus, the muscle work of maximal intensity can be achieved almost immediately. Despite the differences mentioned, EMS and VMC in combination can be considered as two mutually supporting stimuli of a different character and which, with a view to the longer term (e.g. as parts of an RHB program), might influence the resulting effectiveness of training both from the qualitative and quantitative perspectives<sup>48</sup>. In a 2008 study Paillard<sup>49</sup> demonstrated in detail the muscular adaptations with a long-term combination of EMS + AT (or EMS only) in healthy individuals, active sportsmen and patients after knee surgery. Combined training had greater efficacy than voluntary exercise alone, which was interpreted as a cumulative effect in the processes of muscular adaptations. In the context of RHB, it was also shown that EMS was an ideal complement to voluntary exercise. In the early stage of RHB it increased muscular strength, necessary for carrying out the classical training activities. In our study, the AT + EMS group had a higher rate of improvement in the absolute values of those parameters which are generally considered to be main criteria for evaluating the effectiveness of rehabilitation –  $VO_{2\text{peak}}$ and VO<sub>2AT</sub> (an improvement of maximal and submaximal performance). This might be seen as confirmation of the study presumption that the greatest training benefit was expected to result from the combination of AT and EMS. Statistical evaluation, however, did not confirm significant differences between the three groups. In other words, all three training methods had approximately the same positive effect on the functional performance and QoL of CHF patients.

# **Study limitations**

There are several reasons which might explain the fact that greater benefit from AT + EMS combination was not objectively demonstrated in our study. First, it must be taken into account that a large percentage of those studies in which the combination of classical training and EMS brought greater benefit were done in patients after orthopedic and surgical interventions or entirely healthy individuals and active sportsmen. The pathophysiology of the functional and metabolic changes in CHF is so complex that the resulting effect of the combined training need not significantly have manifested itself. Another question relates to the stimulation protocol used. Although the 10Hz frequency is well-established in clinical practice, it cannot be ruled out that a higher rate of improving performance might be achieved using other frequencies (e.g. 25, 35, or 50Hz). Another factor which could significantly affect the final results was the number of patients undertaking the AT + EMS combination (only 22 persons from the original 28 completed the training). Finally, the authors were limited in their possibility to check-up the frequency and regularity of EMS application at home. The only sources of information were the stimulated patients themselves; only 6 patients admitted irregular use of EMS (leading to their elimination from the study). These limitations do not, however, in any way decrease the significance of EMS which should be regarded as a very attractive and effective method of cardiovascular rehabilitation. The use of EMS, however, is still sporadic, even though it has proven to be very useful in improving the functional RHB outcomes in CHF patients.

#### **CONCLUSION**

The main aim of this study was to evaluate the effectiveness of combination of classical ET and EMS in patients with a less advanced form of CHF. The results confirmed the performance improvement using EMS alone or its combination with standard exercise training in patients with heart failure. However, the results of the three studied RHB training protocols did not differ statistically significantly. It can be stated that aerobic ET combined with EMS adds no statistically significant benefit. Nevertheless, a very important positive fact needs to be emphasized - all the studied training methods improved the parameters of functional fitness and quality of life in CHF patients. Further research is needed in order to determine the optimal protocol of EMS and its combinations with other exercise training techniques in the rehabilitation of heart failure.

#### CONFLICT OF INTEREST STATEMENT

The authors stated that there are no conflicts of interest regarding the publication of this article.

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