Functional capacity-based rehabilitation of patients with chronic stable left ventricular heart failure

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Context

Heart failure (HF) is a common and costly condition. Reduced endurance is the main limiting factor of exercise capacity in HF patients. Cardiopulmonary exercise testing (CPX) is considered the most objective method to assess exercise capacity in HF patients.

Aim

To study the degree of improvement among patients with chronic stable left ventricular HF with low and average functional capacity after functional capacity-based rehabilitation program.

Settings and design

Rehabilitation was done at department of cardiology, department of physical medicine and rehabilitation, Ain Shams university. CPX was done at the National institute of research.

Patients and methods

A total of 40 patients with chronic heart failure were randomized to either a control (received their medical treatment with no specific rehabilitation program) or a rehabilitation group. Symptom-limited CPX was performed at baseline and at discharge from the program. Rehabilitation group was further divided according to their functional capacity measures obtained from CPX into group 1 and group 2. Minnesota Living with Heart Failure Questionnaire was obtained from all participants. Group 1 received electric muscle stimulation (EMS) of both lower limbs 5 days/week for 5 weeks. Group 2 received a conventional aerobic rehabilitation program 2 or 3 times/week for ~40 sessions. VO_{2 peak}, VO₂-VT, VE/VCO₂, peak load, heart rate recovery, and Minnesota Living with Heart Failure Questionnaire values were compared before and after the treatment period.

Statistical analysis used

Statistical presentation and analysis of the present study was conducted using the mean, SD, Student's *t*-test, paired *t*-test, χ^2 , linear correlation coefficient, and analysis of variance tests by SPSS, version 17.

Results

EMS produced significant improvement of functional capacity measures in addition to quality of life. It was comparable to the aerobic rehabilitation in group 2. Both rehabilitation protocols caused significant improvement when compared with the control group.

Conclusion

Functional capacity and quality of life were improved after either EMS or aerobic rehabilitation protocol when applied to selected patients with chronic heart failure when compared with control patients who did not receive any rehabilitation program.

Keywords:

aerobic training, chronic heart failure, electromyostimulation, VE/VCO2

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Introduction

The syndrome of chronic heart failure (CHF) has become one of the most common cardiovascular disorders throughout the world, thus placing a heavy financial and social burden on public health funding [1].

Recent evidence examining the underlying pathophysiology of fatigue and dyspnea, the two main symptoms in heart failure (HF), points to structural and functional abnormalities in skeletal muscle besides central hemodynamics disturbance. In symptomatic patients with CHF, maximal exercise capacity is often less than 50% of normal. Exercise intolerance is a widespread and serious problem in patients with CHF [2].

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Cardiopulmonary exercise testing (CPX) proved to be the most accurate way for quantification of cardiorespiratory fitness, grading of the etiology and severity of impairment, and also an objective assessment of the response to intervention [3,4].

The American Heart Association HF guidelines recommend exercise training for all stable outpatients with HF and a reduced left ventricular ejection fraction [5,6].

However, for a variety of reasons, not all patients with HF are able to participate in traditional exercise, as patients with CHF tend to abandon physical training owing to the discomfort related to dyspnea and some even cannot undergo physical training owing to locomotor or central nervous system disorders [7,8].

Neuromuscular electrical stimulation (NMES) of the lower limb muscles may be an alternative to physical training in patients with CHF [9]. NMES has been consistently shown to elicit positive skeletal muscle adaptations at an appropriate stimulus in patients unable to participate in traditional aerobic and/or resistance training programs [10].

Our aim is to study the degree of improvement in patients with chronic stable left ventricular HF with low and average functional capacity after functional capacity-based rehabilitation program.

Patients and methods

This study was conducted on 40 participants with chronic stable left-sided heart failure (LHF) with ejection fraction up to 40%. Participants were recruited from the Cardiology Department and the Outpatient Clinic of Ain Shams University Hospitals. Eligible participants were women and men more than 20 years of age, who had well-compensated LHF at the time of entry into the study, with a diagnosis of HF of more than 3 months in duration, and with a stable medication regimen for at least 2 months. The study was approved by Faculty of Medicine, Ain Shams University Ethics Committee, and consent was obtained from all participants. Patients were excluded for the following conditions: unstable CHF; dyspnea at rest; myocardial infarction less than 3 months in duration before the study; uncontrolled arrhythmia; unstable angina pectoris documented by anginal as pain uncontrollable with medications and ST or T-wave elevation or depression at rest; uncontrolled hypertension or diabetes; obstructive valvular disease; congenital heart disease; cardiac transplantation; severe pulmonary hypertension or other severe pulmonary disease; history of hospitalization for intravenous treatment of HF within at least 3 months of inclusion; patients with coexisting neurological, orthopedic, peripheral vascular diseases, or any intercurrent infective or malignant disease that would interfere with the exercise training program; and participants in a specific exercise program before inclusion in the study.

Patient assessment

All patients who met the inclusion criteria underwent the following at baseline: full medical history taking, thorough clinical examination, and functional capacity assessment according to New York Heart Association classification [11] and the Goldman's specific activity scale [12]. Quality-of-life questionnaire Minnesota Living with Heart Failure using Questionnaire (MLHFQ) to measure the patient's perception of the effects of HF on his or her life [13]. Resting ECG is done to exclude any new ischemia or arrhythmias. Resting echocardiography by 2D Simpson method was used for confirmation of left ventricular ejection fraction, left ventricular dimensions, diastolic function, valvular diseases, and muscle condition. Cardiopulmonary treadmill exercise test was performed as an objective way of assessment of functional capacity [14]. It was done according to modified Naughton protocol [15] and analyzed using CareFusion Oxycon Pro, VIASYS/JAEGER LE200CE (Germany). We started with a warm-up phase with an initial treadmill speed and grade slope of 1.0 mph and 0%, respectively. The speed and/or grade were subsequently adjusted every 2 min to yield an approximate 1-MET increase per stage of exercise. Respiratory gas exchange data were determined continuously throughout the exercise test [14]. After the patients had achieved their peak workload, they were brought to 1 mph and a 0% grade for an active recovery phase. This was maintained for 2 min, after which they were seated for an additional 4 min of passive recovery. Maximum aerobic exercise capacity represented by peak oxygen uptake (VO_{2 p}) was defined as the highest oxygen uptake level achieved during the treadmill test [16]. Ventilatory threshold (VO2-VT) determined by the V-slope method and VE/VCO2 slope calculated over the whole exercise period were determined as powerful markers for disease severity and prognosis [17-19]. Heart rate recovery (HRR) was detected as a measure of the autonomic function. HRR was calculated as the difference between heart rate at peak exercise and at 1 min after exercise into active recovery [20]. Maximum workload achieved and causes of test termination were all noted.

Rehabilitation program

Patients were randomized following baseline assessment into either control (10 patients) or rehabilitation group (30 patients). Rehabilitation group was further subdivided into group 1, including patients with low exercise capacity and poor prognosis represented by VO₂-VT up to 11 ml/min/kg and VE/VCO₂ slope of at least 35, and group 2, including patients with average exercise capacity manifested as VO2-VT more than 11 ml/min/kg and/or VE/VCO2 slope of less than 35 [18,19]. Control patients received their medical treatment and continued their previous level of physical activity at home with no special training program. Group 1 patients received a rehabilitation protocol in the form of electric myostimulation (EMS) of both lower limbs in addition to breathing exercises. Group 2 patients underwent a conventional aerobic training program.

Electric myostimulation program

The quadriceps and gastrocnemius muscles of both legs were electrically and simultaneously stimulated using adhesive electrodes and portable battery-powered fourchannel stimulator (Quadstar II; BioMedical Life Systems Inc., Vista, California, USA). On the quadriceps, two self-adhesive surface electrodes were positioned on the skin ~ 5 cm below the inguinal fold and 3 cm above the upper patellar border. On the gastrocnemius, two electrodes were positioned ~3 cm below the popliteal fossa and 5 cm above the Achilles tendon [21]. Blood pressure and HR were measured before and after each session. EMS was performed for 60 min/day, 5 days/week for a period of 5 weeks. Technical parameters of the stimulation were selected as follows: biphasic electric current with 10-Hz frequency, in 'on-off' operation mode, with pulse duration of 200 µs. The time of ascent and descent of the current was 4 s, and the time of contraction/relaxation was 20 s. The intensity of stimulation was progressively increased to cause a visible contraction tolerable by the patient [19].

Aerobic exercise protocol

Each session is started and ended with a 10-min warmup and 5-min cool down period, respectively [22]. Exercise intensity was started at initial workload corresponding to \sim 50–60% of maximal heart rate value obtained from the CPX. Duration was started at 15 min and was up-titrated gradually every week till the patient was able to perform 30 min continuously on the treadmill. Afterward, exercise intensity was increased gradually and progressively with target intensity of ~85% of maximum heart rate. Sessions were held at a frequency of 2–3 sessions/week for an average of 40 sessions. Once patients demonstrated a tolerance of aerobic training levels (around 8–12 weeks for our patients), resistance training activities were added. Patients performed 10 min of light strength/ resistance training for both upper and lower limbs, focusing on the major muscle groups, using 1–2 sets of 10 repetitions/set [23].

Follow-up

Reassessment of all the recruited participants after the completion of the rehabilitation program was done by the following: clinical assessment, aerobic capacity (using CPX), and quality of life (using Minnesota living with HF questionnaire).

The statistical analysis

Statistical presentation and analysis of the present study was conducted, using the mean, SD, Student's *t*-test, paired *t*-test, χ^2 , linear correlation coefficient, and analysis of variance tests by SPSS, version 17.

Results

A total of 46 patients met the inclusion criteria. Only 40 patients completed at least 90% of the rehabilitation program and the follow-up assessment. Control group had 10 patients, and groups 1 and 2 had 9 and 21 patients, respectively. The three groups were compared regarding age, BMI, EF, HF etiology, functional group, smoking, and history of hypertension and diabetes. There was a significant difference (P < 0.05) between the groups, where group 1 tended to be older, with higher BMI, and almost 90% of them had DM. Other variables did not show significant difference (P>0.05). The control patients showed no statistically significant difference before and after treatment (P>0.05) regarding VO_2 p, ventilatory threshold (VO_2 -VT), maximum workload achieved, and HRR. However, there was a significant difference (P<0.05) regarding VE/VCO₂ slope (35.8±12.035-34.880±11.725) and MLHFQ (34.4±16.695-32.1±16.224). EMS produced inferior improvements in VO_2 p when compared with the conventional aerobic training. However, it elicited superior improvements in VO2 p compared with the control group, but still there was no significant difference in the change between group 1 and group 2. Both EMS and aerobic training produced significant improvement in VO₂-VT after rehabilitation; yet when comparing the degree of increase, there was a significant difference, where group 1 showed greater improvement than both the control and group 2. Both groups 1 and 2 showed significant difference after rehabilitation regarding VE/VCO2 slope; however, group 1 with initial steeper slopes showed greater degree of improvement than control and group 2. Workload was

Table 1	Comparison	between	the	characteristics	of	all	groups
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		Contr	ol group	(10)	(Group I ((9)	Gi	oup II (2	21)
		N		%	N		%	Ν		%
Functional class	11	8		80.00	4		44.44	13		61.90
	III	2		20.00	5		55.56	8		38.10
Smoking	Non	4	40.00		3	33.33		6		28.57
-	Smoker	0		0.00	0		0.00	1		4.76
	Ex-Smoker	6		60.00	6		66.67	14		66.67
Etiology	Ischemic	9		90.00	7		77.78	18		85.71
	Dilated	1		10.00	2		22.22	3		14.29
DM	No	6		60.00	1		11.11	18		85.71
	Yes	4		40.00	8		88.89* ^a	3		14.29
HTN	No	6		60.00	5		55.56	14		66.67
	Yes	4		40.00	4		44.44	7		33.33
Age	Range	30	-	63	50	-	72	25	-	63
-	Mean±SD	52.200	±	9.852	59.556	±	7.601* ^b	48.810	±	10.328
EF	Range	25	-	38	20	-	39	22	-	40
	Mean±SD	32.400	±	4.600	25.889	±	6.679* ^c	31.238	±	5.495
BMI	Range	23.5	-	36	23	-	38	23	-	31
	Mean±SD	28.980	±	3.585	30.378	±	5.374* ^b	26.262	±	2.322

*a=P<0.05, significant among the three groups. *b=P<0.05, significant between group 1 and 2. *c=P<0.05, significant between control and group 1. DM=Diabetes Mellitus; HTN=Arterial Hypertension; EF=Ejection Fraction; BMI=Body mass index.

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V	O2 peak		Groups									AVOI	TUKEY'S Test		
		С	ontro	bl	Group I			Group II			F	P-value	C&I	C&II	1&11
Pre	Range Mean ±SD	6 15.350	- ±	23 5.467	7 12.589	- ±	19 4.988	13 19.410	- ±	26.3 4.087	7.460	0.002*	0.409	0.073	0.002*
Post	Range Mean ±SD	6.2 15.670	- ±	24 5.823	8.5 13.744	- ±	21 5.089	13 21.738	- ±	33 5.193	8.858	0.001*	0.714	0.014*	0.002*
Paired	Differences	-0.320	±	1.028	-1.156	±	0.984	-2.329	±	1.881	6.150	0.005*	0.473	0.005*	0.150
Paired Samples Test		0.351		0.008*			<0.001*								

Table 3 Comparison between the control and rehabilitation patients regarding Vo2-VT pre and post rehabilitation

\	/02-VT		Groups									OVA	TUKEY'S Test		
		Control			Group I			Group II			F	P-value	C&I	C&II	1&11
Pre	Range Mean ±SD	5.9 11.540	- ±	17 3.260	6 8.778	- ±	11 2.279	11.4 15.686	- ±	21 3.033	19.177	<0.001*	0.117	0.002*	<0.001*
Post	Range Mean ±SD	5.3 11.670	- ±	17 3.590	7.3 10.756	- ±	15 2.978	11 16.762	- ±	22 3.279	14.196	<0.001*	0.819	0.001*	<0.001*
Paired Differe		-0.130	±	0.826	-1.978	±	0.992	-1.076	±	0.680	12.906	<0.001*	<0.001*	0.010*	0.019*
Paired Samples Test		0.631			<0.001*			<0.001*							

improved after rehabilitation in both groups 1 and 2, with no significant difference in the degree of increase in WL between EMS and aerobic training. HRR showed only significant improvement after aerobic training in group 2. Quality of life manifested by MLHFQ was improved in all three groups after treatment, with the magnitude of the improvement being greatest in group 1 (Tables 1–7).

Discussion

Reduced exercise capacity is the cardinal symptom of CHF [24]. Almost 20% of stable ambulatory patients with HF are affected by muscle wasting, with serious

clinical implications, evidenced by worse exercise capacity [25]. CPX is considered a valuable tool in identifying patients who respond and those who do not to a given therapeutic intervention, as reflected by the change in CPX [26]. Regular aerobic physical activity is recommended to improve functional capacity and reduce morbidity and mortality in patients with HF [27]. NMES has shown to elicit positive skeletal muscle adaptations in some patients [10].

The value of VO_2 -VT (11 ml/min/kg) [28], along with the enhanced ventilatory response to exercise manifested with a steeper VE/VCO₂ slope of at least 35, a

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v	E/VCO2				Gr	oups	5				AN	OVA	TUKEY'S Test		
		Control			Group I		Group II		F	P-value	C&I	C&II	1811		
Pre	Range Mean ±SD	25 35.800	- ±	65 12.035	36 40.889	- ±	51 5.159	16 27.690	- ±	34 5.510	10.685	<0.001*	0.321	0.022*	<0.001*
Post	Range Mean ±SD	24 34.880	- ±	63 11.725	34 37.444	- ±	44 3.321	16.5 26.952	- ±	35 5.538	8.252	0.001*	0.723	0.019*	0.002*
Paired Differe		0.920	±	0.976	3.444	±	2.351	0.738	±	1.437	9.656	<0.001*	0.004*	0.953	<0.001*
Paired Samples Test		0.015*			0.002*			0.029*							

Table 4 Comparison between the control and rehabilitation patients regarding VE/VCO2 slope pre and post rehabilitation

Table 5 Comparison between the control and rehabilitation patients regarding peak workload (WL) pre and post rehabilitation

	WL		Groups										TUKEY'S Test		
		Control			Group I			Group II			F	P-value	C&I	C&II	1811
Pre	Range Mean ±SD	30 79.800	- ±	110 26.541	30 75.111	- ±	122 40.680	70 109.810	- ±	195 26.832	5.699	0.007*	0.940	0.037*	0.018*
Post	Range Mean ±SD	32 80.600	- ±	112 27.981	40 91.222	- ±	169 52.891	60 118.810	- ±	219 34.698	3.981	0.027*	0.817	0.034*	0.177
Paireo Differe		-0.800	±	3.393	-16.111	±	16.174	-9.000	±	12.724					
Paired Samples Test		0.475			0.017*			0.004*							

Table 6 Comparison between the control and rehabilitation patients regarding Heart rate recovery (HRR) pre and post rehabilitation

	HRR		Groups									OVA	TUKEY'S Test		
		Control			Group I			Group II			F	P-value	C&I	C&II	1811
Pre	Range Mean ±SD	2 10.200	- ±	17 5.554	2 8.333	- ±	16 4.330	2 15.571	- ±	20 4.057	9.946	<0.001*	0.645	0.010*	0.001*
Post	Range Mean ±SD	3 10.500	- ±	16 4.249	4 9.444	- ±	13 3.283	4 16.429	- ±	20 4.285	12.542	<0.001*	0.840	0.002*	<0.001*
Paireo Differe		-0.300	±	2.003	-1.111	±	2.667	-0.857	±	1.621					
Paired Samples Test		0.647			0.247			0.025*							

Table 7 Comparison between the control and rehabilitation patients regarding Minnesota Living With Heart Failure Questionnaire (MLHFQ) pre and post rehabilitation

1	MLHFQ		Groups										
			Control			Group			Group I	1	F	P-value	
Pre	Range Mean ±SD	14 34.400	- ±	73 16.695	26 52.222	- ±	87 21.052	6 32.000	- ±	79 24.619	2.725	0.079	
Post	Range Mean ±SD	13 32.100	- ±	72 16.224	22 31.000	- ±	40 6.285	5 28.381	- ±	97 24.675	0.134	0.875	
Paired	Differences	2.300	±	2.627	21.222	±	16.799	3.619	±	7.372			
Paired Samples Test		0.022*				0.005*			0.036*				

quantitative indicator of exertional hyperapnea, which appears to be a prominent prognostic marker, has been identified previously as able to accurately separate patients by fitness [29,30]. classified randomly into two groups: a control group and a rehabilitation group, which was further divided into group 1 and group 2 according to their functional capacity and prognosis.

A total of 40 patients diagnosed with chronic stable LHF were selected based on their clinical symptoms and with ejection fraction up to 40%. They were Our study showed that both NMES and aerobic training caused a comparable significant improvement of both VO_2 p and VO_2 -VT in both groups 1 and 2 after

rehabilitation, denoting improved maximum aerobic capacity and endurance. Control group, however, did not show significant improvement regarding both markers. This agrees with previous studies [19,31–38] that stated that both aerobic training and EMS could produce beneficial effects regarding VO₂ p and VO₂-VT. Although EMS produces beneficial effects better than only usual care, such effects are inferior to the aerobic training. This was not the case in our study where the magnitude of change in both EMS and aerobic groups was comparable with no significant difference. This again emphasizes the idea that EMS is more efficient in patients with lower functional capacity. Most patients with very low exercise capacity cannot train at work rates high enough to produce significant improvement owing to dyspnea and extreme fatigueability 19. It also might indicate lower effectiveness when applying EMS to candidates whose functional capacity is already beyond the effective range of EMS; therefore, these patients might not benefit enough from the EMS. On the contrary, any increase, even if modest, in the parameters of functional capacity in patients with low functional capacity would be of great importance enhancing the participants' maximum functional capacity and endurance to perform sustained submaximal activities.

An elevated VE/VCO_2 slope has been linked to poor pulmonary perfusion [39], an impaired cardiac output both at rest and during exercise [40], early lactate accumulation, heightened skeletal muscle, and chemoreceptor sensitivity, and deconditioning [41]. The VE/VCO₂ slope parameter has been recently considered as a very important prognostic factor in patients with CHF [42]. VE/VCO₂ slope discriminated high-risk and low-risk patients within a VO₂ p range of 10–18 ml/kg/min [29]. Patients with HF with a VE/VCO₂ slope greater than 35 had a mortality rate that was similar to that in patients with a VO_{2P} up to 10 ml/kg/min [43]. Our study showed that there was a statistically significant improvement of VE/ VCO_2 slope in all three groups after the rehabilitation period reflecting better prognosis, with group 1 showing the highest degree of improvement. VE/ VCO_2 can be positively affected by aerobic training as well as to improvement in function associated with pharmacological (B-blockade, inhibition of the reninangiotensin-aldosterone axis, sildenafil) interventions [4,44]. A previous study [38] showed that there was a significant decrease of VE/VCO₂ slope after either aerobic training, EMS, or combined. The improvement in the EMS group was fully comparable to those of the groups with aerobic training. In our study, improvement was more

pronounced in the EMS group. This result might be owing to the fact that our groups were divided according to their functional capacity parameters obtained from the initial CPX, with group 1 having much higher values of VE/VCO₂. On the contrary, group 2 had near-normal values of VE/VCO₂ slope. Thus, improvement was more obvious in the more impaired group.

HRR1 consistently added prognostic value to the VE/ VCO₂ slope and other CPX responses [3]. Our study showed that mean HRR1 for group 1 was 8.3 ± 4.33 whereas that of group 2 was 15.6 ± 4.1 . There was a direct significant correlation between HRR values obtained from the initial CPX and VO₂ p, VO₂-AT, and WL and inverse correlation with VE/ VCO₂ and MLHFQ, denoting good correlation with patients' functional capacity and prognostic markers. This comes in accordance with the previous studies [20,45,46] stressing the significance of HRR1 in prediction of adverse events and its relation to other prognostic CPX variables (VO_{2 p} and VE/VCO₂ slope and shorter exercise time).

All the patients in our study were on BBs agents as part of their pharmacological management. According to Racine *et al.* [47], while improving left ventricular function and prognosis, β -blocker therapy does not influence HRR.

There was a significant improvement of HRR after rehabilitation in group 2 whereas the difference was insignificant in the control group and group 1. This was not the case with Stacey et al. [46] who declared that aerobic-based cardiac rehabilitation program had no apparent effect on HRR in patients who have higher initial functional capacities and normal HRR responses $(\geq 12 \text{ beats/min})$. This could be attributed to the intensity and duration of exercise program. Another study [48] showed that HRR was significantly more rapid in the exercise group after a 2-month aerobic rehabilitation program compared with control (main effect 12.6 vs. 2.6 beats/min in the trained and control groups, respectively, P<0.005). Dimopoulos et al. [49] suggested that continuous rather than interval exercise training improves early HRR1, a marker of parasympathetic activity, suggesting а greater contribution to the autonomic nervous system. These conflicting results may be because of type of recovery used or the intensity and duration of training. Our results showed that patients of group 1 did not show significant improvement of HRR after EMS. As to our knowledge, no studies are available that examined the effect of EMS on HRR. This could be explained by the fact

that almost 90% of group 1 experienced DM which has a deleterious effect on the autonomic system which in turns affects HRR besides the short duration of the program.

Our study showed a statistically significant difference of workload in both group 1 and group 2 after rehabilitation period, whereas the control group showed no improvement. Although group 2 showed more improvement, still there was no statistically significant difference between the two groups. This agrees with previous studies stating that either aerobic or EMS training has a positive effect on the peak workload [31,33,38].

Comparison of the MLHFQ values in our study before and after the treatment period yielded a statistically significant difference (P < 0.05) in all the three groups, with group 1 showing the most reduction. This agrees with previous studies [37,38,50] that observed a significant improvement in the quality-of-life questionnaires after rehabilitation whether aerobic or EMS.

Although previous studies showed that EMS caused inferior improvements to aerobic training, yet in our study, improvements in the functional parameters in the EMS group were fully comparable to the group of aerobic training, denoting that the physiological response to the increase of oxygen demand during contraction caused by EMS is similar to that caused by conventional physical exercise. This proves our hypothesis that EMS could be equally beneficial when applied to selected patients with lower functional capacity. VO₂-VT and VE/VCO₂ slope were found to be useful parameters in stratifying patients with HF, allowing us for better selection of those who would benefit most from EMS.

As a considerable number of patients with CHF tend to abandon physical training owing to the discomfort related to dyspnea, NMES is considered a very useful technique to improve the functional capacity. NMES could be proposed when the patient lacks the motivation for regular physical activity or when the comorbidities and incapacities associated with CHF make conventional training impossible; NMES is an alternative therapy that can limit loss of muscle volume and strength in patients with CHF, taking into consideration, proper selection of the candidates to gain the maximum benefit. Moreover, the total NMES intervention hours are strongly correlated with change in the functional capacity parameters [37].

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Conflicts of interest

There are no conflicts of interest.

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