Electrical Stimulation of Skeletal Muscles in Patients with Heart Failure: An Alternative to Aerobic Training?

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KOHZUKI ET AL.: ***Electrical Stimulation of Skeletal Muscles in Patients with Heart Failure: An Alternative to Aerobic Training?*** *The exercise training has been shown to improve the functional capacity, quality of life and also the patterns of strength muscles in patients with chronic heart failure (CHF). Most of actual training types, however, are based on the systemic exercises resulting in increased cardiac workload. This could lead to onset of life-threatening side effects such as fatal dysrhythmias. Moreover, most of patients with CHF have low exercise tolerance and poor motivation to exercise. Low-frequency electrical stimulation (ES) has been shown to increase oxidative capacity in the skeletal muscle fibers, to enhance muscular regeneration and to prevent atrophy. We aimed to evaluate the possible benefit of ES in patients with mild to severe CHF, and to compare the results with the conventional bicycle training. In our data, 6 weeks ES (60 min/day) of quadriceps and calf muscles of both legs significantly improved muscle strength and blood flow in patients with advanced CHF. Moreover, a similar improvement of exercise capacity in patients with CHF can be achieved either by aerobic bicycle training or by local ES of the strength muscles of the lower limbs in patients with mild to moderate CHF. Although the effectiveness of conventional exercise protocols in cardiovascular rehabilitation is beyond doubt, the safety and easy application of ES could be of great benefit in the rehabilitation of patients with CHF, especially those with a severe grade of the disease. Future studies should also address the possibility of combining ES with some type of classical exercise training. (J HK Coll Cardiol 2008;16 (Suppl 1):A38-A42)*

Electrical stimulation, exercise, heart failure, skeletal muscle

摘要

運動被證明能夠增強身體的機能、生活品質，並且在慢性心衰竭病人中增強肌肉力量。然而，大多數的運動方式是基於系統訓練並導致心臟負荷加重。這將會引起威脅生命的副作用如致死性的心律失常。不僅如此，絕大多數的慢性心衰竭病人的運動耐受性差，且運動意願低下。低頻率的電刺激能夠增加骨骼肌纖維的氧耗能力，促進肌肉增生，防止肌肉萎縮。我們旨在評估在輕度至重度慢性心衰患者中使用電刺激的可能性，並且與傳統的自行車訓練加以比較。在我們的資料中，6 周的電刺激（每天6 0 分鐘）進展期的心衰竭患者雙下肢股四頭肌和腓腸肌的肌肉力量和血流狀況得以明顯改善。不僅如此，在輕度至中度慢性心衰竭病人中不論通過需氧的自行車運動或者電刺激，運動能力的改善和下肢肌肉力量恢復狀況相似。儘管傳統運動的有效性在心血管病人的康復期中的作用毋庸置疑，但電刺激的安全性和易操作性對於慢性心衰竭病人的康復治療總顯示出巨大的益處，尤其在那些疾病程度嚴重的患者中。我們需要進一步研究電刺激聯合一些經典運動訓練的可能性。

關鍵詞：電刺激　運動　心衰竭　骨骼肌

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Chronic Heart Failure and Exercise Training

Dyspnea and premature fatigue of skeletal muscles are common symptoms of reduced exercise capacity in subjects with chronic heart failure (CHF). CHF is a complex metabolic syndrome with impaired left ventricular function and poor prognosis.[1] The exercise training has been shown to improve the functional capacity, quality of life and also the patterns of strength muscles, and therefore should be considered as an integral part of therapeutic standards in such patients.[2-5] Most of actual training types, however, are based on the systemic exercises resulting in increased cardiac workload.[6-7] This could lead to onset of life-threatening side effects such as fatal dysrhythmias, and for this reason classical rehabilitation programs need medical supervision and assistance. Other problems related to the choice of adequate exercise therapy for these patients are the grade of disease, low exercise tolerance and poor motivation to exercise.

Low-frequency electrical stimulation (ES) of strength muscles has been shown to increase oxidative capacity in the skeletal muscle fibers, to enhance muscular regeneration and to prevent atrophy.[8] Nuhr et al.[9] reported that ES increased functional capacity in patients with advanced CHF compared with sedentary controls. Recently, results from the first randomized trial comparing home-based ES and classical exercise training have demonstrated that both methods could significantly influence functional capacity, muscle strength of patients with mild to moderate CHF.[10] However, chronic effects of ES on systemic blood pressure, heart rate in mild to moderate CHF, or chronic effects of ES on systemic blood pressure, heart rate serum enzymes and functional capacity in severe CHF have not been elucidated. Regarding to the dramatic pathophysiologic changes which deteriorate the organism in conditions of chronic heart failure (including strength muscle mass) there is enough reasons to take the profit from ES also in conditions of CHF. We aimed to evaluate the possible benefit of ES in patients with mild to severe CHF, and to compare the results with the conventional bicycle training.

Electrical Stimulation: Animal Hindlimb Ischaemia Model Study[11]

ES in skeletal muscle at a level far below the threshold of muscle contraction has been reported to promote local angiogenesis in a hindlimb ischaemia model of rats. We completely excised bilateral femoral arteries of male Sprague-Dawley rats. After the operation, electrodes were implanted onto the centre of the fascia of the bilateral tibialis anterior (TA) muscles, tunnelled subcutaneously and exteriorized at the level of the scapulae. The right TA muscles of rats were stimulated continuously at a stimulus frequency of 50 Hz, with a 0.1 V stimulus strength and no interval, for 5 days. The left TA muscles served as controls. We found that angiogenic factors, such as vascular endotherial growth factor (VEGF), and hepatocyte growth factor (HGF) were significantly increased by ES in stimulated muscles compared with control rats.[11] It is concluded that both VEGF and HGF may contribute to the local angiogenesis produced by ES in a hindlimb ischaemia model of rats.[11]

Electrical Stimulation in Patients with Severe CHF[12]

We evaluated 15 patients with advanced grade of CHF (mean age 52±7 years; NYHA class III-IV; EF 19±3%) admitted at hospital for heart graft (Table 1). ES was performed 60 min/day, 7 days a week for 5 consecutive weeks, using dual-channel battery-powered stimulator.[12] The stimulator delivered a biphasic current of 10 Hz frequency. The electrical stimulated muscles were quadriceps and calf muscles of both legs. Self-

Table 1. Characteristics of patients included in the study[12]

Women/men	1/14
Age (years)	56.5±5.2
Heart failure aetiology (ischaemic/nonischaemic)	10/5
NYHA class (III/IV)	4/11
Left-ventricular ejection fraction (%)	18.7± 3.3

adhesive surface electrodes were positioned on the thighs approx. 5 cm under inguinal fold and 3 cm over the upper patella border; in the calf muscles the electrodes position was the area approx. 2 cm under the knee joint and just over the proximal end of Achilles tendon. The current characteristics were set up as follows: "on-off" mode stimulus (20s stimulation, 20s rest), pulse width 200 msec, rise and fall time 1s, and maximal stimulation amplitude 60 mA. The stimulation was performed in supine position, at the same day period and under supervision of medical staff. The first session of stimulation was started with lower amplitudes (around 30 mA). In the following days this value was gradually increased (by 10-15 mA/day) until the final value of 60 mA was achieved and well tolerated by the patient (in 2-4 days).[12]

Effects of ES on the muscle strength and blood flow in patients with advanced CHF were examined before and after 6 weeks of 10 Hz ES of quadriceps and calf muscles of both legs (1 h/day, 7 days/week). Dynamometry was performed weekly to determine maximal muscle strength (F_{max}; N) and isokinetic peak torque (PT_{max}; Nm); blood flow velocity (BFV) was registered before and after 6 weeks of ES using pulsed-wave Doppler velocimetry of right femoral artery. Six weeks of ES increased significantly F_{max} ($p<0.001$), and also PT_{max} ($p<0.01$). Mean BFV in femoral artery increased after 6 weeks ($p<0.05$); BFV values at rest before and after 6 weeks of ES did not differ significantly.[12]

After 6 weeks of LFES, all patients had less dyspnea and a marked decrease in subjective feelings of fatigue during everyday activities, although this change was not statistically significant. Similar results were observed for NYHA classification: 4 patients moved from NYHA IV to NYHA III after 6 weeks of stimulation and the remainder were unchanged but not (e.g., from NYHA III to NYHA IV).[12]

ES did not cause any significant changes of systolic blood pressure and diastolic blood pressure, nor were there significant changes in the recorded values of heart rate. In order to evaluate the possible risk of damage to muscle fiber by stimulation, the activity of both CK and LDH was monitored at the beginning, after 1 week and after 6 weeks of stimulation and only insignificant increases after 1 week of stimulation was observed and after 6 weeks of stimulation, the serum levels of both enzymes returned to baseline.[12] It is concluded that ES may improve the skeletal muscle strength and the blood supply. Thus, this method could be recommended in the treatment of patients with severe CHF.

Electrical Stimulation and Aerobic Exercise Training in Patients with Mild to Moderate CHF[13]

Thirty patients with stabilized form of CHF (mean age 56±6 years, NYHA class II-III, mean EF 35 ±5%) were randomly assigned to a rehabilitation program using either electrical stimulation of skeletal muscles or bicycle training (Table 2).[13] Patients in the first group had 8 weeks of home-based ES applied simultaneously to the quadriceps and calf muscles of both legs (1 h/day for 7 days/week); patients in the second group underwent 8 weeks of 40 min aerobic exercise (3 times a week; 5 min warm-up without workload, 30 min of training alternating 1 min of work - 2 min of relaxation, and 5 min of cool down without workload), The realization of the exercise training was strongly individual, performed at the level of anaerobic threshold determined by spiroergometry, and under supervision of medical staff (doctor, physiotherapist and nurse).

After the 8-week period significant increases in several functional parameters were observed in both groups: maximal VO2 uptake (ES group: $p<0.05$; bicycle group: $p<0.01$), maximal workload (ES group: $p<0.05$; bicycle group: $p<0.01$), distance walked in 6 minutes (ES group: $p<0.05$; bicycle group: $p<0.05$), and exercise duration (ES group: $p<0.05$; bicycle group:

Table 2. Characteristics of patients included in the study[13]

Women/men	7/23
Age (years)	56.3±6.0
Heart failure aetiology (ischaemic/nonischaemic)	24/6
NYHA class (II/III)	22/8
Left-ventricular ejection fraction (%)	34.7±5.0

p<0.05) (Figure 1). The QoL score assessed using the Minnesota Living with Heart Failure. Questionnaire was significantly improved in the bicycle group (from 41.4±5.3 to 27.3±6.3; p<0.03), whereas there was only a slight improvement in the ES group (from 39.6±2.9 to 31.4±4.8; NS). The present results demonstrated the good tolerance and significant improvement of functional capacity after 8 weeks of ES. The increases in VO2peak, Wpeak, and distance walked in 6 minutes, and also the exercise duration after 8 weeks of LFES were very similar to the increases in these parameters in the bicycle group. Other parameters (HRpeak, VO2AT and QoL) significantly increased in the bicycle group but not in the LFES group (only slight improvement was observed). Despite the differences between the 2 methods (myostimulation activity is local, whereas bicycle exercise training challenges the entire body), LFES could be regarded as an acceptable analogue of endurance training which can improve the physiological condition of CHF patients in a period of several weeks, and can be easily performed at home without medical supervision.[13]

Future Perspectives of Electrical Stimulation in Patients with CHF

Electrical stimulation of skeletal muscles in humans has been shown to be a useful therapeutic tool in neurology,[14] postoperative treatment, and in cases of long-term immobilization.[15] In a recent study, LFES was

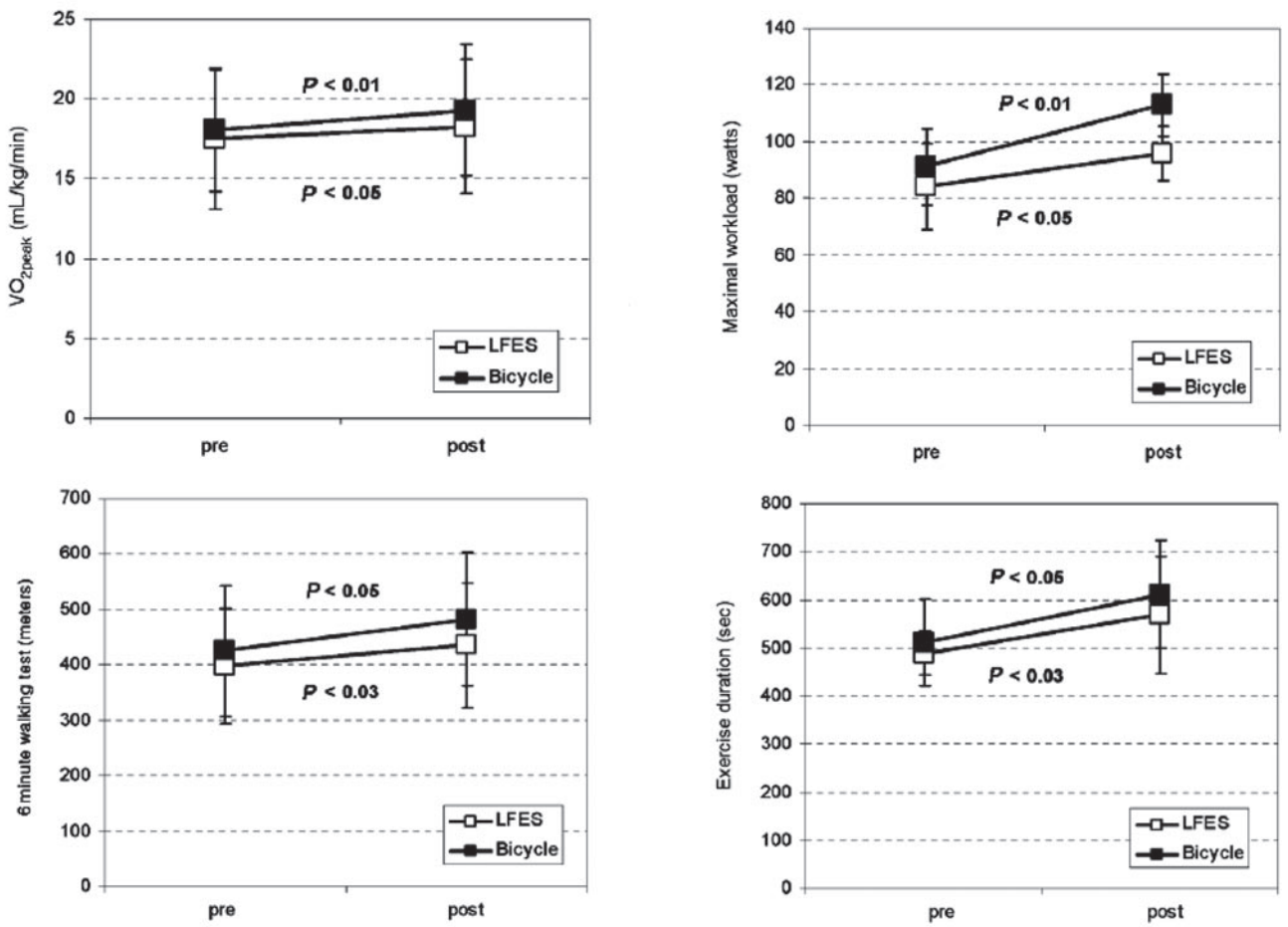

Figure 1. *Results of peak oxygen uptake, peak workload, 6 minutes walking test, and exercise duration in both groups at baseline and after 8 weeks of the given type of rehabilitation.*[13]

reported to improve the functional capacity in claudicants.[16] Hamada, et al.[17] observed enhanced energy consumption, carbohydrate oxidation, and whole body glucose uptake after low-frequency electrical stimulation of the lower limbs, a finding that suggests the possibility of therapeutic application of LFES for diabetic subjects. However, the number of studies concerning the effects of LFES in cardiovascular rehabilitation is still very low. The effectiveness of conventional exercise training in cardiovascular rehabilitation has been sufficiently proven,[18] and LFES is not likely to replace it. But the safety and ease of application could be especially beneficial in patients with advanced CHF (III-IV).

ES should be considered as a valuable alternative to classical exercise training in patients with CHF. Recently, results from the first randomized trial comparing home-based ES and classical exercise training have demonstrated that both methods could significantly influence functional capacity, muscle strength of patients with CHF.[10] Similar results were shown by Nuhr et al in a group of patients with advanced CHF, and an increase of slow myosin heavy chain isoforms at the expense of the fast ones and increased intensity of oxidative enzymatic activity were also found after LFES.[9]

Although the effectiveness of conventional exercise protocols in cardiovascular rehabilitation is beyond doubt, the safety and easy application of ES could be of great benefit in the rehabilitation of patients with CHF, especially those with a severe grade of the disease.

The effectiveness of conventional exercise protocols in cardiovascular rehabilitation is beyond doubt and the patients with mild heart failure would adopt exercise. But the patients with a severe grade of CHF who can not exercise would adopt ES for the safety and easy application. There are scarcely limitations except the allergies of the electrode. Further investigations should yield more detailed data, including information about possible interactions between the central and peripheral cardiovascular mechanisms during muscle stimulation. Future studies should also address the possibility of combining LFES with some type of classical exercise training.

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