

REHABILITATION IN CHRONIC CONGESTIVE HEART FAILURE: COMPARISON OF BICYCLE TRAINING AND MUSCLE ELECTRICAL STIMULATION

EICHER J.C.¹, DOBŠÁK P.², BERTEAU O.¹, WALKER P.³, VERGÈS B.⁴, MAILLEFERT J.F.⁴, CASILLAS J.M.⁴, BRUNOTTE F.³, LOUIS P.¹, WOLF J.E.¹

¹Department of Cardiology, Hôpital du Bocage and University of Burgundy, Dijon, France

²Department of Functional Diagnostics and Rehabilitation, Faculty of Medicine, Masaryk University, Brno, Czech Republic

³Department of Nuclear Medicine, Hôpital du Bocage and University of Burgundy, Dijon, France

⁴Department of Rehabilitation, Hôpital du Bocage and University of Burgundy, Dijon, France

Received after revision November 2004

Abstract

The purpose of this study was to investigate if electrical stimulation of strength muscles could represent an alternative or a complementary way of rehabilitation in congestive heart failure (CHF). Twenty-four patients with chronic stable CHF (NYHA class II-III) were randomly assigned to a rehabilitation program using either a classical bicycle training program (group 1; n=12) or an electrical stimulation of inferior limb muscles (group 2; n=12). Six-minute corridor walk-test and symptom-limited spiroergometry were performed before and after the training program. After the end of rehabilitation a significant increase of distance walked in 6min, oxygen uptake ($\dot{V}O_{2SL}$), maximal heart rate (HR_{max}) and maximal achieved workload (W_{max}) were observed in both groups. There was a close correlation between improvement of $\dot{V}O_{2SL}$ and increase in HR_{max} in the group 1 ($r = 0.64$; $P < 0.05$). A similar relationship was found between $\dot{V}O_{2SL}$ and the increase in W_{max} ($r = 0.65$; $P < 0.05$), and between $\dot{V}O_{2SL}$ and the increase in exercise duration ($r = 0.68$, $P < 0.02$), but only in the group 1. The results showed that an improvement of exercise capacities can be achieved either by classical training method or by electrical stimulation.

Key words

Chronic heart failure, Rehabilitation, Exercise, Electrical stimulation, Strength muscles

Abbreviations used

AV - arterio-venous, CHF - chronic heart failure, ES - electrical stimulation, HR_{max} - maximal heart rate, NO - nitric oxide, NYHA - New York Heart Association, $\dot{V}O_{2SL}$ - symptom-limited oxygen uptake, $\dot{V}O_{2AT}$ - oxygen uptake at anaerobic threshold, W_{max} - maximal workload

INTRODUCTION

Chronic heart failure is a complex metabolic syndrome with impaired left ventricular function and high mortality (1). Several studies reported a strong rise of sympathetic activity, the onset of peripheral vascular remodeling and strength mus-

cle metabolic alterations in response to exercise (2); exercise intolerance in CHF is mainly due to muscle deconditioning (3, 4). 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. (5-7). However, even rehabilitation based on physical exercise can improve both exercise capacity and symptoms, some patients may be too ill to exercise. Several studies reported the increase of oxidative capacity in skeletal muscle fibers, of enhancement of muscular regeneration and of the atrophy prevention by low-frequency electrical stimulation (ES) of strength muscles (8-10). Nevertheless, until now the muscle reconditioning by electrical stimulation (ES) has been studied in few small series, and the effects of this technique compared to classical training in a randomized trial has been poorly evaluated.

PATIENTS AND METHODS

The study population comprised twenty-four patients (5 women, 19 men, mean age 54 ± 9 years) with stable, chronic congestive heart failure. Four patients were in NYHA functional class II, 20 of them were in class III. The etiology of CHF was idiopathic dilated cardiomyopathy (17 subjects), ischemic heart disease (6 subjects), and valvular heart disease (1 subject). All patients gave informed consent. The patients were randomized to enter either a classical bicycle training program, or an electrical stimulation program. Symptom limited spiroergometry was examined before and after training. The patients in the bicycle group (group 1) underwent 25 daily sessions of 20-minute bicycle exercise, at 60-80% of their maximal heart rate. In the electrical stimulation group (group 2), low-frequency (10 Hz) ES was applied to both quadriceps and calf muscles, using ELPHA 2000 stimulators (Danmeter A/S, Odense, Denmark) programmed alternately 20 seconds on and 20 seconds off. Twenty-five daily ES sessions of 1 hour were achieved.

The following parameters were collected before and at the end of the rehabilitation program:

- distance walked in 6 minutes
- symptom limited spiroergometry parameters
- $\dot{V}O_{2SL}$ (symptom-limited $\dot{V}O_2$)
- $\dot{V}O_{2AT}$ ($\dot{V}O_2$ at anaerobic threshold)
- exercise duration
- W_{max} (maximal workload)
- HR_{max} (maximal heart rate)
- using Doppler study of the common femoral artery flow:
 - mean velocity at rest
 - mean velocity after 15 minutes of electrically induced muscle exercise

Statistical analysis was performed using the Wilcoxon paired test, the χ^2 test and the Friedmann test. The P value < 0.05 was considered as significant.

RESULTS

Distance walked in 6 minutes improved significantly in both groups. It improved more in the ES group 2 (+ 72m) than in the bicycle group (+ 29m; *Tables 1, 2, 3 and Fig 1*).

$\dot{V}O_{2SL}$ improved significantly, either by ES (+ 6%) or by bicycle training (+ 8%); the difference between groups is not statistically significant (*Tables 1, 2 and 3*).

$\dot{V}O_{2AT}$ improved non-significantly in the ES group (+ 10%), and significantly (+ 19%) in the bicycle group 1; the difference between groups is significant (*Tables 1, 2, 3 and Fig 2*).

Similarly, exercise duration increased non-significantly in the ES group 2 (+ 31s), and significantly in the bicycle group 1 (+ 82s - *Tables 1, 2 and 3*).

Spiroergometry examinations showed maximal workload, which increased significantly in both groups, as did maximal heart rate (HR_{max}). The difference between groups is non-significant (*Tables 1, 2 and 3*).

Regarding the relationship between the increase in work load, $\dot{V}O_{2SL}$ and the increase in maximal heart rate (HR_{max}), a significant relationship was found in the bicycle group ($r = 0.64$; $P < 0.05$), but not in the ES group. A similar relationship was found between $\dot{V}O_{2SL}$ and the increase in exercise duration ($r = 0.68$; $P < 0.02$), and between $\dot{V}O_{2SL}$ and the increase in maximal workload ($r = 0.65$; $P < 0.05$), but in the bicycle group only.

Doppler study of the common femoral artery flow showed an improvement of vasodilative capacities (i.e. the difference between resting and post-exercise velocities) after rehabilitation, but statistical significance was reached only in the ES group (*Tables 1, 2, 3 and Fig 3*).

Table 1

Symptom limited spiroergometry parameters in the "bicycle" group 1 before and after 5 weeks of exercise training

Bicycle group (group 1)	pre	post	P value
$\dot{V}O_{2SL}$ (ml.kg ⁻¹ .min ⁻¹)	17.28	*18.83	< 0.03
$\dot{V}O_{2AT}$ (ml.kg ⁻¹ .min ⁻¹)	11.32	*13.51	< 0.001
W_{max} (watts)	96.67	*109.7	< 0.02
6-min walking test (m)	468.09	*497.09	< 0.005
Exercise duration (s)	545	*627	< 0.01
HR_{max} (beats.min ⁻¹)	144	*154	< 0.01
Blood flow velocity (cm.s ⁻¹)	21.52	30.23	NS

$\dot{V}O_{2SL}$ - symptom-limited oxygen uptake; $\dot{V}O_{2AT}$ - oxygen uptake at anaerobic threshold; W_{max} - maximal workload; HR_{max} - maximal heart rate

Table 2

Symptom limited spiroergometry parameters in the “ES” group 2 before and after 5 weeks of low-frequency electrical muscle stimulation

ES group (group 2)	pre	post	<i>P</i> value
$\dot{V}O_{2SL}$ (ml.kg ⁻¹ .min ⁻¹)	16.69	*17.67	< 0.05
$\dot{V}O_{2AT}$ (ml.kg ⁻¹ .min ⁻¹)	10.93	12.05	NS
W_{max} (watts)	90.83	*98.33	< 0.04
6-min walking test (m)	408.64	*480.18	< 0.001
Exercise duration (s)	516	547	NS
HR_{max} (beats.min ⁻¹)	148	152	NS
Blood flow velocity (cm.s ⁻¹)	29.09	*41.25	< 0.01

$\dot{V}O_{2SL}$ - symptom-limited oxygen uptake; $\dot{V}O_{2AT}$ - oxygen uptake at anaerobic threshold; W_{max} - maximal workload; HR_{max} - maximal heart rate

Table 3

Comparison of all symptom limited spiroergometry parameters in both groups after 5 weeks of the given type of rehabilitation

ES post	Bicycle	post	<i>P</i> value
$\dot{V}O_{2SL}$ (ml.kg ⁻¹ .min ⁻¹)	18.83	17.67	NS
$\dot{V}O_{2AT}$ (ml.kg ⁻¹ .min ⁻¹)	* 13.51	12.05	< 0.001
W_{max} (watts)	109.7	98.33	NS
6-min walking test (m)	* 497.09	480.18	< 0.01
Exercise duration (s)	627	547	NS
HR_{max} (beats.min ⁻¹)	154	152	NS
Blood flow velocity (cm.s ⁻¹)	30.23	* 41.25	< 0.01

$\dot{V}O_{2SL}$ - symptom-limited oxygen uptake; $\dot{V}O_{2AT}$ - oxygen uptake at anaerobic threshold; W_{max} - maximal workload; HR_{max} - maximal heart rate

DISCUSSION

The global hypo-perfusion and chronic hypoxia in CHF induces gradual damage in functional and metabolic integrity of strength muscle mass. Consequent massive production of variety of pro-inflammatory cytokines stimulates apoptotic pathways leading to fibers atrophy (11), loss of strength, reduction of total muscle mass, global over-expression of anaerobic white fibers (fast glycolytic), and the development of general cachexia (12, 13). Electrical stimulation of strength muscles in humans has been shown to be valuable therapeutic intervention in neurology (14, 15), in post-surgery treatment and in the cases of long-term immobilization (16-18). However, the number of studies concerning the effects of LFES in cardiovascular rehabilitation is still very limited; our trial belongs to a few clinical reports that have focused on the therapeutic potential of low-frequency electrical stimulation in chronic heart failure. Recently, Harris et al. (2004) and Nuhr et al. (2004) published the results of first randomized trials comparing the home-based low-frequency ES training and classical exercise training; the results demonstrated that both methods could significantly influence the muscle strength, improve functional parameters including $\dot{V}O_{2SL}$ and $\dot{V}O_{2AT}$, and improve also the quality of life in patients with CHF (19, 20). These results are very similar to those observed in our present study; 5 weeks of ES or bicycle training led to significant increase of $\dot{V}O_{2SL}$, W_{max} , distance walked in 6 minutes, and of HR_{max} in both groups. Also the exercise duration and $\dot{V}O_{2AT}$ were increased in both groups, but the statistical significance was present only in the bicycle group. In the bicycle group, but not in the ES group, the improvement in $\dot{V}O_{2SL}$ seems to be mediated through the improvement in transport mechanisms, which itself appears to be the result of improved maximal workload and exercise duration. Such a relationship was not found in the ES group, suggesting that electrical stimulation could act through a different mechanism. It is well known that exercise training induces a significant improvement of endothelial functions in patients with CHF (21, 22), and the contractions initiated by local electrical stimulation of the strength muscle may cause similar (or identical) vascular reactions as seen during physical exercises, especially exercise-induced reactive hyperemia in working muscles (23, 24). An acute rise of blood volume increases the shear stress on the vessel wall, which promotes the NO production and liberation (25-27). It is possible to suppose that stimulation-induced changes of blood flow velocity are most probably related to the modification of endothelial functions by long-term electrical stimulation, and thus may be NO-dependent. The significant increase of the blood flow velocity in femoral artery during stimulation observed in our study may reflect the importance of achieved global vascular benefit for the peripheral muscle mass after 5 weeks of ES. Although (from the point of view of effectiveness) it seems that both types of rehabilitation could positively influence the functional capacity and increase the resistance to fatigue. It is important to point out the existing differences between bicycle training and electrical stimulation. Electrical stimulation

RESULTS : anaerobic threshold

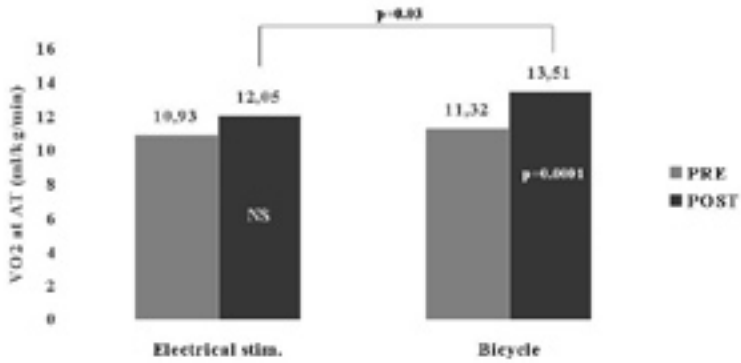


Fig. 1

Comparison of the values of $\dot{V}O_2$ uptake at anaerobic threshold ($\dot{V}O_{2AT}$) in group 1 and 2 before and after 5 weeks of rehabilitation. Statistical significance Wilcoxon paired test

RESULTS : Peak $\dot{V}O_2$

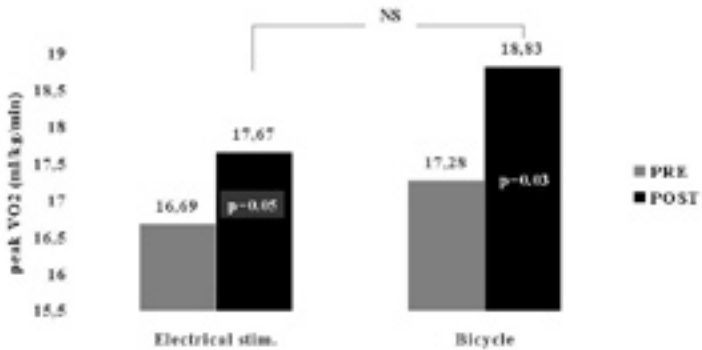


Fig. 2

Comparison of the values of $\dot{V}O_2$ Peak uptake ($\dot{V}O_{2AT}$) in group 1 and 2 before and after 5 weeks of rehabilitation. Statistical significance Wilcoxon paired test

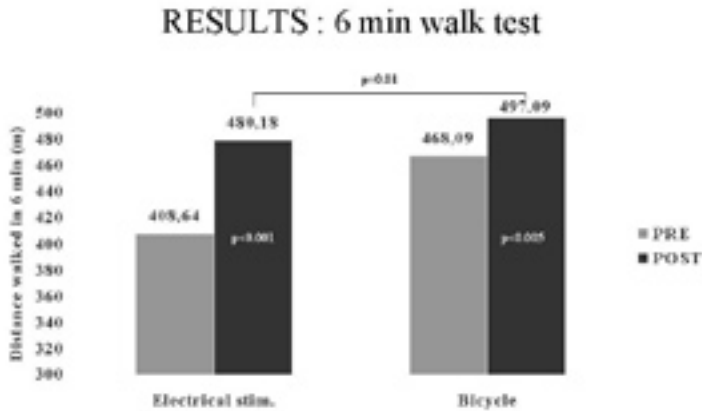


Fig. 3

Comparison of the values of distance walked in 6min (6min walking-test) in group 1 and 2 before and after 5 weeks of rehabilitation. Statistical significance Wilcoxon paired test

concerns only a part of the skeletal muscle mass and its activity is rather local, whereas exercise training on bicycle challenges the entire body. During the periods of stimulation we did not encounter any harmful effects related to the ES application, such as sudden blood pressure or heart rate changes; there were no complaints on muscular pain or skin burn (under the electrodes). Our results are encouraging but we take into account the existing limitations of the trial, first of all the limited number of patients included in the study. From the clinical point of view the most important conclusion resulting from our study is that a significant improvement of functional capacity could be achieved either by ES or by conventional bicycle training. Future investigations should bring more detailed data, especially about possible interactions between the central and peripheral hemodynamic parameters during ES application. It is suggested that clinical trials on larger groups of patients could be useful before the full introduction of ES in cardiovascular rehabilitation.

CONCLUSIONS

This study showed that:

Improvement of exercise capacities in patients with chronic heart failure can be achieved either by classical bicycle training or by electrical stimulation.

Bicycle training improves more $\dot{V}O_{2SL}$, whereas electrical stimulation is more effective on sub-maximal exercise capacities.

In the bicycle group, improvement of $\dot{V}O_{2SL}$ seems to be mainly obtained through the increase in maximal heart rate, and probably through the increased AV difference and improvement of muscle strength.

Electrical stimulation seems to be more effective on the improvement of vascular flow.

Therefore, these two methods may prove to be complementary and could be used in combination, possibly with better results, especially in very sick patients.

A c k n o w l e d g e m e n t

This study was supported by the grant of Czech Ministry of Health IGA MZČR, No. NR 7983-3, 2004.

Eicher J.C., Dobšák P., Berteau O., Walker P., Vergès B., Maillefert J.F., Casillas J.M., Brunotte F., Louis P., Wolf J.E.

REHABILITACE U CHRONICKÉHO MĚSTNAVÉHO SRDEČNÍHO SELHÁNÍ. SROVNÁNÍ DVOU METOD: BICYKLOVÉHO TRÉNINKU A ELEKTRICKÉ STIMULACE

Souhrn

Cílem této studie bylo zjistit, zda elektrická stimulace kosterního svalstva může být alternativou nebo doplňkem v rehabilitaci pacientů s chronickým srdečním selháním (CHSS). Dvacet čtyři pacientů s chronickým stabilizovaným CHSS (NYHA II-III) bylo randomizovaně rozděleno do dvou skupin. Skupina 1 (n = 12) prováděla klasický rehabilitační trénink na bicyklovém ergometru, skupině 2 (n = 12) byla aplikována elektrická stimulace svalstva dolních končetin. Před ukončením rehabilitačního programu a po něm pacienti absolvovali 6-minutový "walk-test" a symptomy limitované spiroergometrické vyšetření ke stanovení $\dot{V}O_{2SL}$. Po ukončení rehabilitace došlo k signifikantnímu zvýšení ušlé vzdálenosti (6 min), hodnoty $\dot{V}O_{2SL}$ a hodnoty $\dot{V}O_2$ při anaerobním prahu, doby trvání zátěže a pracovního výkonu (W_{max}) v obou skupinách. Byla zjištěna úzká korelace mezi zlepšením $\dot{V}O_{2SL}$ a zvýšením maximální tepové frekvence ve skupině 1 ($r = 0.64$, $P < 0.05$). Podobná korelace byla nalezena také mezi $\dot{V}O_{2SL}$ a W_{max} ($r = 0.65$; $P < 0.05$), i mezi $\dot{V}O_{2SL}$ a dobou trvání zátěže ($r = 0.68$; $P < 0.02$), avšak rovněž pouze ve skupině 1. Výsledky prokázaly, že zlepšení funkční kapacity může být dosaženo jak klasickým tréninkem, tak i elektrickou stimulací.

REFERENCES

1. *Böhm M, Kilter H, Kindermann M.* Mechanisms contributing to the progression of left ventricular dysfunction to end-stage heart failure. *Eur Heart J* 2003; 5(Suppl.): 114-21.
2. *Nakamura M.* Peripheral vascular remodeling in chronic heart failure: Clinical relevance and new conceptualization of its mechanisms. *J Cardiac Fail* 1999; 5: 127-38.
3. *Suzuki K, Omiya K, Yamada S et al.* Relations between strength and endurance of leg skeletal muscle and cardiopulmonary exercise testing parameters in patients with chronic heart failure. *J Cardiol* 2004;43(2):59-68.
4. *Senden PJ, Sabelis LW, Zonderland ML et al.* Determinants of maximal exercise performance in chronic heart failure. *Eur J Cardiovasc Prev Rehabil* 2004 Feb; 11(1): 41-7.

5. Coats AJ, Adamopoulos S, Radaelli A et al. Controlled trial of physical training in chronic heart failure. Exercise performance, hemodynamics, ventilation, and autonomic function. *Circulation* 1992; 85(6): 2119-31.
6. Adamopoulos S, Parissis J, Kroupis C et al. Physical training reduces peripheral markers of inflammation in patients with chronic heart failure. *Eur Heart J* 2001; 22(9): 791-7.
7. Schulze PC, Gielen S, Schuler G, Hambrecht R. Chronic heart failure and skeletal muscle catabolism: effects of exercise training. *Int J Cardiol* 2002;85(1):141-149.
8. Pette D, Staron RS. Mammalian skeletal muscle fiber type transitions. *Int Rev Cytol* 1997; 170: 143-223.
9. Maillefert JF, Eicher JC, Walker P et al. Effects of low-frequency electrical stimulation of quadriceps and calf muscles in patients with chronic heart failure. *J Cardiopulm Rehabil* 1998; 18: 277-82.
10. Vaquero AF, Chicharro JL, Gil L et al. Effects of muscle electrical stimulation on peak VO₂ in cardiac transplant patients. *Int J Sports Med* 1998; 19(5): 317-22.
11. Leri A, Claudio PP, Li Q et al. Stretch-mediated release of angiotensin II induces myocyte apoptosis by activating p53 that enhances the local rennin-angiotensin system and decreases the Bcl-2-to-Bax protein ratio in the cell. *J Clin Invest* 1998; 101: 1326-42.
12. Anker SD, Rauchhaus M. Heart failure as a metabolic problem. *Eur J Heart Fail* 1999; 1(2): 127-131.
13. Koller-Strametz J, Pacher R, Frey B, Kos T, Woloszczuk W, Stanek B. Circulating tumor necrosis factor-alpha levels in chronic heart failure: relation to its soluble receptor II, interleukin-6, and neurohumoral variables. *J Heart Lung Transplant* 1998; 17(4): 356-62.
14. Jacobs PL, Nash MS. Modes, benefits, and risks of voluntary and electrically induced exercise in persons with spinal cord injury. *J Spinal Cord Med* 2001; 24(1): 10-8.
15. Hillegass EA, Dudley GA. Surface electrical stimulation of skeletal muscle after spinal cord injury. *Spinal Cord* 1999; 37(4): 251-7.
16. Gibson JN, Morrison WL, Scrimgeour CM, et al. Effects of therapeutic percutaneous electrical stimulation of atrophic human quadriceps on muscle composition, protein synthesis and contractile properties. *Eur J Clin Invest* 1989; 19(2): 206-12.
17. Vinge O, Edvardsen L, Jensen F, et al. Effect of transcatheter electrical stimulation on postoperative muscle mass and protein synthesis. *Br J Surg* 1996; 83: 360-63.
18. Lewek M, Stevens J, Snyder-Mackler L. The use of electrical stimulation to increase quadriceps femoris muscle force in an elderly patient following a total knee arthroplasty. *Phys Ther* 2001; 81(9): 1565-71.
19. Harris S, LeMaitre JP, Mackenzie G, Fox KA, Denvir MA. A randomised study of home-based electrical stimulation of the legs and conventional bicycle exercise training for patients with chronic heart failure. *Eur Heart J* 2003; 24(9): 871-8.
20. Nuhr MJ, Pette D, Berger R et al. Beneficial effects of chronic low-frequency stimulation of thigh muscles in patients with advanced chronic heart failure. *Eur Heart J* 2004; 25(2): 136-43.
21. Hambrecht R, Fiehn E, Weigl C, et al. Regular physical exercise corrects endothelial dysfunction and improves exercise capacity in patients with chronic heart failure. *Circulation* 1998;98(24):2709-15.
22. Linke A, Schoene N, Gielen S, et al. Endothelial dysfunction in patients with chronic heart failure: Systemic effects of lower-limb exercise training. *J Am Coll Cardiol* 2001; 37: 392-397.
23. Duffy SJ, New G, Tran BT, Harper RW, Meredith IT. Relative contribution of vasodilator prostanoids and NO to metabolic vasodilation in the human forearm. *Am J Physiol* 1999;276(2):663-70.
24. Maiorana A, O'Driscoll G, Dembo L, et al. Effect of aerobic and resistance exercise training on vascular function in heart failure. *Am J Physiol Heart Circ Physiol* 2000;279(4):H1999-2005.
25. Sparks HV Jr, Belloni FL. The peripheral circulation: Local regulation. *Ann Rev Physiol* 1978;40:67-92.
26. Fukai T, Siegfried MR, Ushio-Fukai M, et al. Regulation of the vascular extracellular superoxide dismutase by nitric oxide and exercise training. *J Clin Invest* 2000;105(11):1631-9.
27. Kojda G, Cheng YC, Burchfield J, Harrison DG. Dysfunctional regulation of endothelial nitric oxide synthase (eNOS) expression in response to exercise in mice lacking one eNOS gene. *Circulation* 2001;103(23):2839-44.

