*Original article*

# Impact of cardiac resynchronisation therapy on adaptation of circulatory and respiratory systems to exercise assessed by cardiopulmonary exercise test in patients with chronic heart failure

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**Abstract**

**Background:** Cardiac resynchronisation therapy (CRT) has become a valuable therapeutic tool in patients with advanced chronic heart failure (CHF). The search for optimal methods for the assessment of CRT efficacy is still underway.

**Aim:** To evaluate the impact of implantation of CRT devices in patients with CHF on adaptation of circulatory and respiratory systems to maximal exercise assessed by cardiopulmonary exercise tests (CPX) and 6-minute walking tests (6MWT).

**Methods:** We investigated 27 patients (22 males, 5 females, 61.2±9.1 years) with a CRT device implanted due to advanced CHF, which resulted from ischaemic or dilated cardiomyopathy. All patients before implantation underwent echocardiography, CPX with expired gas analysis and 6MWT. Investigations were repeated at 3-6 months after CRT implantation. In CPX we evaluated peak oxygen uptake (peak $VO_2$), oxygen pulse, maximal minute ventilation-carbon dioxide production ($VE/VCO_{2\ max}$), and its slope ($VE/VCO_2$ slope) and $VE/VO_2$ slope, $VO_2$ in anaerobic threshold (AT), and cardiac and respiratory reserve. In 6MWT we evaluated walking distance and heart rate and blood pressure response to exercise.

**Results:** We noted statistically higher mean peak $VO_2$ after CRT implantation in the studied group: 11.34±3.38 vs. 14.56±3.99 ml/kg/min (p <0.0001) and 1.01 ±0.44 vs. 1.4±0.55 l/min (p=0.003) and higher values of expired $CO_2$: 1.00±0.43 vs. 1.43±0.67 l/min (p=0.004). The $O_2$ pulse rose from 9.65±3.39 to 13.23±5.43 ml/beat (p=0.015). We also observed a significant reduction of $VE/VCO_2$ slope from 42.34±13.35 before CRT to 34.77±6.04 after CRT (p=0.0196) and a significant decrease of $VE/VO_2$ slope from 41.32 ±15.46 to 34.01±6.27 (p=0.037). $VE/VCO_{2\ max}$ fell from 58.02±15.86 to 50.1±13.14 (p=0.009). Patients estimated their dyspnoea on the Borg scale at peak exercise at 4.75±0.75 points before CRT and at 3.67±1.15 points (p=0.002) after CRT. Patients could walk a longer distance during 6MWT than before CRT (367±154.9 vs. 231.1±170.3 m, p <0.001).

**Conclusions:** Cardiac resynchronisation therapy improves exercise tolerance measured by means of CPX and 6MWT, improves respiratory system efficiency and restores its adaptive mechanisms during exercise in patients with advanced CHF. Better exercise adaptation after CRT may be objectively measured with CPX parameters, and corelates with improvement of clinical symptoms. CPX seems to be a very helpful tool in assessing the results of CRT.

**Key words:** chronic heart failure, resynchronisation, cardiopulmonary exercise test, exercise tolerance

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## Introduction

Chronic heart failure (CHF) is one of the most common diseases, occurring with the frequency of 0.4-2% in the European population [1]. Studies conducted in Framingham revealed that in men presenting with clinical symptoms of CHF, the risk of death within five years from the onset of symptoms was 75% [2]. Half of all deaths in patients with CHF are due to the progression of CHF; the remaining patients die of sudden cardiac death, resulting from ventricular arrhythmias [3].

Observations of subjects with CHF have led to the conclusion that in about 30% of patients (14-47%, depending on the source) the widening of QRS (caused mainly by left

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bundle branch block, but also by other types of intraventricular conduction abnormalities) plays an important role in the pathogenesis of the disease, and is a manifestation of dyssynchronous contractions of the left ventricle (LV), which leads to unfavourable haemodynamic effects. QRS duration of >140 ms is associated with two times higher mortality [4]. The use of simultaneous pacing of both ventricles – resynchronisation (CRT) – results in a change of the sequence of heart activation, restoring the synchrony of heart contractions, which shortens QRS duration and leads to the improvement of immediate and distant haemodynamic effects. Pilot studies demonstrated that patients who presented with QRS longer than 130-140 ms benefited from CRT. Several trials with CRT (PATH-CHF [5], MUSTIC [6], CONTAK-CD [7], MIRACLE [8], COMPANION [9], CARE-HF [10]) resulted in more precise indications for therapy [11, 12].

Determination of the degree of CHF severity is crucial to define indications for CRT. NYHA classification, based on clinical symptoms, is an inaccurate and insufficient method, allowing only a general assessment of the patient's clinical condition. The cardiopulmonary exercise (CPX) test has been well validated in CHF diagnosis. It enables differentiation of CHF from other causes of exertional dyspnoea and also allows an objective assessment of circulatory capacity and respiratory response to exercise. In many studies with CRT, the CPX test was used as the method of qualifying patients for implantation and allowing the assessment of the results of therapy. The first significant study in which CPX was used to select patients for CRT was the PATH-CHF study [13]. The majority of large randomised studies on CRT were limited to measurements of peak oxygen consumption (peak $VO_2$) in the qualification and evaluation of patients before and after CRT implantation. None of the available studies took into an account the respiratory response to exercise in patients with advanced CHF. From the reports published since 1997 it is known that abnormal respiratory response during exercise in patients with CHF is associated with increased mortality in long-term follow-up [14]. The ventilatory equivalent ratio for carbon dioxide ($VE/VCO_2$) is a particularly important parameter; its pathologic increase during exercise is associated with unfavourable prognosis in patients with CHF [15]. We are not aware of any studies in Poland on use of the CPX test in the assessment of CRT results.

The aim of the study was to assess how much CRT may improve exertional capacity in patients with CHF, the symptoms of dyspnoea as well as to assess whether pathological respiratory activity during exercise changes in patients with CHF treated with CRT.

## Methods

### Inclusion criteria

Patients with advanced CHF who met the following criteria were qualified for CRT implantation:

- CHF in NYHA class III or IV due to ischaemic heart disease (IHD) or dilated cardiomyopathy (DCM)
- CHF in NYHA class II and at least two episodes of acute HF within the previous year
- Optimal pharmacotherapy of CHF (maximum tolerated doses of angiotensin-converting enzyme inhibitor, beta-blockers, loop diuretics and spironolactone)
- Intraventricular conduction abnormalities (LBBB) with QRS >150 ms or QRS 120-150 ms and marked dyssynchrony of LV contractions in echocardiography
- Features of inter- and intraventricular dyssynchrony of the LV in echocardiography
- Reduced ejection fraction in echocardiography
- Left ventricular end-diastolic dimension (LVdD) >55 mm
- Peak oxygen consumption in CPX test <15 ml/kg/min, features of severe aerobic insufficiency, Weber class C, D or E
- The ability to undergo exercise stress testing
- Written consent to participate in the study (the protocol of the study was accepted by the local Ethics Committee).

### Exclusion criteria

The exclusion criteria were as follows:

- CHF in NYHA class I or II
- Mild aerobic insufficiency, Weber class A or B in CPX test
- Severe chronic obstructive pulmonary disease in spirometry testing
- Contraindications to undergo CRT device implantation.

Echocardiography with the assessment of heart chamber dimensions, contractility (ejection fraction evaluation with acoustic quantification – AQ), presence of valve disease and inter- and intraventricular dyssynchrony was performed to qualify patients for CRT implantation. To exclude the presence of severe chronic obstructive pulmonary disease (COPD) and severe bronchial asthma (based on FEV1, FEV1/FVC and lung vital capacity assessment) spirometry testing was performed.

### Cardiopulmonary exercise test

The test was performed according to the Naughton protocol using the Marquette Case 15 system. Measurements of gases were done using the $V_{max}$ 29c system coupled with the treadmill. Cardiopulmonary exercise test was continued until the anaerobic threshold (AT) and maximum heart rate limit ($HR_{max}$) were reached or the patient's refusal to continue walking due to exhaustion even if AT or $HR_{max}$ was not reached.

During CPX the following parameters were assessed:

- Heart rate, blood pressure, the presence of arrhythmias and ischaemic changes in ECG
- Peak oxygen consumption (peak $VO_2$, ml/kg/min, l/min)
- The percentage of predicted age-adjusted normal peak oxygen consumption (calculated according to nomograms)
- Peak expired of $CO_2$ (peak $VCO_2$, l/min)
- Oxygen pulse ($O_2$ pulse, ml/heart beats)
- Maximal ventilation during maximum exercise (VE, l/min)
- Breathing reserve – BR (quotient of maximum voluntary

ventilation (MVV) and maximum ventilation during exercise, presented as percentages of MVV, according to the formula MVV/VE × 100%)
- The achievement of anaerobic threshold (AT – *anaerobic threshold*) ml/kg/min of oxygen consumption
- Maximum value of $CO_2$ ventilatory equivalent (peak $VE/VCO_2$)
- Ventilatory equivalent for $CO_2$ and $O_2$ at anaerobic threshold ($VE/VCO_{2\ AT}$ and $VE/VO_{2\ AT}$)
- $VE/VCO_2$ slope and $VE/VO_2$ slope defining activation of the respiratory system during the whole exercise
- Self-assessed severity of dyspnoea according to modified Borg scale (1-5, where 5 stands for maximum severity).

### 6-minute walk test (6MWT)

During the test measurement of the distance covered by the patient walking at maximum speed for 6 minutes or until exhaustion was done. Resting during the test was allowed. The result of the test was total distance (in metres) covered by the patient during 6 minutes. Before and after the exercise, heart rate and blood pressure were measured.

### CRT implantation

The procedure was performed under local anaesthesia. Three pacing leads were inserted into the right atrium, right ventricle and coronary sinus. Biventricular resynchronising pacing was used in case of persistent atrial fibrillation or when ventricles were synchronised with preserved leading spontaneous atrial activity (tri-chamber stimulation: atrio-biventricular). The procedure was conducted under local anaesthesia. Implantation of the leads into the right atrium and the right ventricle was similar to the implantation of dual-chamber pacemakers. The lead for LV pacing was inserted using right heart catheterisation and contrasting sets through the coronary sinus up to the LV venous branches. The insertion of the lead was preceded by a backward selective venography of the coronary sinus to choose the target vessel and appropriate lead.

After the implantation interrogation of the CRT pacemaker, chest X-ray in order to exclude pneumothorax and lead displacement and echocardiography to exclude haemopericardium were performed. Stitches were removed 9-10 days after the procedure.

### CRT optimisation

In each patient optimisation of CRT was performed using echocardiography. First, the AV delay was optimised during both the sinus rhythm and atrial pacing. The optimum AV delay was established as the shortest interval for which the A wave of the mitral inflow during atrial contraction was not disrupted prematurely (pulse wave Doppler evaluation). After finding optimum AV delay, the optimisation of VV delay was performed based on aortic ejection (assessment of time-velocity integral at the level of the aortic valve using pulse wave Doppler).

### Follow-up

After 3-6 months, cardiopulmonary stress testing, 6MWT test and echocardiography were performed in all patients. The results were compared with baseline results.

### Statistical analysis

The results are presented as mean ± standard deviation or numbers and percentages. Quantitative variables were compared with Student's t-test and qualitative variables with $\chi^2$ test. The value of $p < 0.05$ was considered statistically significant.

## Results

The study included 27 consecutive patients (22 men and 5 women, at the mean age of 61.2±9.1 years) undergoing CRT in our centre in 2005/2006. Initially, 20 patients were diagnosed with CHF in NYHA III class, and 7 patients with CHF in NYHA III/IV class. In 13 patients (12 males, 1 female) CHF resulted from IHD; all these patients had a history of myocardial infarction. In 13 patients (9 males/4 females) CHF was caused by DCM. Patients with DCM were significantly younger (58.3±9.8 years) than patients with IHD (64.0±7.5 years, p=0.013). In one of the patients CHF was caused by decompensated corrected aortic valve disease (he underwent aortic valve replacement 4 years before CRT implantation). Transvalvular pressure gradient was not significantly increased in this patient and he met the inclusion criteria. Two patients who participated in the study presented with persistent atrial fibrillation. None of the patients included in the study died during the 6-month follow-up period (Table I).

The comparison of mean values of CPX parameters before and after CRT implantation is presented in Table II and Figures 1 and 2. A significant improvement of the majority of CPX parameters was found. The mean increase of peak $VO_2$ after device implantation was 3.22 ml/kg/min, constituting a 28% improvement.

All patients completed a 6MWT. After CRT implantation the distance covered by the patients increased from 231.1±170.3 m to 367±154.9 m ($p < 0.001$).

The subgroups of patients with IHD (13 patients, 12 males at the mean age of 64.0±7.5 years) and DCM (13 patients, 9 males, at the mean age of 58.3±9.8 years) were compared. Patients with DCM were significantly younger than patients with IHD (p=0.0128). The gender distribution was not significantly different. The comparison of CPX results in DCM and IHD subgroups is presented in Table II.

## Discussion

Cardiac resynchronisation therapy has recently gained a considerable interest as the method of treatment in patients with CHF. The criteria predicting benefits from CRT in patients with CHF defined by the European Society of Cardiology include: decreased ejection fraction,

**Table I.** The results of CPX

| Parameter | Before CRT | After CRT | p |
|---|---|---|---|
| peak $VO_2$ [ml/kg/min] | 11.3±3.4 | 14.6±4.0 | <0.0001 |
| peak $VO_2$ [l/min] | 1.01±0.44 | 1.40±0.55 | 0.0027 |
| peak $VCO_2$ [l/min] | 1.00±0.43 | 1.43±0.67 | 0.0039 |
| Puls $O_2$ [ml/beat] | 9.65±3.39 | 13.23±5.43 | 0.0146 |
| $VE_{max}$ [l/min] | 48.7±15.1 | 59.5±14.7 | 0.0006 |
| BR [%] | 42.9±17.5 | 27.8±19.1 | NS (0.0510) |
| $VE/VCO_2$ | 58.0±15.9 | 50.1±13.1 | 0.0093 |
| $VE/VCO_2$ slope | 42.3±13.4 | 34.8±6.0 | 0.0196 |
| $VE/VO_2$ slope | 41.3±15.5 | 34.0±6.3 | 0.0368 |
| AT [ml/kg/min] | 11.4±1.4 | 12.6±3.7 | NS |
| $VE/VO_2$ in AT | 44.3±13.6 | 40.0±3.2 | NS |
| $VE/VCO_2$ in AT | 46.0±11.0 | 42.0±8.5 | NS |
| Dyspnoea according to Borg | 4.75±0.75 | 3.67±1.15 | 0.0016 |

**Table II.** Comparison of CPX results in DCM and IHD subgroups

| Parameter | DCM | | | IHD | | | DCM vs. IHD before CRT | DCM vs. IHD after CRT |
|---|---|---|---|---|---|---|---|---|
| | before CRT | after CRT | p | before CRT | after CRT | p | | |
| $pVO_2$ [ml/kg/min] | 12.8±3.5 | 16.2±4.0 | 0.0069 | 10.0±2.7 | 13.1±3.6 | 0.0014 | 0.0306 | NS(0.055) |
| $VO_2$ [l/min] | 1.16±0.37 | 1.52±0.51 | NS (0.07) | 0.82±0.48 | 1.24±0.62 | 0.0162 | NS | NS |
| $VCO_2$ [l/min] | 1.13±0.32 | 1.52±0.66 | NS (0.08) | 0.81±0.53 | 1.32±0.75 | 0.0179 | NS | NS |
| Puls $O_2$ [ml/beat] | 11.01±2.54 | 13.87±5.65 | NS | 7.74±3.75 | 12.34±5.60 | 0.0234 | NS | NS |
| $VE_{max}$ [l/min] | 52.4±14.2 | 63.7±8.7 | 0.0108 | 43.5±16.2 | 53.6±20.2 | NS (0.06) | NS | NS |
| BR [%] | 38.6±20.0 | 31.3±18.7 | NS | 49.0±13.7 | 23.0±20.6 | NS | NS | NS |
| $VE/VCO_2$ | 51.8±9.5 | 49.7±15.8 | NS | 64.2±18.7 | 50.5±10.5 | 0.0011 | 0.0462 | NS |
| $VE/VCO_2$ slope | 36.9±5.2 | 35.9±7.3 | NS | 49.9±18.1 | 38.4±7.9 | NS | NS | NS |
| $VE/VO_2$ slope | 35.1±7.1 | 35.4±7.5 | NS | 50.0±20.5 | 37.9±7.0 | NS | NS | NS |
| Dyspnoea according to Borg | 4.86±0.38 | 4.00±0.82 | 0.0453 | 4.60±1.14 | 3.20±1.48 | 0.0249 | NS | NS |

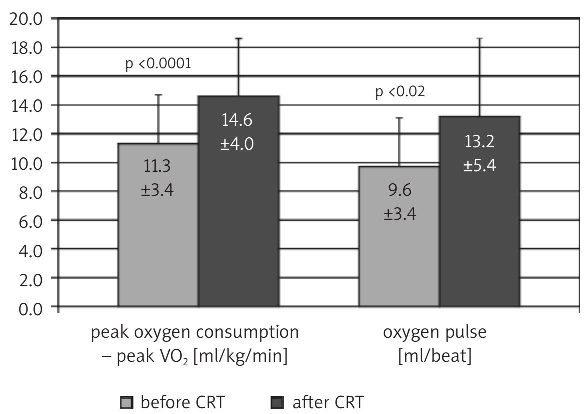


**Figure 1.** Peak oxygen consumption and oxygen pulse in patients before and 3-6 months after CRT implantation

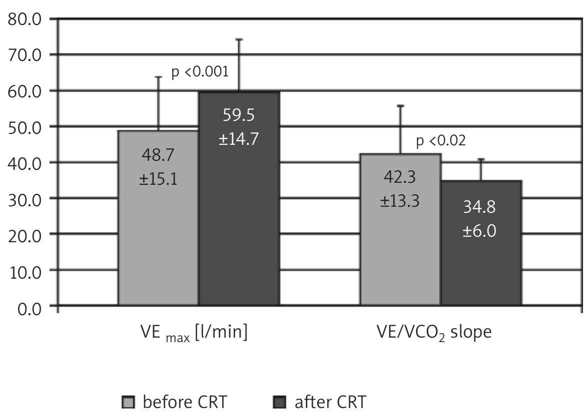


**Figure 2.** Maximal ventilation during exercise ($VE_{max}$) and ventilatory equivalent for expired $CO_2$ ($VE/VCO_2$ slope) in patients before and 3-6 months after CRT implantation

dyssynchrony of heart muscle contractility (widening of QRS complex >120 ms) in patients with NYHA III or IV class despite optimal pharmacological treatment [11, 12]. These guidelines do not include CPX parameters to qualify patients for CRT implantation. The German Society of Cardiology recommended however to consider using peak $VO_2$ <14 ml/kg/min as one of the criteria indicating the need for CRT [16]. In all large-scale randomised studies on CRT the assessment of treatment efficacy was based, among other things, on CPX [5-10]. Attention was however paid mostly to peak oxygen consumption. So far only in the PATH-CHF I [17] and PATH-CHF II [13] studies was the result of CPX considered as an inclusion criterion, and patients with peak $VO_2$ <18 ml/kg/min were included. Based on the results of the CONTAK-CD study it was demonstrated that the initial level of peak $VO_2$ is of significant importance in determining the response to CRT [7]. In that study 490 patients with heart failure in NYHA II-IV class and the width of QRS complexes >120 ms were randomised to ICD or CRT-ICD treatment. Insignificant (0.8 ml/kg/min) improvement of peak $VO_2$ was demonstrated in the whole group. In 176 patients, however, with NYHA III or IV class, a significant increase of peak $VO_2$ of 1.8 ml/kg/min was documented (p=0.001) [18].

Compared with other studies with CRT, patients who participated in our study presented with initially lower peak $VO_2$, and had higher NYHA class before CRT implantation. One of the inclusion criteria was peak $VO_2$ <15 ml/kg/min, and it allowed the selection of patients with the most severe CHF. The mean increase of peak $VO_2$ after CRT implantation in large randomised studies ranged from +0.6 ml/kg/min (INSYNC study) to +1.8 ml/kg/min (CONTAK-CD study, patients with NYHA III) [19]. In our study, despite using strict inclusion criteria, the mean increase of peak $VO_2$ after CRT implantation was +3.2 ml/kg/min.

An improvement of oxygen pulse was also demonstrated (an increase on average of 37%) after CRT implantation. It is the result of the increase of total oxygen consumption (despite higher maximal heart rate) at peak exercise in examined patients. The increase of oxygen pulse results also from the increase of stroke volume during exercise in patients after CRT implantation. Maximum ventilation (VE) at peak exercise increased and the peak level of ventilatory equivalent for $CO_2$ ($VE/VCO_{2max}$) decreased, resulting from a higher increase of $VCO_2$ than of VE. This indicates weaker activation of the respiratory system and an increase of ventilatory reserve at peak exercise despite much greater exercise performed by patients. Self-reported dyspnoea during exercise was reduced. In fact patients were capable of greater exercise, which was reported by patients as lower exercise intensity than during baseline test.

Increased maximal ventilation during exercise, combined with decreased expiratory $CO_2$ concentration (increased $VE/VCO_{2\,max}$ ratio) has been considered an unfavourable prognostic factor [20]. Patients after CRT implantation present with significant decrease of $VE/VCO_{2\,max}$ and such change is of favourable prognostic value.

The $VE/VCO_2$ and $VE/VO_2$ curve slope was also significantly decreased. The value of $VE/VCO_2$ slope has been regarded as a prognostic parameter of CHF. Moreover, increase of $VE/VCO_{2\,max}$ and $VE/VCO_2$ slope in patients with CHF is associated with increased mortality in long-term follow-up. In Francis et al. study the mortality in patients with $VE/VCO_2$ slope between 34.6 and 42.1 was 26% in two-year follow-up [21]. Values of $VE/VCO_2$ slope exceeding 42 were associated with mortality of 49%. In our study a decrease of $VE/VCO_2$ slope to 35 after CRT implantation was achieved. In Corr et al. analysis the level of $VE/VCO_2$ of 35 was considered to be the low-end cut-off value separating high-risk CHF patients from intermediate risk subjects [14]. The prognostic value of the improvement of ventilatory parameters after CRT implantation in our group of patients will be the subject of further analysis.

Despite initial differences in peak oxygen consumption in the subgroup of patients with DCM compared with patients with IHD, no significant differences in the response to CRT were found. However, a trend towards a higher peak $VO_2$ rise after CRT in the DCM subgroup was observed. The remaining CPX parameters did not significantly differ between the two subgroups.

The increase in the distance covered during 6MWT is in line with improved cardiopulmonary test results and further documents benefits of CRT.

Changes observed in patients after CRT implantation reflect the improvement of respiratory parameters and better respiratory adaptation to exercise. The explanation of these favourable changes is not easy and not entirely clear. The improvement of ventilation presumably results from the decrease of respiratory dead space (VD). One of the factors responsible for the improvement of respiratory adaptation after CRT implantation might also be the decrease of pathological activation of chemoreceptors [22] and muscle ergoreceptors [23].

The limited number of patients participating in the study as well as the lack of correlation between obtained results and the results of other additional tests such as echocardiography are the limitations of our study. Echocardiography was performed in each patient before entering the study and in the follow-up period, and the results of more detailed analysis will be presented in following reports.

## Conclusions

CRT in patients with severe CHF improves exercise tolerance, evidenced independently by: the improvement of peak $VO_2$ in cardiopulmonary exercise testing, the increase of the distance covered during 6MWT, and the decrease of self-reported exercise intensity on the Borg scale. CRT also tends to improve respiratory capacity and respiratory adaptation to increased exercise assessed based on VE, VE/$VCO_{2\ max}$ and VE/$VCO_2$ slope. The decrease of self-reported severity of dyspnoea and the improvement of exercise tolerance observed in patients after CRT implantation make them capable of performing much more intense exercise during everyday activities.

## References


1. Remme WJ, Swedberg K; Task Force for the Diagnosis and Treatment of Chronic Heart Failure, European Society of Cardiology. Guidelines for the diagnosis and treatment of chronic heart failure. *Eur Heart J* 2001; 22: 1527-60.
2. Ho KK, Pinsky JL, Kannel WB, et al. The epidemiology of heart failure: the Framingham study. *J Am Coll Cardiol* 1993; 22: 6A-13A.
3. Deedwania PC, Carbajal EV. Current diagnosis and treatment in cardiology, In: Congestive Heart Failure, Appleton and Lange, 1995. (p. 183), In: Crawford M (ed.). Current Diagnosis &Treatment in Cardiology. Lange/McGraw-Hill, 2002.
4. Kashani A, Barold SS. Significance of QRS complex duration in patients with heart failure. *J Am Coll Cardiol* 2005; 46: 2183-92.
5. Auricchio A, Stellbrink C, Sack S, et al. Long-term clinical effect of hemodynamically optimized cardiac resynchronization therapy in patients with heart failure and ventricular conduction delay. *J Am Coll Cardiol* 2002; 39: 2026-33.
6. Linde C, Leclercq C, Rex S, et al. Long-term benefits of biventricular pacing in congestive heart failure: results from the MUltisite STimulation in cardiomyopathy (MUSTIC) study. *J Am Coll Cardiol* 2002; 40: 111-8.
7. Higgins SL, Hummel JD, Niazi IK, et al. Cardiac resynchronization therapy for the treatment of heart failure in patients with intraventricular conduction delay and malignant ventricular tachyarrhythmias. *J Am Coll Cardiol* 2003; 42: 1454-9.
8. Abraham WT, Fisher WG, Smith AL, et al. Cardiac resynchronization therapy for the treatment of heart failure in patients with intraventricular conduction delay and malignant ventricular tachyarrhythmias. *N Engl J Med* 2002; 346: 1845-53.
9. Bristow MR, Feldman AM, Saxon LA. Heart failure management using implantable devices for ventricular resynchronization: Comparison of Medical Therapy, Pacing, and Defibrillation in Chronic Heart Failure (COMPANION) trial. COMPANION Steering Committee and COMPANION Clinical Investigators. *J Card Fail* 2000; 6: 276-85.
10. Cleland JG, Daubert JC, Erdmann E, et al.; Cardiac Resynchronization-Heart Failure (CARE-HF) Study Investigators. The effect of cardiac resynchronization on morbidity and mortality in heart failure. *N Engl J Med* 2005; 352: 1539-49.
11. Swedberg K, Cleland J, Dargie H, et al. Guidelines for the diagnosis and treatment of chronic heart failure: executive summary (update 2005): The Task Force for the Diagnosis and Treatment of Chronic Heart Failure of the European Society of Cardiology. *Eur Heart J* 2005; 26: 1115-40.
12. Hunt SA; American College of Cardiology; American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure). ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure). *J Am Coll Card* 2005; 46: e1-82.
13. Auricchio A, Stellbrink C, Butter C, et al.; Pacing Therapies in Congestive Heart Failure II Study Group; Guidant Heart Failure Research Group. Clinical efficacy of cardiac resynchronization therapy using left ventricular pacing in heart failure patients stratified by severity of ventricular conduction delay. *J Am Coll Cardiol* 2003; 42: 2109-16.
14. Corra U, Mezzani A, Bosimini E, et al. Cardiopulmonary exercise testing and prognosis in chronic heart failure: a prognosticating algorithm for the individual patient. *Chest* 2004; 126: 942-50.
15. Francis DP, Shamim W, Davies LC, et al. Cardiopulmonary exercise testing for prognosis in chronic heart failure: continuous and independent prognostic value from VE/VCO(2)slope and peak VO(2). *Eur Heart J* 2000; 21: 154-61.
16. Stelbrink C, Auricchio A, Lemke B, et al. Policy paper to the cardiac re-sychronization therapy]. *Z Kardiol* 2003; 92: 96-103.
17. Auricchio A, Stellbrink C, Sack S, et al. The Pacing Therapies for Congestive Heart Failure (PATH-CHF) study: rationale, design, and endpoints of a prospective randomized multicenter study. *Am J Cardiol* 1999; 83: 130D-135D.
18. Contak CD subanalysis: www.fda.org. Contak CD CRT-D system. Summary of safety and effectiveness.
19. Lamp B, Vogt J, Schmidt H, et al. Impact of cardiopulmonary exercise testing on patient selection for cardiac resynchronisation therapy. *Eur Heart J Suppl* 2004; 6: D5-D9.
20. Ponikowski P, Francis DP, Piepoli MF, et al. Enhanced ventilatory response to exercise in patients with chronic heart failure and preserved exercise tolerance: marker of abnormal cardiorespiratory reflex control and predictor of poor prognosis. *Circulation* 2001; 103: 916-18.
21. Francis DP, Shamim W, Davies LC, et al. Cardiopulmonary exercise testing for prognosis in chronic heart failure: continuous and independent prognostic value from VE/VCO(2)slope and peak VO(2). *Eur Heart J* 2000; 21: 154-61.
22. Ponikowski P, Chua TP, Anker SD et al. Peripheral chemoreceptor hypersensitivity: an ominous sign in patients with chronic heart failure. *Circulation* 2001; 104: 544-9.
23. Ponikowski PP, Chua TP, Francis DP et al. Muscle ergoreceptor overactivity reflects deterioration in clinical status and cardiorespiratory reflex control in chronic heart failure. *Circulation* 2001; 104: 2324-30.

# Wpływ implantacji układu resynchronizującego u chorych z przewlekłą niewydolnością serca na adaptację układów krążenia i oddechowego do wysiłku fizycznego ocenianą za pomocą ergospirometrii

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**Streszczenie**

**Wstęp:** Głównym objawem przewlekłej niewydolności serca (CHF) jest obniżona tolerancja wysiłku fizycznego. Przypuszcza się, że jej przyczyną jest patologiczna aktywacja i upośledzona adaptacja układów krążenia i oddechowego w czasie wysiłku fizycznego.

**Cel:** Ocena wpływu implantacji dwukomorowego układu resynchronizującego (CRT) u pacjentów z CHF (III–IV klasa wg NYHA) na tolerancję wysiłku fizycznego mierzoną za pomocą ergospirometrii (CPX) i testu 6-minutowego marszu (6MWT) oraz adaptację układu krążenia i układu oddechowego do maksymalnego wysiłku fizycznego.

**Metodyka:** Analiza obejmuje 27 pacjentów (22 mężczyzn, 5 kobiet, w średnim wieku 61,2±9,1 roku) hospitalizowanych w II Klinice Choroby Wieńcowej, u których implantowano CRT z powodu zaawansowanej niewydolności serca na tle kardiomiopatii rozstrzeniowej lub niedokrwiennej. W celu kwalifikacji do wszczepienia CRT wykonywano następujące badania: echokardiografię z oceną dyssynchronii skurczu lewej komory serca, CPX z analizą gazów wydychanych oraz 6MWT. Badania kontrolne przeprowadzono w okresie 3–6 mies. od implantacji CRT. U wszystkich chorych wykonano badanie CPX składające się ze spoczynkowej spirometrii oraz próby wysiłkowej na bieżni ruchomej z analizą gazów wydychanych, ograniczonej objawami niewydolności serca. Analizowano szczytowe pochłanianie tlenu (*peak* $VO_2$, ml/kg/min), $VE/VCO_{2\ max}$, $VE/VCO_2$ slope i $VE/VO_2$ slope, pochłanianie tlenu w progu beztlenowym (AT) oraz rezerwę oddechową i sercową. U wszystkich chorych wykonano 6MWT, w którym badano odpowiedź układu krążenia na wysiłek (tętno, ciśnienie tętnicze) oraz pokonany dystans (w metrach).

**Wyniki:** Stwierdzono istotną statystycznie różnicę w *peak* $VO_2$ przed implantacją CRT *vs* po implantacji CRT dla całej grupy: 11,34±3,38 *vs* 14,56±3,99 ml/kg/min (p <0,0001) i 1,01 ±0,44 *vs* 1,4±0,55 l/min (p=0,003) oraz w wydychanym $CO_2$: 1,00±0,43 *vs* 1,43±0,67 l/min (p=0,004). Stwierdzono także istotny wzrost pulsu tlenowego z 9,65±3,39 do 13,23±5,43 ml/uderzenie (p=0,015). Zaobserwowano istotny statystycznie spadek $VE/VCO_2$ slope z 42,34±13,35 przed CRT do 34,77±6,04 po implantacji CRT (p=0,0196) oraz istotny spadek $VE/VO_2$ slope z 41,32±15,46 do 34,01±6,27 (p=0,037). Poziom $VE/VCO_{2\ max}$ uległ zmniejszeniu z 58,02±15,86 do 50,1±13,14 (p=0,009). Zmniejszył się także subiektywnie odczuwany przez chorych poziom duszności w czasie wysiłku wg skali Borga – z 4,75±0,75 do 3,67±1,15 (p=0,002). Istotnie wzrósł dystans pokonywany przez chorych w 6MWT – z 231,1±170,3 m do 367±154,9 m (p <0,001).

**Wnioski:** Implantacja CRT u chorych z zaawansowaną niewydolnością serca pozwala na istotną poprawę tolerancji wysiłku fizycznego ocenianą za pomocą ergospirometrii oraz wpływa na wydłużenie dystansu pokonywanego przez pacjentów w 6MWT. Implantacja CRT poprawia także wydolność układu oddechowego i jego adaptację do zwiększonego wysiłku. Poprawa parametrów sercowo-oddechowych i tolerancji wysiłku może być obiektywnie stwierdzona za pomocą CPX, która jest bardzo przydatnym badaniem w ocenie skuteczności terapii resynchronizującej.

**Słowa kluczowe:** niewydolność serca, układ resynchronizujący, resynchronizacja, ergospirometria, tolerancja wysiłku

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