

# Cardiac resynchronisation therapy in patients with end-stage heart failure – long-term follow-up

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## Abstract

**Background:** Cardiac resynchronisation therapy (CRT) has been shown to be effective in the treatment of patients with end-stage heart failure (HF). However, long-term results of CRT have not yet been validated.

**Aim:** To assess the sustained benefit of CRT in patients with end-stage HF at long-term follow-up. In addition, predictors of response to CRT were analysed.

**Methods:** Twenty-eight patients with end-stage HF, NYHA class  $\geq$ III ( $\geq$ II in patients with indications for ICD and echocardiographic signs of ventricular mechanical systolic dyssynchrony), left ventricular ejection fraction  $<$ 35%, QRS duration  $>$ 120 ms and left bundle branch block morphology received a biventricular device (BiV). In 27 patients LV pacing was achieved via the coronary sinus tributaries and in 1 patient an endocardial LV lead was introduced transseptally. Ten patients received an ICD-CRT device. The control group consisted of 29 patients fulfilling the criteria for ICD-CRT implantation in whom the CRT system was not implanted for various reasons. At baseline, 3 months after implantation, and then every 6 months the following parameters were evaluated: NYHA class, quality of life (QoL) score, QRS duration on surface ECG, and 6-minute walking distance. The need for hospitalisation assessed one year before and one year after implantation was compared. Follow-up was obtained up to 2 years.

**Results:** The NYHA class and 6-minute walking test were significantly improved in the CRT group after 3 months and continued to improve gradually until 24 months of follow-up. The QoL improvement at 6 months was sustained over 2 years. Hospitalisation rate due to worsening of HF decreased. One-year and two-year survival were significantly better in the CRT group than in the control group (94 and 87 vs. 80 and 73% respectively). The only predictor of clinical improvement after CRT implantation was baseline NYHA class.

**Conclusion:** Clinical improvements with CRT are progressive and sustained over 2 years of follow-up.

**Key words:** cardiac resynchronisation therapy, heart failure

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## Introduction

The demographic prognosis suggests that the most common disease in the human population in the 21<sup>st</sup> century will be heart failure (HF). In spite of enormous progress in medical therapy, HF-related mortality is still very high and many patients, especially those in more severe stages of the disease, are symptomatic despite optimal medical treatment. More than 10 years ago, cardiac pacing, called cardiac resynchronisation therapy (CRT), was proposed to restore normal synchrony of ventricular systole. The present study summarises the results of CRT use in the treatment of patients with

disturbances of intraventricular conduction and advanced HF refractory to optimal medical therapy in our centre.

## Methods

### Patients

Twenty-eight patients (CRT group) were selected, including 19 with ischaemic cardiomyopathy and 9 with non-ischaemic cardiomyopathy, who manifested impaired left ventricular (LV) performance, disturbances of intraventricular conduction, who despite optimal medical treatment still presented symptoms of severe HF (NYHA class III/IV) or had less severe HF (NYHA class II or

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II/III) qualified for cardioverter-defibrillator (ICD) implantation because of echocardiographic signs of mechanical asynchrony of ventricular systole. Ejection fraction  $\leq 35\%$  and increased end-diastolic LV dimension  $\geq 60$  mm as assessed in echocardiography were considered the indices of impaired LV function. Intraventricular conduction disturbances were defined as increase in QRS complex duration  $\geq 120$  ms ( $\geq 170$  ms in patients with a previously implanted cardiac pacemaker). Mechanical asynchrony of ventricular systole was detected if interventricular delay time evaluated in ECG was  $\geq 35$  ms.

The control group involved 29 patients who met the aforementioned criteria but did not undergo CRT system implantation for various reasons (in 11 patients implantation of CRT failed, and in the remainder there was no patient's consent or unavailability of either pacemakers or electrodes at the time of desired implantation).

### CRT system implantation

In all patients, implantation was performed under fluoroscopic guidance. A left ventricular pacing electrode introduced through subclavian vein access was eventually placed in one of the cardiac veins. The preferable site of the left ventricular pacing was the posterior, posterolateral or lateral cardiac vein. The other electrodes of the CRT system were placed in the right atrial appendage and in the right ventricle (RV) – in its apex (RVA) or on the ventricular septum close to its outflow tract. The location of the right ventricular electrode resulted from the LV electrode placement: its site was selected so as to maximise the distance between the two electrodes.

### Echocardiography

All examinations were carried out using a Sonos 2000, Hewlett-Packard equipped with a 2.0-3.5 MHz probe. Mechanical interventricular delay (IVD) was defined as the difference in pre-systolic time at the level of the aortic valve and pulmonary artery, respectively. After the CRT system was implanted in patients found in sinus rhythm, haemodynamically optimal atrio-ventricular delay (AVD) [i.e. when completion of atrial systole (A wave) took place simultaneously with initiation of LV systole] was programmed. Due to the use of various types of pacemakers (Actros DR, Actros SR, Tupos LV and Tripos LV), optimisation of interventricular delay was not possible.

### Clinical evaluation

Prior to CRT system implantation, underlying primary cardiac disease was diagnosed and the form of concomitant disorders as well as stage of HF severity according to NYHA classification was evaluated. Twelve-lead ECG (50 mm/s), echocardiographic examination (2D and Doppler) and 6-minute walking test (6MWT) were

performed. Patients also filled in a questionnaire assessing quality of life (QoL) that was developed based on the *Minnesota Living with Heart Failure Questionnaire*. It included 21 questions regarding symptoms related to HF. The scale of the answers to a given question ranged from 0 to 5 points, where '0' means the lack of a given symptom and '5' means the highest intensity of its manifestation.

In the preoperative period, a standard ECG was recorded and analysis of the parameters describing stimulation and control was carried out. Chest X-ray in PA, RAO 30° and LAO 60° projections were performed to assess the LV electrode location. Subsequent follow-up studies were repeated after 3 and 6 months and every 6 months thereafter. The shortest follow-up time in both groups was 6 months. In both groups the number of hospitalisations for all causes as well as for HF exacerbation was noted. Also the rate of all complications and events associated with pacemaker implantation was evaluated in the CRT group.

### Survival analysis

Survival of patients was assessed throughout the period from the time of enrolment to death or the last follow-up examination or phone contact with a patient. The cause of death was determined and analysis of the survival curves was performed. The shortest follow-up period was 6 months in both examined groups. Two additional CRT patients were included in the survival analysis (the total number of subjects in the CRT group was 30 patients) with a follow-up period less than 6 months. One of them died 15 days after successful CRT system implantation because of stroke and another one who 3 months after CRT implantation underwent heart transplantation. Eleven extra patients (thus the total number in the control group was 40 patients) were recruited for the analysis of the control group. They were qualified for participation in the study, but they were lost during follow-up for various reasons (data regarding these patients were obtained by phone contact or from the civil affairs office).

### Statistical analysis

Demographic and clinical data are presented as means  $\pm$  standard deviation or number and percentages. Variation of the differences between groups was estimated by means of Kruskal-Wallis non-parametric analysis of variance (ANOVA) (hospitalisation time, 6MWT),  $\chi^2$  test,  $\chi^2$  test with Yates' correction,  $V^2$  or Fisher's exact test. The choice of test depended on the actual and predicted number of subjects (the latter one in case of comparison of percentage of patients found in NYHA class  $\geq$  III). Predictors of improvement were searched for using non-parametric Spearman correlation rank test. Kaplan-Meier survival curves were drawn for each group and they were compared by means of Cox F test.

**Table I.** Demographic and clinical data of patients treated with cardiac resynchronisation therapy (CRT group) and control subjects before enrolment in the study

Parameter	CRT group (n=28)	Control group (n=29)	p
Age [years]	62±10 (40-76)	65±12 (47-63)	NS
Male gender	23	22	NS
Cardiac rhythm disturbances			
paroxysmal atrial fibrillation	3 (10%)	8 (28%)	NS
persistent atrial fibrillation	7 (25%)	3 (10%)	NS
paroxysmal ventricular tachyarrhythmias	12 (43%)	9 (31%)	NS
Previously implanted pacemaker	10 (34%)	9 (31%)	NS
VVI pacemaker	4 (16%)	2 (6%)	NS
DDD pacemaker	6 (21%)	7 (24%)	NS
Previously implanted cardioverter-defibrillator	1 (3%)	4 (13%)*	NS
Underlying cardiac disease			
ischaemic cardiomyopathy	19 (68%)	18 (62%)	NS
non-ischaemic cardiomyopathy	9 (32%)	9 (31%)	NS
muscular dystrophy	0 (0%)	2 (7%)	NS
Concomitant disease			
arterial hypertension	9 (32%)	12 (41%)	NS
diabetes mellitus	8 (29%)	11 (38%)	NS
chronic renal failure	5 (18%)	7 (24%)	NS
Conduction disturbances			
AV conduction disturbances	8 (29%)	7 (24%)	NS
LBBB	14 (28%)	11 (48%)	NS
RBBB	2 (7%)	1 (3%)	NS
RBBB+LAH	0 (0%)	2 (7%)	NS
Medical therapy			
ACE-I or ARB	26 (93%)	26 (90%)	NS
beta-blockers	23 (82%)	27 (93%)	NS
furosemide [mg/day]	98.8±73 (0-360)	78.6±87 (0-360)	NS
NYHA class ≥III	24 (85%)	14 (48%)	0.007
QRS complex duration [ms]	180.7±34 (130-240)	180.6±33 (130-240)	NS
Left ventricular ejection fraction [%]	23±4 (14-35)	25±4 (17-35)	NS
Left ventricular end-diastolic dimension [cm]	7.2±0.7 (6.0-8.4)	6.8±7.0 (6.0-10.0)	NS
Interventricular delay [ms]	44±16 (35-80)	52±26 (35-120)	NS
Follow-up time [months]	24±14 (58-8)	25±14 (80-7)	NS

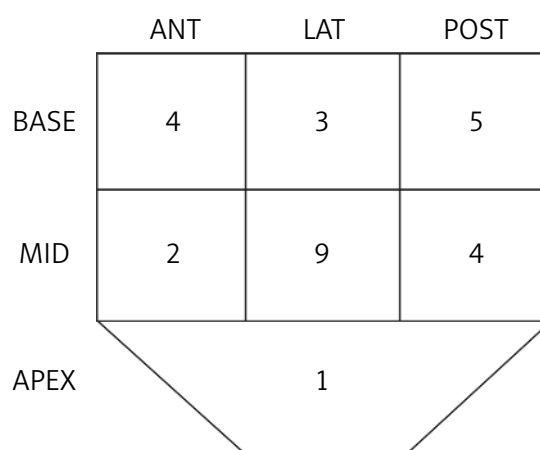
Abbreviations: LBBB – left bundle branch block, RBBB – right bundle branch block, LAH – left anterior hemiblock, ACE-I – angiotensin-converting enzyme inhibitors, ARB – angiotensin-receptor blockers  
\* 6 individuals in the control group had ICD implanted during failed procedure of CRT introduction

## Results

**Patients' clinical characteristics** are presented in Table I. Prior to study enrolment, more patients in the group treated with CRT were found in functional NYHA class III or higher. No other significant differences were noted between examined groups at baseline.

**Pacing system implantation.** Among 28 patients who underwent CRT system implantation, 10 received a biventricular ICD device. In 27 patients, an LV electrode was placed successfully in one of the CS branches. In one case, an attempt to find the orifice of the CS failed, so endocavitary LV pacing after atrial septum puncture was set up. In 7 individuals, the site of right ventricular pacing was within the RV outflow tract and in the remainder the electrode was typically placed in the RVA. Location of the LV electrode was assessed based on chest X-ray in PA, RAO 30° and LAO 60° projections and is presented in Figure 1.

**Complications in the early postoperative period** (up to 30 days following the procedure). Complications of various kinds were noted in 12 (42%) examined subjects, including 9 patients who required repeat procedure. In 1 patient pneumothorax was detected after surgery and was treated with passive drainage; in another subject haematoma in the device pocket was seen but no surgical intervention was necessary. In one case 20 days after the operation infective endocarditis was diagnosed and successfully treated with antibiotics so that there was no need for pacing system explantation. In 4 (14%) cases, dislocation of the LV electrode to the RV was noted. In the latter group of patients, successful procedures of electrode repositioning were carried out. In another 3 subjects increased threshold of biventricular pacing in CS >7.2 V/1.0 ms (*exit block*) was found and it

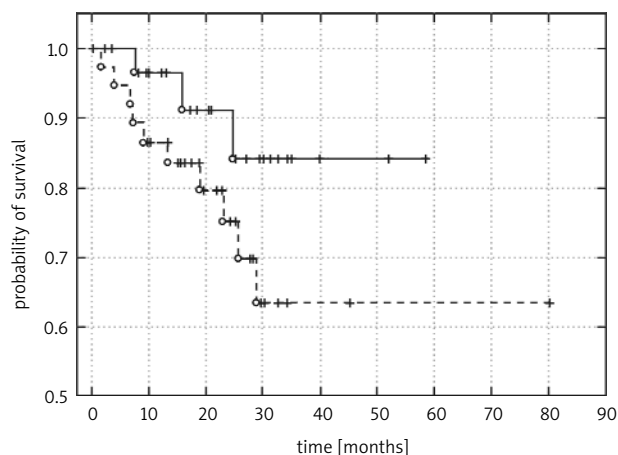


**Figure 1.** Location of left ventricular electrode in patients treated using cardiac resynchronisation therapy

Abbreviations: ANT – anterior wall, LAT – lateral wall, POST – posterior wall, BAS – basal part of the left ventricle, MID – middle part of the left ventricle, APEX – left ventricular apex

**Table II.** Death causes in the CRT and control groups

Death cause	CRT group	Control group
Heart failure deterioration	3 (10%)	8 (20%)
Sudden cardiac death	0	1 (2.5%)
Stroke	1 (3%)	1 (2.5%)
Complications following heart transplantation	1 (3%)	1 (2.5%)
Unknown reason	0	2 (5%)
Total	5 (16%)	13 (33%)

**Figure 2.** Kaplan-Meier curves displaying – probability of survival in CRT (solid line, n=30) and control (dashed line, n=40) group  
° complete, + cut

was fixed by electrode repositioning. In 2 individuals marked elevation of pacing threshold in the right atrium was detected and again a change of electrode position solved the problem.

**Complications during follow-up.** In 3 patients ineffective biventricular pacing due to late LV electrode dislocation was noted. In 1 case it resulted from electrode dislocation to the RV, and in the remaining 2 subjects within a cardiac vein. Eventually, in the group of 28 patients who underwent successful CRT system implantation, pacing was still maintained in 26 of them (92%) during follow-up of 24±14 months.

**Changes of QRS duration.** Prior to the procedure in the CRT group, QRS duration was 186±36 ms and after implantation was shortened to a mean of 171±25 ms ( $p=0.06$ ).

**Survival analysis by means of Kaplan-Meier method.** Causes of deaths in both groups are outlined in Table II. A statistically significant difference ( $p=0.002$ ) with respect to survival free from any cardiac events, defined as death from HF deterioration or sudden cardiac death (SCD), was observed (Figure 2) between the groups. Eight of 13 patients who died in the control group (62%) had RVA pacing during examination. In the CRT group, one-year

**Table III.** Percentage of patients in functional NYHA class ≥III in the CRT and control groups during successive follow-up examinations ( $\chi^2$  test)

Time [months]	N	NYHA ≥III [%]		p
		CRT group	Control group	
0	57	82.1	48.3	0.0074
3	57	21.4	55.2	0.0089
6	57	14.3	62.0	0.0002
12	43	4.6	63.6	<0.0001
18	40	13.3	71.4	0.0015
24	30	14.3	77.8	0.0023

**Table IV.** Mean result of 6-min walking distance (in meters) in the CRT and control groups during successive follow-up examinations (Kruskal-Wallis test)

Time [months]	CRT group	Control group	p
0	299±137	326±144	NS
3	340±153	298±156	NS
6	393±169	265±162	<0.05
12	404±133	278±154	<0.05
18	443±107	305±119	<0.05
24	473±129	281±190	<0.05

**Table V.** Comparison of quality of life in the CRT and control groups (Student's t-test)

Time [months]	CRT group	Control group	p
0	69.1±23.4	41.5±21.4	<0.001
6	56.9±24.4	48.3±23.1	NS
12	47.9±23.9	50.3±27.2	NS
24	43.5±25.2	59.3±32.7	NS

survival was 94% and two-year 87%, while in the control group they were 80% and 73%, respectively.

**Functional NYHA class.** In both groups, comparable proportions of patients were found in functional NYHA class III or higher. At baseline more such patients were in the CRT group. However, from the 3<sup>rd</sup> month of follow-up significantly fewer patients were found in functional NYHA class ≥III as compared to the control group and this difference was seen throughout the whole period of the study (Table III).

**6-minute walking test.** A significant difference in mean result of 6MWT was observed at 6 months after the procedure and in magnitude of distance extension in the CRT group compared with the control one. This trend was also seen in the later follow-up (Table IV).

**Quality of life.** At baseline assessed QoL was higher in the control subjects. However, during the subsequent examinations no differences with respect to this parameter were noted (Table V).

**Table VI.** Comparison of mean hospitalisation time of all causes and of heart failure deterioration in the CRT and control groups (Kruskal-Wallis test)

Parameter	Hospitalisation time [days]		p
	CRT group	Control group	
Heart failure			
one year before	19.6±15.8	9.6±16.2	0.001
one year after	4.9±9.1	15.6±17.8	0.004
All causes			
one year before	29.9±16.2	19.9±29.9	0.0007
one year after	20.3±12.4	31.8±41.4	0.41

**Hospitalisations.** In the year preceding recruitment to this study, patients in the CRT group required significantly longer in-hospital treatment both for all causes and for those related to HF deterioration. However, in the first year following enrolment average hospitalisation time due to HF was significantly shorter in the CRT group than in the control one. A similar trend was observed regarding hospitalisation time for all causes, although this difference was not of statistical significance (Table VI). In the CRT group, complications and failures associated with the use of this method (total 335 days in the whole group) caused 59% of all hospitalisations during follow-up. In 24% of the cases, hospitalisation was for HF deterioration, and in 17% was for other reasons.

**Predictors of improvement after CRT employment.** In the CRT group, clinical improvement defined as a reduction in functional NYHA classification by at least one class was observed in 17 (61%) patients. However, in 8 (29%) patients a decrease of LV end diastolic volume (LVEDV) by at least 10% was seen. The only factor predicting improvement, defined as a reduction in NYHA classification by  $\geq 1$  class, was baseline NYHA class ( $p=0.04$ ; Spearman rank correlation index 0.3836) (Table VII). No factors predicting improvement defined as a decrease in LVEDV by  $\geq 10\%$  were revealed.

## Discussion

The presented study is a summary of a two-year follow-up of patients with CRT. Until today no such extensive study dedicated to this issue has been published in Poland. Our analysis revealed that the use of CRT in patients with moderate or severe HF accompanied by intraventricular conduction disturbances led to improved clinical status, better exercise capacity and higher QoL as well as to a decrease in cardiovascular-related hospitalisation time and longer survival of patients. The results of our study broaden previous experience with CRT by longer follow-up (2 years). In some large clinical trials, outcomes after CRT implantation were evaluated during 6-month follow-up (MIRACLE, MUSTIC, PATH-CHF, In-Sync, COMPANION,

**Table VII.** Evaluation of correlation between improvement after CRT system implantation defined as reduction by  $\geq 1$  class according to NYHA classification and form of cardiomyopathy, baseline NYHA class as well as such parameters as LVEDV, LVEF, degree of mitral regurgitation, QRS complex duration or IVD and degree of decrease in these parameters after use of the CRT system

Parameter	N valid cases	R Spearman	p
Improvement & ischaemic cardiomyopathy	19	-0.2793	0.15
Improvement & non-ischaemic cardiomyopathy	9	0.2793	0.15
Improvement & NYHA class	28	0.3836	0.04
Improvement & QRS	28	0.0581	0.76
Improvement & QRS delta	28	0.0554	0.77
Improvement & interventricular delay	28	0.0809	0.68
Improvement & interventricular delay delta	28	0.18399	0.34
Improvement & left ventricular end-diastolic volume	28	0.2177	0.27
Improvement & left ventricular ejection fraction	28	-0.1122	0.57
Improvement & mitral regurgitation	28	0.0566	0.77

MIRACLE-ICD) [1-6]. Later, the results of prolonged (by half a year) follow-up regarding patients enrolled in the PATH-CHF, In-Sync and MUSTIC trials were published [1, 4, 7], although the only parameter assessed at the last 12-month follow-up examination was QoL. In the longest multi-centre CARE-HF study [8] the follow-up period was 18 months. Then this study was prolonged by a further 8 months to perform additional analysis of CRT impact on patients' mortality [9]. In our study the long-term and progressive nature of clinical improvement was shown, indicating a permanent and progressive favourable impact of CRT system implantation in patients with HF. Our findings are consistent with the two reports regarding CRT with the longest follow-up: by Stahlberg M et al. [10] (follow-up of 3 years) and Molhoek S et al. [11] (mean time of 23 months). They revealed long-term improvement with respect to parameters such as NYHA class, 6-minute walking distance and QoL.

Based on the survival curves analysis, significant differences with respect to survival between the CRT and control group were noted. This was found to be consistent with the findings of the CARE-HF trial [8], where among subjects with the CRT system an overall mortality reduction by  $>30\%$  compared to the medically treated group was observed ( $p=0.002$ ). However, in the COMPANION study [6], the use of CRT decreased the risk of death of any cause by 24%, although this result was

found to be close to the threshold of statistical significance ( $p=0.059$ ). A decreased risk of death was obvious in the case of combination of two therapeutic methods, CRT and ICD, and was 36% ( $p=0.003$ ). In our study, mortality associated with HF deterioration was 10% in the CRT group and 20% in the control group. In the CRT group no SCD cases were observed, contrary to 2.5% in the control group. In the previously mentioned CARE-HF trial, mortality related to SCD was 8 and 13% in the CRT group and 7 and 9% in the control one, respectively. The SCD rate was lower in our patients. This probably resulted from the fact that 4 (13%) individuals of the control group had undergone ICD implantation before enrolment in the study and an additional 6 subjects (25% in total) had the ICD implanted during failed procedure of biventricular device (BIV) implantation. Eventually, altogether 11 (36%) subjects in the BIV group received a CRT-ICD system that certainly decreased the risk of death of SCD. Our findings can also be explained by the longer follow-up period of our study. In the discussion of the results of the prolonged (by an average of 37.4 months) follow-up in the CARE-HF study [9], the authors suggested that ability of the CRT system to reduce the incidence of SCD could increase with time of therapy (enhanced cardiac performance as a pump, reverse remodelling).

The use of CRT markedly decreased hospitalisation time of all causes as well as for HF deterioration. These findings are consistent with the observations of other authors [1-6, 8]. The number of hospitalisations in the HF population in Poland is approximately 100 thousand per year (1995 data) [12]. It has been shown that independent risk factors of subsequent hospital admissions are previous hospitalisation due to HF deterioration, duration of HF symptoms over 18 months, ischaemic aetiology of cardiomyopathy, chronic HF and functional NYHA classes III – IV [13]. The majority of patients enrolled in our study met all aforementioned criteria and were in the group at high risk for repeat hospitalisation. Thus, reduced time of in-hospital treatment for HF deterioration due to CRT implantation deserves special attention. However, mean hospitalisation time of all causes in the CRT group during the first year following system implantation did not differ from the control group. We should pay attention to the relatively high number of complications and failures of therapy with the use of pacing that contributed to 59% of total hospitalisation time in this group. It should be expected that with increasing experience in the CRT use, the number of these failures will decrease systematically and in consequence also the necessity of hospitalisation for these reasons.

In our study the only significant factor predicting improvement after CRT implantation was functional status evaluated according to NYHA classification. Patients with more advanced HF at baseline responded better to CRT therapy. Baseline degree of mitral valve regurgitation (MR) was found to be close to statistical

significance ( $p=0.08$ ) as a predictor of clinical improvement. Patients with a higher degree of MR responded better to CRT implantation. Data in the literature regarding the importance of clinical patient status and MR in the assessment of prognosis of CRT outcome are contradictory. According to some authors, HF deterioration evaluated on the basis of NYHA classification may predict response to therapy [14]. Other studies do not support this correlation [15, 16]. However, MR severity is not predictive according to some authors [15] while others, like Diaz-Infante et al. [17], have shown that a high degree of MR was associated with poor response to CRT implantation. Contrary to the above-mentioned reports, Oguz et al. [18] and Reuter et al. [19] showed better improvement in patients with more severe MR at baseline.

Follow-up of the control group revealed interesting findings. At baseline they were found to be in better shape, including higher QoL, than patients who underwent CRT system implantation. In this group fewer patients were in NYHA classes III to IV and one year prior to enrolment they needed in-hospital treatment less frequently both for all causes and for HF deterioration than the CRT subjects. However, after 3 months of follow-up differences in the examined parameters did reverse unfavourably for the control group. In spite of optimal medical therapy they manifested a tendency towards worse clinical status, poorer exercise tolerance and worse QoL. Progression of HF symptoms was even more pronounced than observed in the MIRACLE trial in the control group treated only medically. In this study, deterioration of functional status by at least one class according to the NYHA classification was observed only in 4% of patients compared to 20% in the control group in our study.

Observed progression may result from not only natural HF course but also from the fact that 19 (68%) subjects had an implanted pacemaker or ICD and RVA pacing was used in this group. In 7 of them the rate of pacing was  $>50\%$ , so altogether in 16 (55%) individuals pacing of the apex of the RV was used throughout the whole follow-up period. Ritter et al. [20] provided evidence that RVA pacing was harmful. They evaluated retrospectively patients with mild and moderate HF who had an implanted standard system with RVA pacing and also individuals who received CRT because of severe HF. Despite the patients with RVA pacing at baseline presenting less expressed HF symptoms, after 6 months of follow-up they were hospitalised more frequently than patients in the CRT group (12 vs. 6%,  $p < 0.05$ ) and their LVEF decreased from 43 to 38% ( $p < 0.05$ ). The results of the DAVID (21) and MADIT II [22] trials also indicate clearly adverse consequences of RVA pacing in the group of patients with decreased LVEF. The findings of the follow-up of our patients confirm the harmful effects of RVA pacing. Thus, CRT system implantation should be

considered in patients with HF symptoms and decreased LVEF requiring permanent ventricular pacing.

### Study limitations

The most important limitation of this study is the fact that conventional apical right ventricular pacing was employed in some patients in the control group, which might have had an adverse impact on mortality and complication rate. The second limitation is the relatively low number of patients enrolled in our study.

### Conclusions

1. CRT pacing in patients with moderate or severe HF and intraventricular conduction disturbances leads to:
  - improvement in clinical status, tolerance of physical exercise and QoL that are progressive, indicating a permanent and progressive favourable impact of CRT,
  - prolongation of overall survival and survival free from any cardiac events,
  - decreased hospitalisation time related to HF deterioration as well as to all other reasons.
2. Baseline clinical status evaluated according to the functional NYHA classification is a predictor of improvement following CRT implantation

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# Długoterminowa obserwacja chorych z zaawansowaną niewydolnością serca po implantacji stymulatora dwukomorowego

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## Streszczenie

**Wstęp:** Niewydolność serca (HF) jest bardzo istotnym problemem współczesnej kardiologii. Jak już udowodniono, poprawę kliniczną można uzyskać dzięki zastosowaniu terapii resynchronizującej (CRT).

**Cel:** Długoterminowa ocena kliniczna efektów zastosowania CRT u chorych z zaburzeniami przewodzenia śródkomorowego i ciężką, oporną na leczenie farmakologicznie HF, a także analiza czynników predykcyjnych poprawy po zastosowaniu CRT.

**Metodyka:** Badaniem objęto 28 chorych w wieku średnio  $62,3 \pm 10,3$  roku (40–76 lat), z frakcją wyrzutową lewej komory (LV)  $\leq 35\%$ , wymiarem końcoworozkurczowym  $\geq 60$  mm oraz QRS  $\geq 120$  ms ( $\geq 170$  ms u chorych z implantowanym wcześniej stymulatorem serca), u których pomimo stosowania optymalnego leczenia farmakologicznego występowały nasilone objawy HF (III/IV klasa wg NYHA), oraz chorych z mniej zaawansowaną HF (II lub II/III klasa wg NYHA) kwalifikowanych do wszczęcia kardiowertera-defibrylatora (ICD) serca, u których w badaniu echokardiograficznym stwierdzano cechy mechanicznej asynchronii skurczu komór IVD  $\geq 35$  ms. Grupę kontrolną stanowiło 29 chorych spełniających wyżej wymienione kryteria, u których z różnych powodów nie zastosowano CRT. Minimalny okres obserwacji chorych w obu grupach wynosił 6 mies. Badania kontrolne obejmowały ocenę stanu klinicznego (klasa wg NYHA, test 6-minutowego marszu) oraz jakości życia chorych. Ponadto w obu grupach odnotowano hospitalizacje związane z HF, a także dokonano analizy krzywych przeżycia.

**Wyniki:** U 27 chorych zastosowano przezżylną stymulację LV poprzez zatokę wieńcową, a u jednego endokawitarną stymulację LV. Dziesięć osób otrzymało dwukomorowy ICD. Od 3. mies. obserwowano istotną poprawę kliniczną (zmniejszenie się liczby chorych pozostających w III/IV klasie wg NYHA – 82,1 vs 21,4%,  $p < 0,001$ ), wydłużenie dystansu pokonywanego podczas testu 6-minutowego marszu ( $299 \pm 137$  vs  $340 \pm 153$  m,  $p < 0,05$ ), a od 6. mies. poprawę jakości życia ( $69,1 \pm 23,4$  vs  $56,9 \pm 24,4$ ,  $p < 0,05$ ). W 2-letniej obserwacji poprawa miała charakter progresywny. Zastosowanie stymulacji dwukomorowej (BIV) znacząco skróciło także średni czas hospitalizacji ze wszystkich przyczyn, a także z powodu zaostrzenia HF ( $p = 0,04$  i  $p = 0,0003$ , odpowiednio). W grupie kontrolnej obserwowano tendencję do pogarszania się stanu klinicznego, tolerancji wysiłku oraz jakości życia chorych oraz wydłużania czasu hospitalizacji. Na podstawie analizy krzywej przeżycia stwierdzono znamienne statystycznie różnice w przeżywalności całkowitej, a także w przeżywalności bez incydentów sercowych między grupami BIV i kontrolną ( $p = 0,03$  i  $p = 0,002$ , odpowiednio). Jedynym istotnym czynnikiem predykcyjnym poprawy po zastosowaniu leczenia stymulacją BIV okazał się stan kliniczny oceniany wg klasyfikacji NYHA.

**Wnioski:** Stymulacja BIV u chorych z umiarkowaną i ciężką HF oraz z towarzyszącymi zaburzeniami przewodzenia śródkomorowego prowadzi do poprawy stanu klinicznego, tolerancji wysiłku fizycznego oraz jakości życia chorych. Poprawa ta ma charakter progresywny, co sugeruje trwałą i postępującą w miarę upływu czasu korzystny efekt stymulacji BIV. Zastosowanie stymulacji BIV wydłuża przeżywalność całkowitą oraz przeżywalność bez incydentów sercowych, zmniejsza częstość hospitalizacji z powodu progresji niewydolności serca, a także z wszystkich przyczyn.

**Słowa kluczowe:** stymulacja resynchronizująca, niewydolność serca

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