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Original Research Article

Upgrading Patients with Pacemakers to Resynchronization Pacing: Predictors of Success

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Abstract

The investigations of predictors of success or failure of cardiac resynchronization therapy (CRT) were studied previously. But assessment of success in patients already on dual or single pacemakers and upgraded to CRT were not extensively studied before. How to select patients in whom this may be the most optimal strategy is unclear. We sought to determine factors associated with success or failure in this group of patients who were already paced for heart block. 81 pts were subjected to upgrade to CRT implantation after being on pacemaker. The study was conducted in Germany. Data was presented as Median (Min. – Max.) for abnormally distributed data or Mean ± SD. for normally distributed data. Parameters that revealed no statistical significance in response: Age, sex, EF, diabetes, renal disease, GFR, MR, QRS duration (all above 150 msec), AF and CRT optimization. The following parameters revealed significant influence on response to CRT: Less responders with: Higher CRP, presence of TR, presence of PHN, presence of previous MI, being ischemic vs nonischemic cardiomyopathy (less responders with ischemic CM). EF improved in responders from 30±8.6 to 39.86±9.77. The findings through light on specific parameters that predict response to upgrade to CRT after usual pacemaker. It confirms the benefit of upgrading to CRT from DDD or VVI in patients with EF less than 35%.

Keywords: Heart failure, Resynchronization Therapy, CPR, Ischemic vs Non-ischemic Cardiomyopathy

INTRODUCTION

Cardiac resynchronization therapy (CRT) has a broader range of therapeutic benefits in appropriately selected patients. The improvement includes cardiac function symptoms and quality of life and reductions in HF-related hospitalizations and death (Dickstein et al., 2010; McMurray et al., 2012; Bristow et al., 2004; Cleland et al., 2005; Gervais et al., 2009; Moss et al., 2009). The investigations of predictors of success or failure of cardiac resynchronization therapy were studied previously. But assessment of success in patients already on dual or single pacemakers and upgraded to CRT were not extensively studied before. How to select patients in whom this may be the most optimal strategy is unclear. We sought to determine factors associated with success or failure in this group of patients who were already paced for heart block.

Aim

The aim of this work is to study the predictors of success or failure of upgrade of RV pacing to cardiac resynchronization therapy.

METHODS

The study included 81 patients who fulfilled the inclusion

criteria (Previous pacemaker implantation for conventional indication > 6 ms, new symptoms of heart failure, documented reduction of LVEF after RV pacing < 40%, RV pacing >40% of time) , the study was conducted in Germany. The study was conducted from January 2010 to June 2012.

Coronary angiography was done in all. Heart failure was assessed by symptoms and ejection fraction. The diagnosis of ischaemic cardiomyopathy was made by history of myocardial infarction.

All patients gave written informed consent and the study was approved by the Ethics Committee of the hospital.

Exclusion criteria

Only patients with RV pacing in who CRT implantation failed were excluded (5 patients)

How success was assessed

By improvement in NYHA class > one level at least, improvement in EF > 5% at least, improvement of LV end systolic volume by 15% at least. 6 min walk distance, if the distance increased than before CRT by > 25% (not done in all so not included in the statistics).

Device therapy

Transvenous biventricular pacemaker implantation was done using standard steps under local anaesthesia. Optimization of atrioventricular delay was done in most patients after implantation and at 3, 6 months. Transmitral Doppler was utilized for optimization. In patients with atrial fibrillation biventricular pacing was triggered by ventricular mode. Patients were followed-up in a device therapy clinic.

Study design

A clinical assessment and echocardiography was done on the day prior to implantation and at 1, 3, and every 6 months thereafter.

Clinical assessment and echocardiography: Assessments included documentation of NYHA class, transthoracic echocardiography, left ventricular volumes were estimated using Simpson's equation by planimetry of apical four-chamber views.

Follow up

Patients were followed one year after CRT implantation.

Parameters assessed were

Sex, Age, CRP, LVEF, Tricuspid incompetence, pulmonary hypertension, previous infarction, QRS duration and etiology of HF (ischemic or cardiomyopathy).

Statistical analysis of the data

Data were fed to the computer and analyzed using IBM *SPSS software package version 20.0.* Qualitative data were described using number and percent. Quantitative data were described using mean and standard deviation. Comparison between different groups regarding categorical variables was tested using Chi-square test. When more than 20% of the cells have expected count less than 5, correction for chi-square was conducted using Fisher's Exact test. Correlations between two quantitative variables were assessed using Pearson coefficient. Significance of the obtained results was judged at the 5% level. Data was presented as Median (Min. – Max.) for abnormally distributed data or Mean ± SD. for normally distributed data.

RESULTS

In tables 1-3. Of 81 cases, 24 (29.6%) were nonresponders and 57 (70.3%) were responders.
Data was presented as Median (Min. – Max.) for abnormally distributed data or Mean ± SD. for normally distributed data. Data presented in coming lines of nonresponders then responders respectively then P value:
EF: 30.17 ± 9.19 vs 30.30 ± 8.60, P=NS
Age years: 75 vs 72, P=NS
Sex: Males 16.7% vs 17.5%, P=NS
Mitral incompetence: 97.6% vs 99.4%, P=NS
Tricuspid incompetence: 100% vs 79%, P= 0.001
Pulmonary Hypertension: 77% vs 59%, P= 0.037
Previous infarction: 87.5% vs 56%, P= 0.032
Ischemic vs nonischemic cardiomyopathy: 87.5% vs 59.6%, P= 0.014
Optimization after procedure: not recorded in all cases so cannot be compared.
Atrial fibrillation: 12.5% vs 22.8%, P=NS
Rate of hospitalization during one year after procedure:
Renal function GFR: 49% vs 50%, P=NS
QRS duration msec: 180 vs 190, P=NS
Diabetes: 41.7% vs 43.9%, P=NS
CRP: 11 vs 3.35, P=0.001
Revascularization: 87.5% vs 50.9%, P=0.002 (ischemic cases and those with precious infarction were less responders than nonischemic cardiomyopathy; revascularization of course was done in these ischemic patients).

Table 1. Comparison between before and after in each of responder, no responder and total according to different parameters

	Non responder			Responder			Total sample		
	before	After	p	before	After	p	before	After	p
GFR	49.28±13.10	46.35±16.04	0.729	50.43±12.36	50.15±11.59	0.436	50.10±12.47	49.20±12.78	0.388
CRP	11(0.80 – 74)	10.5(0.8 – 74)	1.000	3.4(0.3 – 20.6)	3.6(0.3 – 20.6)	1.000	3.9(0.3 – 74.0)	4.0(0.3 – 74.0)	1.000
EF	30.17±9.19	31.50±12.13	0.741	30.30±8.60	39.86±9.77	<0.001*	30.26±8.72	37.52±11.03	<0.001*
pace	91.62±11.08	98.90±0.32	0.164	92.74±11.62	97.45±3.10	0.027*	92.41±11.40	97.91±2.64	0.007*
QRS duration	182.29±21.26	148.70±16.87	<0.001*	188.04±23.42	148.82±16.21	<0.001*	186.33±22.83	148.78±16.30	<0.001*

Normally quantitative data was expressed in mean ± SD and was compared using Paired t-test, abnormally distributed data was expressed in median (Min. - Max.) and was compared using Wilcoxon signed ranks test. *: Statistically significant at $p \leq 0.05$

Table 2. Comparison between responder, no responder according to different parameters

	Response		Total
	Non responder No. (%)	Responder No. (%)	
Age	75.83 ± 6.70	72.19 ± 8.96	73.27 ± 8.47
Sex			
Male	20(83.3%)	47(82.5%)	67(82.7%)
female	4(16.7%)	10(17.5%)	14(17.3%)
Revascularization			
0	3(12.5%)	28(49.1%)	31(38.3%)
1	10(41.7%)	15(26.3%)	25(30.9%)
2	3(12.5%)	7(12.3%)	10(12.3%)
3	8(33.3%)	7(12.3%)	15(18.5%)
DCM			
0	21(87.5%)	34(59.6%)	55(67.9%)
1	3(12.5%)	23(40.4%)	26(32.1%)
DM			
0	14(58.3%)	32(56.1%)	46(56.8%)
1	10(41.7%)	25(43.9%)	35(43.2%)
MR			
0	2(8.3%)	5(9.6%)	7(9.2%)
1	13(54.2%)	28(53.8%)	41(53.9%)
2	9(37.5%)	12(23.1%)	21(27.6%)
3	0(0.0%)	7(13.5%)	7(9.2%)
PHN			
0	5(22.7%)	20(40.8%)	25(35.2%)
1	7(31.8%)	19(38.8%)	26(36.6%)
2	10(45.5%)	10(20.4%)	20(28.2%)
Ablation0			
0	2(66.7%)	13(100.0%)	15(93.8%)
HIS	1(33.3%)	0(0.0%)	1(6.3%)
operative success			
0	1(4.2%)	5(8.9%)	6(7.5%)
1	23(95.8%)	50(89.3%)	73(91.3%)
0&1	0(0.0%)	1(1.8%)	1(1.3%)

Qualitative data were described using number and percent. Normally quantitative data was expressed in mean ± SD

Table 3. Comparison between responder, no responder according to different parameters "continue"

	Response		Total
	Non responder No. (%)	Responder No. (%)	
Devices			
CRT P	4(16.7%)	21(36.8%)	25(30.9%)
CRT D	20(83.3%)	36(63.2%)	56(69.1%)
Echo responder			
0	6(85.7%)	2(6.9%)	8(22.2%)
1	0(0.0%)	26(89.7%)	26(72.2%)
2	1(14.3%)	1(3.4%)	2(5.6%)
Clinical response 3m			
Non responder	24(100.0%)	5(8.8%)	29(36.8%)
Responder	0(0.0%)	52(91.2%)	52(64.2%)
Clinical response 1y			
Non responder	13(86.7%)	10(22.2%)	23(38.3%)
Responder	1(6.7%)	35(77.8%)	36(60.0%)
Worsened	1(6.7%)	0(0.0%)	1(1.7%)
Clinical response 2y			
Non responder	9(90.0%)	6(24.0%)	15(42.9%)
Responder	1(10.0%)	19(76.0%)	20(57.1%)
previous infarction			
Non previous infarction	3(12.5%)	25(43.9%)	28(34.6%)
previous infarction	21(87.5%)	32(56.1%)	53(65.4%)
Etiology			
ICM	21(87.5%)	34(59.6%)	55(67.9%)
DCM	3(12.5%)	23(40.4%)	26(32.1%)
Responder			
0	24(100.0%)	0(0.0%)	24(29.6%)
1	0(0.0%)	57(100.0%)	57(70.4%)
Kidney dis			
0	13(54.2%)	33(57.9%)	46(56.8%)
1	11(45.8%)	24(42.1%)	35(43.2%)

Qualitative data were described using number and percent.

Parameters that revealed no statistical significance in response: Age, sex, EF, diabetes, renal disease, GFR, MR, QRS duration (all above 150 msec), history of ablation, AF recurrence, previous pacemaker, optimization. The following parameters revealed significant influence on response to CRT: Less Responder with: Higher CRP, presence of TR, presence of PHN, presence of previous MI, being ischemic vs nonischemic cardiomyopathy (less responder with ischemic CM). EF improved in responders from 30$\pm$8.6 to 39.86$\pm$9.77

DISCUSSION

In the present study, we found that biventricular pacing through the insertion of a transvenous LV lead in previously RV-paced patients offers a remarkable benefit in symptoms, functional status and rate of hospitalizations. Also this is accompanied by an improvement in echocardiographic measurements and a decrease in QRS duration.

The results presented in this work are, in general, consistent with the published reports (Finlay et al., 2004; Lemos and Atallah, 2009; Valentina et al., 2013; Jonathan et al., 2012), and suggest that it is possible to partially reverse the harmful effect of chronic RV pacing.

In most studies, the benefits of CRT have been elucidated in patients with dyssynchrony due to an “intrinsic” LBBB, but patients with HF and previous RV-pacing systems were excluded from most clinical trials of CRT.

In the current study, beneficial treatment effects of BiV pacing were shown in patients with RV-pacing–induced dyssynchrony (paced LBBB). Patients with HF and an RV pacemaker often fulfill the current indications for CRT.

These patients may have significant interventricular dyssynchrony, although the severity and frequency of these abnormalities in this group remain poorly explored.

A number of studies have reported on the effects of upgrading from RV pacing to biventricular pacing in either the acute setting or in the short term (Adelstein et al., 2014; Sideris et al., 2014; Christophe, 2008; Tomoyuki et al., 2010). Early reports examining the feasibility of

adapting chronic RV pacemaker systems to provide biventricular stimulation showed improvements in quality of life in patients with HF, but without thoroughly assessing the echocardiographic response to resynchronization therapy.

Similar improvement in symptoms, functional capacity and quality of life emerged from additional crossover observational and retrospective studies (Sideris et al., 2014; Christophe, 2008; Tomoyuki et al., 2010)..

Other reports examining the impact of CRT upgrade on the acute echocardiographic and hemodynamic effects of biventricular pacing indicated an acute increase in EF and a reduction in intraventricular mechanical delay.

Several of these studies found overall similar improvements induced by CRT in patients having a primary implantation as compared to patients receiving an upgrade procedure after chronic RV pacing.

CONCLUSIONS

This study elucidates the benefit of upgrading RV pacing to CRT and reveals the factors affecting response. The following parameters revealed significant influence on response to CRT: Less responders with: Higher CRP, presence of TR, presence of PHN, presence of previous MI, being ischemic vs nonischemic cardiomyopathy (less responders with ischemic CM). The study confirms the benefit of upgrading to CRT from DDD or VVI in patients with EF less than 35%.

Conflict of Interest

There is no conflict of interest

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