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Original Research Article

Evaluation of left ventricular longitudinal function and synchrony after dual chamber pacemaker implantation

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ARTICLE INFO

Article history:

Received 28 May 2014

Accepted 18 November 2014

Available online 28 November 2014

Keywords:

Biomedical electronics

Dyssynchrony

Myocardial deformation imaging

Dual chamber pacemaker

ABSTRACT

Background and objective: To evaluate left ventricular (LV) longitudinal function and dyssynchrony mechanisms after dual chamber pacemaker implantation.

Materials and methods: The speckle tracking imaging technique was used for quantification of global longitudinal function of the left ventricle and for dyssynchrony evaluation before pacemaker implantation and after 3-month follow-up. The study group consisted of 98 patients with conventional indications for dual chamber pacemaker implantation.

Results: Speckle tracking echocardiographic methods and image postprocessing revealed impairment of global longitudinal strain and significant LV dyssynchrony derived from 12 basal and mid-septum segments usually untraceable with conventional echocardiographic methods. Despite good physical performance and ejection fraction, global longitudinal strain significantly decreased in all patients from -15.08 ± 0.46 to -13.56 ± 0.5 ($P < 0.05$) as well as mitral annulus movement decreased from 11.57 ± 2.41 to 8.46 ± 1.74 cm/s ($P < 0.001$) and from 12.55 ± 2.75 to 10.78 ± 2.82 mm ($P < 0.001$). It was expected that patients with dual chamber pacemaker will develop inter- and intraventricular dyssynchrony, but our study showed that pacing lead position did not prevent from LV dyssynchronisation and only changed the mechanism.

Conclusions: Global longitudinal strain and LV dyssynchrony assessment enables us to detect early signs of LV dysfunction. Mechanisms of dyssynchrony development will be useful for pacemaker programming choices in order to prevent further dyssynchronisation.

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Peer review under responsibility of Lithuanian University of Health Sciences.



<http://dx.doi.org/10.1016/j.medici.2014.11.010>

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1. Introduction

Dual-chamber (DDD/R) pacing was developed two decades ago, to restore atrioventricular (AV) synchronization in patients with AV block and represented a significant technological advance at that time. Multiple studies have demonstrated the hemodynamic superiority of AV sequential pacing over single ventricular pacing (VVI/R). A properly timed atrial systole improves stroke volume through the Frank-Starling mechanism. Higher left ventricular (LV) end-diastolic pressures and volumes – higher systolic and mean blood pressures and lower right atrial and pulmonary capillary wedge pressures have been reported with AV synchronous pacing [1]. A variety of invasive and noninvasive hemodynamic studies have documented a 10% to 53% improvement in cardiac output with AV sequential pacing compared with VVI pacing [1,2].

These generally consistent improvements in cardiac output led to conclusions that AV sequential pacing would reduce the risk of heart failure, reduce mortality, and improve quality of life [1]. Also DDD/R was described as the physiological pacing mode.

Despite this, research data in patients with pacemakers for sick sinus node dysfunction or AV block provide increasing evidence showing that dyssynchronization of ventricular electrical activation and contraction, induced by right ventricular pacing (RV) worsens long-term cardiac morbidity and mortality.

The risk of heart failure is increased even in hearts with initially normal pump function and in case of part-time ventricular pacing. These epidemiologic data fit with knowledge from decades of pathophysiological research, indicating that RV pacing creates abnormal contraction, reduced pump function, causes hypertrophy and ultrastructural abnormalities [2].

The aim of our study was to evaluate mechanism of LV remodeling and dyssynchronisation by using 2D echocardiography with speckle tracking imaging.

2. Materials and methods

The study group consisted of 98 subjects with a mean age of 70.51 ± 13.46 years. All of them were admitted to the Clinic of Cardiology, Hospital of Lithuanian University of Health Sciences, due to conventional indications for dual chamber pacemaker implantation: sick sinus node syndrome or second to third degree AV block.

Before procedure and at 3-month follow-up, physical examination, electrocardiography, 6-minute walk test (6-MWT), and echocardiography were performed and evaluated by using conventional and speckle tracking imaging (STI) techniques. Only patients with certain (at least 90%) right ventricular pacing percentage were selected for further analysis. Patients with lower ventricular pacing could misrepresent LV remodeling mechanisms.

The patients were divided into two groups: 46 patients (45.1%) with apical ventricular lead position (first group) and 52 patients (54.9%) with mid-septum ventricular lead position (second group). Lead positioning was not predefined before pacemaker implantation – a decision was made by a surgeon regarding anatomical situation.

2.1. Conventional echocardiography

Echocardiographic technique and calculations of morphometric parameters were performed in accordance with the recommendations of The American Society of Echocardiography 2005 [3–5]. The biplane Simpson's rule was used for calculation of global LV ejection fraction (EF). To evaluate longitudinal left ventricle function we used measurement of mitral annular longitudinal movement assessed by M-mode and by tissue Doppler imaging (TDI).

2.2. Interventricular and intraventricular dyssynchrony

Interventricular dyssynchrony represents the discordance between the times of right ventricular (RV) and LV contraction. Pulsed wave (PW) or continuous wave (CW) Doppler images of aortic and pulmonary flow velocities were used to measure the interventricular mechanical delay (IVMD), which includes recording of LV outflow tract (apical 5-chamber view) and RV outflow tract (parasternal short-axis view of the great vessels) and calculating the difference in time between ECG-derived Q wave onset and the onset of LV outflow and the time between the onset of Q and the onset of RV outflow. These time intervals respectively reflect LV and RV pre-ejection period (PEP). IVMD values of >40 ms and values of LV PEP of >140 ms are considered as pathological [6,7].

Intraventricular dyssynchrony was evaluated by using two methods. First one was M-mode-derived septal-to-posterior wall motion delay (SPWMD), i.e., the difference in timing of septal and posterior wall contraction [7]. The SPWMD is the difference between the time from the onset of ECG-derived Q wave to the initial peak posterior displacement of the septum, and the time from the onset of QRS to the peak systolic displacement of posterior wall. SPWMD >130 ms was considered pathological. Second method was based on STI techniques which measure the standard deviation of the averaged time-to-peak-strain (TP-SD) of 12 LV basal and mid-segments obtained from the three standard apical views: a TP-SD of >60 ms was considered as pathological [8].

2.3. Automated single speckle tracking imaging

For 2D speckle tracking echocardiography analysis we used Vivid 7 (GE Vingmed Ultrasound AS, Horten, Norway) equipment. Tissue harmonic images were scanned at long-axis apical three standard apical views with the M3S probe. The mean frame rate was 60 frames per second (range 40–80). Data were stored on the hard disc of the echocardiographic machine, and transferred to a workstation (EchoPAC PC, GE Vingmed) for offline analysis. For further analysis LV was divided into 6 long axis segments in each view.

The system calculates mean global strain and strain rate (SR) values for all predefined LV segments.

2.4. Statistical analysis

Statistical analysis was performed with software SPSS version 20.0 (IBM SPSS, Inc., Chicago, IL, USA).

A P value less than or equal to 0.05 was considered as statistically significant.

All parametric data were expressed as the mean and standard deviation (SD). The Student's *t* test was used for comparison of quantitative sizes of two independent samples. The chi-square test was used for comparing frequencies of qualitative and nonparametric variables. Pearson correlation coefficients were obtained to describe relations for parameters of different methods.

3. Results

The main clinical and echocardiographic parameters are presented in [Table 1](#).

All patients significantly improved their physical performance as assessed in the 6-MWT: from 209.01 ± 37.45 to 564.86 ± 14.09 m after 3 months of DDD/R pacemaker implantation ($P < 0.001$). This can be easily explained by decreased physical activity and quality of life due to symptomatic bradycardia before pacemaker implantation.

Global EF evaluated by Simpson biplane method remained the same in all patients after 3-month follow-up ($P < 0.001$).

Despite good physical performance and EF, global longitudinal strain (GS) significantly decreased in all patients from -15.08 ± 0.46 to -13.56 ± 0.5 ($P < 0.05$).

Also there was a decrease in peak systolic velocity of mitral annular longitudinal movement measured by PW TDI and in mitral annular longitudinal movement (MAM) measured by M-mode: from 11.57 ± 2.41 to 8.46 ± 1.74 cm/s and from 12.55 ± 2.75 to 10.78 ± 2.82 mm respectively ($P < 0.001$). These data show that LV dysfunction usually is underestimated in standard clinical practice.

Inter-ventricular dyssynchrony evaluation revealed no significant change after 3 months. But all patients developed various degree of intra-ventricular dyssynchrony – TP-SD derived from 12 LV segments increased from 35.27 ± 3.66 to 48.51 ± 3.61 ms ($P < 0.01$). Even if TP-SD significantly increased

in all patients – intraventricular dyssynchrony remained between physiological normal limits.

3.1. Correlation between methods

As mentioned above, there were used four different methods to evaluate LV longitudinal function – LV EF, MAM derived from M-mode, MAM derived from PW-TDI and GS assessed by using STI techniques. There was a strong correlation between these four methods at *P* value of 0.01. Each method is eligible to evaluate global longitudinal function, but STI techniques gives opportunity to assess not only global but also precise local myocardium segment not in qualitative but in quantitative values.

The same must be mentioned about different methods used to evaluate intra-ventricular dyssynchrony. A correlation between SPWMD (M-mode) and TP-SD (STI techniques) was detected at *P* value 0.05. Interestingly, the SPWMD data derived from M-mode showed no significant difference after 3 months, but TP-SD derived from twelve basal and mid segments revealed tendency to intra-ventricular dyssynchrony after pacemaker implantation. This fact also can be explained by more accurate quantitative myocardium dyssynchrony evaluation in particular segments by using STI techniques vs. M-mode measurements.

3.2. Right ventricular pacing site impact

Patients were divided into two groups: first one consisted of patients with apical RV lead position and second group, with mid-septum RV lead position. Lead position was selected by doctor who was performing pacemaker implantation regarding anatomical situation.

There was no significant difference between those two groups with different RV lead position while evaluating their clinical status, physical performance during 6-MWT or echocardiographic parameters. Only few parameters have implications for further research.

Table 1 – Main clinical and echocardiographic parameters of patients with dual chamber pacemaker.

Variable	Before pacemaker implantation	3 months after pacemaker implantation	P
6-MWT, m	209.1 (37.45)	564.86 (14.09)	0.001
BSA, m ²	1.98 (0.35)	1.88(0.40)	NS
EF, %	49.5 (5.01)	50.5(4.50)	NS
GS, %	-15.08 (0.46)	-13.56 (0.50)	0.043
MAM, mm	12.55 (2.75)	10.78 (2.82)	0.001
MAM, cm/s	11.57 (2.41)	8.46 (1.74)	0.001
SPWMD, ms	88.06 (31.21)	107.56 (38.90)	NS
IWMD, ms	16.05 (21.05)	18.85 (10.99)	NS
TP-SD, ms	35.27 (3.66)	48.51 (3.61)	0.005

Values are mean (standard deviation).

NS, not significant; 6-MWT, 6-minute walk test; BSA, body surface area; EF, left ventricular ejection fraction; GS, global longitudinal strain; MAM, mitral annulus longitudinal movement; SPWMD, septal-to-posterior wall motion delay; IWMD, interventricular mechanical delay; TP-SD, standard deviation of the averaged time-to-peak-strain.

Table 2 – Parameters of patients of group 1 – RV apical lead position (n = 46).

Variable	Before pacemaker implantation	3 months after pacemaker implantation	P
6-MWT, m	265.63 (98.43)	543.75 (99.09)	0.003
BSA, m ²	1.87 (0.45)	1.9 (0.50)	NS
EF, %	52.5 (5.0)	54.5 (4.5)	NS
GS, %	-16.54 (2.18)	-15.32 (1.58)	0.006
MAM, mm	11.86 (1.98)	10.78 (2.82)	0.014
MAM, cm/s	11.13 (2.55)	10.75 (3.51)	0.014
SPWMD, ms	89.37 (30.21)	82.50 (14.38)	NS
IWMD, ms	6.38 (11.74)	14.25 (10.45)	NS
TP-SD, ms	47.60 (21.42)	65.13 (16.75)	0.005

Values are mean (standard deviation).

NS, not significant; 6-MWT, 6-minute walk test; BSA, body surface area; EF, left ventricular ejection fraction; GS, global longitudinal strain; MAM, mitral annulus longitudinal movement; SPWMD, septal-to-posterior wall motion delay; IWMD, interventricular mechanical delay; TP-SD, standard deviation of the averaged time-to-peak-strain.

Table 3 – Parameters of patients of group 2 – RV mid-septal lead position (n = 52).

Variable	Before pacemaker implantation	3 months after pacemaker implantation	P
6-MWT, m	166.00 (98.00)	580.95 (40.93)	0.001
BSA, m ²	1.99 (0.55)	1.85(0.38)	NS
EF, %	48.20 (12.50)	50.29(12.50)	NS
GS, %	-15.23 (3.12)	-11.62 (2.76)	0.008
MAM, mm	13.07 (1.18)	10.81 (2.25)	0.001
MAM, cm/s	11.90 (2.80)	8.62 (1.63)	0.014
SPWMD, ms	87.05 (32.67)	126.67 (41.02)	0.001
IWMD, ms	23.43 (22.9)	22.45 (10.24)	NS
TP-SD, ms	25.86 (18.32)	35.84 (16.43)	0.001

Values are mean (standard deviation).
 NS, not significant; 6-MWT, 6-minute walk test; BSA, body surface area; EF, left ventricular ejection fraction; GS, global longitudinal strain; MAM, mitral annulus longitudinal movement; SPWMD, septal-to-posterior wall motion delay; IWMD, interventricular mechanical delay; TP-SD, standard deviation of the averaged time-to-peak-strain.

Different parameters of both groups are presented in Tables 2 and 3.

The first group of patients developed pathological intra-ventricular dyssynchrony after 3 months of observation – measured TP-SD was >60 ms, but this group had initial significantly higher level of LV dyssynchrony. Also a theoretical approach suggests that apical lead position causes not only longitudinal but radial dyssynchrony, increased untwisting rate and impaired torsional LV behavior [9].

Second group of patients revealed significant septum to posterior wall motion delay. This parameter was neither valuable in the general patients group nor between patients with apical lead position. This phenomenon can be explained by altered cardiac mechanics due to lead position in mid-septum. Probably implanted lead is suspending normal wall movement and leads to septum delay. This mechanism leads to increasing intra-ventricular dyssynchrony, even though mid-septum lead position was believed to normalize LV dyssynchronization caused by RV pacing [9].

4. Discussion

It is known that large randomized clinical trials in sinus node disease or atrioventricular block have reached a consensus that despite maintenance of AV synchrony, DDD/R pacing does not reduce death, compared with VVI/R and has surprisingly modest or even negative benefits for progression of heart failure and atrial fibrillation, that emerge only after many years of follow-up [10].

The Canadian Trial of Physiological Pacing (CTOPP) was reported in 2000. In this trial 2568 patients (mean age 73 years) with symptomatic bradycardia requiring permanent pacing, were randomized to atrial (AAI, AAIR, DDD, or DDDR) or ventricular pacing groups (VVI or VVIR) and monitored for an average of 3 years. There were no differences in the incidence of heart failure hospitalization [11].

The DAVID (The Dual Chamber and VVI Implantable Defibrillator) trial tested the hypothesis that DDD/R pacing

at rate of 70 bpm would enable optimal heart failure management and reduce heart failure hospitalization and death risk compared with ventricular-only backup pacing (VVI, 40 beats/min) [12]. The study was terminated prematurely and unexpectedly because of an excess of heart failure and deaths in the DDD/R pacing group.

Because of data mentioned above, DDD/R pacing with large percentage of ventricular pacing (more than 90%) was accepted as a simple clinical model for myocardial remodeling. DDD/R pacing creates the same ECG pattern as left bundle branch block (LBBB). Electrical activation and contraction geometry in LBBB are close to right ventricle pacing model with unchanged atrioventricular synchrony.

Despite these provocative observations, clinical experience indicates that the majority of pacemaker patients tolerate chronic right ventricle pacing. In the MOST (The Mode Selection Trial) study, only about 10% of patients had new heart failure onset during follow-up and were more likely to have a lower ejection fraction, myocardial infarction, and a worse New York Heart Association functional class compared with patients who did not experience heart failure. But also it means that from 1000 patients who have conventional indications for DDD/R pacing and normal ejection fraction, one hundred of them are at risk of heart failure due to right ventricle pacing.

Our goal is to recognize patients, who will worsen from conventional DDD/R pacing. And if we do so, what pacing model should be chosen – cardiac resynchronization therapy (even with normal ejection fraction) or DDD/R system, which should be adapted for patients evaluating not only electrophysiological, but also hemodynamical aspects. Our results showed that all patients developed subclinical LV dysfunction; therefore, it is still unclear who will develop clinical heart failure and observations are continued.

The main question is the mechanism of LV dysfunction. Animal studies have shown that the mechanical effect of asynchronous electrical activation is important, because the various LV segments differ not only in time of onset of contraction, but also in quality of contraction [13]. Contraction disturbances due to right ventricular pacing have been proven not only in animal studies, but also in patients – perfusion defects and wall motion abnormalities have been shown in up to 65% of the patients with angiographically normal coronary arteries, exposed to chronic RVA pacing [14]. Modern echocardiographic techniques such as strain, strain rate and single speckle tracking have the same value for research of new criteria to evaluate risk factors of heart failure progression. Our research showed several criteria for early dyssynchrony evaluation which can be followed by subsequent DDD/R system optimization.

We evaluated only patients with high ventricular pacing rate (≥90% of right ventricle pacing) and results revealed interventricular dyssynchrony in patients with different pacing sites (right ventricle apex vs. mid-septum position). The main difference was the mechanism for developing dyssynchrony.

There are some limitations in our research. The first is that we evaluated only longitudinal LV function. Authors in two-dimensional speckle tracking echocardiography field demonstrated that right ventricle apical pacing impairs left ventricle

twist and untwisting properties [15] so this should be next step in our this stage analysis.

The second limitation is focus only on a single heart chamber, meanwhile left atrial or right ventricle function also may contribute to heart failure development.

And finally, at this research stage we just observed LV function changes without any intervening in to everyday pacemaker follow-up and programing, based on mostly timing and capture parameters. There is a possibility to optimize AV delay and to influence LV function through preload modulation, thereby atrial function could be preserved and maximized [16]. Despite automated specialized algorithms for AV optimization which are provided by various pacemaker industries, there are some reliable echocardiographic methods for AV optimization and we are willing to use them in next our research stage.

5. Conclusions

Global longitudinal strain and LV dyssynchrony assessment enables us to detect early signs of LV dysfunction in patients with dual chamber pacemaker.

This study revealed that all patients with dual chamber pacing, despite pacing site and good clinical performance, develop a decrease in global longitudinal ventricular strain, left ventricular long axis dysfunction and an increase in intra-ventricular dyssynchrony.

More accurate studies could give a hint for pacing strategy selection and heart failure prevention.

Conflict of interest

The authors state no conflict of interest.

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