

Influence of DDD rate response pacing with integrated double sensors on physical efficiency and quality of life

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Received 19 April 2008; accepted after revision 25 July 2008; online publish-ahead-of-print 18 August 2008

KEYWORDS

Rate response pacemaker;
Quality of life;
Cardio-pulmonary
exercise test

Aims The aim of this study was to evaluate whether the use of a double sensor gives additional benefits for patients in improving physical efficiency as well as quality of life (QoL) as compared to the accelerometer sensor alone.

Methods and results The presented research is a prospective, randomized, single-blind clinical trial. Double-sensor (accelerometer and minute-ventilation) pacemakers (Guidant, Pulsar Max DR) were implanted in 20 patients with sinus node dysfunction (SND) and chronotropic incompetence. After randomization, patients were placed in one of two groups: 1, only the accelerometer sensor was activated; 2, both sensors were activated. After a 3-month follow-up, an initial cardio-pulmonary exercise test was performed, after which the patients were placed in the opposite group for a further 3 months. Finally, the second tests were performed. In 75% of the patients an improvement in QoL was observed in the double-sensor group ($P = 0.0242$) when compared with the single-sensor group. The addition of a ventilating sensor had no influence on the duration of exercise test (A: 11 ± 3.19 vs. B: 11 ± 2.92 $P = 1.0000$). The parameters of cardio-pulmonary exercise tests recorded in situations A and B before exertion, and 6 minutes after exertion were not statistically different.

Conclusion The use of double-sensor pacemakers does not improve physical efficiency; however, it does improve QoL.

Background

Chronotropic incompetence is defined as the inability of the sinus node to react adequately with an increase in heart rate to exercise or other metabolic stress.^{1,2} For patients suffering from this disease, rate-response pacemakers (AAIR, VVIR, and DDDR) were invented.^{3–5} The key element of such pacemakers is their activity sensor(s). The most common types of sensors include: accelerometer, minute-ventilation, or those that operate based on QT measurement. Accelerometer sensors are used most often due to their low cost and ease of programming.^{6,7} Unfortunately, their sensors have some disadvantages, e.g. lack of acceleration in the case of increased metabolism without vibration of the body. Joining two different types of sensors in a single pacemaker to fully use their advantages and eliminate defects solved this problem. Many companies offered this kind of solutions. An example of one of these pacemakers is the Pulsar Max DR model 1270 (Guidant,

USA), which is equipped with two sensors (accelerometer and minute-ventilation) that work together. This type of device should theoretically ensure more 'physiological' steering of the frequency of heart rhythm (HR) than the traditional rate-response pacemakers with accelerometer sensors. The disadvantages of this solution are higher power consumption, reduced lifespan, and higher price. Additionally, patients who have these types of pacemakers implanted need follow-up visits more often.

The analysis of respiratory gases during cardio-pulmonary exercise (CPx) tests in patients with implanted pacemakers plays an essential role in the objective evaluation of physical efficiency during work in different modes of pacing. An example of this kind of cardio-pulmonary parameter is the ability of the body to take up oxygen through— $\dot{V}O_2$ max—maximal oxygen consumption (aerobic capacity). This is the more stable and credible parameter that describes physical efficiency during the exercise. Another useful parameter recorded during CPx tests is EQ VE/ $\dot{V}CO_2$ ventilatory equivalent ratio for carbon dioxide. All analysed CPx parameters are presented in Table 1.^{8–11}

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Table 1 Analysed cardio-pulmonary parameters together with units and abbreviation used in the text

Abbreviation	Units	Explanation
T_{Exercise}	min	Time of duration of exercise test
M Load	Watt	Maximum load during exercise test
VO ₂ max (peak)	mL/kg/ min	Maximal oxygen consumption (aerobic capacity) during exercise test
VO ₂ AT	mL/kg/ min	Submaximal oxygen consumption during exercise test
EQ VE/VCO ₂	–	Ventilatory equivalent for carbon dioxide
R VE/VCO ₂	–	Factor R for ventilatory equivalent for carbon dioxide
VE/VCO ₂ peak/ rest	–	Relation of ventilatory equivalent ratio for carbon dioxide at the top of exercise to the rest

Some aspects of life and health are very difficult to estimate with the help of objective investigations, especially when they concern the ability to function normally and efficiently at home, with the family and at work. Determining the importance of these subjective aspects of physical and psychological health led to the creation of the term quality of life (QoL) as well as the tools to evaluate it. The choice of a suitable questionnaire for a given population with implanted pacemakers is very difficult. The main problem is connected with the specificity of this group of patients. The Minnesota Living with Heart Failure Questionnaire (MLWHFq) could be useful in cases where the clinical symptoms of chronotropic incompetence are similar to those of circulatory failure.^{12,13}

Rapid technological progress means that innovative models of pacemakers with new activity sensors have been introduced, as well as models with combinations of sensors. In the literature on the subject, there is a lack of objective clinical research evaluating the usefulness of these kinds of solutions.

The aim of the study was to evaluate whether the use of the double sensors in the Pulsar Max DR (Guidant, USA) gives additional benefits for patients such as improvement of physical efficiency as well as QoL when compared with the single accelerometer sensor. An additional purpose was to evaluate whether the QoL in patients studied correlated with the results of CPx tests.

Methods

Study population

This trial was a prospective, randomized clinical study. Twenty patients were included (14 women, 6 men) aged 62.7 ± 10.3 years and hospitalized in the Electrocardiology Department between 2003 and 2005, suffering from symptomatic sinus node dysfunction (SND) with co-existent chronotropic incompetence. In three of the patients included (15%), transient atrioventricular block I/II degree was also confirmed. Only patients with the classic form of chronotropic incompetence where the increase in HR during effort was <75% of the maximum HR for a given age (220 minus age in years) were included. In 16 patients (80%) arterial hypertension was observed, in 8 (40%) coronary heart disease, and in 12 (60%) paroxysmal atrial fibrillation. Of those patients included in the study,

diabetes was confirmed in 3 patients (15%), 10 patients (50%) were overweight, and 4 suffered from obesity (20%). For the patients included in the study, the degree to which a patient was overweight or obese was determined using weight and height to calculate their 'body mass index' (BMI). The following criteria were used:

- BMI 18.5–24.9 Healthy weight
- BMI 25.0–29.9 Overweight
- BMI 30 or higher Obese

Ethical consideration

The study was approved by the Local Bioethical Committee (Silesian Medical University; research no. NN-6501-21/1/05) and conducted in accordance with the Helsinki Declaration. Patients volunteered to participate in the study. Spoken and written informed consent was obtained.

Exclusion criteria

- Lack of patient agreement form
- Symptomatic heart failure (NYHA class II or higher)
- Coronary arterial disease (CCS class II or higher)
- Significant problems related to mobility that made it impossible to perform the exercise test
- Chronic obstructive pulmonary disease
- Mental disorders
- Active neoplastic disease
- Participation in a different clinical trial
- Pregnancy or lactation

Scheme of the research

A Holter ECG, echocardiographic examination, and CPx test using Jaeger treadmill to calculate chronotropic incompetence were performed on each patient qualified for the study before pacemaker implantation. Pulsar Max DR pacemakers (Guidant, USA) with Synox SX leads (Biotronik, Germany) were implanted in all of the patients. Pacemaker implantation was performed using standard procedures, and 2 days after implantation, both sensors were activated. At the same time, optimal programming was performed for each patient. During the first follow-up visit (1 month after implantation), if the pacemaker was working properly, after the CPx test, randomization was done. All patients were randomly placed in one of the following so-called 'situations':

- Situation A: patients with a DDDR pacemaker using an accelerometer sensor.
- Situation B: patients with a DDDR pacemaker using both accelerometer + minute-ventilation sensors.

After a 3-month observation period, each patient was requested to fill in the MLWHFq questionnaire and a CPx test was also performed. Subsequently, the patients were moved into the opposite group for the next 3 months. Finally, the QoL questionnaire was filled in and CPx tests were performed once again. Patients were not informed which situation they were in during the research.

Quality of life

To evaluate QoL, a 21-question Minnesota questionnaire (MLWHFq) was used. Questions in this questionnaire refer to the different activities of everyday life. The answers to each question the patient answered defined the intensification of given symptoms, as well as the degree to which the patient could not participate in these activities. Each answer had to be evaluated on a scale of 1–6—the higher the number of points, the less the possibility of

freely performing the action in the patient's subjective opinion. Moreover, each patient answered five additional questions relating to mobility, self-sufficiency, common actions, pain, and depression, each of which was awarded points from 1 to 3. The patient's score on the MLWHFq indicated the patient's subjective opinion about either the improvement in their QoL and its deterioration.

Cardio-pulmonary exercise test

Cardio-pulmonary exercise tests were performed on a Jaeger treadmill (Marquette 2000 Series) by using a modified Bruce protocol. Both tests were performed under the same conditions (in the morning after a light breakfast), while undergoing the same pharmacological treatment without any change in dosages of medications being used. In each case, it was a maximal test—this means that the moment a patient felt shortness of breath that would make it impossible to continue to exercise, the test was stopped (6–8 points on the Borg scale). The HR, blood pressure, and an ECG during the exercise test were monitored.

Pacemaker programming

The basic parameters of pacing (the basic frequency, atrioventricular delay, and maximal frequency) were optimized for each patient after the first month of clinical observation and were not changed between the first and second exercise tests. The optimum configuration of sensors was programmed after the end of trial.

Statistical consideration

Statistical calculations were done using Statistica 6 (StatSoft Inc., USA, Polish version). All statistical analyses were performed using small group tests. Statistical significance was calculated using a multi-factorial analysis. The Student's *t*-test was used for parametric data and the Wilcoxon test for non-parametric data. To compare groups with and without improvement in physical activity or QoL in situations A and B, Mann–Whitney's *U* test was used. Correlations of physical activity with QoL were obtained using Pearson's tests.

Results

The comparison of cardio-pulmonary exercise tests in situations A and B

The results of both CPx tests (in situations A and B) were in the patients' subjective feeling of their maximum efforts, which was expressed as the approximate score on the Borg scale (A: 7.14 vs. B: 7.23, $P=0.76486$) as well as the almost identical values of the respiratory factor RER (1.07 ± 0.12). The parameters of CPx tests recorded in situations A and B before exertion and 6 min after exertion were not statistically different (both during *t*-test analysis as well as Wilcoxon test). Comparison of the average values of the analysed parameters at the peak of the exertion in situations A and B are presented in *Table 2*. None of the presented parameters did showed statistically significant changes. The addition of a ventilating sensor had no influence on the duration of exercise test (A: 11 ± 3.19 vs. B: 11 ± 2.92 , $P=1.0000$). In 13 patients, when both sensors were activated (situation B in relation to A), an improvement of physical efficiency was confirmed, deterioration was observed in 6 patients, and a lack of any change in 1 patient. The improvement of average physical efficiency was observed in women more often than men, but did not reach a statistically significant level in the bilateral Fisher test ($P=0.3201$).

The evaluation of quality of life using the MLWHFq in situation A and B

Changes in the QoL in situations A and B are presented in graphic form in *Figure 1*. The results showed a significant decrease in the number of points at the 3-month follow-up when compared with the single accelerometer sensor (A: 54.65 ± 16.67 vs. B: 47.25 ± 15.11 , $P=0.0242$; Wilcoxon test), which indicates an improvement in the QoL in the subjective opinion of patients studied. An improvement in QoL in situation B was observed in 75% of the group studied, when compared with situation A. An analysis of regress executed for factors that have an influence on changes QoL in situation B in relation to situation A showed that none of the factors of regress had reached the statistical significance (Mann–Whitney *U* test).

In *Figure 2*, the results of the comparative analysis of the groups without improvement and with improvement of QoL in situation B are presented. Patients who obtained more benefits are characterized by a younger age, lower BMI, a longer duration of the exercise test, larger maximum load, and larger maximal oxygen consumption. However, the above-mentioned differences were not statistically significant.

Correlation of quality of life changes with the results of exercise tests

An analysis of the correlation between QoL changes at the 3-month follow-up in patients with both sensors activated (situation B) with the results of exercise tests (the analysis of correlation and the regress by Spearman's method) did not show statistical changes for any of the identified relationships. An analysis of multiple backward regress did not show a statistical influence of the cardio-pulmonary parameters in situations A and B in relation to the QoL results.

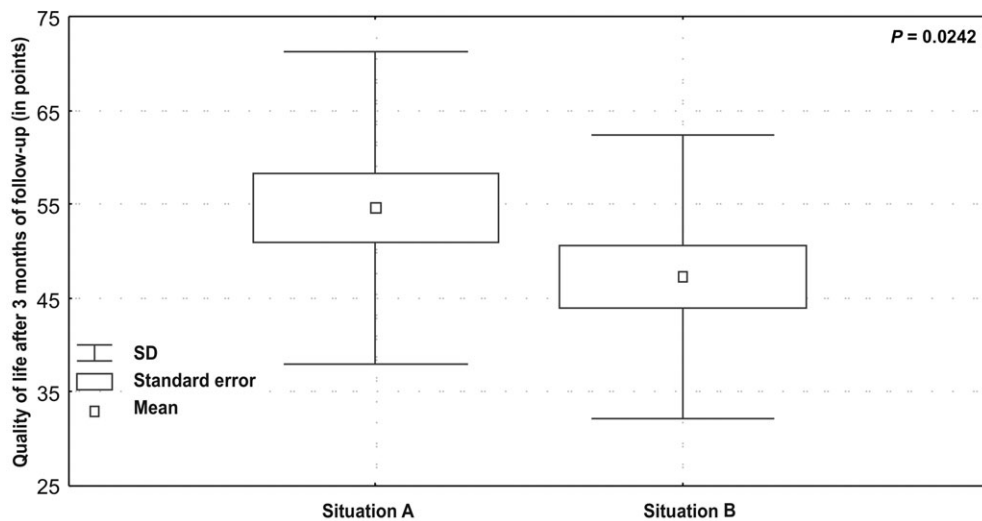
Discussion

A review of the literature on the subject shows that chronotropic incompetence remains a problem. This influences the development of new activity sensors in rate-response pacemakers, or sometimes even a combination of sensors in order to allow for a more physiological growth of HR in situations of the increasing metabolic demand of the organism. However, to date, an ideal solution does not seem to exist. Example of pacemakers with both sensors integrated have been presented by many manufacturers (Medtronic—Legend Plus, ELA Medical—Twin Trace, and Guidant—Pulsar Max, Pulsar Max II and Insignia). There is a lack of complex research evaluating the influence of double-sensor pacemakers on QoL as well as on the physical activity of patients with SND accompanied by chronotropic incompetence. This is why the authors decided to undertake research in this area.

An analysis of the CPx tests in the group with both sensors activated showed that of the seven recorded parameters used to evaluate physical efficiency, one parameter remained the same, two showed an insignificant decrease in physical efficiency, and four showed a slight improvement in physical efficiency. It is possible to conclude that the activation of the double sensor did not bring about significant improvement in physical efficiency as determined by a treadmill test for the patients studied. A possible reason for this might be that in the majority of the cases while the patient was walking on the treadmill, the vibration of

Table 2 Comparison of average values parameters analysed in this trial on the top of exercise in the A and B situations

Measured parameters on the top of exercise	Situation A	Situation B	P (Wilcoxon)
Heart rhythm (min^{-1})	138.55 \pm 16.94	140.60 \pm 22.29	0.4878
Systolic pressure (mmHg)	164.50 \pm 23.03	169.40 \pm 27.65	0.7234
RER	1.07 \pm 0.12	1.07 \pm 0.12	1.0000
Minute-ventilation (L/min)	50.09 \pm 18.80	49.99 \pm 26.45	0.9747
Time of exercise (min)	11 \pm 3.19	11 \pm 2.92	1.0000
M load (Watt)	155.5 \pm 61.59	158.0 \pm 77.48	0.4630
VO ₂ max (mL/kg/min)	22.33 \pm 6.35	21.62 \pm 6.90	0.2049
VO ₂ AT (mL/kg/min)	20.58 \pm 4.31	20.24 \pm 5.1	0.9588
EQ VE/VCO ₂	30.45 \pm 4.27	30.17 \pm 3.78	0.2471
R VE/VCO ₂	28.62 \pm 3.82	28.12 \pm 3.35	0.4009
VE/VCO ₂ peak/rest	0.84 \pm 0.08	0.83 \pm 0.19	0.7227

**Figure 1** Average values \pm standard deviation ($X \pm SD$) on the scale of MLWHFq after 3 months of follow-up.

whole of the body was high and were correctly recorded through the accelerometer sensor, so that the acceleration of the HR was adequate for the intensity of the exertion. The use of the second (minute-ventilation) sensor caused the HR to accelerate more smoothly, but it had no significant influence on the parameters obtained during the CPx test. The smoother acceleration during exertion could, however, have an influence on the patients' feelings, which can be translated into an improvement of mood noted on the questionnaire about QoL.

The significant subjective improvement of QoL registered on the Minnesota questionnaire was independent from the improvement of physical efficiency observed when both sensors were working simultaneously. More advantages were confirmed in younger patients with a double-sensor device, who achieved large maximal loads during exercise tests and were characterized with high peak oxygen consumption. In this group of patients, cardio-pulmonary parameters do not usually improve significantly. It seems, therefore, that the subjective improvement of QoL mainly in the group of younger, active patients, and in good physical condition may be caused by the fact that these individuals usually perform a wide variety of physical activities. They are also usually more active in their emotional life.

One of the most important recent researches is a Dutch multi-centre, prospective, single-blind study that was

performed on patients by van Hemel *et al.*¹⁴ The research was performed in three phases: 3 months sensor off, 2 months minute-ventilation sensor on (to learn the intrinsic rhythm) and finally 2 months with either an accelerometer sensor or a minute-ventilation sensor. A different QoL questionnaire was used (Aquarel questionnaire) in contrast to the one used in our study (Minnesota questionnaire). Both of these questionnaires are, however, fully acceptable to evaluate QoL. The authors concluded that pacemaker implantation itself strongly improves QoL. They did not confirm any additional advantages in QoL whether single- or dual-sensor pacing was used.¹⁴

On the basis of the gathered material, the Dutch authors came to the conclusion that in patients with standard indications, permanent rate response pacing of the heart equipped in a single-activity sensor improves the QoL. In additional, a second sensor does not significantly improve QoL in the initial months after implantation. This statement, however, is in contradiction with the results obtained in this study. The divergence of results might possibly be explained by the different situations being compared and the use of different tools to evaluate QoL. The influence of sensors was not estimated on physical efficiency in this trial.

In 1996, Sulke published the preferences of 10 patients according to the sensor used.¹⁵ VVIR pacemakers with a single sensor were compared with a combination of sensors

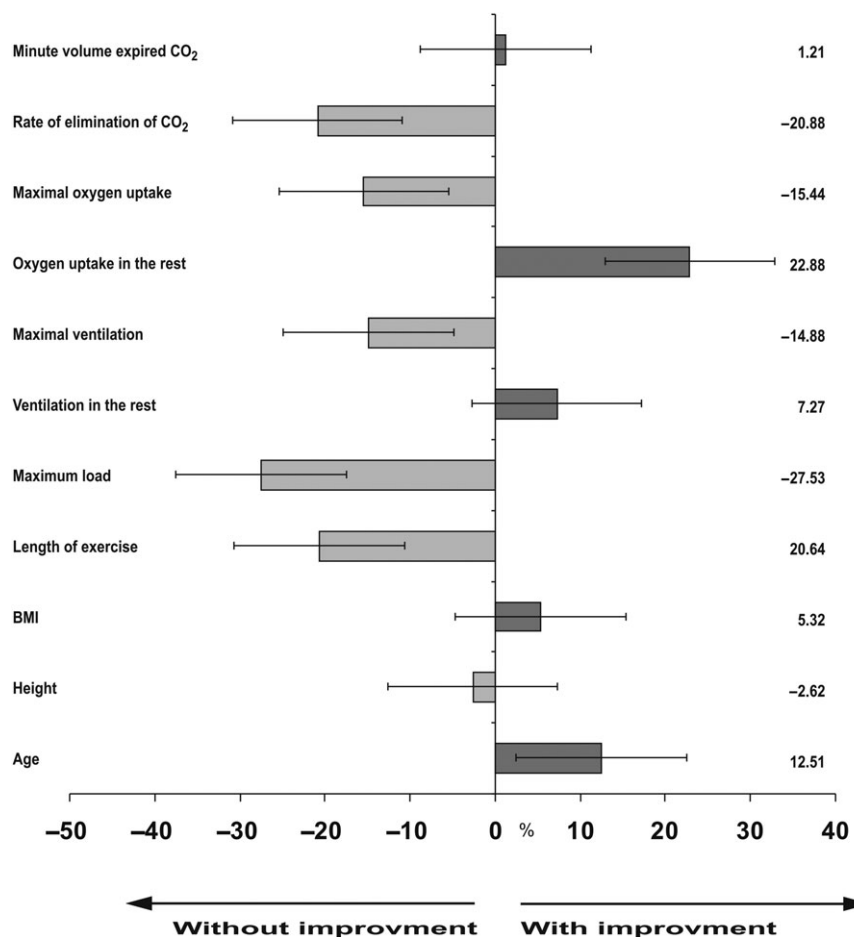


Figure 2 Relative differences between groups with and without an improvement.

(accelerometer and minute-ventilation). The results did not confirm any improvement in QoL with both sensors activated. The authors concluded that the use of a double sensor does not provide additional benefits; however, it increases the costs of treatment, as well as making the process of follow-up more difficult and time-consuming. Only the subjective opinion regarding mood was used without making use of any of the generally accepted QoL questionnaire. Exercise tests performed by those patients showed the superiority of VVIR pacing. However, the differences were not statistically significant. In contrast to our research, British authors used VVI/VVIR pacing. A different method of pacing significantly influences QoL, which has already been shown in multi-centre researches such as MOST and CTOPP.^{16,17} The results, nevertheless, agree with regard to the range of influence of sensors on the efficiency of exertion.

Lascault *et al.*¹⁸ from the Saint Denis Centre investigated 12 patients with DDDR pacemakers working in either double-sensor or single-sensor mode (accelerometer or minute-ventilation), in which cardio-pulmonary tests as well as an evaluation of QoL were performed. Only a tendency to improve physical efficiency when both sensors were activated was observed (which is comparable to the results set forth in this paper); however, the QoL evaluated by the French authors did not improve significantly.

In January 2006 in PACE, the results of a multi-centre DUSISLOG trial under the direction of Padeletti *et al.*¹⁹ were published. It was the first large trial of this type

whose main aim was to evaluate the potential advantages of using double-sensor pacemakers. Physical efficiency was evaluated by means of a 6 min walk test as well as QoL after using the DDDR double sensor (accelerometer and minute-ventilation) for 3 months in relation to the single sensor (accelerometer or minute-ventilation). Physical efficiency as well as QoL with a device with a single sensor was very similar; however, activation of both of them did not produce additional benefits. In conclusion, the authors confirm that in a majority of the cases, the single sensor allows the patient to obtain satisfactory results. It is possible that only intensified chronotropic incompetence in a chosen patient population can expect additional advantages from the use of double-sensor pacemakers. This is fully comparable with our results and conclusions.

The review of literature on the effectiveness of rate response pacing in patients with chronotropic incompetence shows the necessity for additional research to find new solutions.

Study limitations

A small group is a limitation of the research presented. This limitation has an unfavourable influence on the obtained results. This is caused by the fact that it is very difficult to find patients with SND and chronotropic incompetence in order to create a homogenous research group. Other researchers also are faced with this kind of problem. Most

researchers usually include 10–20 patients. Only large multi-centre study materials have more than 100 patients.^{14,19}

Conclusions

The study presented showed that using double sensors (accelerometer and minute-ventilation) in pacemakers like the Pulsar Max DR does not bring any additional, objective benefits in the improvement of physical efficiency during cardio-pulmonary tests when compared with the accelerometer sensor. It was not proven that in the group with subjective improvement in QoL, physical efficiency was also significantly improved.

Funding

Research grant from the Medical University of Silesia.

Conflict of interest: none declared.

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