Correlation Among Closed Loop Stimulation, Cardiopulmonary Capacity, and Quality of Life

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Summary

Improving patient's quality of life (QoL) is currently one of the major goals for the development and optimization of cardiac pacing. The Closed Loop Stimulation (CLS) sensor system integrates the pacemaker into the autonomic nervous system, rendering it sensitive to physical and mental stress. To evaluate CLS and its relationship to QoL and vital capacity (VO_{2max}), we designed a prospective, randomized, controlled, double-blind, crossover study that included patients with sinus node disease and implanted Inos^{2+} CLS pacemakers. The patients were randomized to receive DDD or DDD-CLS pacing. The first evaluation was performed after 3 months and included the application of a QoL Short-Form-36 (SF-36) questionnaire and an ergospirometric test. After the examinations, the modes were crossed over. Three months after the mode crossover, a new evaluation was performed with the same parameters. Student's t-test and ANOVA statistical methods were applied for validation of the data. Fifty patients with an average age of 62 ± 8 years, among them 27 male, were included. According to the SF-36 QoL questionnaire, the patients with DDD-CLS demonstrated a significant improvement of the physical and emotional aspects (p-value < 0.05). The comparison between DDD-CLS and DDD modes with respect to the indices of vital capacity (obtained by the ergospirometric testing) such as maximum oxygen consumption, myocardial oxygen consumption, and cardiac output showed a significant difference in favor of DDD-CLS pacing (p-value < 0.05). CLS provides a pronounced difference in heart rate, allowing a natural physiological answer to physical and emotional stress, thus improving not only tolerance to maximum exercise but also QoL.

Key Words

Closed Loop Stimulation (CLS) sensor system, chronotropic incompetence, ergospirometric test, quality of life

Introduction

Although cardiac arrhythmias can be effectively managed by cardiac pacing, pacemaker patients may still be faced with some restrictions in their daily lives. A failure to reproduce normal sinus function will likely reduce quality of life (QoL) in patients with sinus node disease (SND), requiring application of a rate-adaptive pacing system. The latter can improve hemodynamic (and possibly neurohumoral) responses during exercise, symptomatology, and QoL in SND patients.

The Closed Loop Stimulation (CLS) sensor system has been developed to integrate the pacemaker into the natural cardiovascular control loop using myocardial contractility monitoring [1]. Myocardial contractility is supposed to be the most suitable parameter for rate-responsive pacing [2]. The CLS system monitors continuously myocardial contractility and converts intrinsic information into rate regulation [3]. Several studies [3-5] have defined this concept as a feedback of current heart rate, rendering CLS very sensitive to physical and mental stress. The interaction between CLS and the autonomic nervous system directly via circulatory centers causes heart rate variations similar to those in healthy individuals [6].

Several studies have demonstrated good cardiopulmonary performance in CLS patients during treadmill testing [5,7-9], and one study has reported on improvements in patients' QoL with respect to the pre-implantation score [10]. No study has examined potential correlation between improvement in QoL and enhancement in the vital capacity (VO_{2max}) in patients treated with CLS. The main goal of our study was to evaluate the cardiopulmonary performance during treadmill exercise in chronotropic incompetent patients treated with CLS. The secondary goal was to correlate the impact of CLS on patients' vital capacity and QoL.

Materials and Methods

The investigation was designed as a prospective, randomized, double-blind, crossover trial (Figure 1). The study protocol was approved by the institutional review committee. All patients gave their written informed consent before enrollment.

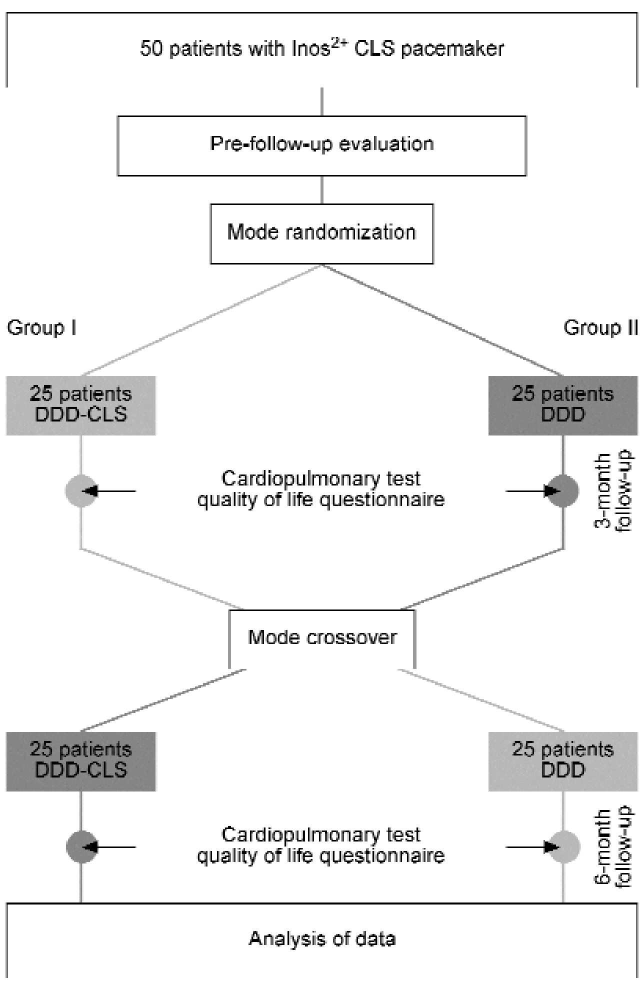

Figure 1. Study design and follow-up flowchart.

Study Population

Fifty patients with SND and implanted $Inos^{2+}$ (Biotronik, Germany) DDD-CLS pacemakers participated in the study. The mean age of the patients was 64 ± 8 years; 54% were male. Baseline physical and additional examinations were performed prior to the study. The patients were in NYHA functional class I or II, all physically active, and had normal left ventricular systolic function according to the Doppler echocardiography. No patient suffered from a pulmonary disease or any condition that might limit his or her exercise performance.

Follow-up Schedule

After verifying pacemaker functional integrity, the pacing mode was randomized to DDD (group I) or DDD-CLS (group II) with maximum pacing rate of 150 beats/min in all patients. Three months after mode randomization, a cardiopulmonary exercise test was performed to assess patients' physical capacity and exercise tolerance. The patients then completed the SF-36 QoL questionnaire, supervised by personnel unaware of the programmed pacing mode and exercise test results. At the end of the QoL examination, the mode was crossed to DDD-CLS in group I and to DDD in group II. Three months after mode crossover, the functional integrity of the pacemakers was verified, a new cardiopulmonary test was performed, and the SF-36 questionnaire was completed in the same way as at the previous follow-up.

Cardiopulmonary Exercise Test

The cardiopulmonary exercise test consisted of a symptom-limited treadmill exercise. Before the test, patients were instructed how to walk on a treadmill and breath while being connected to the spirometry system. The speed was increased by (1.3 km/h) every 2 min starting with 2.7 km/h, without changing the grade of the treadmill of 10%. Patients who had to interrupt at least one of the exercise tests due to angina, intermittent claudication, or arrhythmias were excluded from the comparative analysis. Because of low specificity in detecting ischemia in our patients, changes of the ST segment in a surface ECG during exercise were not regarded as signs of myocardial ischemia. These changes were not considered as criteria for interrupting the test when they occurred without chest pain. Expiratory gases were analyzed with a Medical Graph System 2001 analyzer

(Medical Graph System, USA). Cardiac output was obtained from maximum oxygen consumption according to Hossack [18]. According to the American Heart Association and American College of Cardiology, chronotropic incompetence is defined as the inability of the heart to increase its rate sufficiently during exercise to reach two standard deviations from the expected increase.

Short-Form-36 (SF-36) QoL Questionnaire

The SF-36 (Medical Outcomes Trust, USA) is a multipurpose, short-form health survey with only 36 questions. It yields an eight-scale profile of scores (Figure 2 modified by Ware [11]) as well as physical and mental health summary measures. Accordingly, the SF-36 has been useful in comparing general and specific populations, differentiating the health benefits resulting from a wide range of treatments, and screening individual patients [12]. Among the most frequently studied conditions evaluated via the SF-36 are cardiovascular diseases [12]. The eight health concepts were selected from the 40 concepts included in the Medical Outcomes Study (MOS) [13]. The concepts chosen represent those that are most frequently measured in widely used health surveys as well as those most affected by disease and treatment [11]. Reliability and validity estimates for physical and mental summary scores usually exceed 0.80 [11,14].

Statistics

All explanatory data are given as the mean ± 1 standard deviation (SD). The paired Student's t-test and the McNemar's chi-square test were used to analyze differences in mean values for continuous and categorical variables, respectively. Linear regression was used to verify the correlation between cardiopulmonary test results and QoL scores. A p-value < 0.05 was considered statistically significant. The analysis was performed with the STATA statistical software version 7.0 (STATA Corporation, USA).

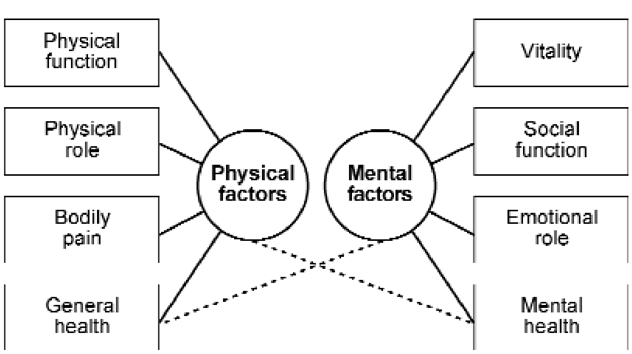

Figure 2. SF-36 scales measure physical and mental health components.

Results

The comparative results for the DDD-CLS and DDD modes during cardiopulmonary testing are provided in Table 1. There was a significant difference in favor of the DDD-CLS mode with respect to maximum oxygen consumption, myocardial oxygen consumption, cardiac output, chronotropic deficit, and chronotropic reserve (p-value < 0.05). The improvement in maximum exercise capacity with DDD-CLS pacing is also illustrated in Figure 3. Due to individual differences in exercise capacity, the number of patients completing each step decreased with the severety of exercise. The SF-36 QoL scores were more favorable during CLS pacing, with respect to both physical and mental aspects (Figures 4-6). Figure 8 indicates that the positive improvement in vital capacity (VO_{2max}) during physical exercise was often associated with a better QoL score.

	DDD	DDD-CLS	p-value
Chronotropic deficit (beats/min)	22.1 ± 18	10.1 ± 8	0.001
Chronotropic reserve (beats/min)	44.9 ± 19	68.1 ± 16	0.003
Maximum heart rate (beats/min)	118.2 ± 21	143.3 ± 19	0.001
Cardiac output (l/min)	13.2 ± 3	14.2 ± 4	0.018
MVO_{2max} (ml/kg/min)	24.1 ± 8	28.3 ± 7	0.007
VO_{2max} (ml/kg/min)	29.7 ± 9	34.2 ± 12	0.004

Table 1. Intraindividual comparison of cardiopulmonary test results for the two modes. Chronotropic reserve = maximum heart rate – heart rate at rest; chronotropic deficit = (220 – age/years) beats/min – maximum heart rate;VO_{2max} = maximum oxygen consumption per body weight; MVO_{2max} = myocardial oxygen consumption, respectively.

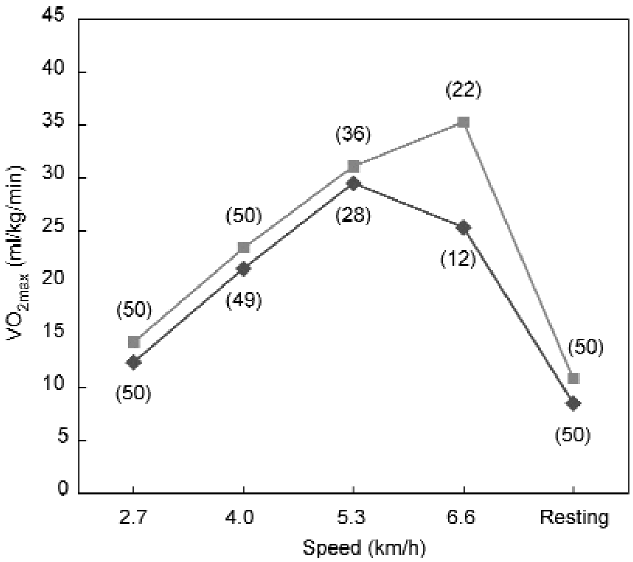

Figure 3. Comparison of the maximum vital capacity in the DDD-CLS mode (upper line) and DDD mode (bottom line) during treadmill exercise. The number of patients at each treadmill stage is shown in brackets. The treadmill speed was increased by 1.3 km/h every 2 min, starting from 2.7 km/h. The grade was 10% at all stages.

Discussion

Many studies have validated the importance of cardiopulmonary testing to evaluate chronotropic answers in patients with SND [15,16]. It is well known that conventional DDDR pacemakers with simple artificial sensors are unable to re-establish the complex cardiovascular function in SND patients adequately. The insufficient increase in heart rate during exertion in pacemaker patients with SND can potentially cause dyspnea, palpitations, and other symptoms. Consequently, the patient's QoL deteriorates. Physicians should optimize conventional, open-loop systems by completing extensive programming of several rate-adaptive parameters. By comparing different rate-adaptive pacing sensors, Malinowski [17] showed that most single- and dual-sensor controlled systems have difficulties in determining an appropriate pacing rate in at least one type of physical or mental stress. In contrast, the CLS system provided heart rates comparable to normal patients without SND.

The current study has shown a significant improvement of vital capacity in patients with DDD-CLS pacing systems compared to patients with DDD pacing. The improvement is reflected in a better cardiopulmonary performance. The difference between the two pacing modes with respect to exercise testing could result in a significant improvement of patients' QoL, which means an enhanced heart rate response during physical and mental stress.

Kuly et al. [9] have compared CLS pacing with conventional DDD pacing during treadmill tests. Their findings show that the CLS system provides physiological rate regulation and intensifies cardiopulmonary performance in chronotropically incompetent patients. In comparison to our study, Kuly did not link the exertion tolerance to an improvement in patients' QoL. Another multicenter study has researched the best CLS pacing adaptation (without any need of special programming [4]) to physiologic demands during exercise

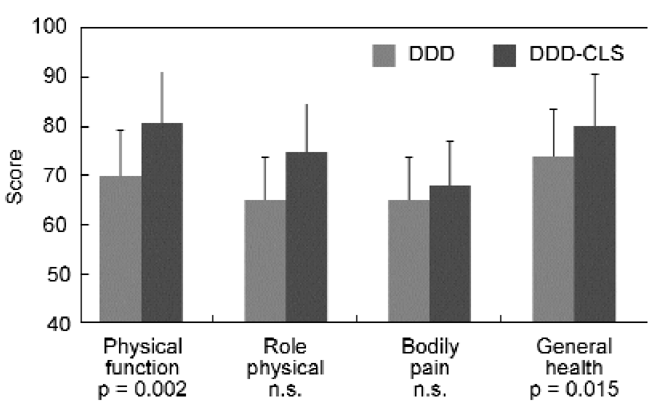

Figure 4. Comparison of SF-36 physical health scores for the two modes (a higher value is more favorable). Corresponding p-values are indicated; n.s. = non-significant.

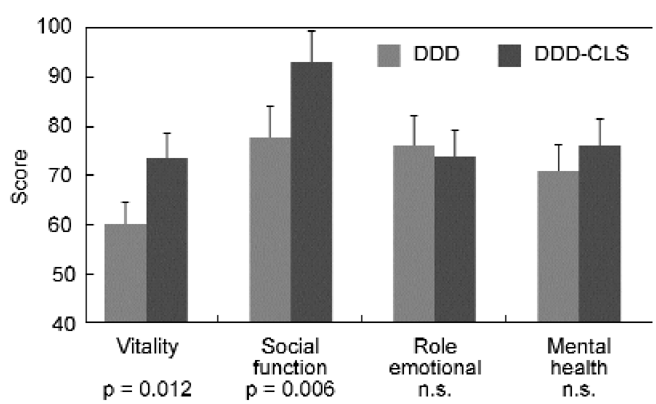

Figure 5. Comparison of SF-36 mental health scores for the two modes (a higher value is more favorable). Corresponding p-values are indicated; n.s. = non-significant.

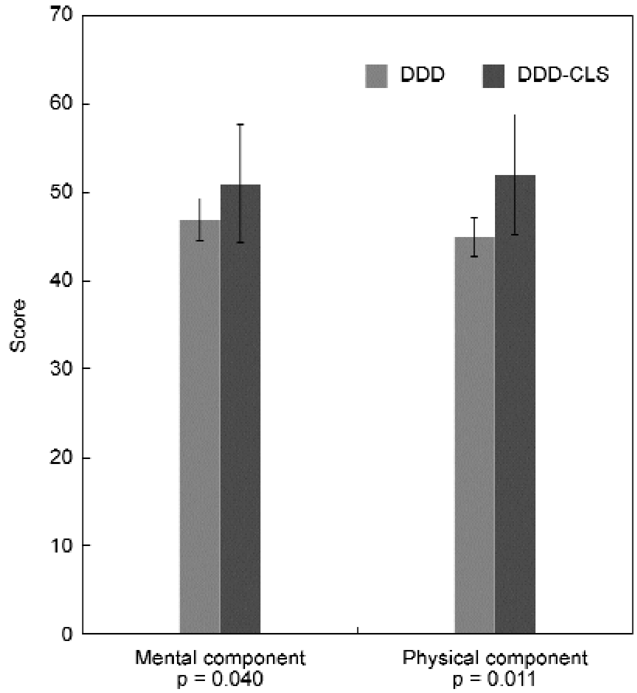

Figure 6. Comparison of mental and physical components of the SF-36 score for the two modes (a higher value is more favorable). Corresponding p-values are indicated.

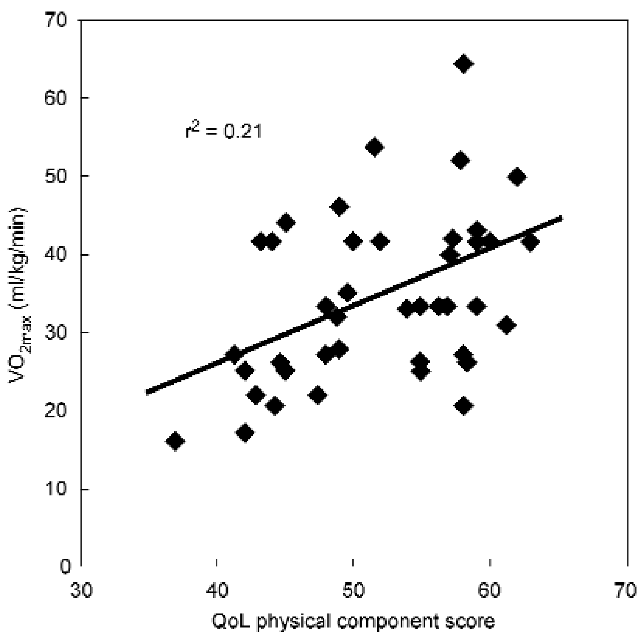

Figure 7. Linear regression test indicates a correlation between the physical component in the SF-36 score and vital capacity (VO_{2max}) during treadmill test.

tests. The CLS system proved to be effective in maintaining intrinsic circulatory regulation and integrating the pacemaker into the natural control system, thus enabling the heart rate to be managed by the autonomic nervous system (ANS). Some studies using CLS and heart rate variability have proven that upgrading autonomic heart modulation improves the capacity of the cardiovascular system as well [6].

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