Evaluation of Closed Loop Stimulation through Symptom-Limited Exercise Testing of DDD-CLS versus DDD Pacing

S. KULY, V. SCHIBGILLA*, U. HARTUNG, S. MANG, M. WILHELM, M. SCHLEGEL, W. G. DANIEL
University of Erlangen-Nuremberg, Medical Clinic II, Erlangen, Germany
* University of Würzburg, Clinic Coburg, Medical Clinic II, Coburg, Germany

Summary

Since the development of rate-adaptive pacing almost 20 years ago, a variety of different sensor principles such as motion detectors and accelerometers have been invented to control the pacing rate according to the patient's need. The Closed Loop Stimulation of the Inos² CLS pacemaker is a new approach to rate regulation. This system offers the advantage of directly monitoring the action of the natural control loop on the myocardium and thus integrating the rate regulation of the Inos² CLS into the cardiocirculatory control system. The aim of this study was to evaluate quantitatively the clinical benefit of Closed Loop Stimulation in chronotropic incompetent patients. Thirteen patients implanted with an Inos² CLS pacemaker were enrolled in this study. The patients had to perform a symptom-limited treadmill test at two consecutive follow-up examinations. The first examination was performed with the pacemaker set to the non-rate regulative DDD mode. The second examination was conducted two weeks later with the pacemaker set to the rate regulating DDD-CLS mode. With the pacemaker set to the DDD-CLS mode, we found a general increase in peak exercise performance, VO_2, and in the maximum achieved heart rate. In DDD-CLS mode, the mean achieved heart rate increased from 83 ± 9 bpm to 111 ± 12 bpm. VO_2 increased from 15 ± 3 ml/kg/min to 18.5 ± 4 ml/kg/min, and the maximum achieved workload increased from 72 ± 18 watt to 109 ± 21 watt. These results demonstrate that CLS provides physiological rate regulation and increases exercise tolerance and the cardiopulmonary performance of chronotropic incompetent patients.

Key Words

Closed Loop Stimulation, symptom-limited exercise testing

Introduction

The development of rate-adaptive pacing almost 20 years ago has revolutionized cardiac pacing [1]. Rate-adaptive pacing has become a standard therapy for bradycardiac, chronotropic incompetent patients. The clinical benefit of rate-adaptive pacing is well established and there is ample of evidence that rate-adaptive pacing enhances exercise tolerance in these patients [2-5,11,12].

The performance of many modern rate-adaptive pacemakers is based on the analysis of extracardiac signals such as motion, acceleration, or respiratory minute volume. Dual-sensor systems have been developed to overcome some of the problems encountered with single-sensor pacemakers [4,6]. These systems blend external signals (motion or acceleration) with more physiological information such as respiratory minute volume or QT-interval. However, despite the progress in technology and the computational power of pacemakers, even these very sophisticated systems lack some of the functionality of the cardiocirculatory system's golden standard [4].

Closed Loop Stimulation (CLS) represents a new approach in rate regulation. The CLS system permanently monitors the contractile state of the myocardium and converts the intrinsic information into rate regulation. Since the contractility of the myocardium is modified by the action of the cardiocirculatory system, the regulation of CLS is coupled directly to the cardiocirculatory system and thus integrated into the natural control loop. Ruppert et al. [10] demonstrated the sensitivity of CLS to the Valsalva maneuver, indicating a direct action of the baroreceptor reflex on the rate regulation of the CLS. During Valsalva, the CLS regulated the heart rate properly and mimicked the known rate regulation of healthy subjects. Malinowski [4] reported appropriate rate regulation of the CLS system under varying ambulatory conditions. A quantitative clinical evaluation of the clinical benefit of CLS pacing under defined and reproducible conditions is of major importance for clinical application. Here, we report first the clinical results of our study which show the impact of CLS pacing on the exercise performance of chronotropic incompetent patients.

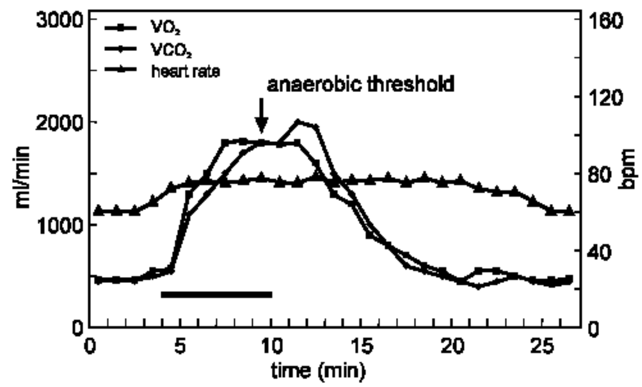

Figure 1. Symptom-limited treadmill test with the patient in DDD mode, same patient as in Figure 2. The solid bar indicates the exercise duration. For further explanation see text.

Methods

Thirteen patients (5 m; 8 f; mean age 71.3 ± 8.2 years) participated in the study and received an Inos² CLS pacemaker (Biotronik, Germany). Indications were chronotropic incompetence combined with intermittent or high-degree AV-block. Patients were required to perform a symptom-limited treadmill protocol with the pacemaker set either to the non-rate-regulative DDD mode or to the rate-regulative DDD-CLS mode. The first examination was conducted in the DDD mode with the basic pacing rate set to 60 bpm in all patients. The second one was conducted two weeks later in the DDD-CLS mode. The basic pacing rate was set to 60 bpm and the maximum closed-loop rate was programmed to 120 bpm to 140 bpm according to the patient´s need. The treadmill protocol used in this study followed the Alt protocol [13] with a stepwise increase in workload of about 25 watt every two minutes. A gas-analyzer (CPX Medical Graphics, USA) was used to monitor oxygen consumption (VO_2) and carbon dioxide production (VCO_2). The heart rate (bpm) was recorded continuously via conventional ECG.

Results

All patients enrolled in this study showed a general increase in cardio-pulmonary performance with the pacemaker set to the rate-regulating DDD-CLS mode. Figure 1 and 2 show the results of one patient with the pacemaker set to the DDD mode (Figure 1) and to the DDD-CLS mode (Figure 2). In the DDD mode, this patient achieved a peak exercise performance of about 75 watt. At rest, the heart rate was 60 bpm; it increased slightly at the beginning of the exercise and reached a plateau of about 80 bpm at 25 watt. The VO_2 increased with increasing workload and reached a plateau of 1700 ml/min at a workload of 50 watt. VCO_2 increased and crossed VO_2 at an exercise performance of about 75 watt, indicating that the patient reached the anaerobic threshold. At that stage, the patient experienced the first symptoms of dyspnea and terminated the test. With the pacemaker in the DDD-CLS mode, this patient achieved a higher heart rate, a higher VO_2, and a higher peak exercise performance. As shown in Figure 2, the heart rate increased steadily as the workload increased and reached a maximum of about 130 bpm two minutes after exercise cessation. In the CLS mode, the peak exercise performance was at 150 watt. The VO_2 reached a plateau of 2150 ml/min at 75 watt and was thus about

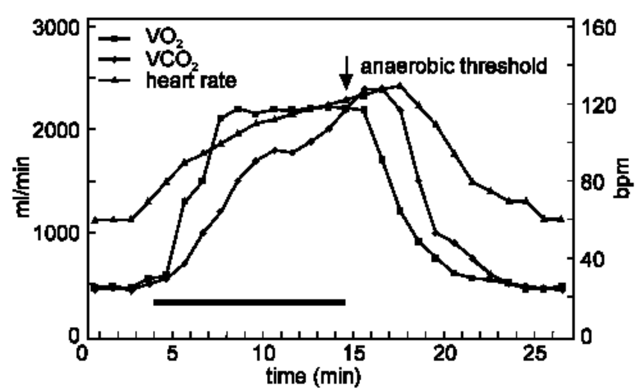

Figure 2. Symptom-limited treadmill test in DDD-CLS mode, same patient as in Figure 1. Note the increase in exercise duration and achieved heart rate. The solid bar indicates the exercise duration. For further explanation see text.

25 % higher than in the DDD mode. Accordingly, the anaerobic threshold was shifted to a greater exercise intensity, with the VCO_2 crossing the VO_2 at 150 watt instead of at 75 watt in the non-rate-regulating DDD mode. In DDD-CLS mode, the exercise intensity at the anaerobic threshold was about 100 % higher than in the DDD mode. Despite individual differences in physical fitness, we found similar trends in all the patients enrolled in this study. Figure 3 summarizes the results. With the pacemaker set to DDD-CLS, all patients achieved higher rates, higher VO_2, and higher exercise performance. At peak exercise, the mean achieved heart rate in the DDD mode was 83 ± 9 bpm and 111 ± 12 bpm in the DDD-CLS mode. The VO_2 at peak exercise increased by about 23 % from 15 ± 3 ml/kg/min in DDD mode to 18.5 ± 4 ml/kg/min in DDD-CLS mode. The mean maximum achieved workload increased more than 50 % from 72 ± 18 watt in the DDD mode to 109 ± 21 watt in the DDD-CLS mode. Since all patients reached their maximum workload at their anaerobic threshold, the increase in peak exercise is equal to an increase in the anaerobic threshold.

Discussion

Rate-adaptive pacing systems have been extensively studied to evaluate the clinical benefit of rate-adaptive therapy [3-6,12]. Currently, more than half of all pacemaker systems implanted function rate-adaptively. Our object was to determine the clinical benefit of the

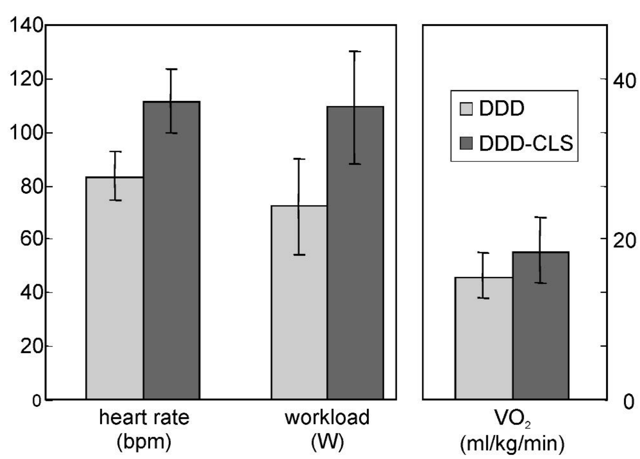

Figure 3. Mean peak heart rates, mean achieved workload and oxygen consumption (VO_2) with the pacemaker set either to DDD mode or DDD-CLS mode.

Inos[2] rate-regulating CLS system. For that purpose, we used the symptom-limited Alt [13] treadmill protocol and monitored the respiratory oxygen consumption and carbon dioxide production, comparing the individual performance when the patient was in the DDD mode with patient performance in the DDD-CLS mode. With CLS pacing, we found a general increase in achieved heart rate and VO_2, and the mean maximum achieved exercise performance increased by more than 50 %. These results are similar to those of other studies on different rate-adaptive pacemakers [3,5,14,15]. However, a direct comparison between the results of other studies and our study is hard to obtain. Differences in age, exercise testing, and pacemaker settings make a direct comparison impossible. For example, while using the same treadmill protocol but different pacemaker systems, Schlegel et al. [14] reported an increase in maximum VO_2 from 16.4 ± 5.6 to 23.2 ± 11.1 ml/kg/min in their group I patients; furthermore, the maximum achieved heart rate in these patients was 72 ± 13 bpm in the non-rate-adaptive mode and 130 ± 16 bpm in the rate-adaptive mode. Here, we report an increase in VO_2 from 15 ± 3 to 18.5 ± 4 ml/kg/min and an increase in heart rate from 83 ± 9 bpm in the DDD mode to 111 ± 12 bpm in the DDD-CLS mode. The obvious differences of our study and the study by Schlegel et al. regarding VO_2 are certainly due to age differences between the two groups (59.9 ± 12 vs. 71 ± 8 years). The differences in the achieved heart rate during exercise are probably due to differences in the pacemaker settings. In our study, the maximum closed loop rate of all patients was set to 120 bpm to 140 bpm. In the study of Schlegel, the maximum rate adaptive pacing rate was kept constant at 160 bpm. The different pacemaker settings reflect the age differences of the two groups of patients. In general, depending on the underlying disease, younger patients tolerate higher maximal pacing rates than elderly patients.

Malinowski [4] compared different sensor principles for rate-adaptive pacing using a variety of ambulatory exercise and mental stress tests. In his study, Malinowski showed that most single- and dual-sensor controlled systems have difficulties in determining an appropriate pacing rate in at least one form of stress. In contrast, the CLS provided heart rates comparable to those of the control subjects with normal sinus node function under all conditions. Furthermore, CLS is sensitive to the Valsalva maneuver and regulates the heart rate adequately during the entire course of the maneuver [10]. The appropriate response of the CLS system to the Valsalva maneuver and to mental stress tests [4] indicates the successful integration of the CLS system into the natural control loop. Together with our study, these results show that CLS provides physiological rate regulation and increases the exercise tolerance and the cardio-pulmonary performance of chronotropic incompetent patients.

References

[1] Benditt DG, Mianulli M, Lurie K, et al. Multiple sensor systems for physiologic cardiac pacing. Ann Intern Med. 1994; 121: 960-968.

[2] Haennel RG, Logan T, Dunne C, et al. Effects of sensor selection on exercise stroke volume in pacemaker dependent patients. PACE. 1998; 21(9): 1700-1708.

[3] Candinas R, Jakob M, Buckingham TA, et al. Vibration, acceleration, gravitation, and movement: activity controlled rate adaptive pacing during treadmill exercise testing and daily life activities. PACE. 1997; 20(7): 1777-1786.

[4] Malinowski K. Interindividual comparison of different sensor principles for rate-adaptive pacing. PACE. 1998; 21(2): 2209-2213.

[5] Lau CP, Butrous GS, Ward DE, et al. Comparison of exercise performance of six rate-adaptive right ventricular cardiac pacemakers. Am J Cardiol. 1989; 63: 833-838.

[6] Lau CP, Mehta D, Toff WD, et al. Limitations of rate response of an activity-sensing rate-responsive pacemaker to different forms of activity. PACE. 1988; 11: 141-150.

[7] Schaldach M. What is Closed Loop Stimulation? Prog Biomed Res. 1998; 2(3): 49-55.

[8] Lang R, Dörnberger V, Kühlkamp V, et. al. Kontraktionsdynamik vs. Accelerometer: Intraindividueller Sensorvergleich bei physischer und psychischer Belastung. Herzschrittmacher & Elektrophysiologie. 1998; 9(Suppl. 1): 13-14.

[9] Witte J, Reibis R, Pichlmaier AM, et. al. Frequenzadaptive Stimulation mittels eines Kontraktilitätssensors - Eine multizentrische Studie. Herzschrittmacher. 1996; 16(1): 8-16.

[10] Ruppert T, Hubmann M, Lang E. Closed Loop Stimulation is Sensitive to the Valsalva Maneuver. Prog Biomed Res. 2000; 2(5): 123-125.

[11] Benditt DG, Mianulli M, Fetter J, et al. Single-chamber cardiac pacing with activity- initiated chronotropic response: evaluation by cardiopulmonary exercise testing. Circulation. 1987; 75(1): 184-191.

[12] Humen DP, Kostuk WJ, Klein GJ. Activity-sensing, rate-responsive pacing: improvement in myocardial performance with exercise. PACE. 1985; 8(1): 52-59.

[13] Alt E, Gastmann U, Schmid S. A new exercise protocol to compare treadmill and bicycleergometry in cardiac pacing. Circulation. 1993, 88: 1-22.

[14] Schlegel M, Matula M, Alt E. Verbesserung der Sauerstoffaufnahmekapazität durch frequenzadaptive Schrittmacherstimulation: Einfluß der Herzeigenfrequenz. Z. für Kardiol. 1994; 83: 912-920.

[15] Capucci A, Boriani G, Specchia S. Evaluation by cardiopulmonary exercise test of DDDR versus DDD pacing. PACE. 1992; 15: 1908-1913.