Influence of Permanent Right Ventricular Pacing on Cardiorespiratory Exercise Parameters in Chronic Heart Failure Patients With Implanted Cardioverter Defibrillators*

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Study objectives: **Patients with chronic heart failure and implanted cardioverter-defibrillators (ICDs) may have a higher incidence of new-onset or worsening heart failure requiring hospitalization with dual-chamber ICDs compared with single-chamber ICDs.**

Design and setting: **The purpose of this study was to show the impact of permanent right ventricular (RV) pacing on exercise capacity and related cardiorespiratory parameters in patients with chronic heart failure and ICDs.**

Patients and interventions: **Seventeen patients with chronic heart failure and a dual-chamber ICD performed cardiopulmonary exercise testing (CPX) on 3 different days. After CPX 1, patients were randomized either to back-up pacing or permanent RV pacing. After 3 months, CPX 2 was performed and patients changed groups (crossover design); CPX 3 was performed after 3 additional months.**

Measurements and results: **Maximal values for workload (108 ± 46 W vs 117 ± 48 W, $p < 0.01$), oxygen uptake ($\dot{V}O_2$) [21.0 ± 5.3 mL/min/kg vs 22.5 ± 6.4 mL/min/kg, $p < 0.05$], oxygen pulse (13 ± 3.7 mL vs 14 ± 4.0 mL, $p < 0.05$), and metabolic equivalent (6.0 ± 1.5 vs 6.4 ± 1.8, $p < 0.05$) were significantly lower with permanent RV pacing compared to back-up pacing. Workload, $\dot{V}O_2$, and oxygen pulse were significantly reduced at the ventilatory anaerobic threshold, while workload and $\dot{V}O_2$ were significantly lower at the respiratory compensation point. No differences were found for maximal heart rate, minute ventilation $\dot{V}E$, and respiratory exchange ratio. The $\dot{V}E$/carbon dioxide production slope was significantly steeper with permanent RV pacing compared to back-up pacing.**

Conclusions: **Permanent RV pacing significantly reduced maximal and submaximal measures of exercise. For patients with chronic heart failure and sufficient atrioventricular conduction, every effort should be made to minimize permanent right ventricular pacing.**

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Key words: cardiopulmonary exercise testing; dual-chamber implantable cardioverter defibrillator; maximal oxygen consumption; minute ventilation/carbon dioxide production slope; respiratory compensation point; ventilatory anaerobic threshold; ventilatory efficiency

Abbreviations: CPX = cardiopulmonary exercise testing; DDD = dual-chamber pacemaker; ICD = implantable cardioverter defibrillator; LVEF = left ventricular ejection fraction; RV = right ventricular; $\dot{V}CO_2$ = carbon dioxide production; $\dot{V}E$ = minute ventilation; $\dot{V}O_2$ = oxygen uptake; $\dot{V}O_2max$ = maximal oxygen uptake

The implantable cardioverter-defibrillator (ICD) improves survival in patients with life-threatening ventricular arrhythmias.[1] Recently, prophylactic implantation of a defibrillator in patients with prior myocardial infarction and advanced left ventricular dysfunction has been shown to be superior to standard medical therapy.[2] However, a higher incidence of new-onset or worsening heart failure requiring hospitalization was found with dual-chamber ICDs.[2] The Dual Chamber and VVI Implantable Defibrillator trial[3] confirmed these findings in chronic heart failure patients without an indication for antibradycardia pacemaker therapy. Direct comparison of back-up pacing using right ventricular (RV) back-up pacing programming to permanent atrioventricular-sequential RV pacing showed a significantly lower number of deaths or first hospitalizations for congestive heart failure in ICD patients with back-up pacing.[3] The different components of the composite end point, mortality, and hospitalization for congestive heart failure also trended in favor of RV back-up pacing.

Information from the atrial chamber allows better device programming and individualization of drug therapy for ventricular arrhythmias.[4] Therefore, most currently implanted ICDs are dual-chamber devices.[3] Moreover, positive short-term and long-term effects of dual-chamber RV pacing in the treatment of end-stage idiopathic dilated cardiomyopathy have been shown.[5–7] However, 4 to 18% of ICD patients were found to need antibradycardia pacing.[3,8] At the moment, however, it is unclear whether dual-chamber pacemakers (DDDs) should be implanted, or whether permanent DDD pacing should be activated in modern ICDs in every patient with chronic heart failure regardless of the intrinsic atrioventricular conduction delay.

The maximal oxygen uptake ($\dot{V}O_2$max) is used for risk stratification in chronic heart failure patients.[9] In some cases, $\dot{V}O_2$max might be underestimated because of reduced patient motivation or premature termination of exercise on the examiner's decision. Furthermore, patients with severe heart failure tend to perform activities of daily life that involve submaximal measures of exercise.[10] Submaximal exercise parameters such as the ventilatory anaerobic threshold, the respiratory compensation point, and ventilatory efficiency (minute ventilation [$\dot{V}E$]/carbon dioxide production [$\dot{V}CO_2$] slope) are less subject to these influences.[10–13] The $\dot{V}E/\dot{V}CO_2$ slope in particular was found to be a reliable predictor of prognosis in patients with chronic heart failure.[11,12,14] The purpose of this study was to show the impact of permanent RV pacing on exercise capacity and submaximal cardiorespiratory parameters in patients with chronic heart failure and dual-chamber ICDs.

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Materials and Methods

A monocentric, prospective, randomized pilot study was performed in a crossover design. Patients were blinded to the setting of the device, as were the physicians and technicians who performed and analyzed the cardiopulmonary exercise testing (CPX) results (double-blind design). Patients were informed of the nature, risks, and benefits of the investigation and gave their written informed consent to participate in the study. The Institutional Ethics Committee of the University of Graz, Austria, approved the study protocol.

Inclusion Criteria

Inclusion criteria included the following: a class I indication for an ICD[1] (*ie*, history of ventricular tachycardia or survivor of sudden cardiac death), age > 18 years, left ventricular ejection fraction (LVEF) $< 40\%$, permanent sinus rhythm, and medication not changed during the investigation period.

Exclusion Criteria

Exclusion criteria included the following: chronic atrial fibrillation, history of paroxysmal atrial fibrillation, sick sinus syndrome, need for permanent atrioventricular-synchronous RV pacing, an atrioventricular delay < 150 ms, female patients with child-bearing potential, age > 80 years, and hypertrophic obstructive cardiomyopathy.

Programming of the ICD

Antitachycardia Parameters: The device was programmed individually according to the underlying ventricular arrhythmia. This programming was maintained during the 6-month follow-up period unless ventricular tachyarrhythmias developed for which the antitachycardic stimulation therapy was inappropriate or ineffective.

Antibradycardia Parameters: The lower rate was programmed to 40 to 50 beats/min for all patients. The upper rate of the pacemaker was programmed according to the age-predicted maximal heart rate, 130 to 160 beats/min.

Patients were randomized in a crossover design to either of the following: (1) intrinsic atrioventricular-sequential conduction without ventricular stimulation (DDD with a long atrioventricular delay or DDI) [back-up pacing group]; or (2) fixed atrioventricular delay of 100 to 120 ms ensuring permanent RV stimulation. At the 3-month follow-up, programming was switched to correspond to the other group so that the study patients served as their own control group.

CPX

Subjects completed CPX on an electronically braked cycle ergometer (ER 900; Jaeger; Wuerzburg, Germany) to volitional exhaustion on 3 different days: The first test (CPX 1) was intended to familiarize patients with the testing procedure and to determine their maximal workloads. To obtain baseline values, patients were asked to sit quietly on the cycle ergometer for 10 min. Resting values were collected in the last minute before the onset of the workload. Exercise was started with a workload of 10 W followed by an increase of 10 W for men and 7 W for women every minute thereafter. A 12-lead ECG (Jaeger) was used to monitor and record ECG tracings. A physician supervised each test. During CPX, subjects wore an airtight mask over their nose and mouth. Oxygen uptake ($\dot{V}O_2$) and $\dot{V}CO_2$ were analyzed continuously during the tests using a breath-by-breath system