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Implantable Cardioverter Defibrillator Incorporated with Biventricular Pacing Among Heart Failure Patients

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CHAN ET AL.: Implantable Cardioverter Defibrillator Incorporated with Biventricular Pacing Among Heart Failure Patients. Implantable cardioverter defibrillator (ICD) with biventricular pacing (BiV) is available for drug-refractory heart failure patient who has class I indication for ICD and inter-ventricular conduction delay. We studied 32 patients with mean age of 61 years (M:F=9:1) with mean ejection fraction about 30% who has underwent implantation of implantable cardioverter defibrillator incorporated with left ventricular pacing. It showed its efficacy in terms of improvement in functional status and ejection fraction as confirmed by echocardiogram, episodes of cardiac related rehospitalization ($p<0.05$) and appropriate therapy for ventricular tachycardia among our patients in the mean follow up period of 22 months. Permanent left ventricular pacing is achieved by pacing of the distal branches of coronary sinus with a specially designed left ventricular (LV) lead. The optimal placement of LV lead is identified by a satisfactory pacing threshold, ventricular sensing and late sensing of LV electrical activity in order to optimize the resynchronization process. At the end of follow-up, all LV leads were fully functional with stable thresholds and appropriate sensing. Eight episodes of ventricular fibrillation and 18 episodes of ventricular tachycardia were successfully detected. The detection of ventricular arrhythmia detection was 100%. Four patients received 28 inappropriate shocks secondary to supraventricular tachycardia. **Conclusion:** Implantable cardioverter defibrillator incorporated with biventricular pacing is an efficient and safe mean of providing patient with cardiac resynchronization therapy in patient with drug refractory heart failure with interventricular conduction delay. (*J HK Coll Cardiol* 2003;11:50-57)

Cardiac resynchronization therapy, Heart failure, Implantable cardioverter defibrillator

摘要

植入式心臟復律除顫器聯合雙室起搏器，對於藥物抵抗性心衰病人有著植入式心臟復律除顫器 I 類指征和室內傳導阻滯是適用的。我們研究了 32 位患者，平均年齡為 61 歲，男女比例 9:1，平均射血分數約為 30%，他們接受了植入式心臟復律除顫器聯合左室起搏器的治療。我們這組病人平均 22 個月的隨訪表明這種治療是有效的，表現為心功能的改善和超聲心動圖證實的射血分數的提高，心臟病相關的再入院時間的減少 ($p<0.05$)，以及對室性心動過速的適宜治療。永久性左心室起搏器是通過與左心室特殊導聯相連的冠狀竇遠端分支而實現起搏的。左心室導聯放置的最佳位置是依據令人滿意的起搏閾值、室性感應、左心室電活動晚期感應而定的，由此而實現最佳的再同步過程。在隨訪的終點，所有左心室導聯均功能完整，表現為閾值穩定、靈敏度適宜。8 次室顫和 18 次室性心動過速均被成功的發現。室性心律失常的發現率為 100%。有 4 位病人接受了 28 次不適當的電擊而發生了室上性心動過速。結論：植入式心臟復律除顫器聯合雙室起搏器，對於伴隨室內傳導阻滯的藥物抵抗性心衰病人是安全有效的，它為病人提供了良好的心臟再同步治療。

關鍵詞：心臟再同步治療 心衰 植入性心臟復律除顫器

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Background

Implantable cardioverter defibrillator (ICD) has become an important therapeutic modality for patients who have had aborted cardiac arrest or are at risk for life-threatening ventricular arrhythmias. Clinical trials have already confirmed the role of ICD for patients with sustained ventricular arrhythmias¹ and have expanded the indications to include patients with coronary artery disease, left ventricular dysfunction with or without and non-sustained ventricular tachycardia.^{2,3} Many heart failure patients remain highly symptomatic.⁴ Population morbidity and mortality still remain high.⁵ There is a need to identify subgroups of patients particularly those at high risk for newer non-pharmacological therapeutic strategies. Previous studies have documented the deleterious haemodynamic effects of left bundle branch conduction delay with resultant dyssynchronous activation of the left ventricle. Cardiac resynchronization therapy (CRT) involves atrio-ventricular (AV) pacing to optimize AV timing and biventricular (BiV) pacing to synchronize right and left ventricular contractions. It has been shown that CRT results in acute improvement in haemodynamics,⁶⁻⁸ functional class, 6 minutes walking distance⁹⁻¹³ and probably anti-arrhythmic event in recent studies.^{13,14} CRT becomes more widely applicable since the introduction of endocardial transvenous pacing leads for left ventricular (LV) pacing via the cannulation of branches of the coronary sinus (CS), thus avoiding thoracotomy surgery. The aim of this study was to report our clinical experience and long-term outcome in patients being implanted with ICD incorporated with CRT.

Materials and Methods

Patient Population

The study population consisted of 32 patients who underwent successful implantation of ICD incorporated with BiV pacing from December 1999 to June 2002. All patients were in New York Heart Association (NYHA) functional class II to III with optimal medical therapy at maximal tolerated dose for congestive heart failure and they were not dependent on inotropic support.

All patients also have the usual indications for CRT, namely, LV systolic dysfunction with ejection fraction <35% on echocardiography or angiography, echographic LV end diastolic diameter >60 mm, and intrinsic QRS interval >140 ms. Clinical characteristics of the patients studied are summarized in Table 1.

Implantation of ICD Incorporated with BiV Pacing

The devices implanted in this study were CONTAK CD (model 1832) and the newer CONTAK Renewal model (Guidant Inc, Minneapolis, USA) and InSync 7272 ICD (Medtronic Inc., Minneapolis, USA) which are capable of delivering ICD therapies and CRT. Both devices have a special five-port header for connection of four leads, which have three pacing electrodes (one atrial lead, one right ventricular [RV] lead and one LV lead) and two defibrillation coil. CRT and antitachycardia pacing (ATP) can be programmed to the right, left or biventricular stimulation in InSync ICD and Renewal ICD but not the earlier generation CONTAK CD. The CONTAK CD incorporated both RV and LV sensing in the detection algorithm while

Table 1. Patient characteristics

	N=32
Age (years)	61±12 (37-83)
Male (n, %)	30 (94%)
Underlying etiology of heart failure:	
Ischemic cardiomyopathy	14 (44%)
Dilated cardiomyopathy	14 (44%)
Valvular heart disease	3 (10%)
Sarcoidosis	1 (2%)
Left ventricular ejection fraction (%)	24.2±11
Follow-up (months)	22±12 (2-37)
ECG (intervals):	
PR (ms)	246±22
QRS (ms)	176±20
Rhythm:	
VF	8 (25%)
VT	18 (56%)
Syncope with positive induction at EPS	6 (19%)

VF=ventricular fibrillation; VT=ventricular tachycardia; EPS=electrophysiological study

both ventricular sensing and detection remain on the right side lead only in InSync ICD and Renewal CD.

The LV pacing lead was inserted transvenously via the subclavian venous route. Coronary sinus venogram was obtained during balloon occlusion, and specially designed LV pacing lead was inserted through the CS into distal epicardial branch with the help of dedicated 8Fr guiding catheters. Essentially, two different specially designed transvenous CS pacing leads were used. The over-the-wire design was used in 18 patients. It is a unipolar 6-French tined electrode which contains a central lumen and an open tip through which a 0.014 inch guidewire can be passed through and guide the advancement of pacing lead. The second LV pacing lead used was a pre-shaped unipolar 4.1 French passive fixation lead and was implanted in 14 patients. The atrial lead was positioned at the high right atrium and the defibrillation lead positioned in the RV apex respectively (Figure 1). Proper testing of the sensing and capture thresholds of the three pacing leads

were performed. Diaphragmatic stimulation or phrenic nerve stimulation (more commonly seen with LV lead stimulation) were evaluated. The total implant procedure duration, LV lead implantation time, fluoroscopic time and defibrillation thresholds (DFT) were measured.

Clinical Evaluation and Follow-up

Prior to implantation of the device, all patients' underwent the following assessment: New York Heart Association (NYHA) classification and echocardiography for determination of the LV systolic and diastolic diameter and LV ejection fraction. After implantation, all patients underwent optimization of CRT by determining the optimal AV intervals for systolic LV function using Doppler echocardiography. The device was first programmed to a lower rate to ensure an intrinsic sinus rate. The sensed AV delay was programmed to 200 ms. At this setting, mitral valve closure is delayed to the end of the A-wave. The sensed AV interval was decreased at 20 ms intervals until the



(a)



(b)

Figure 1. Chest X-rays (PA view) of a patient with previous coronary bypass surgery implanted with ICD with biventricular pacing performed at a) immediately after implantation and b) 1 year after. Note the significant reduction in cardiothoracic ratio and improvement in pulmonary venous congestion.

mitral valve Doppler signal caused truncation of the A-wave. The optimal AV interval was programmed to ensure that the mitral valve closure Doppler signal coincided with or occurred shortly after the end of the A-wave.

Patients were evaluated at outpatient clinic at 1 and 3 months, and then 6 monthly after implantation. Arrhythmic episodes were retrieved from the device memory and examined by the physicians. Follow up data were acquired for up to 3 years. Cardiovascular endpoints were defined as arrhythmic death, sudden cardiac death, or death attributable to congestive heart failure or myocardial infarction or other events resulting in terminating the BiV ICD functions (for example, heart transplantation). Hospitalizations for cardiovascular events were defined as hospital admission secondary to congestive heart failure, ischaemia (for example, acute myocardial infarction and unstable angina) or cardiac arrhythmia events. The number of cardiac related hospitalization was compared before and after BiV ICD implantation. The rate of re-admission was determined by dividing the number of hospitalizations experienced by the total number of person-years of follow-up.

Statistical Analysis

Continuous data were expressed as mean±SD. Student's t test was used to compare the results at baseline and during their most recent follow-up. For all tests, a p value<0.05 was considered significant.

Results

Implantation Procedure

LV lead implantation at the distal branches of coronary sinus was successful in 91% of patients. The reasons for unsuccessful LV lead implantation were failure of coronary sinus branches cannulation in 2 patients and high LV capture thresholds at various distal branches in another patient. Therefore, a total of 32 patients were entered in final analysis. The acute mean LV pacing thresholds in those 32 patients was 1.1±0.5 V. The mean defibrillation threshold, measured

by T-wave shock induction, was 9.5±5 joules. The procedural time was 3.8±1.2 hours and mean fluoroscopy time was 37.1±22.4 minutes. The chronic LV pacing thresholds, sensing and impedance were not significantly different between the two types of leads utilized in this study (Figure 2).

Patients' Clinical Parameters and Outcome

The ICD function and BiV pacing function were activated in all patients after optimization of AV intervals using doppler echocardiography. The baseline and long-term follow up results are listed in Table 2. There is significant improvement of mean LV ejection fraction from 24.4% to 34% (p<0.05). There is significant reduction in LV systolic and diastolic dimensions. Interestingly, there was a decrease in QRS duration but did not reach statistically significant. The cardiac related hospitalization rate was also significantly reduced (p<0.05). Two patients died from multi-organ failure at 14 months and intractable heart failure at 22 months after implantation respectively. Three other patients subsequently underwent orthotopic cardiac transplantation for congestive heart failure. The total event free survival without heart transplantation was 27 (84%) of 32 patients.

Long Term Device Follow-up

There were 3 device related late complications (1 wound infection and 2 LV leads dislodgement) for which repositioning of leads was successful. Eight patients received 19 appropriate therapies for ventricular tachyarrhythmias (average 2.4 episodes/pt). All ventricular tachyarrhythmias were correctly identified; hence, sensitivity of ventricular arrhythmias detection was 100%. Two patients initially programmed to RV antitachycardia pacing (ATP) were programmed to BiV ATP which was significantly more effective in terminating ventricular tachycardia. Four patients received 28 inappropriate shocks secondary to supraventricular tachycardia (SVT) (n=26) and oversensing of diaphragmatic myopotentials (n=2). There was no inappropriate detection arising from double counting of RV and LV signal during SVT amongst our patients.

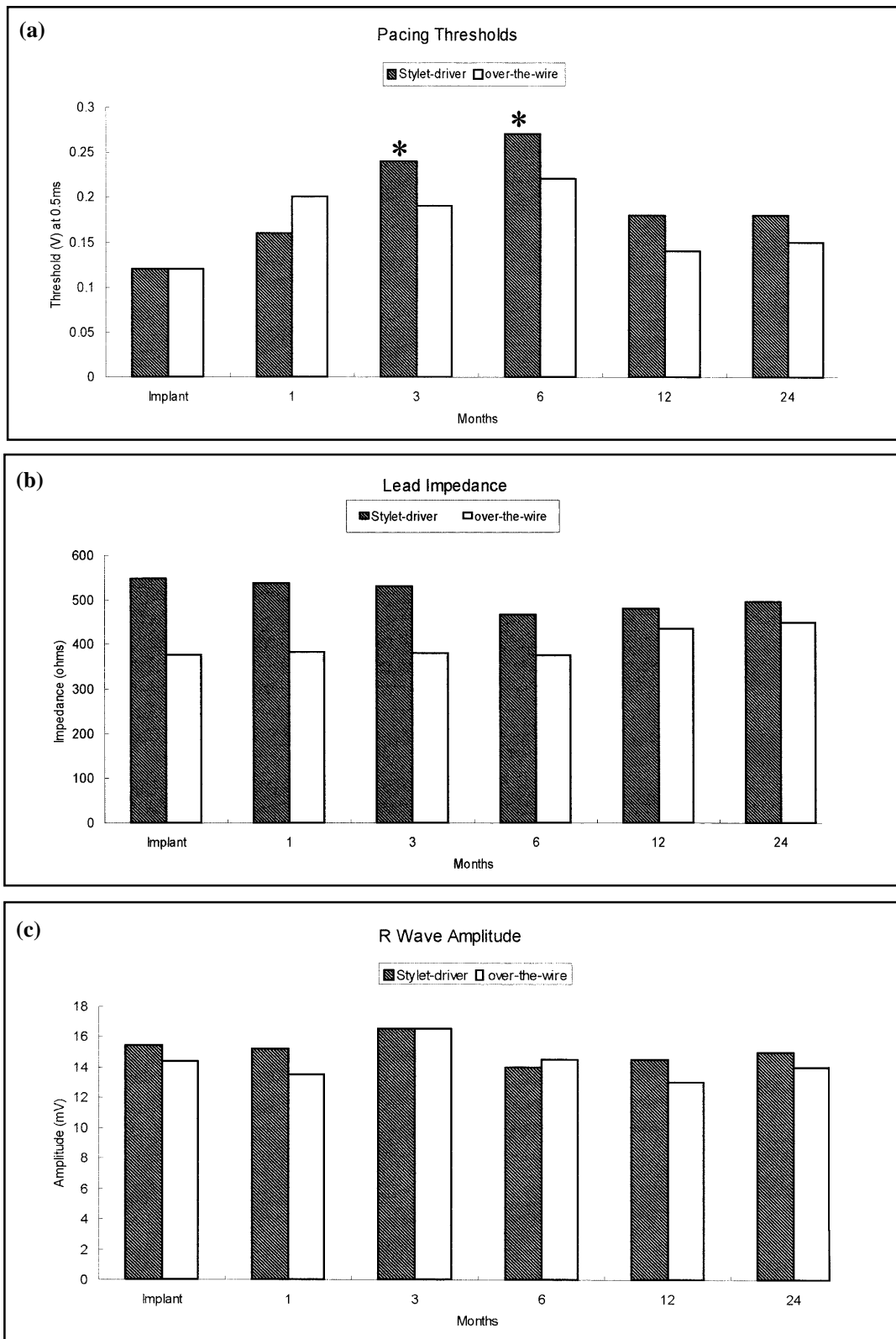


Figure 2. Comparison of two types of left ventricular (LV) pacing leads with respect to their chronic a) chronic pacing thresholds b) sensing and c) impedance. * $p < 0.05$ when compared with implant.

Table 2. Clinical parameters before and after ICD incorporated with BiV pacing

	Baseline	Post BiV ICD	P value
QRS duration (ms)	176±20	146±15	0.34
LVDD (cm)	6.8±1.1	6.15±0.9	<0.001
LVSD (cm)	5.74±1.1	5.01±1.1	<0.001
EF (%)	24.4±11	34±16	0.02
Cardiac-related Rehospitalization (episodes/year)	8.6±8.2	3.6±6.2	<0.0001

Discussion

This report describes our clinical experience with ICD capable of CRT in patients with severe systolic heart failure considered at risk of malignant ventricular tachyarrhythmias. The significant improvement in functional class and LV dimensions together with significant reduction in cardiac related hospital admissions is in agreement with other recently reports.⁹⁻¹³ Therefore, heart failure patients with prior cardiac arrest and marked interventricular conduction delay should be considered as the optimal candidates to the ICD implantation combined with BiV pacing. Furthermore, our findings that significant QRS narrowing was not constantly achieved with BiV pacing despite much improved mechanical systolic response was consistent with other studies.¹³

The MIRACLE-ICD (Multicenter InSync-ICD Randomized Clinical Evaluation) was conducted in a near-identical way to the MIRACLE trial,⁸ with implantation of ICD with CRT devices into 362 patients with a conventional indication for ICD, LVEF <35% and NYHA III/IV heart failure. This study showed a marked reduction in days in hospital for heart failure (77%; $p=0.012$), in the use of intravenous therapy for heart failure (57%; $p<0.001$) and the outcome of death or worsening heart failure (40%; $p=0.033$) during long-term follow-up. In the CONTAK-CD trial, which was designed to assess if BiV pacing could reduce short-term morbidity and mortality in patients with heart failure, the primary endpoint (a composite of all-cause mortality, hospitalization for heart failure, worsening of heart failure requiring intervention or appropriate ICD discharges) was reduced by 21%, which failed to achieve statistical significance. Similar to MIRACLE-

ICD trial, CRT was associated with important trends to benefit, including reductions in mortality (23%), hospitalization for heart failure (13%), worsening heart failure events (26%), and appropriate ICD discharge (9%). CRT was associated with a significant reduction in echocardiographic LV dimensions, control-group subtracted increase in peak oxygen of 1 mL/kg/min, and improved NYHA class (33% of control group in class I/II vs 80% of patients on CRT).

The recently completed COMPANION study randomized patients to receive with CRT (with or without backup defibrillator) versus optimal medical therapy.¹⁴ The primary end-point is all-cause mortality and all-cause hospitalization. As patients who have an existing indication for an ICD are excluded from COMPANION, it will effectively be assessing the use of prophylactic ICD in patients deliberately stratified for not being at risk of arrhythmias. This study has just been terminated prematurely in late November 2002 because of highly significant reduction in combined all cause mortality and all cause hospitalization in CRT and ICD arm itself.

Incidence of Ventricular Tachyarrhythmias and Efficacy of Therapy

Whether BiV pacing affects the incidence of sustained ventricular tachyarrhythmias remains an important question. Data from the beta-blocker studies support the concept that improving heart failure reduces sudden death, suggesting that the incidence of ventricular arrhythmias is decreased.¹⁵ Some small studies have shown positive effects on the incidence of ventricular arrhythmias^{16,17} while recent larger studies showed equivocal results.¹⁸ With BiV pacing, two distinct pacing sites are used which may enhance the

efficacy to terminate VT by antitachycardia pacing (ATP) as the site of stimulation may modify the ability of a stimulated impulse to enter the re-entry circuit and terminate VT. Kuhlkamp et al has shown that biventricular ATP delivery was more effective than right ventricular ATP and a trend was seen that BiV pacing did result in fewer acceleration than right ventricular ATP.¹⁸ Our clinical experience demonstrated better efficacy of ATP when delivered biventricularly in selected patients as well.

Inappropriate Detection of Ventricular Tachyarrhythmias

A hybrid bipolar ventricular sensing configuration is adopted in the first generation CONTAK CD (Guidant Inc.). The electrograms from both RV and LV leads are fed into a single amplifier; as a result, a composite electrogram wider than the device post-sense blunting period of 135 ms could result in double counting. BiV pacing was not associated with significant problems as long as continuous pacing in the ventricles was achieved. However, when spontaneous ventricular activity occurred, sensing of both components of the composite RV/LA electrograms resulting in double counting was seen. As a result, double-counting occurs leading to inappropriate therapy in up to 14% of patients, usually in the situation of sinus tachycardia with spontaneous AV conduction.¹⁹⁻²¹ Similarly, atrial fibrillation with intrinsic conduction could cause double sensing of the intrinsic QRS complex despite a mode switching option if AV conduction were rapid. The Medtronic InSync 7272 ICD and Guidant Renewal ICD incorporate two separate ports for RV and LV leads. The LV lead does not sense and is used only for pacing. Electrograms from RV lead only is used for detection and is unchanged when compared with standard ICDs, thus effectively preventing the possibility of double counting.

Conclusions

In a selected group of heart failure patients with primary indication for ICD therapy, adjunctive CRT by implanting "an ICD combined with BiV pacing"

improved ejection fraction, LV dimensions and functional status, with reduced hospital admissions. Implantation of ICD capable of BiV pacing is a safe procedure in patients with severe congestive heart failure. Ventricular tachyarrhythmia episodes in these patients were all appropriately treated. Thus the use of an ICD with CRT should be considered in patients with ventricular tachycardia with evidence of intraventricular dyssynchrony.

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HEART FAILURE, CRT, ICD

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