The Clinical Observation of Biventricular Pacing in Patients with Congestive Heart Failure

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HUA and CHEN: ***The Clinical Observation of Biventricular Pacing in Patients with Congestive Heart Failure.*** *Congestive heart failure is one of the leading health problems in medicine. Intraventricular conduction delay is associated with contraction abnormalities, prolonged mitral regurgitation and a shortened left ventricular filling time in patients with conduction defects and dilated cardiomyopathy. Biventricular pacing is a promising new strategy for correcting the ventricular activation sequence and potentially improving myocardial function and clinical outcome in patients with congestive heart failure. Uncontrolled and controlled studies have shown that biventricular pacing could help to improve patients by at least one functional class, increases the 6-minute walk distance by 20-40%, and improves quality of life (as assessed by the Minnesota living with heart failure questionnaire) by 20-50%. Left ventricular lead implantation requires more time than implantation of traditional pacemaker leads. New technology and techniques are likely to reduce the time required for implantation in the future. (J HK Coll Cardiol 2002;10:11-16)*

Biventricular pacing, clinical observation, congestive heart failure

摘要

充血性心力衰竭是醫學領域面臨的主要問題之一。在充血性心力衰竭患者，心室內傳導延遲與心肌收縮不同步，二尖瓣返流延長及左室充盈時間縮短相關。雙心室同步起搏可糾正心室激動不同步，改善患者心功能，是一個有前途的治療方法。一些對照和非對照的臨床研究已經證明雙心室同步起搏可改善患者心功能一級，6分鍾步行距離 20-40%，以及生活質量20-50%〔明尼蘇達生活質量評分〕。植入左心室電極導線比植入傳統電極導線要更長時間，隨著技術的不斷改進，植入時間將減少。

關鍵詞：雙心室同步起搏　臨床觀察　充血性心力衰竭

Introduction

The aging of the population has made chronic heart failure (CHF) an increasingly important health problem. It is the leading medical cause of hospitalization and its economic cost continues to increase. In recent years, pharmacological treatment made considerable progress. Angiotensin converting enzyme (ACE) inhibitors and B blockers have significantly reduced mortality and morbidity in New York Heart Association (NYHA) class II-IV patients, while improving their quality of life. But that benefit is probably not permanent and will be limited in time. A variety of non-pharmacological approaches is available to treat these refractory heart failure patients. Heart transplant remains the best solution but can only be applied to a restricted number of patients.

Intraventricular conduction delay is associated with asynchronous ventricular contraction, even in patients without heart failure. Contraction abnormalities, prolonged mitral regurgitation and a shortened left

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ventricular filling time have also been documented in patients with conduction defects and dilated cardiomyopathy.[1-4] Biventricular pacing is a promising new strategy for correcting the ventricular activation sequence and potentially improving myocardial function and clinical outcome in patients with heart failure.[5-8] Although large controlled clinical trials of biventricular pacing have yet to be completed, currently available data suggest that patients with advanced heart failure and ventricular conduction abnormalities may benefit from such therapy.

Intraventricular Conduction Delay and Biventricular Pacing

Wide QRS are frequently observed in patients with chronic heart failure associated with left ventricular (LV) systolic dysfunction. Some studies revealed a prevalence of intraventricular conduction delay (as defined by QRS duration >120 ms) in chronic heart failure patients, estimation at 27-53%.[9] These conduction abnormalities - intraventricular conduction delay in particular is considered to be an independently predictive factor of mortality. Thus in the Vesnarinone Trial (VEST) study,[10] the 6 years mortality rate in patients with chronic heart failure with altered LV function (LV ejection fraction <40%) was significantly higher in patients whose QRS duration exceeded 110 ms (65%) than in those where it did not (40%), regardless of the degree of LV impairment.

In addition, these conduction disorders have deleterious effects both on systolic function and on LV filling, and they can induce or enhance mitral "functional" regurgitation. Xiao and colleagues[11] demonstrated, in dilated cardiomyopathy (DCM) patients, that the presence of a left bundle branch block (LBBB) was associated with a more than 80% increase in LV pre-ejection contraction time and 60% increase in LV relaxation time; there was also a negative correlation between the QRS duration and the +dp/dt. So, the wider the QRS, the lower the contractility. In the same studies, analyzing the parameters of LV diastolic function revealed that the LV filling time was significantly reduced (by nearly 40%) in DCM patients in the presence of LBBB or a significant prolongation of the PR interval (>200 ms). In parallel, the quality of atrial contribution to LV filling was impaired, as reflected on transmitral Doppler by a single phase flow linked to E wave and A wave superimposition. Lastly, in patients with LV systolic dysfunction, the presence of an LBBB or prolonged PR interval is associated with an increase in the duration of mitral regurgitation. Incidentally, the presence of an LV-left atrial diastolic gradient-frequently found in patients with DCM and atrioventricular conduction disorders which can be the origin of diastolic mitral regurgitation.

The aim of multisite biventricular pacing is to correct not only the atrioventricular asynchrony but also the nonuniformity of ventricular activation, contraction and relaxation sequences. It is proposed primarily for patients with drug refractory heart failure with LV systolic dysfunction and wide QRS complex. In 1994 Cazeau et al[12] from France reported the remarkable benefit of biventricular pacing in a patient with drug-refractory CHF due to dilated cardiomyopathy, and left bundle-branch block (QRS=200 ms). The left ventricle (LV) and right ventricle (RV) were paced simultaneously to achieve a more physiologic depolarization sequence. Since this report, a substantial number of short-term studies have shown that biventricular pacing improves haemodynamics in CHF patients with severe left ventricular systolic dysfunction and major left sided intraventricular conduction disorders.[6,7,13,15,16] A longer spontaneous QRS complex may be predictive of a greater positive response to pacing. Intraventricular conduction delays cause an inefficient dysynchronous pattern of left ventricular activation with segments contracting at different times. The rationale of biventricular pacing is to improve the sequence of electrical activation (resynchronization) and create a more coordinated and efficient left ventricular contraction. Resynchronization may also reduce functional mitral regurgitation.[14-16] Reversal of left ventricular remodeling by synchronous biventricular pacing in heart failure was reported.[17]

Patients with chronic atrial fibrillation may also benefit. In this instance, continual biventricular pacing often requires radiofrequency ablation of the Atrial-ventricular (AV) junction to ensure control of ventricular depolarization by the pacemaker.[18] Optimized AV delay played an important role in improvement of hamodynomics particularly in patients accompanied by atrioventricular conduction delay. Shortening AV interval could reduce presystolic regurgitation and improve filling pattern of the left ventricle.[19]

Left Ventricular Pacing Technique

To achieve biventricular pacing, left ventricular lead placement is the most important part. The cardiac venous structures differ among individual patients, with wide variations in the location and size of the coronary sinus and its side branches. Consequently, adequate visualization of the venous anatomy is very important in transvenous left ventricular lead placement. The venous phase of the coronary angiogram sufficiently outlines the coronary sinus ostium and a number of its branches in about 20% of patients. Selective coronary sinus catheterization from the subclavian route undoubtedly provides better visualization of potential sites for lead placement. The use of an occlusive balloon enhances the quality of the images. AP, RAO, and LAO views of the coronary sinus will help in guiding the leads, and a knowledge of the position, angulations, and size of the side branches will assist in lead selection and placement.

The lead most commonly used for left ventricular pacing is the attain LV model 2187, a unipolar, polyurethane lead, available in 65 cm or 75 cm length, with a curved distal body and a soft tip. The tip can be straightened using the stylet. Withdrawal of the stylet alters the curve, allowing angulation of the lead to the desired location. Recently, the new transvenous over-the-wire and side wire (Figure 1) left ventricular lead system has been used in clinical practice.[20,21] The left ventricular lead is implanted via the subclavian vein and, ideally, placed in a vein in the posterolarteral or lateral wall of the heart, where the sensed endocardial signals occur late in the QRS complex. The right ventricular lead is then placed at a site anatomically remote from the left ventricular lead, with good electrical separation and, preferably, early in the QRS complex.

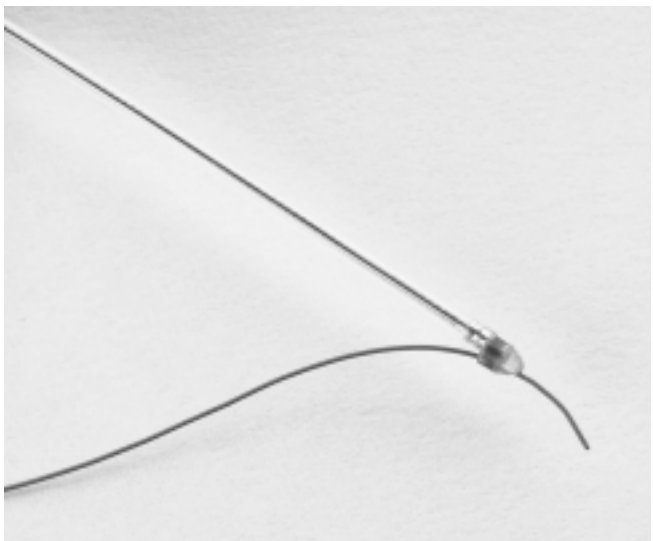

Figure 1. *Side-wire left ventricular lead system*

Successful transvenous ventricular lead implantation is defined as (1) a stable left ventricular lead position, (2) satisfactory pacing thresholds and (3) good electrical and anatomic separation of the right and left ventricular leads. The clinical experience shows that success rate for transvenous left ventricular lead implantation was 84-93%.[22,23] Left ventricular lead implantation requires more time than implantation of traditional pacemaker leads. New technology and techniques are likely to reduce the time required for implantation in the future.

Clinical Observation of Biventricular Pacing

Results from uncontrolled studies suggest that multisite pacing improves selected heart failure patients. One of the largest of these is the InSync study.[24,25] It comprised 103 patients with severe heart failure of mixed etiology. All patients had severe heart failure, NYHA functional class III-IV, and a QRS duration of at least 150 ms. Significant improvements by biventricular pacing were seen in most patients after 12 months of pacing compared to baseline with regard to NYHA class, 6-minute walk distance, and quality of life. Moreover, pacing reduced the QRS duration significantly and normalized the intraventricular delay as an indication that ventricular resynchronization had been achieved.

There are a number of randomized trials on the efficacy and safety of biventricular pacing, the results of some of them remain to be published (Figure 2). In the Pacing Therapies for Congestive Heart Failure (PATH CHF) trial,[26] patients with severe heart failure (120 ms) were included. After an extensive acute invasive evaluation performed during implantation, the patients were randomized during implantation, the patients univentricular mode - that is, right or left ventricular pacing only, no pacing, and biventricular pacing. The study enrolment ended in 1998 and included 54 patients. Interim results indicate a 40% improvement

in the 6-minute walk distance and a 50% improvement in quality of life after 1 month of the best univentricular mode cases constituted by left ventricular pacing, and 1 month of biventricular pacing.

The Multisite Stimulation in Cardiomyopathy (MUSTIC) study[22] involves 67 patients. Enrolment was completed in June 1999. This study includes only NYHA class III heart failure patients with a sinus rhythm, QRS duration of at least 150 ms. The patients were randomized in a single blind crossover fashion to 3 months each of biventricular pacing or fixed rate ventricular pacing at a rate of 40 beats per minute. The primary end points are the 6-minute walk distance and maximal oxygen uptake, with quality of life as a secondary end point. The result shows that the mean distance walked in 6 minutes was 23% greater with active pacing, the quality-of-life score improved by 32%, peak oxygen uptake increased by 8%, hospitalizations were decreased by two thirds, and active pacing was preferred by 85% of the patients.

The Multicenter Insync Randomized Clinical Evolution (MIRACLE) study[23] is a large prospective, randomized, double-blind, controlled trial designed to more definitively evaluated the clinical efficacy and safety of cardiac resynchronization for heart failure. Until July 2000, this study has being enrolled 370 patients with NYHA class III and IV systolic heart failure and QRS durations of 130 ms or more. The primary end points is defined the effects on functional status (quality of life, NYHA class, 6-minute hall walk distance) at 6 months. The result was presented in the North American Society of Pacing and Electrophysiology, 22nd Annual Scientific Sessions (NASPE 2001). The success rate for transvenous left ventricular lead was 93%. The 6-minute walk distance was 350 meters in active pacing and 300 meters during control phase. The quality of life score was improved 22%. The peak oxygen uptake was a trend to increase but no significant difference (p=0.056).

Biventricular pacing is a promising treatment in patients with severe heart failure with intraventricular conduction disturbances. It helps to improve patients by at least one functional class, increases the 6-minute walk distance by 20-40%, increases the oxygen uptake by 8-40%, and improves quality of life (as assessed by

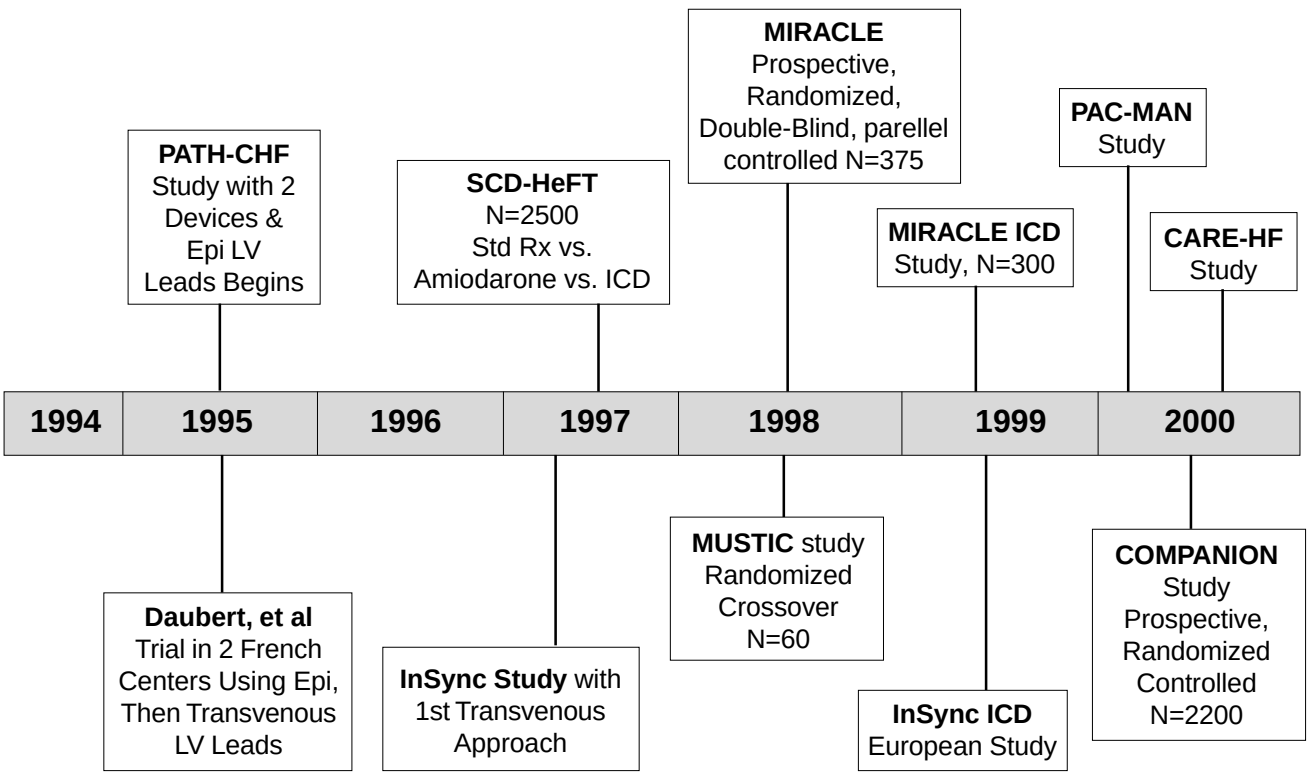

Figure 2. *Clinical studies about resynchronization therapy.*

the Minnesota living with heart failure questionnaire) by 20-50%. These figures are impressive. From uncontrolled and controlled studies it is also clear that not all patients respond to this treatment. Clinical, electrical or echocardiographic predictors of response to pacing are needed in view of the costs involved in pacemaker implantation and follow up. The ultimate success of the ambitious efforts to resynchronize cardiac activity in CHF will depend on defining its real benefit in a variety of circumstances by rigorous scientific evaluation and the development of new technology or further refinement of existing technology. For example, adjusted RV-LV stimulation delay - rather than simultaneous activation - may enhance the hemodynamic response. Left ventricular dual-site pacing seems to improve haemodynamics compare to single site left ventricular pacing. Implantable Cardioverter-Defibrillator (ICD) encompass the biventricular pacing could reduce episodes of ventricular tachyarrthmias by improve heart function in patients with intraventricular conduction delay.[27,28] Ongoing clinical studies (InSynch-ICD, CONTAKCD, COMPANION) will prove ICD combine biventricular pacing could further improve the quality of life and survivals.

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