# BIVENTRICULAR PACING THERAPY FOR HEART FAILURE: A REVIEW OF THE LITERATURE

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Given its wide spread and poor prognosis, heart failure (HF) is a true challenge in modern cardiology. To address HF, many therapeutic modalities have been developed, such as cardiomyoplasty [1], implantable devices to help heart pumping function [2, 3], transcatheter radiofrequency ablation of atrioventricular (AV) junction in atrial fibrillation [4, 5], intracardiac cardioversion in HF complicated with tachyarrhythmias [6, 7], heart transplantation, and others.

Booming pacemaking technique exceeded by far the original need for correction of bradyarrhythmias: by early 1980s, new areas for application of pacing have been identified. In 1990-1992 M.Hochleitner et al. [8, 9] published surprising results of successful use of permanent bicameral (atrial and ventricular) pacing with shortened AV delay to treat the last-stage HF caused by dilatation cardiomyopathy.

In 1994, two teams of researchers S.Cazeau et al. [10] and P.Bakker et al. [11] were first to use tricameral (atrio-biventricular) pacing in patients with severe HF and intraventricular block and managed to improve dramatically their condition. To correct the myocardial dyssynchrony, one of the components of chronic HF, various pacing modalitites have been tried: pacing of the right and left ventricles (RV and LV), combined bifocal RV pacing, and biventricular pacing [12]. P.Jais et al. [13] first implanted a biventricular pacing system in a patient with the end-stage congestive HF and sick sinus syndrome through puncture of the atrial septum after having failed to place an LV lead in the coronary sinus. F.Leclerq et al. [14] recommended the wider use of transseptal puncture for placing permanent pacing leads in the LV. What has not been tried yet is a direct transarterial endocardial LV pacing as it is associated with high risk of thromboebolism [15]. In a survey of inadvertent positioning of leads in the LV [16] the incidence of cerebral embolism events exceeded 25%. D.Warfield et al. [17] believe anticoagulation can help reduce, though not eliminate fully, the number of thromboebolic complications. However, the need for anticoagulation in early postoperative period does result in the increased incidence of hematomas in the pacemaker pocket [18].

Alternative ways of permanent RV pacing and various modes of multifocal pacing would normalize the electrical systole and increase the cardiac index [19]. Nonetheless, since the first implantation of endocardial pacemaker in 1959 by S.Furman, J.Schwedel [20] in a Stokes-Adams seizure patient, with an electrode positioned in the RV apex, the latter site is still being traditionally used for obvious ease of lead placement and no major complications postoperatively. The RV apex pacing has proved to have negative inotropic effect and cause a long-term myocardial dysfunction, especially in patients with heart failure and ventricular conduction disturbance. The MOST (Mode Selection Trial) findings demonstrated that asynchronous contractions of the right and left ventricles seen in permanent RV pacing in clinically significant sinus node dysfunction and normal length QRS do increase the risk of hospitalization for chronic heart failure (CHF) and atrial fibrillation even with preserved synchrony in AV conduction [21].

Apical pacing distorts normal conduction pattern in the myocardium, causing in particular an abnormal motion of the septum, asynchronous ventricular contractions and prolonged relaxation phase, thus impairing central hemodynamics. The cardiac output is diminished both in single-chamber, and sequential pacing, with intact AV synchrony [22]. B.Stojnic et al. [23] demonstrated that bicameral apical VDD pacing vs. only atrial AAI pacing does result in delayed excitation in various sites of the RV and the LV.

Other authors [24], while confirming this finding, discovered that the same patients with bicameral pacing from the apex and resultant decrease in cardiac output, would increase the cardiac output when switched to exclusively atrial pacing (with St-Q interval less than 220 ms). Thus, there was demonstrated the hemodynamic benefit of 'natural' propagation of the excitation vs. 'artificial' one from the apex.

These findings and numerous echocardiographic data in ventricular septum pacing [25] prompted the search of new hemodynamically more efficient ways of ventricular pacing from alternative sites, new ways of delivery and fixation of leads. Variously shaped leads have been designed to prevent them from dislodgement and ensure safe pacing as far as pacing threshold, adequate sensing and avoidance of perforation of ventricular wall are concerned. In 1991 E.Barin et al. [19] published a series of 33 patients successfully treated with permanent pacing where the lead was placed in the RV outflow tract. C.DeCock et al. [26] reported a considerable (17%) increase of the cardiac index associated with permanent pacing of the RV outflow tract.

Currently, the following alternative ways of pacing have been proposed and being evaluated:

1. Single monofocal endocardial RV outflow tract pacing, also called septal pacing.
2. Bifocal RV pacing: the RV is simultaneously paced from two sites, by convention, the outflow tract and the apex.
3. Biventricular pacing: both the RV, and the LV are paced. The RV is paced in a conventional endocardial mode from the apex, while the LV is paced either endocardially, or epicardially. Various ways of delivering the LV lead have been tried: transvenously via coronary sinus, via punctured atrial septum, and finally via thoracotomy for epicardial pacing.

As mentioned above, the RV outflow tract pacing has not been convincingly advantageous compared to apical pacing. P.Bakker et al. [27] used biventricular pacing (the LV epicardially, and the RV endocardially) to treat congestive heart failure. The need for thoracotomy was one big disadvantage of this method.

First successful permanent LV pacing using leads placed via cardiac veins dates back to 1994 [28], though technically it is difficult to place regular leads into the coronary sinus. J.Daubert et al. [29] tested a number of specially designed leads for permanent left atrial pacing via the coronary sinus. They managed to position leads in the heart veins in 74% cases only.

Currently, guidewire and tine containing 4.1 Fr leads (Select Secure, model 3830; Medtronic, Inc.) are delivered and positioned in various sites of the heart for direct His bundle vs. septum or para-hisian/outflow tract pacing [30].

In recent decade cardiac resynchronization therapy (CRT) has been actively translated into practice as a relatively new and efficient way for addressing the CHF [31]. CRT, also known as biventricular pacing or multisite ventricular pacing, involves simultaneous pacing of the RV and the LV. To this end, a coronary sinus lead is placed for LV pacing in addition to a conventional RV endocardial lead (with or without a right atrial [RA] lead). Alternatively, the lead can be sutured to the LV epicardium.

The basic goal of CRT is to restore LV synchrony in patients with dilated cardiomyopathy and a widened QRS, which is predominantly a result of left bundle branch block, in order to improve the mechanical functioning of the LV. Randomized clinical trials have confirmed the effectiveness of CRT for improving cardiac hemodynamics and symptoms; preventing hospitalization; and improving mortality as compared with conventional therapy in patients with advanced heart failure symptoms and severe left ventricular dysfunction.

Evidence suggests that CRT may even be beneficial in patients with mildly symptomatic heart failure (New York Heart Association [NYHA] class II). A study of 659 heart failure patients who underwent successful CRT found the procedure safe to use in patients with clinically significant mitral regurgitation (MR). At 12-month followup, patients with more than mild MR had comparable results to patients with mild or no MR. Most of the benefits appear to be associated with the presence of left bundle branch block (LBBB) on electrocardiography (ECG); the longer the QRS duration (particularly >150 ms), the more beneficial CRT is likely to be. In light of this and other accumulating evidence, the American College of Cardiology, American Heart Association and Heart Rhythm Society modified the Class I indication for CRT to include not only patients with NYHA class III and IV symptoms, but also those with NYHA class II symptoms and left-bundle-branch block with a QRS duration that is greater than or equal to 150 ms.

In patients with other forms of conduction disturbance (eg, right bundle branch block [RBBB] or RV pacing), CRT is of questionable utility and therefore cannot be recommended at this time.

Successful resynchronization can be achieved with placement of the LV lead in almost any CS branch, provided that the site is in the proximal third to the middle third of the LV. Placement of the lead in areas with maximal dyssynchrony has been associated with better CRT outcomes.

Coronary sinus is accessed via peripheral veins, such as axillary, subclavian or cephalica, The LV lead is delivered using multiple sheaths, allowing the delivery of a 6F to 4F pacing leads via the inner catheter. Selection of pacing leads is dictated predominantly by the anatomy of the branch and the ease of deliverability. Bipolar leads are used in most cases, with unipolar leads reserved for patients with extremely small branches (i.e., branches that are too small to accommodate a 4F bipolar lead). In Europe, multipolar leads with 4 separate pacing electrodes are available; these have been associated with improved implantation success. Left ventricular pacing leads are typically secured either with active fixation using tines or with passive fixation using the multiple curves of the lead to fit it tightly in the target vein.

Although it may be possible to place the LV lead without knowing the anatomy of the coronary sinus (CS) and its branches, it is prudent to obtain a CS phlebogram to direct the selection and placement of this lead. In most patients, a balloon angiography catheter should be used for contrast injection to achieve optimal opacification of the CS and its branches.

Complications of CRT include the dissection or perforation of the coronary sinus or rupture of its branch (in most cases, this is of no clinical consequence,though pericardial effusion should be echocardiographically monitored for continuing accumulation or development of tamponade physiology) and lead dislodgment (5%-7% of cases) as well as diaphragmatic capture or a change in the capture threshold soon after implantation, which may require electronic repositioning .

Appropriate device programming should yield reliable biventricular pacing. Only patients with at least 95% of biventricular pacing will benefit from CRT; therefore, the AV delay should be programmed to be short. The various device manufacturers have developed several algorithms that allow automatic programming of AV delay as well as RV-to-LV delay. However, these algorithms have not been associated with improved outcomes as compared with programming of the AV delay to 130 and 100 ms (paced and sensed, respectively). Another option is to use echocardiography-based parameters for AV optimization, although this is not supported by clinical outcome data.

Typically, the lower pacing rate should be programmed to be about 50 beats/min unless sinoatrial (SA) node dysfunction is present. The maximum tracking rate should be extended as far as is feasible in the device to allow biventricular pacing throughout a wide span of sinus rates. In patients who have SA node dysfunction, rate response should also be programmed.

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## ТҮЙІН


Жүрек жетіспеушілікте жүрекке қос қарыншалық (бивентрикулярлық) электр ырғақ беру терапиясы: әдебиет шолуы

Жүрек жетіспеушілікте жүрекке қос қарыншалық (бивентрикулярлық) электр ырғақ беру саласындағы күні бүгінгі деректер келтірілген.

Өзекті сөздер: Жүрек жетіспеушілігі, дилатациялық кардиомиопатия, кардиоресинхронизациялық ем, бивентрикулярлық электр ырғақ беру.


## РЕЗЮМЕ


**Бивентрикулярная электрокардиостимуляция в лечении сердечной недостаточности: обзор литературы**

Представлены современные данные по применению бивентрикулярной электрокардиостимуляции при сердечной недостаточности.

Ключевые слова: Сердечная недостаточность, дилатационная кардимиопатия, кардиоресинхронизирующая терапия, бивентрикулярная электркардиостимуляция.