Biventricular Pacing: A Promising Therapeutic Alternative for Patients with Severe Congestive Heart Failure

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Summary

Biventricular pacing is a novel therapy for patients with heart failure and severely diminished left ventricular function associated with intracardiac conduction delay. The primary aim of biventricular pacing is to re-synchronize the ventricular activation pattern and to improve hemodynamics. Results of early and recent studies including large-scale, multicenter, randomized trials demonstrated the efficacy of this treatment modality showing improved hemodynamics, exercise tolerance and quality of life in patients with severe heart failure. Preliminary data suggest that patients with atrial fibrillation may also benefit. There is growing evidence showing that the frequency of life-threatening arrhythmias is decreased using biventricular pacing in this patient population. However, the effect of biventricular pacing on mortality is still unknown. Ongoing trials will clarify the important issues regarding the influence on mortality and the problem of appropriate patient selection.

Key Words

Biventricular pacing, heart failure

Introduction

Heart failure is a highly prevalent disease, and despite recent advances in medical therapy it remains a growing health problem [1]. Intraventricular conduction delay is an independent predictor of mortality in patients with severe congestive heart failure (CHF) [2]. Multisite or biventricular pacing was recently developed as a possible novel pacing modality for patients with CHF and intraventricular conduction delay [3]. In patients with drug refractory heart failure and a severely diminished left ventricular function associated with significant intracardiac conduction delay, biventricular pacing can be used to improve mechanical synchrony [4]. Results of available controlled and uncontrolled studies show improvement in hemodynamics, exercise tolerance, and quality of life in patients with heart failure [3-7]. The aim of this review is to summarize the current knowledge regarding biventricular pacing as well as the potential mechanism of the effectiveness of this pacing modality, including the evaluation of the optimal pacing sites. Furthermore, on the basis of our experience, we provide a description of the implantation technique. The possible role of a combined biventricular pacing and ICD therapy is also discussed, particularly the influence of biventricular pacing on the recurrence of ventricular tachyarrhythmias.

Rationale for Biventricular Pacing

A considerable proportion of patients with severe CHF often have significant intraventricular conduction delay and left bundle branch block [2]. This intraventricular conduction delay – indicated by prolonged QRS duration – may cause an abnormal contraction pattern that is recognized as ventricular dyssynchrony [4]. Segments of the left and right ventricle contract at different times. Ventricular dyssynchrony results in abnormal interventricular septal wall motion, decreased contractility (dP/dt), reduced diastolic filling

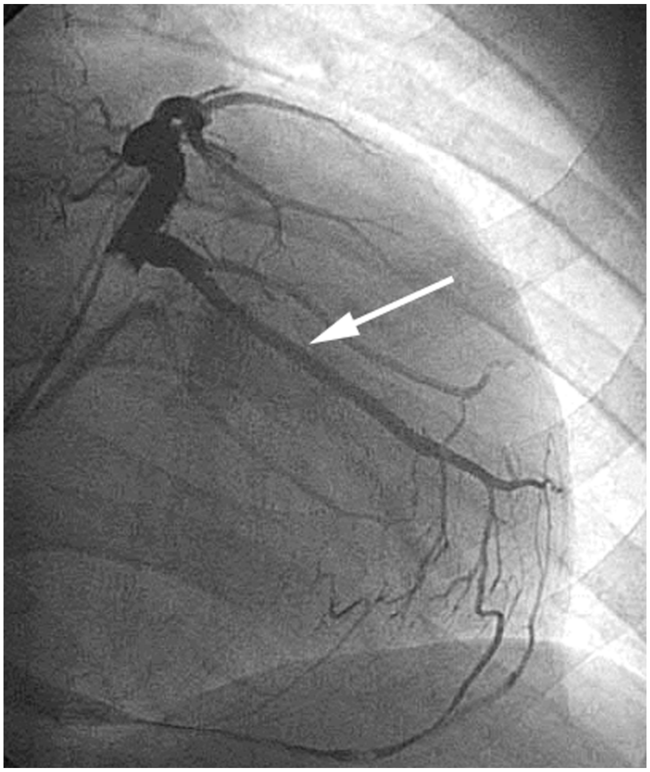

Figure 1. Occlusion venogram of the distal coronary sinus shows appropriate side branches (arrow) for biventricular pacing.

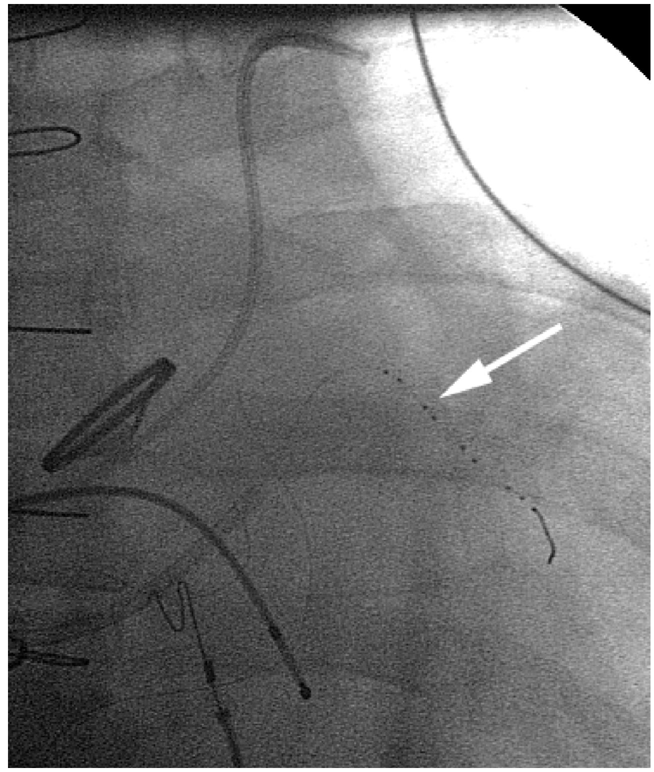

Figure 2. Temporary multipolar electrode catheter (arrow) is used for acute hemodynamic study.

times, and prolonged duration of mitral regurgitation causing a significant mechanical disadvantage for the failing heart [8,9]. Theoretically, multisite or biventricular pacing may resynchronize the contraction pattern of the ventricles [3-5]. This idea serves as a rationale for biventricular pacing in this severely ill patient population. Re-coordination of the activation pattern can normalize the so-called functional mitral regurgitation and may optimize left ventricular filling [4]. However, the trend towards a superior hemodynamic benefit has to be interpreted with caution because the atrioventricular delay was optimized in most of the studies, which has had a major impact by itself [10]. Recent data suggest that patients with atrial fibrillation may also benefit, but to achieve sufficient pacing time, radiofrequency catheter ablation of the atrioventricular node is often required [11].

A number of randomized trials have provided information on the efficacy and safety of biventricular pacing. Patients with severe heart failure (NYHA III or IV) and wide QRS complex were included in the Pacing Therapy in Congestive Heart Failure trial (PATH-CHF). During implantation invasive testing was performed and patients were then randomized to a one-month period of either univentricular pacing, no pacing, or biventricular pacing. The study utilized a three-month crossover period between pacing modes. The chronic pacing mode was optimized according to the results of the crossover period. Results showed a 40 % increase in the six-minute walking distance and a 50 % improvement in the quality of life with biventricular and preferred univentricular (usually left ventricular) pacing. The Multisite Stimulation in Cardiomyopathies (MUSTIC) trial randomized 67 patients with severe heart failure associated with a QRS duration > 150 ms. This single-blind, randomized, controlled crossover study compared the responses of patients during two different pacing situations: three months of inactive pacing and three months of atriobiventricular pacing. The study concluded that although the procedure is technically complex, atriobiventricular pacing significantly improves exercise tolerance and quality of life in patients with chronic heart failure and significant intraventricular conduction delay [6]. These results were confirmed by the Multicenter InSync Randomized Clinical Evaluation Trial (MIRACLE) [12], which were presented at the 2001 Scientific Session of the American College of Cardiology. The MIRACLE trial statistically proved the therapeutic benefit of cardiac resynchronization therapy. The functional status of the patients significantly improved; this was quantified by objective measures such as a reduction in systolic and diastolic volumes, increase in left ventricular ejection fraction and reduction of mitral regurgitation.

Selection of the Optimal Right and Left Ventricular Pacing Sites

Despite the strong theoretical basis, a considerable proportion of patients do not respond to biventricular pacing therapy even if a decreased duration of the QRS complex is achieved. Different approaches are used to select patients who will benefit most from biventricular pacing. In our center, a conventional electrophysiologic induction study is combined with an acute hemodynamic evaluation of biventricular pacing. Standard diagnostic catheters are used to stimulate the high right atrium and the right ventricle at different sites. The coronary sinus is cannulated with a specially designed vascular sheath (Vue Port, Cardima, USA) that contains an inflatable balloon that is capable of performing a venogram without the need of a separate balloon catheter (Figure 1). After the anatomical situation is assessed and recorded for future use, a very thin 1.5 F multipolar electrode catheter (Pathfinder, Cardima) is inserted into the CS to perform the pacing study (Figure 2). At least two different side branches – that seem feasible according to the venogram – are cannulated by this multipolar electrode catheter. Intracardiac electrograms are recorded and the pacing threshold is evaluated at each site at different atriobiventricular pacing rates and atriventricular delays. A non-invasive, continuous photoplethysmograph with an optional model flow analysis (Portapres, TNO Biomedical Instrumentation, Amsterdam) that measures complex hemodynamics throughout the whole study including cardiac output, stroke volume and total peripheral resistance is connected to the patient. A transthoracic echocardiography that assesses transmitral flow completes the setup. The optimal pacing site is selected according to the results of the acute hemodynamic measurements. There is growing evidence showing the disadvantageous effect of right ventricular apical pacing on left ventricular function [13]. Therefore, in the case of a non-responding patient, the right ventricular lead is repositioned from the right ventricular apex to alternative pacing sites (i.e., the right ventricular outflow tract), and the measurements are repeated. However, improved acute hemodynamics does not necessarily mean an improved clinical outcome including a reduction in mortality. The evaluation of this issue necessitates large-scale randomized trials.

The Technique of Left Ventricular Lead Positioning

Transvenous implantation of the left ventricular lead via the coronary sinus (CS) is well-developed; however, there is still a need to describe the optimal implantation technique. The methodology developed at the Thorax Center in Rotterdam, the Netherlands, is based on our own, as well as adopted international experience. After puncture of the subclavian vein, the CS is cannulated with a non-steerable diagnostic catheter using a combined electrophysiologic and anatomical approach. After successful cannulation of the CS, a 9 F delivery sheath is placed over the catheter distal to the CS, providing a stable and multipurpose access to the targeted vein which is selected according to the acute hemodynamic study (see above). The "peel away" sheath is then used to deliver a permanent, unipolar pacing lead, preferably at the lateral wall, midway between the apex and the base. Other lateral and posterior sites are also acceptable, but the great cardiac vein and the middle cardiac vein are used only when the other veins are not suitable.

Biventricular ICD Therapy and Recurrences of Ventricular Tachyarrhythmias

Although most of the recent studies demonstrated the beneficial effects of biventricular pacing on this patient population, the mortality rate still remains fairly high [14]. Nevertheless, none of the studies mentioned above aimed to assess the mortality in a randomized fashion. The high mortality rate suggests the natural course of this severe, advanced stage of heart failure disease because this pacing modality is used mainly for very sick patients with CHF, which is usually refractory to drug therapy. Since the incidence of sudden cardiac death accounts for 30 – 50 % of the deaths in this patient population [14], combined biventricular pacemaker and defibrillator therapy should be considered. Improved hemodynamics with biventricular pacing may reduce the need for interventions by the implanted device. This possible and logical synergistic effect was proposed and studied by Higgins and his colleagues [15]. They reported that biventricular pacing diminished the need for ICD therapy for patients with tachyarrhythmias [15]. The decreased number of interventions by the ICD was possibly related to the improved hemodynamics. A decrease in ventricular conduction delay with biventricular pacing reduces macro-reentry and pause-dependent tachyarrhythmias because the dispersion of refractoriness is decreased, compared with right ventricular pacing [15,16]. The decrease in plasma nor-epinephrine levels and decreased sympathetic activity may also play a role [17,18]. Zagrodzky et al. showed that acute biventricular pacing decreases the inducibility of sustained monomorphic tachycardias in patients with ischemic cardiomyopathy [16]. In contrast, in a retrospective study conducted by Theuns et al., the time between implantation and the first recurrence of ventricular tachyarrhythmias was not modified by biventricular pacing in a virtually identical patient population [19]. Furthermore, subgroup analysis revealed a slightly earlier recurrence of ventricular tachyarrhythmias with a cycle length slower than 350 ms in the group treated with biventricular pacing, compared with groups having a dual-chamber ICD either with a narrow or broad QRS complex [19]. According to these results, the proarrhythmic effect of the left ventricular lead cannot be excluded. However, the potential and probably temporary disadvantage of this therapy's effect exists in the peri-procedural period. There is no available data comparing the late recurrence of the same arrhythmias with the recurrence of index arrhythmias.

Conclusion

So far, biventricular pacing is based on a modified conventional pacing setup. The placement of a permanent endocardial left ventricular lead using a transseptal technique seems technically feasible; however, the potential for life-threatening, thrombo-embolic complications has not yet been investigated. The enhanced hemodynamic response of multisite, left ventricular pacing in various clinical circumstances, such as the adjusted right ventricular-left ventricular stimulation delay, also necessitates further controlled studies.

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