Biventricular pacing and congestive heart failure: the wave of the future

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"O body swayed to music, O brightening glance,
How can we know the dancer from the dance?"
William Butler Yeats

Congestive heart failure (CHF) remains one of the enormous challenges of our time. In Ireland, it is estimated that there are over 80,000 people with CHF. There are over 10,000 new cases annually. With Ireland's ageing population, high coronary artery disease prevalence and increased longevity, it is projected that by the end of the next decade as many as 300,000 people will carry a diagnosis of CHF.

Despite the remarkable progress in pharmacological development over the past two decades, much needs to be accomplished. Angiotension-converting enzyme (ACE) inhibitors, beta-blockers, digoxin and spironolactone have made a significant impact on decreasing mortality and hospitalisation, and greatly improving quality of life. Nevertheless, the five year survival rate for all New York Heart Association (NYHA) classes is approximately 50%. Thus, the epidemic of CHF continues to gather momentum. Over one-half of CHF patients have three or more co-morbidities. CHF patients take an average of six medications. Over three-quarters of CHF patients have at least two hospital admissions per year. The resource utilisation of providing care to these patients continues to rise exponentially.

Mechanism of death

The aetiology of CHF in the majority of cases occurs predominantly as a consequence of ischaemic heart disease. Initially, patients with CHF symptoms can be stabilised. Patients can function almost normally provided they are compliant with their medications. However, over time there is a progressive deterioration of their symptoms, with decreased exercise tolerance, increasing shortness of breath, which leads to acute decompensation with increasing hospitalisations and rehospitalisations. Death in patients with CHF is due to either sudden cardiac death, typically a ventricular tachyarrhythmia or pump failure.

Sudden cardiac death

The majority of sudden cardiac deaths are due to either ventricular tachycardia or ventricular fibrillation. Paradoxically, the proportion of sudden cardiac deaths is highest in those patients who are stable with NYHA class II symptoms. Conversely, the proportion of pump failure deaths is highest in the most symptomatic patients with class IV symptoms. Deaths in patients resuscitated from ventricular arrhythmias can be decreased by 39% with the placement of an implantable cardioverter defibrillator (ICD) compared with amiodarone/sotalol. Patients with ischaemic CHF, a left ventricular ejection fraction of <35% and non-sustained ventricular tachycardia have been shown to have a decreased mortality after placement of an ICD. More recently, placement of an ICD has been shown to decrease mortality in mostly stable patients with CHF and a left ventricular ejection fraction of <30% (see Figures 1 and 2). However, despite these impressive results, patients continue to die from pump failure related events.

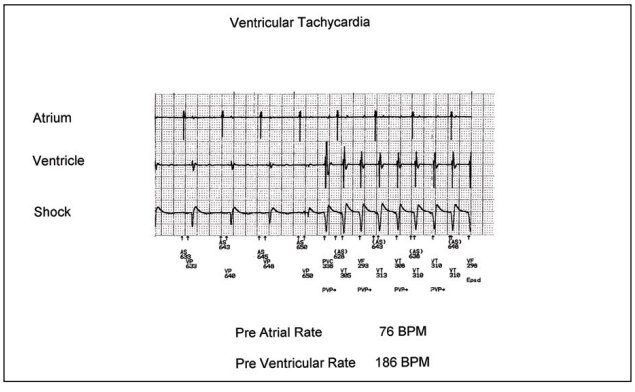

Figure 1. Monomorphic ventricular tachycardia in a patient with CHF, who received an implantable cardioverter defibrillator (ICD) as part of the MADIT II study. These electrograms from the ICD show there is AV dissociation. The atrial rate is 76bpm and the ventricular rate is 186bpm.

Pump failure deaths

Cardiac transplantation is a very effective option for patients with class IV heart failure. However, the need for heart transplants greatly exceeds the number of donor hearts that become available. Over the years, several other strategies with varying degrees of success have been pursued. Recently,

biventricular pacing has shown great promise in improving pump failure in patients with CHF and intraventricular conduction delay (wide QRS morphology).

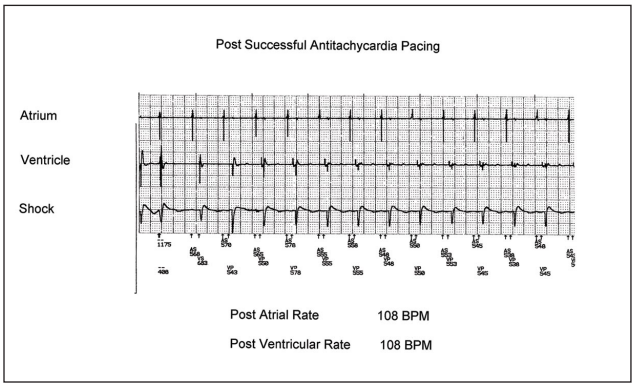

Figure 2. Electrogram following successful overdrive pacing of ventricular tachycardia in Figure 1 by the ICD. Post therapy the atrial and ventricular rate are identical at 108bpm.

Wide QRS complex

Delays in ventricular conduction leads to wide QRS complexes (see Figure 3), typically left or right bundle branch block. In patients with CHF and left bundle branch block (LBBB), ventricular dyssynchrony is seen during ventricular contraction. Conduction to the lateral wall is delayed. This leads to a disorganised ventricular contraction with a decrease in pumping efficiency. In LBBB, the interventricular septum is activated early. The later activation of the left ventricular lateral-free wall leads to a left ventricular contraction with paradoxical septal motion, causing a further decrease in pumping efficiency.

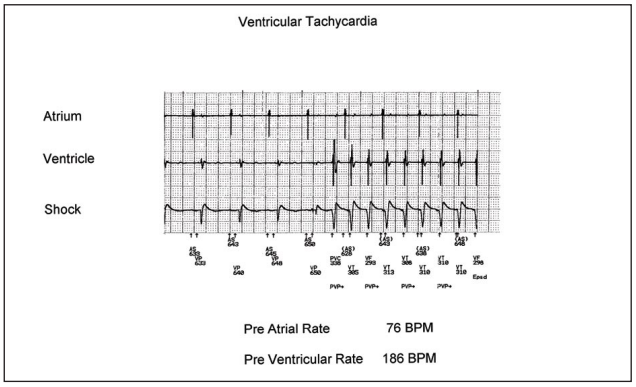

Figure 3. Electrocardiograph of a patient with CHF and wide QRS before cardiac resynchronisation therapy with an atriobiventricular pacemaker.

Almost a decade ago, it was proposed that the simultaneous activation of both the right and the left ventricles could be accomplished by biventricular pacing. The consequences of biventricular pacing included an organised ventricular

activation sequence and a coordinated septal and freewall contraction, leading to improved pumping efficiency, the so-called cardiac resynchronisation therapy.

It was also known that a delay in intra-atrial and AV nodal conduction prolonged PR interval in patients with CHF leading to a sub-optimal contribution of atrial systole, a limited filling time and diastolic mitral regurgitation. Diastolic mitral regurgitation occurs because the atrial pressures after atrial systole decrease below the left ventricular diastolic pressures. Blood returns to the atrium after the atrial contraction, but before the ventricular contraction due to the prolonged PR interval. Atrioventricular sequential pacing at a shorter AV interval (shorter PR interval) would abolish the diastolic mitral regurgitation.

Background to assessment of benefits of biventricular pacing

Small studies demonstrated a significant improvement in stroke volume during left ventricular or biventricular pacing. Previous studies of oral inotropic agents showed that there was an increased mortality associated with the use of these agents. The unexpected outcomes after the chronic use of these agents was due to increased energy demands of the failing heart that were required to achieve an increased systolic function. Concerns were expressed initially that, like several oral inotropic agents, biventricular pacing might also increase energy demands. Biventricular pacing was able to achieve a similar increase in cardiac output at a lower energy when compared to dobutamine that was titrated to achieve a similar heart rate.

Several parameters have been studied including norepinephrine levels, oxygen consumption, quality of life, echocardiographic parameters and many other markers associated with poor outcomes in CHF patients. Although the studies included small numbers of patients, all have shown encouraging trends towards reversal or significant improvement in these parameters.

Effects of wide QRS on mortality

Several studies have now shown a consistent finding. One year mortality in patients with CHF incrementally increases with progressive widening of the QRS, independent of other risk factors. Mortality at one year was 10% when the QRS was <90ms, rising to over 20% with QRS between 120 and 170ms, to almost 40% with QRS >220ms. This makes sense: the sicker the heart, the slower the ventricular activation, the longer the QRS complex. It was not clear if shortening the QRS duration would improve the prognosis (see Figures 3 and 4).

Biventricular pacing: a technical approach

To achieve the concept of biventricular pacing, both ventricles need to be simultaneously activated. This requires one pacing lead activating the right ventricle and another pacing lead activating the left ventricle. To maintain atrioventricular synchronised contraction, a lead is also required in the right atrium. The coronary sinus drains venous blood from the heart into the right atrium. Branches of the coronary sinus, specifically

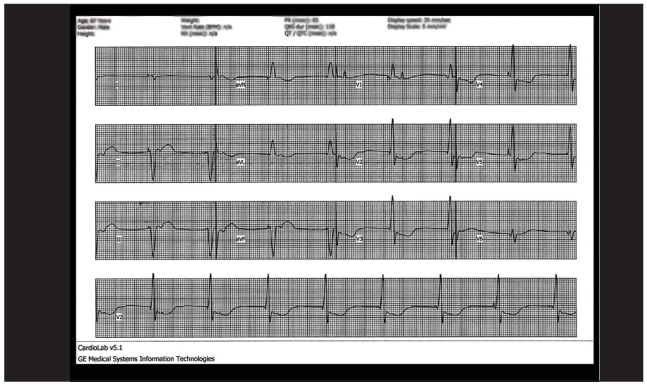

Figure 4. Electrocardiograph of the patient in Figure 3 after biventricular pacemaker placement. QRS duration decreased from 134ms to 118ms.

the lateral or posterolateral branches, lay over the lateral wall of the left ventricle.

The most common approach is transvenous. A sheath is advanced into the mouth of the coronary sinus. Once the coronary sinus is cannulated, a retrograde venogram is obtained to identify the target branch. An angioplasty guidewire is passed deep into the lateral branch. A passive fixation pacing lead is advanced over the guidewire into a stable position in the branch. The right atrial and right ventricular leads are placed as for a routine pacemaker. The supporting sheath is removed. The leads are connected to the biventricular pacemaker and placed in the pocket below the left clavicle (see Figure 5).

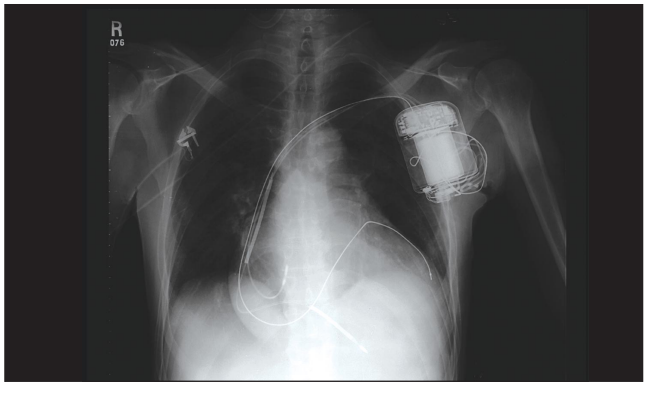

Figure 5. Chest x-ray of an atriobiventricular pacemaker and leads.

In approximately 7-10% of patients, it is not possible to place a left ventricular pacing lead transvenously. Several reasons have been identified and include absence of the coronary sinus, failure to cannulate the coronary sinus, failure to obtain a stable branch for the lead, absence of venous branches draining from the lateral or posterolateral wall, and left diaphragmatic stimulation of the phrenic nerve. In this situation, the right atrial and right ventricular leads are placed transvenously. A transthoracic approach is used to place a left lateral lead directly on the epicardium. The lead is then tunnelled to the biventricular pacemaker pocket and connected to the device. Follow up is routine as for regular dual chamber pacemakers.

MIRACLE study

The largest randomised published trial to date is the Multicenter InSync Randomized Clinical Evaluation (MIRACLE) study. In this study, 453 patients were assigned either biventricular pacing programmed on or off for six months. All these patients had a left ventricular (LV) ejection fraction ≤35%, QRS duration >130ms and a six minute walk of <450m. All patients were on stable medical therapy for several months. The mean LV ejection fraction was 22% and the mean QRS duration was 166ms. Over 90% were NYHA class III. There were significant improvement in exercise duration and quality of life. Over two-thirds of patients had one NYHA class improvement in their symptoms versus 38% with the device programmed off. Hospitalisation days decreased from 363 to 83 days, a 77% reduction. There were significant improvements in myocardial oxygen consumption, systolic function, and there was evidence of remodelling of the left ventricle on echocardiography.

The results of this study prompted the regulatory authority approval of this technology in many countries. Although this study was not powered to address mortality issues, there was a trend towards a lower mortality in the patients with biventricular therapy programmed on. Several larger trials that will address the mortality benefits are ongoing.

Special situations

Patients with right bundle branch block and CHF may also benefit from biventricular pacing therapy. In these patients, echocardiography identified LV dyssychrony, and this subset of patients benefited from therapy. Atrial fibrillation in the presence of CHF is a marker of poor outcome. Although atrioventricular pacing cannot be performed, these patients have been shown to benefit from therapy. However, it is important to note that these patients need to pace in the ventricular 100% of the time in order to obtain benefit from biventricular pacing. In those patients not pacing 100% of the time, they will require an AV node ablation. This will prevent the rapid ventricular response that is often seen with atrial fibrillation.

Delivery of biventricular services

To optimise the management of patients with CHF, a multidisciplinary approach is required to provide the patients with the best practice care possible. The team should be led by a heart failure specialist who coordinates the programme. The team should include nurse specialists, pharmacists, social worker support, administrative support and data-based management services. As many of these patients need device therapy to either treat or prevent sudden cardiac death with an ICD or improve cardiac output with a biventricular pacemaker, a trained electrophysiologist or rhythm specialist is required to facilitate device placement in these high risk patients. As part of this approach, it is important to continue to participate in research protocols that better define those patients likely to benefit from device therapy.

Future directions

Currently, patients with wide QRS complexes (>130ms) are thought to benefit from biventricular therapy. Estimates of CHF patients who also have wide QRS complexes varied between 10% and 40%. However, patients with CHF and QRS complexes <130ms may have LV dyssynchrony and may benefit from biventricular pacing. These populations are currently being studied. Intra-atrial conduction delay may limit the contribution of the left atrial systole. The mitral valve may already have closed before the left atrium gets activated. Perhaps a left atrial pacing lead will be required to improve the electromechanical timing of the cardiac cycle. Again, this will be evaluated in the future. The tools that facilitate cannulation of the coronary sinus are improving all the time. This may reduce the number of patients that require the much more invasive epicardial approach.

Finally, identification markers of those that benefit most need to be determined, and biventricular pacing needs to be made available to those at highest risk as early as possible.

Further reading

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