REVIEW

Role of resynchronisation therapy and implantable cardioverter defibrillators in heart failure

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Postgrad Med J 2006;82:16–23. doi: 10.1136/pgmj.2005.034199

The worldwide prevalence of heart failure is increasing in part because of an aging population. In the developed world, heart failure affects 1%–2% of the general population, accounting for 5% of adult hospital admissions. There is now convincing evidence supporting the beneficial effects of cardiac resynchronisation therapy for the treatment of heart failure. Numerous observational studies, as well as a series of randomised controlled trials, have shown the safety, efficacy, and long term benefits for patients with chronic systolic heart failure who have broad QRS complexes and refractory symptoms despite optimal medical therapy. These studies have consistently found statistically significant improvements in quality of life, New York Heart Association functional class, exercise tolerance, and left ventricular reverse remodelling. Recent evidence suggests that the benefit may at least in part be because of a reduction in mechanical dyssynchrony.

For more than a decade several pacing modalities have been considered for patients with severe drug refractory heart failure, with varying results. More recently randomised clinical trials, observational studies, and mechanistic studies have produced unequivocal support for the use of biventricular pacing in patients with NYHA III–IV refractory heart failure and evidence of ventricular conduction delay, most commonly seen as left bundle branch block (LBBB) on the electrocardiogram. These studies have consistently shown an improvement in objective functional status, quality of life, and exercise capacity in these patients.

ROLE OF PACING IN HEART FAILURE

Right ventricular pacing

The possible role of pacing in heart failure was first considered three decades ago. Hochleitner *et al*⁸ initially reported that right sided dual chamber pacing, with a short AV interval was of benefit in patients with heart failure who had no conventional indication for pacing. They described a reduction in NYHA class, fall in cardiothoracic ratio, and an increase in both systolic and diastolic blood pressure. The benefit was attributable to a reduction in pre-systolic mitral regurgitation, and hence an increase in left ventricular filling period. Pre-systolic mitral regurgitation was most pronounced in those patients with a prolonged AV delay and an increased left ventricular end diastolic pressure. The acute haemodynamic results in these and other studies^{9–10} were impressive, however, the longer term results were disappointing.^{11–13}

Subsequently there have been reports of haemodynamic benefits by pacing from the right ventricular outflow tract¹⁴ and from the His bundle.¹⁵ However, there are currently no published randomised trials comparing different right ventricular pacing sites.

More recently the dual chamber and VVI implantable defibrillator (DAVID) study¹⁶ and the mode selection (MOST) study¹⁷ have suggested that right ventricular pacing in itself may increase the incidence of heart failure. It is believed that despite restoring AV synchrony, RV pacing causes abnormal left ventricular electrical activity resulting in dyssynchronous mechanical activity.

Abbreviations: NYHA, New York Heart Association; LBBB, left bundle branch block; CRT, cardiac resynchronisation therapy; ICD, implantable cardioverter defibrillator; TDI, tissue Doppler imaging; TSI, tissue synchronisation imaging; LYG, life year gained

The worldwide prevalence of heart failure is increasing in part because of an aging population. In the developed world, heart failure affects 1%–2% of the general population,¹ and accounts for 5% of all adult hospital admissions.² It is estimated that 0.2% of the population are admitted to hospital with this condition each year. In the developed world, the major aetiological factors are ischaemic heart disease, hypertensive heart disease, idiopathic dilated cardiomyopathy, and valvular heart disease. Patients with advanced heart failure (New York Heart Association (NYHA) class III–IV), have both a poor quality of life and a poor prognosis. Death for these patients is usually attributable to disease progression, or less commonly is sudden. In contrast, death occurring in patients with NYHA I and II heart failure is more commonly sudden.

Within the first year of diagnosis mortality is up to 40%, with an additional 10% each year after this. In those with drug refractory symptoms the mortality is even higher. There have been several therapeutic advances in the treatment of heart failure over recent years, with the use of β blockers,³ angiotensin converting enzyme inhibitors,⁴ angiotensin II receptor blockers,⁵ and mineralocorticoid receptor blockers^{6,7}; however the prognosis remains extremely poor and there is probably limited potential for therapeutic benefit from additional neurohumoral block.

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Submitted
28 February 2005
Accepted 10 May 2005

Biventricular pacing for heart failure was first undertaken by Bakker in 1993. The initial cohort of heart failure patients assessed were those with a LBBB pattern on their ECG. This was based on the known adverse effects of LBBB. With LBBB there is late left ventricular activation via the septum from the right ventricle; this results in a delay between the onset of left and right ventricular mechanical contraction. LBBB is also associated with a delay in the opening and closure of the aortic valve and a delay in mitral valve opening, but has no effect on the timing of right ventricular events. This results in a significant reduction in the duration of left ventricular filling time. The presence of LBBB also results in abnormal ventricular septal motion, which in turn is related to interventricular dyssynchrony and an abnormal pressure differential between the right and left ventricle. The abnormal septal motion results in an increase in the left ventricular end systolic diameter and reduction in the left ventricular ejection fraction, cardiac output, mean arterial pressure, and dp/dt. Consequently LBBB is associated with more severe symptoms of heart failure and also a higher mortality in heart failure patients.^{18 19}

Biventricular pacing

Simultaneous ventricular pacing was therefore thought to reduce the dyssynchrony, hence the term cardiac resynchronisation therapy (CRT), improving ventricular contractility and hence the symptoms of heart failure. Numerous acute haemodynamic studies have been undertaken comparing the efficacy of biventricular, right ventricular, and left ventricular temporary pacing modalities.^{20 21} With biventricular pacing, these have consistently shown an improvement in left ventricular filling and contractile function, with a reduction in both pre-systolic and systolic mitral regurgitation and a reduction in pulmonary capillary wedge pressure. The increased contractile function is not associated with increased oxygen cost, implying an improvement in myocardial efficiency.²² Left ventricular pacing has also been shown to produce contractile and haemodynamic benefit in a small number of studies.^{23 24}

The initial clinical studies of long term biventricular pacing reported high perioperative mortality figures, related to the early invasive epicardial lead placement procedure, involving thoracotomy under a general anaesthetic.²⁵ Daubert *et al*²⁶

described the first transvenous approach for placing the left ventricular lead via the coronary sinus.

Several long term studies, of differing study design, have reported impressive results from biventricular pacing in heart failure patients with a prolonged QRS duration (>130 ms) who were severely symptomatic (NYHA III-IV) despite optimal medication. The InSync study²⁷ reported significant improvements in exercise capacity, NYHA class, and quality of life; the multisite stimulation in cardiomyopathy (MUSTIC) study²⁸ a significant improvement in exercise tolerance, NYHA score, peak oxygen uptake, and cardiac ejection fraction; the multi-centre InSync randomised clinical evaluation study (MIRACLE)²⁹ a significant improvement in exercise capacity and quality of life, and a 50% reduction in hospitalisation in the first six months. Core centre analysis of the echocardiography data from the MIRACLE study also provides evidence of reverse remodelling of the left ventricle. These studies were not powered to address mortality or morbidity as primary end points, however a meta-analysis of four studies (Contak CD, MUSTIC, MIRACLE, InSync ICD) with a total of 1634 patients³⁰ reported a 51% reduction in progressive heart failure mortality from 3.5% to 1.7%, and a 21% reduction in hospitalisation. The comparison of medical therapy, pacing and defibrillation in heart failure (COMPANION)³¹ study was a comparison of no pacing, biventricular pacing, and biventricular pacing with ICD. It was halted prematurely because the ICD limb showed a 40% reduction in the combined end point of death from or hospitalisation for heart failure, compared with a 34% reduction in the biventricular limb. This has resulted in biventricular pacing being granted a class IIa indication by ACC/AHA/NASPE.

The results of CARE-HF have recently been published. The trial was designed to evaluate the long term effects of cardiac resynchronisation on the mortality and morbidity of patients with heart failure attributable to left ventricular systolic dysfunction with a QRS duration >120 ms who were already receiving optimal medical therapy. A total of 813 patients were randomised to device therapy or control and followed up for a mean of 29.4 months. The trial reported a 37% reduction in combined all cause mortality (death) or unplanned cardiovascular hospitalisation, and a 36% reduction in all cause mortality.³² Table 1 summarises the effect of CRT on morbidity and mortality.

Figure 1 Changes in ventricular volumes with volume unloading. (A) Normal. (B) Heart failure with diastolic ventricular interaction. LBNP, lower body negative pressure.

Figure 2 Mechanisms of improvement in cardiac function with cardiac resynchronisation therapy.

ROLE OF IMPLANTABLE DEFIBRILLATORS IN HEART FAILURE

The major causes of death in patients with congestive heart failure are death from progressive pump failure and sudden cardiac death. The rates for total mortality and sudden death vary by functional class. In symptomatically mild (NYHA class II) patients the overall annual mortality is 5%–15%, with 50%–66% of these deaths being sudden. In NYHA class III, annual mortality increases to 30%–50%, and in class IV it often exceeds 50%. However, the proportion of deaths that are sudden decreases: in class III it falls to 20%–50% and in class IV to 5%–30%.³³

The implantable cardioverter defibrillator (ICD) has been shown in multiple studies to be the most effective available therapy to treat life threatening ventricular arrhythmias and to prevent sudden cardiac death. Three early randomised, prospective, controlled trials have shown conclusively that ICD is the treatment of choice in the primary prevention of sudden cardiac death in patients with a history of previous myocardial infarction (MADIT-I, MUSTT, MADIT-II).^{34–35} However, the results of MADIT-I and MUSTT have limited applicability to patients with symptomatic heart failure because less than 20% of patients recruited had advanced heart failure, and only a minority received β blocker therapy. These were followed up by MADIT-II. Patients with advanced heart failure were better represented in this trial, and all patients had LVEF < 30%. ICD therapy reduced the risk of death by 31% and was shown to be clearly superior to conventional anti-failure therapy for prolonged survival.³⁶

Several randomised controlled trials have shed new light on the appropriate treatment to prevent secondary cardiac death. The AVID trial compared ICD therapy with medical therapy (amiodarone or sotalol). More than half of all patients had congestive heart failure, with a mean LVEF of 31%. The trial was terminated early because of a significantly better overall survival in the group receiving ICD therapy. The benefit was most profound in those patients with LVEF < 35%.³⁷

For patients with ischaemic cardiomyopathy, data from MADIT-I and MADIT-II strongly support the use of ICD

therapy for the prevention of sudden cardiac death. For patients with idiopathic dilated cardiomyopathy the results of the CAT³⁸ and AMIOVERT³⁹ trials found no mortality benefit with ICD therapy. However, the COMPANION³¹ trial found a significant reduction in mortality in heart failure patients treated with a combined AICD/biventricular pacing device. There was a non-significant reduction in mortality in those treated with biventricular pacing alone. Subgroup analysis showed significant improvements in survival in the context of both ischaemic and non-ischaemic aetiology. This is supported by the results from SCD-HeFT.⁴⁰ In this trial ICD therapy was compared with amiodarone and with placebo in patients with an LVEF $\leq$ 35% and NYHA class II/III heart failure symptoms. There was a 23% reduction in mortality in the ICD group, and the benefit was similar for both the ischaemic and non-ischaemic group. However, most benefit was derived in the group with NYHA class II symptoms, with no benefit seen in patients with NYHA class III symptoms. Amiodarone did not affect mortality.

MECHANISMS OF BENEFIT FROM BIVENTRICULAR PACING

Several mechanisms are thought to be responsible for the benefit seen with biventricular pacing in patients with heart failure (see fig 2).

Electrical and mechanical resynchronisation

As stated previously, biventricular pacing is currently advocated for patients with NYHA III and IV class symptoms despite optimal medical therapy who have prolonged QRS durations (>120 ms). The latter is based on the original rationale that biventricular pacing acts via an improvement in cardiac “electrical synchrony”, hence the commonly used term “resynchronisation therapy”. The phenomenon of dyssynchrony is a consequence of progressive, global, or focal degradation of the myocardium. This leads to heterogeneous propagation of cardiac electrical activity.

Intraventricular dyssynchrony

This refers to the pronounced heterogeneity in the timing of mechanical events between different segments of the left

Table 1 Effect of cardiac resynchronisation therapy (CRT) on morbidity and mortality

Study	Follow up	Therapy	Risk reduction with CRT or CRT-ICD therapy			
			Mortality and hospitalisation (%)	Mortality and heart failure hospitalisation (%)	Mortality (%)	Heart failure mortality (%)
COMPANION (n = 1520)	12 months	CRT+ICD	19.3	39.5	43.4	
		CRT	18.6	35.8	23.9	
MIRACLE (n = 453)	6 months	CRT		39	27	50
JAMA meta-analysis (n = 1634)	3–6 months	CRT			23	29
CARE-HF (n = 813)	29.4 months	CRT		37	36	

ventricle that is frequently seen in patients with heart failure. Although partly attributable to electrical dyssynchrony, other factors seem to contribute to mechanical dyssynchrony.^{41–42} Hence echocardiographic markers of mechanical dyssynchrony show considerable variation in patients with broad QRS duration, and pronounced mechanical dyssynchrony may be present in heart failure patients with narrow QRS duration.^{42–43} Biventricular pacing (which reduces QRS duration) reduces parameters of mechanical dyssynchrony, but curiously, despite increasing QRS duration, LV pacing also reduces mechanical dyssynchrony.⁴² Furthermore, the BELIEVE study reported comparable clinical benefit from left ventricular and biventricular pacing. Nevertheless, several studies, using a variety of techniques have shown that biventricular pacing produces the greatest echocardiographic, haemodynamic, and clinical benefit in those patients with the greatest mechanical dyssynchrony at baseline and reductions in dyssynchrony with pacing also predict these benefits.^{44–46}

There is as yet no gold standard technique for quantifying intraventricular mechanical dyssynchrony. Studies have shown that measuring time to peak tissue velocity (Ts) from myocardial velocity curves using tissue Doppler imaging (TDI) are useful for quantitative assessment of systolic dyssynchrony. In particular, the dyssynchrony index (Ts-SD), or standard deviation of Ts in a 12-segment model, was a powerful predictor of LV reverse remodelling after CRT therapy.^{43–47} Tissue synchronisation imaging (TSI) is a technological advancement in the assessment of systolic dyssynchrony by transforming the Ts into different colour coding. It has the advantage of providing a visual aid for quick identification of regional delay within the LV wall. Yu *et al* have validated the good correlation between Ts or Ts-SD derived from both TDI and TSI.⁴⁸

Left ventricular remodelling

Biventricular pacing has been shown to have a beneficial effect on left ventricular remodelling. Increased ventricular ejection efficiency resulting from coordinate contraction, a reduction in mitral regurgitation, and a reduction in sympathetic/parasympathetic imbalance may contribute to chronically unload both ventricles and initiate reverse remodelling. In a non-randomised study Yu *et al* evaluated 25 NYHA class III–IV patients with an ejection fraction <40% and a QRS duration >140 ms, who received biventricular pacing. Continued pacing at three months in these patients resulted in significant improvements in ejection fraction, left ventricular volumes, left ventricular dp/dt max, myocardial performance index, and the degree of mitral regurgitation. Withholding pacing for a four week period resulted in a progressive, but not immediate, loss of effect. It was concluded that the improvement in left ventricular mechanical dyssynchrony was the mechanism for this.

Data from several randomised trials consistently show that CRT is able to induce reverse remodelling in the vast majority of patients. Stellbrink *et al*⁴⁹ analysed 25 patients included in the PATH-CHF trial, focusing on changes in left ventricular volumes after CRT. Left ventricular end diastolic (LVEDD) and end systolic dimensions (LVESDs) were significantly reduced after six months, as were left ventricular volumes. These findings are supported by data from the MIRACLE, CONTAK-CD, Vigor-CHF, and INSYN-ICD trials.

Activation of the neuroendocrine system is an early phenomenon in patients with coronary heart failure and left ventricular dysfunction, and has been recognised as a predictor of death. Saxon *et al*⁵⁰ recently reported no significant change in noradrenaline levels during three months of biventricular pacing. In contrast, Hamdan and colleagues found that CRT decreased sympathetic nerve activity, which closely correlates with plasma noradrenaline concentration.⁵¹ Braun *et al* reported a significant decrease in noradrenaline and NT-proBNP after short term CRT, but this effect was attenuated after 24 months of follow up.⁵²

Reduction in mitral regurgitation

As discussed previously, short AV delay pacing reduces pre-systolic mitral regurgitation.⁵³ The presence and magnitude of this is related to left ventricular end diastolic pressure (LVEDP) and to prolongation of the A-V interval. Pacing increases the effective diastolic filling period by a reduction in pre-systolic mitral regurgitation. However, this is believed to make only a modest contribution to the overall haemodynamic benefit of biventricular pacing in most patients. Biventricular pacing may also reduce the magnitude of systolic “functional” mitral regurgitation, by a reduction in ventricular sphericity, and/or by an increase in mitral valve “closing pressure” leading to improved coaptation of the mitral valve leaflets.^{54–55} Reverse remodelling may also aid in the reduction in longstanding mitral regurgitation.

Improvement in left ventricular filling

Cardiac resynchronisation therapy may improve the diastolic filling time of the left ventricle in several ways:

- A reduction in pre-systolic mitral regurgitation (see above).
- By improving ventricular synchrony during active relaxation, biventricular pacing might theoretically improve diastolic filling, although two studies have reported no improvement in Tau^{42–56}
- By a reduction in external constraint to left ventricular filling.

Atherton *et al*⁵⁷ and Dauterman *et al*⁵⁸ have shown that in many heart failure patients the filling of the left ventricle may be impeded by external constraint from the raised pressure in the stretched pericardium (pericardial constraint)

Table 2 Current guidelines for device therapy in heart failure

	CRT therapy	ICD therapy
NICE guidelines	Criteria <ul style="list-style-type: none"> • Drug refractory • NYHA class III-IV • EF < 35% • QRS Duration > 120 ms • LVEDD > 6 cm • Non-reversible cause 	Primary prevention <ul style="list-style-type: none"> • History of MI + NSVT on Holter + Inducible VT on EPS + LVEF < 35% + NYHA III at worst Secondary prevention <ul style="list-style-type: none"> • Sustained VT • LVEF < 35% • NYHA III at worst
ACC/AHA/NASPE guidelines	Class IIa indication <ul style="list-style-type: none"> • Drug refractory <ul style="list-style-type: none"> • NYHA class III-IV • Dilated or ischaemic cardiomyopathy <ul style="list-style-type: none"> • QRS duration > 130 ms • LVEDD ≥ 55 mm • LVEF ≤ 35% 	Class IIa indication <ul style="list-style-type: none"> • LVEF ≤ 30% AND > 1 month after MI or > 3 months after CABG Class III indication <ul style="list-style-type: none"> • NYHA class IV drug refractory heart failure in patients who are not candidates for transplantation

and from the right ventricle via the interventricular septum (diastolic ventricular interaction). In these circumstances reducing central blood volume may acutely increase left ventricular diastolic volume despite reducing left ventricular diastolic pressure. This is because the reduction in external constraint from the right ventricle and pericardium increases the true left ventricular distending pressure. Bleasdale and colleagues recently showed that left ventricular pacing reduces this external constraint, effectively recruiting preload, presumably by causing the left ventricle to fill comparatively earlier, and therefore reducing the external constraint acting on the left ventricle at mid-diastole (see fig 1).⁵⁹

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PATIENT SELECTION

Cardiac resynchronisation therapy

At present, guidelines do exist for patient selection for biventricular pacing, based on the aforementioned larger trials. The present criteria, as published by the National Institute for Health and Clinical Excellence (NICE, 2003) are: drug refractory symptoms, NYHA III-IV, ejection fraction < 35%, QRS duration > 120 ms, non-reversible cause, left ventricular end diastolic dimension > 6 cm.⁵⁹ Despite the positive results of CRT trials, more than a third of patients receiving CRT are non-responders. As mentioned earlier, a number of recent studies have aimed to identify non-responders based on various echocardiographic techniques, in particular TDI.⁴³⁻⁴⁵

Some patients with narrow QRS complexes (who do not fulfil current criteria) may benefit. A better understanding of the mechanisms of benefit of biventricular and left ventricular pacing may lead to improved patient selection and optimisation of pacing strategy in individual patients.

In addition to those patients with a comparatively normal QRS duration, scarce data are available on biventricular pacing in those patients in atrial fibrillation, although several studies are ongoing. The MUSTIC trial reported favourable one year results of biventricular pacing in patients with severe heart failure and major intraventricular conduction disturbances. However, the results for the atrial fibrillation group were less impressive.²⁸ A recent study by Molhoek *et al* evaluated the clinical response and long term survival rate of CRT in patients with heart failure and chronic atrial fibrillation and compared the results with those in patients in sinus rhythm. NYHA class, Minnesota quality of life score, and six minute walking distance improved significantly in both groups after six months of CRT. The rate of non-responders was greater among patients with atrial fibrillation. Nevertheless, the long term survival rate was comparable between the two groups.⁶⁰ The question of earlier implantation of a biventricular device in those patients with NYHA class II heart failure, to possibly slow disease progression has not been fully addressed. Table 2 summarises current guidelines.

Implantable defibrillators

Guidelines do exist for the use of ICD therapy in patients with left ventricular dysfunction and congestive heart failure. According to the 2002 ACC/AHA/NASPE guidelines,⁶¹ ICD

therapy has been granted a class IIa indication in patients who meet the following criteria: LVEF $\leq 30\%$ that are at least one month after MI or three months after CABG surgery. NYHA class IV drug refractory heart failure in a patient who is not a candidate for cardiac transplantation is currently a class III indication. However, there are no data from large randomised controlled trials to support the use of ICD therapy in this context. Table 2 summarises current guidelines from both NICE⁶² and ACC/AHA/NASPE.

CRT alone compared with CRT-ICD

When the decision to implant a CRT device has been made, the question arises as to whether to implant a device incorporating cardioverter defibrillator properties. The MIRACLE ICD trial was a prospective, randomised, double blind, parallel controlled clinical trial intended to assess the safety and clinical efficacy of a combined ICD and cardiac resynchronisation system in patients with an LVEF $\leq 35\%$, a QRS duration ≥ 130 ms, and NYHA class III-IV symptoms. Primary and secondary outcomes were similar to those in the MIRACLE trial, but also showed the efficacy of anti-tachycardia therapy with biventricular pacing.⁶³ Patients who meet the criteria for CRT are all high risk for sudden cardiac death. Although no guidelines are currently in place to dictate practice, results from the COMPANION trial may support the idea that patients receiving CRT should receive a device with defibrillator capabilities. This study shows that ICD-CRT is superior to CRT alone in terms of mortality. However, CRT-ICD is considerably more costly than CRT alone (see below). Until guidelines are in place, it would seem sensible to recommend that all patients with a class I indication for ICD therapy, as well as those patients meeting the criteria in the MADIT-I, MADIT-II, and MUSST trials receive combination CRT-ICD therapy.

Cost effectiveness

The economic cost of managing heart failure is considerable and largely attributable to the cost of hospitalisation.⁶⁴ Current estimates suggest that about £1 billion is spent on heart failure each year in the UK. About 7%–10% of patients with heart failure may be suitable for CRT (excluding those patients with atrial fibrillation). The cost of CRT devices is substantial, a basic system costing at least twice that of a conventional pacing system. However, the time and resources associated with implantation of the device and management of complications are more difficult to quantify. However, the impact of CRT on health care budgets is probably only a fraction of that for ICD therapy.

In the USA and UK, a cost per life year gained (LYG) of less than \$50 000 (£27 000) is generally considered cost effective, while costs in excess of \$100 000 (£54 000) would generally be considered cost ineffective. A recent analysis of data from the SCD-HeFT study suggested that ICDs were fairly cost effective, with a cost per LYG of \$33 000 (£18 000). There was a powerful interaction between NYHA class and outcome. ICDs did not seem effective (and therefore not cost effective) in patients who had NYHA III heart failure. Patients with NYHA II heart failure had a cost of \$26 000 (£14 000) per LYG. However, this is based on the cost of a simple device and leads of \$17 500 (£9400), without implantation costs, and is considerably lower than implantation costs in the UK, which are on average £14 000.

Accurately estimating the cost of CRT is difficult as it is directed primarily at improving symptoms and quality of life, as compared with preventing sudden cardiac death. No analysis of quality adjusted LYG has yet been reported. As most heart failure expenditure is driven by hospitalisations and length of stay, a reduction in these end points would suggest cost effectiveness. In the MIRACLE trial,⁶³ CRT reduced hospitalisation for heart failure by 50% and the

total number of days in hospital from 363 to 83 days. Subsequently, the COMPANION trial³¹ reported a 34% reduction in deaths from or hospitalisations for heart failure in patients receiving CRT compared with optimal pharmacological therapy, and a 40% in those receiving combined CRT-ICD therapy.

As data arise supporting the use on CRT devices with combined cardioverter defibrillator capabilities, implementation of this therapeutic strategy threatens to have an impact significantly on public healthcare spending. Possible cost limiting mechanisms include price cuts because of increasing use, identification of subgroups at higher risk of sudden death and, with regards to ICD therapy, the use of cheaper devices with limited diagnostic and therapeutic options.

CONCLUSION

There is now convincing evidence supporting the beneficial effects of CRT for the treatment of heart failure. Numerous observational studies, as well as a series of randomised controlled trials, have been completed, showing the safety, efficacy, and long term benefits for patients with chronic systolic heart failure and ventricular dyssynchrony. These studies have consistently shown statistically significant improvements in quality of life, NYHA functional class, exercise tolerance, and left ventricular reverse remodelling. A comprehensive meta-analysis has showed reduction in mortality and hospitalisation rates for worsening heart failure.

However, even though CRT has been shown to work in patients with drug refractory, symptomatic heart failure, it is not without its limitations. A high degree of operator skill is required. Implant times are often prolonged and procedural failure not uncommon. Accurate patient selection is crucial. TDI will probably remain the most feasible and valuable method for the rapid assessment of large numbers of patients. Further studies are required to assess the efficacy of CRT in patients with atrial fibrillation, in those with a narrow QRS duration on surface ECG, and in patients with milder symptoms of heart failure.

MULTIPLE CHOICE QUESTIONS (TRUE (T)/FALSE (F); ANSWERS AFTER THE REFERENCES)

- Left bundle branch block is characterised by the following:
 - A delay in the opening and closure of the aortic valve
 - No effect on mitral valve opening
 - Simultaneous left and right ventricular contraction
 - A reduced left ventricular filling time
 - No effect on the timing of right ventricular events
- Mechanisms responsible for the benefit seen with biventricular pacing:
 - Both biventricular and left ventricular pacing modes have a beneficial effect on left ventricular mechanical dyssynchrony
 - Patients with a narrow QRS complex derive no benefit from biventricular pacing as they have no mechanical dyssynchrony
 - Biventricular pacing has no effect on ejection fraction and left ventricular volumes
 - A decrease in pre-systolic mitral regurgitation and a reduction in the magnitude of functional mitral regurgitation are seen in patients undergoing biventricular pacing

- (E) Biventricular and left ventricular pacing have no effect on diastolic ventricular interaction and left ventricular filling pressures
3. With regards to dual chamber and right ventricular pacing:
- (A) Right ventricular pacing results in an increase in the incidence of heart failure
- (B) Right ventricular pacing results in abnormal left ventricular electrical activity and mechanical dyssynchrony
- (C) Dual-chamber pacing has no effect on pre-systolic mitral regurgitation
- (D) Several published randomised trials have proven a haemodynamic benefit by positioning the right ventricular lead in the outflow tract
- (E) Dual chamber pacing results in acute haemodynamic improvements in LV filling
4. Regarding the role of implantable defibrillators in heart failure:
- (A) In NYHA class III the proportions of deaths attributable to sudden cardiac death is 50%–66%
- (B) MADIT I, MUSTT, and MADIT II showed no benefit of ICD therapy when used as primary prevention
- (C) ICD therapy has been proved to reduce mortality in cardiomyopathy of both ischaemic and non-ischaemic aetiology
- (D) The COMPANION trial reported a significant reduction in mortality in patients treated with biventricular pacing alone
- (E) Patients with an EF < 35% show the greatest benefit from ICD therapy when used for secondary prevention
5. Diastolic ventricular interaction and heart failure:
- (A) In health the LVEDP is a measure of the true distending pressure of the left ventricle
- (B) The pericardium lacks the capacity to grow to accommodate long term increases in cardiac size
- (C) Acute balloon occlusion of the inferior cava in patients with heart failure results in an increase in left ventricular volumes
- (D) In a canine rapid pacing heart failure model, LV stroke work was inversely related to LVEDP but linearly related to true LV filling pressure
- (E) LV pacing has no effect on LV stroke work in patients with heart failure
6. The following statements apply to the results of the COMPANION and SCD-HeFT trials:
- (A) A significant reduction in mortality was seen in patients receiving a combined defibrillator/biventricular pacing device in the COMPANION trial
- (B) A significant reduction was seen in patients receiving a pacing only device in the COMPANION trial
- (C) Patients with both ischaemic and non-ischaemic cardiomyopathy were represented in the COMPANION trial
- (D) The SCD-HeFT trial reported a significant reduction in mortality in the ICD group in patients with ischaemic cardiomyopathy only
- (E) In the SCD-HeFT Trial patients with NYHA class III symptoms derived no benefit from ICD therapy

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Funding: none.

Conflicts of interest: none declared.

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ANSWERS

1. (A) T, (B) F, (C) F, (D) T, (E) T; 2. (A) T, (B) F, (C) F, (D) T, (E) F; 3. (A) T, (B) T, (C) F, (D) F, (E) T; 4. (A) F, (B) T, (C) T, (D) F, (E) T; 5. (A) T, (B) F, (C) T, (D) T, (E) F; 6. (A) T, (B) F, (C) T, (D) F, (E) T.