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Is cardiac resynchronisation therapy feasible, safe and beneficial in the very elderly?

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Abstract

Objective To evaluate whether cardiac resynchronisation therapy (CRT) implantation was feasible and safe in octogenarians and the association with symptoms. **Methods** Consecutive patients undergoing CRT implantation were recruited from two UK centers. Patients grouped according to age: < 80 & ≥ 80 years. Baseline demographics, complications and outcomes were compared between those groups. **Results** A total of 439 patients were included in this study, of whom 26% were aged ≥ 80 years. Octogenarians more often received cardiac resynchronization therapy pacemaker in comparison to cardiac resynchronisation therapy-defibrillator. Upgrade from pacemaker was common in both groups (16% < 80 years *vs.* 22% ≥ 80 years, P = NS). Co-morbidities were similarly common in both groups (overall diabetes: 25%, atrial fibrillation: 23%, hypertension: 45%). More patient age ≥ 80 years had significant chronic kidney disease (CKD, estimated glomerular filtration rate < 45 mL/min per 1.73 m^2, 44% *vs.* 22%, P < 0.01). Overall complication rates (any) were similar in both groups (16% *vs.* 17%, P = NS). Both groups demonstrated symptomatic benefit. One-year mortality rates were almost four fold greater in octogenarians as compared with the younger cohort (13.9% *vs.* 3.7%, P < 0.01). **Conclusions** CRT appears to be safe in the very elderly despite extensive co-morbidity, and in particular frequent severe CKD. Symptomatic improvement appears to be meaningful. Strategies to increase the appropriate identification of elderly patients with CHF who are potential candidates for CRT are required.

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1 Introduction

Chronic heart failure (CHF) is common and predominantly affects the elderly; data collected on 43,894 patients hospitalized with heart failure from the National Heart Failure Audit in England and Wales in 2012/2013 showed the median age was 80 years, 66% were aged > 75 years and 30% > 85 years.[1] Patients with heart failure in general practice in the UK are on average 77 years old.[2]

The outlook for patients with CHF and left ventricular dysfunction (LVSD) has been transformed over last two decades with advances in medical therapy primarily directed towards antagonism of activated neurohormonal systems. The mainstream of treatment includes a combination of beta-blockers,[3] angiotensin converting enzyme inhibitors,[4] and mineralocorticoid antagonists.[5] Yet, many patients remain symptomatic with impaired prognosis. Up to 30% of patients with severe LVSD have broad QRS duration on electrocardiograph (in particular left bundle branch block, LBBB), which itself is independently associated with adverse prognosis.[6] Cardiac resynchronisation therapy [with pacemaker alone (CRT-P) or with additional defibrillator capabilities (CRT-D)] involves implanting a pacing device with both right and left ventricular leads and is of additional benefit in such patients reducing the death rate or unplanned hospitalisation for major cardiovascular event by 16%.[7] In patients with CHF, CRT is also associated with symptomatic benefit and improvement in quality of life.[7–9] Despite proven and well documented benefit of CRT, the mean age of all patients receiving CRT-P and CRT-D in the UK in 2010 was 72 and 67 years, respectively.[10]

These data suggest that CRT may be underutilised in elderly patients with CHF. Potential reasons include clinical

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concerns regarding co-morbidities and potential complications of an invasive procedure and difficulties in accessing heart failure services. We sought to evaluate whether CRT implantation is feasible and safe in very elderly patients with CHF and whether it was associated with improved symptoms.

2 Methods

This was a retrospective cohort study conducted at two hospitals on the south coast of England with overall catchment population of 1.2 million. Consecutive patients undergoing attempted CRT implantation over 36 months were included in the study.

Data were gathered by two clinicians through comprehensive review of case notes and electronic records including procedural data, clinic letters, imaging, pacing data, blood tests and ECGs where available at both centres. Clinic letters provided information about demographics, aetiology, co-morbidities and symptomatic benefits. In an attempt to capture all significant complications a rigorous evaluation of relevant data were performed: (1) failure to implant a new system or lead displacement — patients' notes, electronic records, pacing record data and imaging; (2) pneumothorax — review of all chest X-rays post procedure; (3) infection resulting in system explant — notes, electronic records, pacing data and blood tests; and (4) severe contrast induced nephropathy necessitating renal replacement therapy – blood tests, electronic records and medical notes

Baseline data included demographics and New York Heart Association (NYHA) class before implantation and at follow up between three and six months when documented (Table 1). Data were evaluated to one year for all patients. All-cause mortality at one year was assessed. In line with common clinical practice at both centres, most patients had blood tests immediately prior to device implantation. The indication for the device was documented: (1) primary heart failure — symptomatic patients with severe LVSD and (2) primary arrhythmia — patients with documented ventricular arrhythmic episode (generally receiving a defibrillator) but also severe LVSD and broad QRS.

All patients were grouped according to age at implantation, ≥ 80 years and < 80 years; comparison between these groups was performed. Local audit committee and the national research ethics committee approvals were obtained for each participating site. The anonymous amalgamated data were analyzed.

Data were analysed for normal distribution and compared using *t*-test and chi-squared tests as appropriate. Cumulative values were expressed as percentages and mean ± SD. All values were 2 tailed and $P < 0.05$ was considered significant.

Table 1. NYHA functional classification.

NYHA class	Symptoms
I	No limitation in normal physical activity
II	Mild symptoms only in normal activity
III	Marked symptoms during daily activities, asymptomatic only at rest
IV	Severe limitations, symptoms even at rest

NYHA: New York Heart Association.

3 Results

Over the study period, 458 patients had CRT implantation attempted and formed the study population. Of these, 19 (4%) patients (16 < 80 years, 3 ≥ 80 years) did not receive a working left ventricular lead due to failure to implant or a lead was implanted but switched off (generally when it is anticipated that frequent pacing would be required in the future). As such, a total of 439 patients with initial successful CRT implantation were included in this study, 115 (26%) of patients were ≥ 80 years old. The groups differed at baseline as the ≥ 80 years group had significantly higher rates of underlying ischaemic heart disease and were more likely to have a primary diagnosis of heart failure as the indication for CRT device. A greater proportion of ≥ 80 years group had severe chronic kidney disease (CKD) as manifest by estimated glomerular filtration rate (eGFR) < 45 mL/min per 1.73 m^2 at baseline (44% compared with 22% in the < 80 years group, $P < 0.01$). Major co-morbidities including atrial fibrillation, hypertension and type 2 diabetes were similarly common in both groups (Table 2).

Table 2. Baseline demographics in 439 patients who underwent CRT implantation.

Characteristic	Age < 80 yr (*n* =324)	Age ≥ 80 yr (*n* = 115)	*P*
Age, yr	69 ± 8	83 ± 2	< 0.01
Male, %	73	77	0.31
Ischaemic aetiology, %	54	69	< 0.01
Indication: heart failure, %	81	92	< 0.01
CRT-D, %	51	14	< 0.01
Upgrade from PPM, %	16	22	0.13
eGFR, mL/min per 1.73 m^2	57 ± 17	46 ± 19	< 0.01
History of hypertension, %	44	46	0.72
History of diabetes, %	27	19	0.08
Atrial fibrillation at implant, %	22	29	0.15

Data are presented as mean ± SD or percent. CRT: cardiac resynchronization therapy; CRT-D: cardiac resynchronization therapy defibrillator; eGFR: estimated glomerular filtration rate; PPM: permanent pacemaker.

An upgrade of existing pacemaker system to a CRT device was frequently observed. Patients in the younger cohort were more likely to receive a CRT-D than those ≥ 80 years, (51% *vs.* 14%, $P < 0.01$).

Overall complication rates (any) were similar in both groups (16%–17%). The only significant difference between the groups was observed in increase in pneumothoraces in the group aged ≥ 80 years (Table 3). There were no apparent events of severe contrast induced nephropathy necessitating renal replacement therapy.

Improvement in symptoms was considered clinically significant if patients were documented to have an increase in function corresponding to ≥ 1 reduction in NYHA class at their follow up appointment. Data were available for NYHA class both before implantation and at follow up for 171/324 (53%) of < 80 years old group and 61/115 (53%) of ≥ 80 years group; an improvement of ≥ NYHA class 1 was seen in 60% and 69% patients, respectively ($P = 0.23$). All cause mortality at one year was significantly greater in patients aged ≥ 80 years as compared with the younger cohort (13.9% *vs.* 3.7%, $P < 0.01$).

4 Discussion

Our study showed, in elderly patients aged 80 or above, that CRT implantation is safe and feasible when compared to a population on average nearly 15 years younger. There were no significant differences in overall complication rates. Whilst this is a retrospective study, the proportion of patients experiencing an improvement of NYHA class by one or more (a predictor of quality of life[11]), appears to be of similar magnitude in the elderly and younger cohorts.

Major co-morbidities were common in both groups, a finding that has been observed in previous clinical trials.[12] The prevalence of significant CKD was greater in those aged greater than 80 years old and it might have been anticipated that this might be associated with higher complication rates, in particular since the implantation of the left ventricular lead generally involves imaging with radio-opaque contrast with theoretical potential for contrast induced nephropathy. No patients in this study developed severe renal dysfunction as a consequence of the procedure necessitating renal replacement therapy. Whilst overall complication rates were similar, a significant difference between the groups was observed in number of pneumothoraces. This might related to frailty and body habitus in the very elderly and in addition a large number of patients in this study had an upgrade procedure (17%). It is generally accepted that an upgrade procedure carries more risks than the de novo implant;[13] of the five patients over the age of 80 years who suffered a pneumothorax two were during upgrade procedures.

Table 3. Complications in 439 patients undergoing CRT implantation.

Complications	Age < 80 year (n = 324)	Age ≥ 80 year (n = 115)	P
Pneumothorax, %	1.2	4.3	< 0.05
Lead displacement, %	8.6	6.9	0.571
Infection + system explants, %	3.1	1.7	0.447
*Overall (%)	17	16	

*Overall includes failed left ventricular implants, redo procedures, haematomas and superficial infections. CRT: cardiac resynchronisation therapy.

There are few studies evaluating complication rates of CRT in the very elderly. The mean ages in intervention arms in CRT clinical trials were 67[7,14], 64[8], and 65[9] years old. In the CARE-HF trial, the only randomized trial of CRT powered for mortality, only 6.1% patients were ≥ 80 years.[7] A single centre study over six years found that the short term (30 day) complication rate was 12.2% in 728 patients receiving CRT implant of whom 90 (12.4%) were older than 80 years, with no difference between the age groups.[15] Similar improvements in NYHA class and left ventricular remodelling measurements, checked at 6–12 months post implant, between older and younger patients receiving CRT have been demonstrated.[15–20] Our findings (albeit limited by the nature of the study) are consistent with this. The finding in the current study that mortality rates at 1-year were over three times greater in patients aged over 80 years is unsurprising given such an age difference between the groups. Previous studies have also shown that survival in octogenarians after CRT is worse than that among younger patients,[21,22] whereas others have suggested comparable survival between the groups.[23,24]

Data from randomized studies demonstrate that the combination of optimal medical therapy (beta-blockers, angiotensin converting enzyme inhibitors and mineralocorticoid antagonists) and CRT can beneficially impact on both survival and quality of life. Data from the National Heart Failure Audit in 2012/2013 revealed that as patients get older they are far less likely to be on adequate OMT.[1] The National Institute for Clinical Excellence (NICE) have provided recommendations for CRT-P or CRT-D as treatment options for people with CHF who have left ventricular ejection fraction (LVEF) of 35% or less with no age limit (Table 4).[25] Similarly, current European Society of Cardiology Guidelines recommend CRT in patients with CHF and LVEF ≤ 35% who remain in NYHA functional class II, III or ambulatory IV despite adequate medical treatment and LBBB with QRS duration >150 ms (class I) or LBBB with QRS duration 120–150

Table 4. Treatment options with ICD or CRT for people with heart failure*.

QRS Interval	NYHA			
	I	II	III	IV
120–149 ms without LBBB	ICD	ICD	ICD	CRT-P
120–149 ms with LBBB	ICD	CRT-D	CRT-P or CRT-D	CRT-P
≥ 150 with or without LBBB	CRT-D	CRT-D	CRT-P or CRT-D	CRT-P

*The patients have left ventricular dysfunction with an LVEF of 35% or less (according to NYHA class, QRS duration and presence of LBBB). CRT-D: cardiac resynchronisation therapy defibrillator; CRT-P: cardiac resynchronisation therapy pacemaker; ICD: implantable cardioverter defibrillator; LBBB: left bundle branch block; NYHA: New York Heart Association.

ms (class I) or non-LBBB with QRS duration >150 ms (class IIa) and even non-LBBB with QRS duration 120–150 ms (class IIb).[26] Whilst these guidelines do not suggest that age should impact on whether an individual patient should receive a CRT-D or CRT-P, given the large difference in mean age between the groups, it is unsurprising that a larger proportion of the very elderly received CRT-P. Patient involvement in decision making is the key.

Heart failure predominantly affects the elderly, but only a quarter of our patients who underwent CRT were over the age of 80. Around a third of patients[6] with CHF have broad QRS on ECG and it therefore appears we are failing to identify potential elderly candidates, since in the UK the average age of CRT-D implant is 67 years and CRT-P implant 72 years. Reasons for this might include lack of access to specialist heart failure services for the elderly, perceived higher risk of complications or lack of benefit, or patients not wanting to undergo the procedure. Whilst it would be wrong to suggest that all patients with symptomatic CHF and broad QRSD duration should have CRT, recently published NICE guidelines on acute heart failure recommending that all patients should be managed by a specialist heart failure team may help in the appropriate identification of candidates.[27] A change in service delivery with multidisciplinary communication and education with clear guidelines and pathways, either local or national is required.

There are potential limitations of our study. For example, it is a retrospective cohort study and may be influenced by selection bias. It is likely that less frail elderly patients were considered/referred for CRT, although the 1-year mortality rate in patients over 80 years was still high at around 14%. Yet the large numbers of very elderly subjects included across two different sites may help in the generalizability of the results. We do not have comprehensive data on medications following CRT and acknowledge that drug therapy is likely to influence the outcomes following CRT, in terms of NHYA class and likely survival. The main purpose of this study was to evaluate the complication rates and thereby safety of the implant procedure and therefore this is what we focused our data collection on. Whilst we acknowledge that this is a limitation in our study, we do not believe that a difference in medication utilization between the groups would impact on the complication rates.

It is possible that some minor complications were missed, such as small haematomas or minor skin infections. With meticulous data collection/evaluation it is less likely that a serious complication was missed and there does not appear to be any reason as to why the detection of complications might be different between the age groups.

Implantation of CRT is feasible and safe in the very elderly despite extensive co-morbidity and frequent CKD. Despite the fact that the majority of patients with heart failure are elderly, the mean age of CRT implants in the UK is considerably lower suggesting that many patients may not be being considered for the procedure. Strategies to ensure that all patients, irrespective of age, have access to specialist heart failure services are required.

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