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Cardiac resynchronization therapy pacemaker or cardiac resynchronization therapy defibrillator: what determines the choice?—findings from the ESC CRT Survey II

Camilla Normand[1,2]*, Cecilia Linde[3], Nigussie Bogale[1], Carina Blomström-Lundqvist[4], Angelo Auricchio[5], Christoph Stellbrink[6], Klaus K. Witte[7], Wilfried Mullens[8,9], Christian Sticherling[10], Germanas Marinskis[11], Elena Sciaraffia[4], Giorgi Papiashvili[12], Svetoslav Iovev[13], and Kenneth Dickstein[1,2]

[1]Cardiology Division, Stavanger University Hospital, Stavanger, Norway; [2]Institute of Internal Medicine, University of Bergen, Bergen, Norway; [3]Heart and Vascular Theme, Karolinska University Hospital and Karolinska Institutet, Stockholm, Sweden; [4]Department of Medical Science and Cardiology, Uppsala University, Uppsala, Sweden; [5]Clinical Electrophysiology Unit, Fondazione Cardiocentro Ticino, Lugano, Switzerland; [6]Department of Cardiology, Klinikum Bielefeld, Germany; [7]Leeds Institute of Cardiovascular and Metabolic Medicine, University of Leeds, Leeds; [8]Department of Cardiology, Ziekenhuis Oost-Limburg, Genk, Belgium; [9]Biomedical Research Institute, Faculty of Medicine and Life Sciences, Hasselt University, Diepenbeek, Belgium; [10]University Hospital Basel, University of Basel, Switzerland; [11]Clinic of Heart Diseases, Vilnius University, Lithuania; [12]Arrhythmia Department, Helsicore - Israeli-Georgian Medical Research Clinic, Tbilisi, Georgia; and [13]Cardiostimulation and Electrophysiology sector at "St. Ekaterina" University Multi-profile Hospital for Active Treatment, Sofia, Bulgaria

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Aims The decision to implant a cardiac resynchronization therapy pacemaker (CRT-P) or a cardiac resynchronization therapy defibrillator (CRT-D) may be challenging. There are no clear guideline recommendations as no randomized study of cardiac resynchronization therapy (CRT) has been designed to compare the effects of CRT-P with those of CRT-D on patients' outcomes. In the CRT Survey II, we studied patient and implantation centre characteristics associated with the choice of CRT-P vs. CRT-D.

Methods and results Clinical practice data from 10 692 patients undergoing CRT implantation of whom 7467 (70%) patients received a CRT-D and 3225 (30%) received a CRT-P across 42 ESC countries were collected and analysed between October 2015 and January 2017. Factors favouring the selection of CRT-P implantation included age >75 years, female gender, non-ischaemic heart failure (HF) aetiology, New York Heart Association functional Class III/IV symptoms, left ventricular ejection fraction >25%, atrial fibrillation, atrioventricular (AV) block II/III, and implantation in a university hospital.

Conclusion In a large cohort from the CRT Survey II, we found that patients allocated to receive CRT-P exhibited particular phenotypes with more symptomatic HF, more frequent comorbidities, advanced age, female gender, non-ischaemic HF aetiology, atrial fibrillation, and evidence of AV block. There were substantial differences in the proportion of patients allocated to receive CRT-P vs. CRT-D between countries.

Keywords Heart failure • Cardiac resynchronization therapy • Implantable cardioverter-defibrillator • Cardiac resynchronization therapy pacemaker • Cardiac resynchronization therapy defibrillator

Introduction

Cardiac resynchronization therapy (CRT) reduces morbidity and mortality in patients with symptomatic heart failure (HF), reduced left ventricular ejection fraction (LVEF), and prolonged QRS durations, and therefore, international cardiology guidelines have provided a Class I recommendation for CRT in such patients.[1,2] However, guideline task forces are not able to provide strong

* Corresponding author. Tel: +4751518000; fax: +47 51519892. *E-mail address*: camilla.normand@doctors.org.uk

What's new?

- An analysis of 11 088 cardiac resynchronization therapy implantations in 42 ESC countries demonstrates large national variations in the percentage of cardiac resynchronization therapy pacemaker (CRT-P) vs. cardiac resynchronization therapy defibrillator devices implanted as well as substantial differences in the selection criteria for the choice of device type.
- Factors associated with choice of CRT-P include age >75 years, female gender, non-ischaemic heart failure aetiology, New York Heart Association functional Class III/IV symptoms, left ventricular ejection fraction >25%, atrial fibrillation, atrioventricular block II/III, and implantation in a university hospital.

recommendations regarding which patients should receive cardiac resynchronization therapy pacemaker (CRT-P) and which patients should receive cardiac resynchronization therapy with a defibrillator (CRT-D) since no randomized controlled trial (RCT) has been designed to compare the effects on clinical outcomes of these two device types. The choice between CRT-P and CRT-D is therefore left to the discretion of the clinicians and implanters.[3] The decision is complicated by the fact that many patients with HF and a reduced LVEF eligible for CRT also have an overlapping indication for primary prophylaxis against sudden arrhythmic death with an implantable cardioverter-defibrillator (ICD).[2]

Despite strong recommendation in international cardiology guidelines,[1,2] CRT implementation practice varies considerably across Europe.[4,5] In order to describe the current clinical practice in patients implanted with a CRT device, the CRT Survey II collected data on 11 088 CRT recipients in 42 ESC member countries over a 15-month period. The purpose of the present analysis was to describe which patient and hospital characteristics were associated with a choice between a CRT-P and a CRT-D device.

Methods

Recruitment

The design and rationale of CRT Survey II along with the details of the electronic case report form (eCRF) have been published previously.[4,6] The survey was designed as a joint European Society of Cardiology (ESC) initiative between the European Heart Failure Association (EHRA) and the Heart Failure Association (HFA) following the success of the first CRT Survey. We invited all 47 ESC member states detailed in the 2014 EHRA White Book[7] to join and 288 centres in 42 countries participated in the survey. Sites were asked to enter consecutive patients implanted with a CRT between October 2015 and January 2017.

Data collection, management and analyses

The Institut für Herzinfarktforschung Ludwigshafen (IHF) together with the CRT Survey II scientific committee revised the eCRF used in the first ESC CRT Survey in 2009[5] and developed the statistical analysis plan. The IHF was also responsible for data collection, monitoring, and verification. The day-to-day logistics of running of the survey was coordinated by Operations at Stavanger University Hospital/University of Bergen, Norway.

Survey population and questionnaires

Any patient undergoing a CRT implantation procedure was eligible for inclusion. This included both successful and unsuccessful implantations. *De novo* CRT devices and upgrades from a previous pacemaker (PM) or ICD were included, but generator replacements or revisions of existing CRT devices were excluded as the survey was designed to capture only first-time CRT implantations.

Implanting centres were asked to complete a web-based eCRF of all consecutive patients. The eCRF collected information on patient characteristics, diagnostic workup, indications for CRT, implant procedures, and short-term outcomes including adverse events and complications during the index hospitalization. Information on longer-term outcomes was not collected. The eCRF was designed to be completely anonymized in order to facilitate site and patient recruitment. Each implanting centre was also requested to complete a one-time site questionnaire describing hospital type, size, population served, operator specialty, infrastructure, facilities, and implantation routines for their CRT device programme.

Statistical analysis

All data analyses were performed by IHF using SAS®, release 9.4 (SAS Institute Inc., Cary, NC, USA) on a Microsoft® Windows® 8 Enterprise platform. All percentages were relative to the total number of patients with available information. Numerical data were summarized by means of standard statistics (i.e. number of available data, median, and interquartile range). *P*-values were calculated using Mann–Whitney–Wilcoxon test when comparing medians and χ^2 test or Fisher's exact test, if necessary, when comparing percentages. A *P*-value <0.05 was considered statistically significant. *P*-values <0.001 were considered highly significant. We did not impute missing values.

A logistical regression analysis identified factors associated with implantation of a CRT-P using a stepwise selection procedure to calculate maximum likelihood estimates. To avoid a previous PM or ICD implantation acting as confounding factors, patients upgraded to CRT were excluded from this analysis. The following factors were included in the regression analysis: age, gender, admission type (elective vs. non-elective), referral from another centre, HF aetiology, cardiovascular comorbidities (hypertension, atrial fibrillation, valvular heart disease), and non-cardiovascular comorbidities (chronic obstructive lung disease, diabetes, anaemia, and chronic kidney disease), recent hospitalizations for HF, New York Heart Association (NYHA) functional class, LVEF, QRS duration, bundle branch morphology, atrioventricular (AV) block, hospital CRT implantations per year, type of hospital (university vs. non-university), and implanter clinical specialty. Odds ratios for selection of a CRT-P vs. CRT-D were calculated. The Hosmer and Lemeshow test for goodness-of-fit was used to test the validity of the regression model.

Results

Patients analysed

Of the 11 088 patients included in the survey, 10 692 had sufficient data collected to be included in the present analysis and of these 3225 (30%) received a CRT-P device and 7467 (70%) a CRT-D device (*Figure 1A*). From the cohort of 7305 patients implanted *de novo* a regression analysis was performed for demographic and clinical factors associated with receiving a CRT-P (*Figure 1B*).

Clinical characteristics

Table 1 describes the clinical characteristics of the total cohort. Patients implanted with a CRT-P device were significantly older,

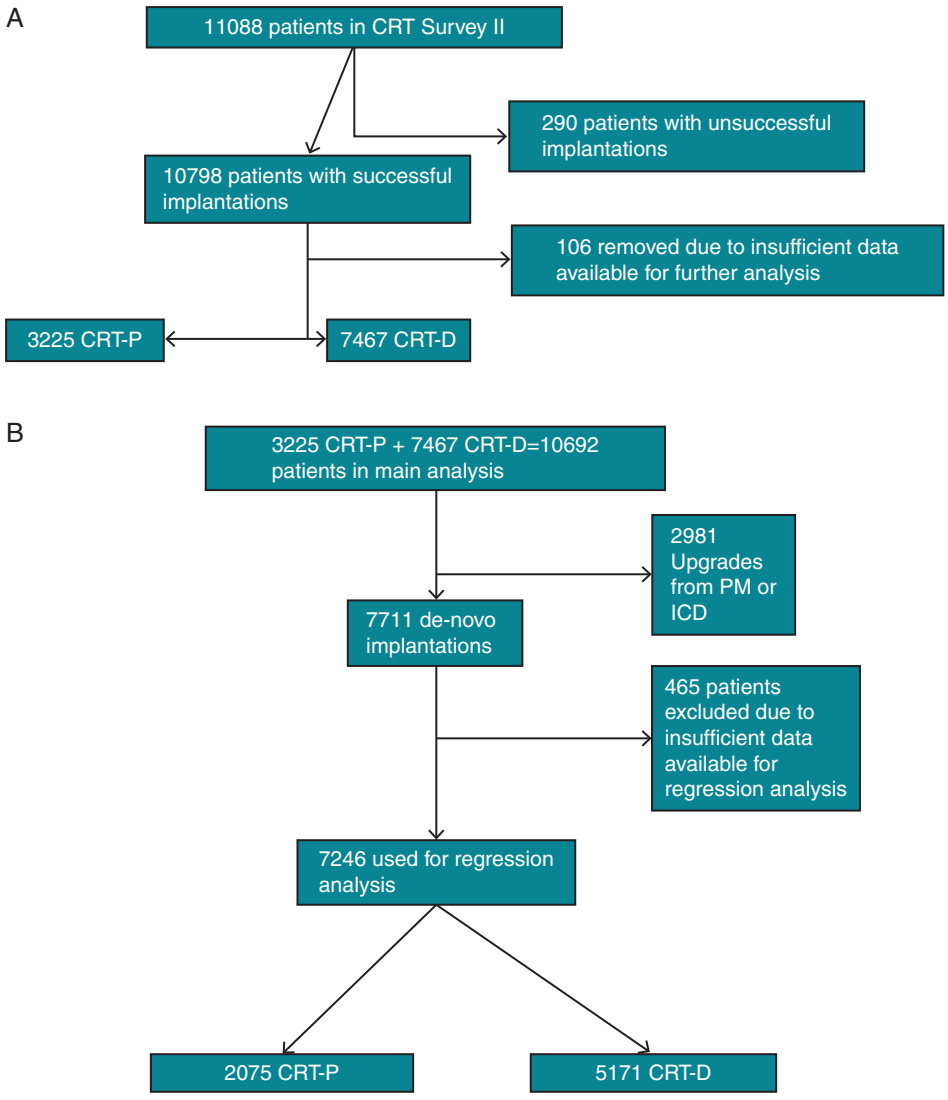

Figure 1 Consort diagrams. (*A*) Patients included in main analysis (*Tables 1–4*). (*B*) Patients used in regression analysis (*Table 5*) (patients with previous device are excluded from analysis). CRT-D, cardiac resynchronization therapy defibrillator; CRT-P, cardiac resynchronization therapy pacemaker; ICD, implantable cardioverter-defibrillator; PM, pacemaker.

more often female and were less likely to have ischaemic aetiology. They also had significantly more cardiovascular and non-cardiovascular comorbidities including AF, valvular heart disease, hypertension, anaemia, and chronic kidney disease. Patients in the CRT-P group were more likely to be receiving an upgrade from a previous device either a permanent PM or ICD.

Pre-implant clinical evaluation and ECG

Table 2 presents the baseline clinical assessments in the population divided by device received. Patients receiving a CRT-P device were more likely to have either NYHA functional Class III or IV symptoms and also had a higher median N-terminal pro-B-type natriuretic peptide (NT-proBNP) level. On the other hand, whilst the two groups were not very different in terms of median LVEF and left ventricular end-diastolic diameter, substantially more patients receiving a CRT-P device had a baseline LVEF greater than the guideline recommendation level of ≤35%. For patients receiving a CRT-P due to AV block II/III the mean LVEF was 37% compared with 28% in those receiving it primarily for HF.

QRS durations were similar between the two groups, but patients receiving CRT-P were less likely to have left bundle branch block (LBBB) morphology and more likely to have atrial fibrillation and AV block II/III at the time of implantation. Patients in the CRT-P group were also more likely to be PM-dependent.

Implanters were able to select more than one option for clinical indication for implantation of the CRT. In the CRT-P group the most commonly selected indication was HF with wide QRS duration and 43% selected a PM indication and expected right ventricular pacing dependence. In patients receiving a CRT-D the most commonly selected indication was HF or left ventricular

Table 1 Clinical characteristics of patients implanted with a CRT-P vs. CRT-D

	CRT-P ($n = 3225$)	CRT-D ($n = 7449$)	*P*-value
Demographics			
Age (years), median (IQR)	75 (67–80)	68 (61–74)	<0.00001
Age ≥75 (%)	51.2% (1652/3224)	23.6% (1758/7464)	<0.00001
Female gender	31.0% (998/3223)	21.3% (1592/7463)	
Currently enrolled in a clinical trial	6.5% (209/3218)	9.2% (684/7449)	<0.00001
Primary HF aetiology			
Ischaemic	32.9% (1054/3207)	49.4% (3668/7421)	<0.00001
Non-ischaemic	55.8% (1790/3207)	47.2% (3505/7421)	
Other	11.3% (363/3207)	3.3% (248/7421)	
Past history and major comorbidity			
Myocardial infarction	25.1% (804/3204)	40.8% (3022/7413)	<0.00001
PCI/CABG	27.7% (888/3203)	43.6% (3231/7413)	<0.00001
Valvular heart disease	30.3% (971/3209)	25.9% (1914/7402)	<0.00001
Valve surgery	35.9% (441/1229)	29.4% (709/2414)	0.00006
Hypertension	67.1% (2145/3195)	62.3% (4612/7399)	<0.00001
Diabetes	29.9% (959/3209)	31.8% (2352/7405)	0.05516
Obstructive lung disease	11.9% (383/3208)	12.0% (891/7406)	0.89359
Anaemia	17.8% (571/3207)	13.8% (1021/7402)	<0.00001
eGFR <60 mL/kg/min	35.4% (1135/3207)	29.2% (2159/7392)	<0.00001
HF hospitalization during last year	44.4% (1425/3209)	47.2% (3496/7399)	0.00699
Atrial fibrillation	49.8% (1597/3207)	36.8% (2724/7404)	<0.00001
Paroxysmal	30.1% (481/1597)	37.8% (1031/2724)	
Persistent	21.7% (346/1597)	23.0% (626/2724)	
Permanent	47.8% (763/1597)	38.5% (1048/2724)	
Previous device	25.8% (828/3214)	20.6% (1534/7461)	<0.00001
PM	25.3% (812/3214)	8.2% (614/7461)	
ICD	0.5% (16/3214)	12.3% (920/7461)	

CABG, coronary artery bypass grafting; CRT-D, cardiac resynchronization therapy defibrillator; CRT-P, cardiac resynchronization therapy pacemaker; eGFR, estimated glomerular filtration rate; HF, heart failure; ICD, implantable cardioverter-defibrillator; IQR, interquartile range; PCI, percutaneous coronary intervention; PM, pacemaker.

dysfunction and an indication for an ICD, PM dependence and expected RC pacing dependence as an indication was only selected in 14% of the cases.

CRT implantation procedural complications

Table 3 presents the CRT implantation procedural and periprocedural complications for the entire cohort. Patients receiving a CRT-P were slightly less likely to receive it during an elective admission and also less likely to receive a multipolar left ventricular lead. Periprocedural complications were similar, with both groups reporting a 5% complication rate. The most common complication was pocket haematoma followed by coronary sinus dissection and pneumothorax. There were four procedural-related deaths in the CRT-P group and three in the CRT-D group.

Post-cardiac resynchronization therapy implantation

Table 4 details the post-CRT implantation course. The total length of hospital stay was 3 days for both groups, and there was similar adverse events rate during hospitalization reported of <5%, with worsening of renal function occurring more commonly in the CRT-P recipients and arrhythmias more commonly in patients implanted with a CRT-D. There were 42 deaths during the hospital stay, 25 in the CRT-P group and 17 in the CRT-D group.

Recipients of CRT-P were less likely to be taking optimal guideline-directed medical therapy at discharge than recipients of CRT-D with lower rates of beta-blocker, angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker and mineralocorticoid receptor antagonist prescription. More patients were anticoagulated in the CRT-P group and significantly fewer were prescribed antiplatelet agents. The planned follow-up was similar for the two groups with 99% of patients scheduled for appointments at follow-up clinics. However, there was much less planned remote monitoring in the CRT-P group. Device optimization was more commonly performed in the CRT-D group.

Characteristics associated with selection of cardiac resynchronization therapy pacemaker

Table 5 describes patient and hospital characteristics associated with selection of a CRT-P vs. a CRT-D. Characteristics

Table 2 Pre-implant clinical evaluation and ECG

	CRT-P (n = 3225)	CRT-D (n = 7467)	P-value
NYHA class			
I	3.4% (109/3188)	3.3% (246/7358)	<0.00001
II	32.3% (1031/3188)	40.0% (2944/7358)	
III	58.2% (1855/3188)	52.9% (3891/7358)	
IV	6.1% (193/3188)	3.8% (277/7358)	
BMI (kg/m^2), median (IQR)	27 (24–30) n = 3078	27 (25–31) n = 7112	<0.00001
Systolic BP (mmHg), median (IQR)	125 (112–140) n = 3148	120 (110–135) n = 7269	<0.00001
Diastolic BP (mmHg), median (IQR)	71 (65–80) n = 3146	72 (67–80) n = 7268	0.31060
LVEF, median (IQR)	30 (25–37) n = 3167	27 (21–31) n = 7354	<0.00001
LVEF >35%	27.4% (869/3167)	6.6% (488/7354)	<0.00001
LVEDD by echo (mm), median (IQR)	60 (55–66) n = 2480	64 (59–70) n = 5924	<0.00001
Mitral regurgitation			0.58197
None	21.2% (627/2958)	19.7% (1336/6773)	
Mild	45.2% (1338/2958)	47.1% (3187/6773)	
Moderate	26.5% (784/2958)	26.4% (1786/6773)	
Severe	7.1% (209/2958)	6.9% (464/6773)	
Laboratory measurement, median (IQR)			
NT-proBNP (pg/mL)	3035 (1212–7213) n = 1014	2158 (992–4948) n = 2385	<0.00001
Haemoglobin (g/dL)	13 (12–14) n = 3023	14 (12–15) n = 6965	<0.00001
Serum creatinine (μmol/L)	103 (83–133) n = 2042	99 (83–126) n = 3839	0.00020
Pre-implantation ECG			
Heart rate (b.p.m.), median (IQR)	70 (60–80) n = 3153	70 (61–80) n = 7283	0.01934
Atrial rhythm			
Sinus	59.2% (1881/3179)	73.8% (5437/7371)	<0.00001
Atrial fibrillation	34.3% (1090/3179)	21.7% (1601/7371)	
Atrial paced	3.6% (114/3179)	2.4% (180/7371)	
Other	3.0% (94/3179)	2.1% (153/7371)	
PR interval (ms), median (IQR)	180 (160–220) n = 1782	180 (160–210) n = 5316	0.15056
AV block II/III	30.8 % (970/3147)	13.9 % (1009/7268)	<0.00001
Paced QRS duration (ms), median (IQR)	180 (160–200) n = 654	183 (160–200) n = 756	0.02825
Intrinsic QRS duration (ms), median (IQR)	160 (140–173) n = 2609	160 (142–174) n = 6676	0.00016
<120	11.3% (294/2609)	6.0 % (399/6676)	
120–129	5.9% (153/2609)	5.1% (341/6676)	
130–149	17.2% (448/2609)	19.1% (1273/6676)	
150–179	44.3% (1156/2609)	48.1% (3214/6676)	
≥180	21.4% (558/2609)	21.7% (1449/6676)	
QRS morphology			
LBBB	71.1% (2136/3005)	77.1% (5504/7138)	<0.00001
RBBB	7.0% (211/3005)	6.5% (461/7138)	0.29771
Other	21.9% (658/3005)	16.4% (1173/7138)	<0.00001
Pacemaker dependant	21.5% (680/3167)	10.7% (782/7300)	<0.00001
AV node ablation (patients with AF)[a]	35.1% (378/1077)	27.6% (438/1587)	0.00004
Performed	25.1% (95/378)	21.5% (94/438)	
Planned	74.9% (283/378)	78.5% (344/438)	
Clinical indication for CRT[b]			
HF with wide QRS	63.3% (2025/3197)	58.8% (4368/7428)	
HF or LV dysfunction and indication for ICD	5.8% (187/3197)	65.9% (4898/7428)	0.00001
PM indication and expected RV pacing dependent	43.1% (1379/3197)	14.1% (1044/7428)	<0.00001
Evidence of mechanical dyssynchrony	14.8% (472/3197)	10.2% (754/7428)	<0.00001
Other	6.4% (205/3197)	3.6% (267/7428)	<0.00001

AF, atrial fibrillation; AV, atrioventricular; BMI, body mass index; BP, blood pressure; CRT, cardiac resynchronization therapy; CRT-D, cardiac resynchronization therapy defibrillator; CRT-P, cardiac resynchronization therapy pacemaker; ECG, electrocardiogram; HF, heart failure; IQR, interquartile range; ICD, implantable cardioverter-defibrillator; LBBB, left bundle branch block; LV, left ventricular; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; PM, pacemaker; RBBB, right bundle branch block; RV, right ventricular.

[a]AV nodal ablation only regards patients with atrial fibrillation.

[b]More than one indication could be given.

Table 3 CRT implantation procedure and periprocedural complications

	CRT-P ($n = 3225$)	CRT-D ($n = 7467$)	*P*-value
Admissions			
Elective	72.8% (2341/3215)	78.6% (5816/7403)	<0.00001
Referral	25.5% (819/3212)	25.4% (1882/7398)	0.94905
Operator			
Electrophysiologist	77.9% (2531/3250)	76.7% (5758/7505)	0.06516
HF physician	5.8% (189/3250)	4.7% (351/7505)	
Invasive cardiologist	11.8% (384/3250)	12.6% (942/7505)	
Surgeon	3.7% (119/3250)	4.5% (339/7505)	
Other	0.8% (27/3250)	1.5% (115/7505)	
Prophylactic antibiotics	97.9% (3128/3195)	99.0% (7376/7454)	0.00002
Procedure time (min), median (IQR)	90 (62–120) $n = 3133$	94 (69–125) $n = 7278$	<0.00001
Fluroscopy time (min), median (IQR)	13 (8–21) $n = 3109$	14 (8–23) $n = 7217$	<0.00001
LV lead type			
Unipolar	0.7% (22/3191)	0.7 % (55/7390)	<.00001
Bipolar	49.2% (1570/3191)	39.3% (2903/7390)	
Multipolar	50.1% (1599/3191)	60.0% (4432/7390)	
LV position optimized	33.2% (1034/3114)	34.1% (2447/7178)	0.38313
Electrical delay such as QLV	60.0% (613/1021)	59.5% (1438/2418)	
Paced QRS duration	63.7% (650/1020)	59.1% (1426/2413)	
Other means	19.4% (198/1018)	26.4% (636/2406)	
Periprocedural complication	4.8% (155/3256)	5.3% (401/7513)	0.21397
Death	2.6% (4/155)	0.7% (3/401)	0.09883[a]
Bleeding	16.8% (26/155)	19.2% (77/401)	0.50879
Requiring intervention	38.5% (10/26)	32.9% (25/76)	
Pocket haematoma	73.1% (19/26)	80.3% (61/76)	
Pneumothorax	23.9% (37/155)	18.5% (74/401)	0.15190
Haemothorax	2.6% (4/155)	1.2% (5/401)	0.27338[a]
Coronary sinus dissection	31.6% (49/155)	30.7% (123/401)	0.82983
Pericardial tamponade	3.2% (5/155)	4.2% (17/401)	0.58250
Other	23.9% (37/155)	29.4% (118/401)	0.19021

CRT-D, cardiac resynchronization therapy defibrillator; CRT-P, cardiac resynchronization therapy pacemaker; IQR, interquartile range; HF, heart failure; LV, left ventricular.
[a]The Fisher's exact test used to calculated the *P*-value due to small sample size.

significantly associated with a decision for CRT-P ($P < 0.05$) included past medical history of hypertension, non-elective admission and non-LBBB. Characteristics highly significantly ($P < 0.001$) independently associated with choice of CRT-P were age >75 years, female gender, non-ischaemic HF aetiology, NYHA functional Class III/IV, LVEF >25%, AF, AV block, and being implanted in a university hospital.

Cardiac resynchronization therapy pacemaker vs. cardiac resynchronization therapy defibrillator per country

There was a large variation in both the total number of CRT implantations and the proportion of CRT-P vs. CRT-D implanted per country (Supplementary material online, *Table S1*). Analysing countries that provided >200 patients to the Survey, we found that in some countries the percentage of CRT-P was as high as 88% and in others as low as 2% (*Figure 2*).

Discussion

In the largest ever prospective cohort study of international CRT implantation practice, we have described patient selection for CRT-P and CRT-D. Overall, we showed that 70% of CRT recipients in Europe received a device with defibrillation capacity. Cardiac resynchronization therapy pacemaker recipients were older, more commonly had NYHA functional Class III–IV symptoms, were more often female, had higher NT-proBNP levels and more frequently had comorbidities and additional conduction tissue disease. On the other hand, patients implanted with a CRT-D device were more likely to have ischaemic HF aetiology probably reflecting the stronger guideline levels of evidence for an ICD in patients with ischaemic aetiology than in those with non-ischaemic aetiology.[2] Patients receiving a CRT-P were slightly less likely to receive it during an elective admission, suggesting that CRT-P was a more likely choice during an acute admission, which may reflect that amongst CRT-P recipients AV block II/III was an indication for CRT implantation.

Table 4 Post CRT implantation

	CRT-P (*n* = 3225)	CRT-D (*n* = 7467)	*P*-value
Paced QRS duration (ms), median (IQR)	135 (120–150) *n* = 2954	138 (120–151), *n* = 6958	0.00006
Device programming			
AV optimization	54.2% (1699/3136)	60.6% (4382/7234)	<0.00001
VV optimization	58.9% (1844/3131)	56.7% (4095/7225)	0.03619
Device optimization	32.6% (1010/3098)	38.8% (2790/7185)	<0.00001
Discharge status			
Alive	99.2% (3162/3186)	99.8% (7351/7368)	0.00007
Death	0.8% (25/3186)	0.2% (17/7368)	
Length of hospital stay (days), median (IQR)	3 (2–7) *n* = 3168	3 (2–7) *n* = 7316	0.02122
Major adverse events after procedure			
AE during hospitalization after procedure	4.7% (153/3225)	4.7% (350/7467)	0.89853
MI	0.1% (2/3182)	0.1% (6/7346)	1.00000[a]
Stroke	0.0% (1/3182)	0.1% (5/7346)	0.67510[a]
Infection	0.5% (15/3182)	0.6% (42/7346)	0.51939
Worsening HF	0.7% (23/3182)	0.7% (48/7346)	0.68949
Worsening renal function	1.3% (40/3182)	0.8% (61/7346)	0.03915
Arrhythmias	0.8% (25/3182)	1.3% (96/7346)	0.02123
Other	2.1% (68/3182)	1.8% (132/7346)	0.24040
Planned follow-up	98.7% (3184/3225)	98.6% (7366/7467)	0.73608
Implantating centre	85.1% (2711/3184)	87.0% (6408/7366)	0.01086
Other hospital	8.5% (271/3184)	7.8% (576/7366)	0.23013
Private cardiologist	7.2% (228/3184)	4.5% (332/7366)	<0.00001
Primary care physician	1.3% (40/3184)	0.7% (50/7366)	0.00307
CRT/pacemaker clinic	10.2% (326/3184)	10.5% (770/7366)	0.74001
HF management programme	2.4% (78/3184)	2.5% (182/7366)	0.94893
Other	0.4% (14/3184)	0.2% (15/7366)	0.0337
Remote monitoring planned	18.2% (578/3169)	35.3% (2581/7303)	<0.00001
Drug therapy at discharge			
Loop diuretic	78.9% (2457/3113)	81.9% (5935/7249)	0.00046
ACEi/ARB	81.8% (2542/3107)	88.3% (6380/7222)	<0.00001
MRA	52.9% (1636/3095)	67.5% (4861/7204)	<0.00001
Betablocker	82.7% (2579/3119)	91.8% (6656/7254)	<0.00001
Ivabradine	3.1% (95/3092)	6.7% (478/7177)	<0.00001
Digoxin	11.8% (364/3092)	9.8% (700/7178)	0.00206
Calcium channel blocker	12.6% (388/3087)	7.4% (531/7171)	<0.00001
Amiodarone	14.6% (452/3092)	18.5% (1328/7182)	<0.00001
Other anti-arrhythmic agent	1.6% (50/3082)	1.7% (125/7176)	0.6147
Oral anticoagulant	52.9% (1641/3103)	43.7% (3145/7201)	<0.00001
Anti-platelet agent	36.0% (1161/3225)	47.8% (3567/7467)	<0.00001

ACEi, angiotensin-converting enzyme inhibitor; AE, adverse event; ARB, angiotensin II receptor blocker; AV, atrioventricular; CRT, cardiac resynchronization therapy; CRT-D, cardiac resynchronization therapy defibrillator; CRT-P, cardiac resynchronization therapy pacemaker; HF, heart failure; ICD, implantable cardioverter-defibrillator; IQR, interquartile range; MI: myocardial infarction; MRA, mineralocorticoid receptor antagonist; PM, pacemaker; VV, ventriculo–ventricular.
[a]The Fisher's exact test used to calculated the *P*-value due to small sample size.

Complications and adverse events

Reassuringly, despite the differences in clinical characteristics between recipients of CRT-P and CRT-D, periprocedural complication rates and adverse events during hospitalization and the length of stay were the same between both groups. The addition of a defibrillator lead and more bulky CRT device could increase the complication rates in CRT-D procedures compared with CRT-P procedures, but a recent cohort study of 3008 patients found similar results to our study, that peri-complications rate were equal in the two groups.[8] The similar periprocedural complication rates between CRT-P and CRT-D recipients could therefore possibly reflect a choice for CRT-P in patients deemed at higher risk for complications.

Table 5 Characteristics associated with CRT-P vs. CRT-D implantations-regression analysis

Characteristics	Odds ratios (95% confidence interval	*P*-value
Male gender	0.66 (0.58–0.66)	<0.0001
Age ≤75 years	0.27 (0.24–0.27)	<0.0001
Elective admission	0.86 (0.75–0.86)	0.0279
Ischaemic aetiology	0.45 (0.39–0.45)	<0.0001
Past medical history		
Hypertension	1.13 (1.00–1.13)	0.0478
Atrial fibrillation	1.42 (1.22 –1.42)	<0.0001
Pre-implant clinical evaluation		
NYHA functional class III/IV	1.37 (1.21–1.37)	<0.0001
LVEF ≤25%	0.50 (0.45–0.50)	<0.0001
Pre-implantation ECG		
Atrial fibrillation	1.45 (1.22–1.45)	<0.0001
AV block II/III	2.85 (2.37–2.85)	<0.0001
LBBB	0.84 (0.73–0.84)	0.0128
Hospital characteristic		
University hospital	2.11 (1.87–2.11)	<0.0001

AV, Atrioventricular; CRT-D, cardiac resynchronization therapy defibrillator; CRT-P, cardiac resynchronization therapy pacemaker; ECG, electrocardiogram; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association.

Post-cardiac resynchronization therapy implantation

The rates of formal follow-up plans were similar for both groups although significantly more patients in the CRT-D group had a plan to be followed-up by remote monitoring. Remote monitoring of ICD patients is more common due to the desire to monitor arrhythmia and device safety, which could contribute to this observed difference.

Perhaps reflecting the fact that most participating centres in the CRT Survey II were teaching or university centres, the adherence to optimal medical treatment for HF was high in the survey overall.[4] Cardiac resynchronization therapy defibrillator patients tended to have more intensive HF medication than CRT-P recipients. Thus it appears that physicians tend to apply guideline-based optimal medical therapy more rigorously when caring for CRT-D patients. Alternatively, the age difference could suggest that the older patients in the CRT-P cohort did not tolerate medical therapies as well or that uptitration of medication was not possible in patients with AV block receiving CRT within the short hospital stay.

Factors associated with cardiac resynchronization therapy pacemaker rather than cardiac resynchronization therapy defibrillator

We found age ≥75 years, female gender, non-ischaemic cardiomyopathy, NYHA Class III/IV, AF, AV block II/III, LVEF >25%, and being implanted in a university hospital to be highly significantly related to the choice of a CRT-P over a CRT-D. Overall, it appears possible that in patients selected for CRT-P, operators are appreciating the limited clinical effectiveness of ICD therapy in older and frailer patients. This is consistent with the limited guidance provided in the most recent EHRA guidelines from 2013 on CRT, which recommend CRT-P in advanced HF, major comorbidities and frailty.[1] Implanters also appear to favour CRT-P implantation over CRT-D in patients with non-ischaemic cardiomyopathy, perhaps reflecting the increasing evidence of lesser benefit of an ICD in this group and the weaker evidence level awarded by the most recent HFA guidelines for primary prevention of sudden cardiac death in patients with non-ischaemic HF aetiology.[2,9]

Previously available data on cardiac resynchronization therapy pacemaker vs. cardiac resynchronization therapy defibrillator

CARE HF clearly demonstrated a reduction in total mortality with CRT compared with optimal medical therapy in eligible patients.[10] In the extended follow-up dataset, CRT-P was associated with a reduction in sudden cardiac death closely correlated to left ventricular reverse remodelling.[11,12] There remains the question, however, of whether CRT-D offers additional protection to patients receiving a CRT device. No study has been designed or powered to directly compare CRT-P vs. CRT-D on clinical outcomes limiting the ability of guidelines to comment or advise.[3] Only one head-to-head study of CRT-D vs. CRT-P has ever been published. However, this study (COMPANION) was not designed to compare different CRT devices; rather, it focused on the overall concept of CRT vs. optimal medical therapy. It established the benefit of a CRT over medical therapy in eligible patients but was underpowered to compare any difference between the two device arms. Although total mortality was only reduced compared with medical therapy in the CRT-D arm, the CRT-P and CRT-D curves largely overly one another.[13] In addition, the REVERSE study demonstrated that CRT does not induce ventricular tachycardia (VT) but that significant reverse left ventricular remodelling was associated with a reduction in VT.[14]

In order to address concerns about making a choice in clinical practice, the most recent EHRA guidelines provide a list of factors to be considered in selecting a CRT-P vs. a CRT-D; such as advanced HF, severe renal insufficiency, other major co-morbidities, frailty and cachexia.[1] The 2014 United Kingdom (UK) National Institute for Health and Care Excellence (NICE) Guidelines (TA314) provide clear recommendations on when to consider CRT-P vs. CRP-D based on QRS duration and morphology and NYHA class but remain silent on the effects of comorbidities and age on the relative benefit of CRT-D over CRT-P.[3]

In our survey, we found that women were less likely to receive a CRT-D. This is consistent with the findings from recent European Registry in which only 19% of primary preventive ICD recipients were female.[15] In another meta-analysis women represented 22% of 7229 patients. In contrast to men, these datasets reported that women had a lower mortality and experienced fewer appropriate shocks than men.[16]

In the French CeRtiTuDe registry 1705 recipients of either a CRT-P or a CRT-D were followed for adjudicated causes of death over 2 years.[17] As in CRT Survey II and in a recent cause-of-death

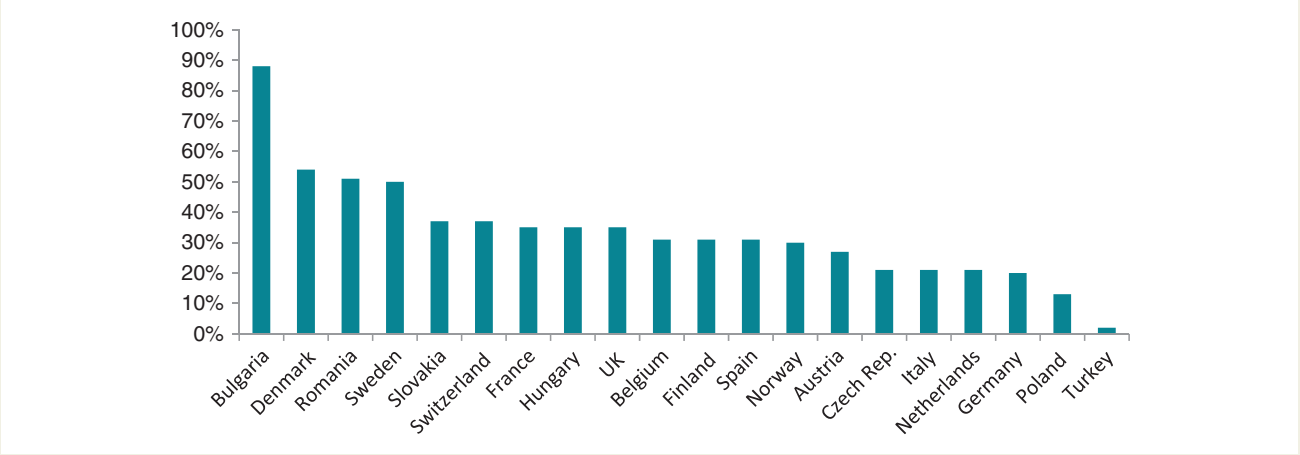

Figure 2 Percentage CRT-P per country (for countries with >200 patients in CRT Survey II). CRT-P, cardiac resynchronization therapy pacemaker.

analysis of 18 874 patients with CRT-P or CRT-D, CRT-P patients were older, more symptomatic, more often had AF and less often had ischaemic aetiology.[18] Indeed, CRT Survey I already indicated that >30% of CRT patients were older than 75 years.[5] Importantly, outcome in the elderly CRT population has been shown to be comparable with age-matched patients.[19] Although mortality was double in CeRtiTuDe in the CRT-P vs. the CRT-D group, this increased mortality rate was due to non-sudden cardiac death in the CRT-P group. A large single-centre study published in 2017 showed similar results to the CeRtiTuDe registry, namely that despite being younger and fitter, recipients of CRT-D systems did not have a clear mortality benefit over those that received CRT-P systems.[20] In short, CRT reduces but probably does not completely abolish the risk of sudden cardiac death likely through reverse remodelling.

The only recent RCT of defibrillator over standard care—the DANISH study—described that the benefits of ICD in patients with dilated cardiomyopathy were limited to the younger patients (<68 years of age). In CRT recipients (58%) CRT-D was not obviously better than CRT-P.[9] Indeed, the incidence of sudden cardiac death was overall relatively low in CRT-P (<5% at 2 years) and the events were likely to be preceded by recorded sustained ventricular arrhythmias. This finding suggests that regular CRT-P device memory interrogation/remote monitoring might be warranted to timely upgrade patients from CRT-P to CRT-D in case of sustained VT.[17] These findings call for maintaining an individualized approach when selecting a defibrillator in conjunction with CRT implantation. Indeed, compared with non-ischaemic cardiomyopathy patients with ischaemic heart disease have substantially less improvement in ventricular function after CRT, yet their benefit on prognosis is remarkably similar.

Economic considerations

Our findings indicate that clinical information alone does not explain the large variations in implantation rate of CRT-P vs. CRP-D which our analysis found. These cannot be explained only on medical grounds, other factors such as reimbursement policies may come into play as countries with comparable financial resources show markedly different implantation behaviours. We performed a linear regression analysis based on gross domestic product per capita in the countries contributing >200 patients to the Survey and showed that the likelihood of implanting a CRT-P vs. CRT-D could not be explained simply by the country's economic status, so clearly other factors are motivating physicians to make choices between CRT-P and CRT-D in the absence of clear guidelines. However, the question of whether there is a benefit of CRT-D over CRT-P and at what cost is important since ICD implantation is considerably more expensive, the devices frequently have a more intensive follow-up programme, and complication rates due to the device are more frequent.[21] This question deserves to be addressed in a well-designed randomized head-to-head comparison.

Limitations

The ability of a survey to describe practice is related to the strength of its methodology, its representativeness and size. Although the number of patients enrolled in this survey was large, there were substantial differences amongst countries. Overall, we estimate that about 11% of patients implanted with CRT in participating countries during the recruitment period were enrolled in the survey. We cannot assess the degree of selection bias in the choice of enrolled patients. Although we requested enrolment of consecutive patients, we were not able to verify this, and sites may have been less likely to report unsuccessful implants or cases with a poor outcome, accounting for low complication and mortality rates. The eCRF was designed to be user-friendly and anonymous in order to maximize the number of patients enrolled. Unavailable patient data could be omitted on the eCRF so that the analyses were based on the available data, which resulted in variation in the sample size for each data point. Furthermore, the interpretation of questions was up to the discretion of the investigator. Although there was no formal independent monitoring of the data collection, the IHF conducted 'front-end' data check and post database lock quality control analyses designed to prevent incorrect data being analysed. For the regression analysis we

did not include the full cohort to avoid adding upgrades as a confounding factor in our analysis.

Conclusions

RT Survey II is the largest available comparison of patients receiving CRT-P or CRT-D. In Europe CRT-P recipients were older and had greater comorbidity. Independent patient characteristics that were found to be predictors of receiving a CRT-P included age ≥75 years, female gender, non-ischaemic HF aetiology, NYHA Class III/IV, LVEF >25%, AF, and AV block II/III and implantation in a university hospital. Our survey has demonstrated wide variations in the percentage of CRT-P vs. CRT-D in ESC member countries. We believe that these variations in clinical practice partially arise from the limited specific recommendations regarding choice of device type provided by the current ESC guidelines; such large variations emphasize the need for increasing evidence in this area. Our findings can assist in the design of future studies in this field as we have identified factors that clinicians appear to consider when making the choice of device type. It is clinically relevant to identify the degree to which these factors are predictive of clinical outcomes in a randomized clinical trial of CRT-P vs. CRT-D.

Supplementary material

Supplementary material is available at *Europace* online.

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