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The European cardiac resynchronization therapy survey

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Aims The European cardiac resynchronization therapy (CRT) survey is a joint initiative taken by the Heart Failure Association and the European Heart Rhythm Association of the European Society of Cardiology. The primary aim of this survey is to describe current European practice associated with CRT implantations.

Methods and results A total of 140 centres from 13 European countries contributed data from consecutive patients successfully implanted with a CRT device with or without an ICD between November 2008 and June 2009. The total number of patients enrolled was 2438. The median age of the patients was 70 years (IQR 62–76) and 31% were ≥75 years. It was found that 78% were in NYHA functional class III or IV and 22% in I or II. The mean ejection fraction was 27% ± 8 and the mean QRS duration 157 ms ± 32. The QRS duration was <120 ms in 9%. Atrial fibrillation was reported in 23%. It was found that 26% of patients had a previously implanted permanent pacemaker or ICD; 76% of procedures were performed by an electrophysiologist; 82% had an elective admission for implantation and the median duration of hospitalization was 3 days (IQR 2–7); and 73% received a CRT-D device which was more often implanted in men, younger patients, and with ischaemic aetiology. The mean QRS duration was reduced to 133 ms ± 27 ($P < 0.0001$) at discharge. Peri-procedural complication rates were comparable to the rates reported in randomized trials.

Conclusion This CRT survey provides important information describing current European practice with regard to patient demographics, selection criteria, procedural routines, and status at discharge. These data should be useful for benchmarking individual patient management and national practice against wider experience.

Keywords Cardiac resnchronization therapy (CRT) • European practice • Survey

Introduction

The recent ESC Heart Failure Guidelines,[1] the ESC/European Heart Rhythm Association (EHRA) Guidelines for Cardiac Pacing,[2] and the ACC/AHA/HRS Guidelines for Device Therapy[3] provide a class I recommendation with the level of evidence A for cardiac resynchronization therapy (CRT) treatment with or without an ICD in patients with symptomatic heart failure (NYHA III and IV) despite adequate medical treatment, a QRS duration >120 ms and an EF < 35%, in order to improve survival and reduce morbidity. Guidelines provide little guidance on which patients should have CRT-P or CRT-D, reflecting the lack of relevant data from randomized clinical trials (RCTs).[4–6] The implantation rate of CRT-P or CRT-D in Western Europe was 100/million inhabitants in 2008; 25% of these devices were CRT alone (CRT-P) and 75% were devices in combination with an ICD (CRT-D).[7]

The data from RCTs on CRT are largely based on selected patients and there is also limited data in elderly patients with co-morbidity. It is likely that many patients who would benefit

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from device therapy do not receive it. In contrast, some patients who receive a device do not fulfil guideline criteria.[8] Recent publications suggest that patients with higher left ventricular ejection fractions (LVEF), milder symptoms, atrial fibrillation, right bundle branch block (RBBB), or narrower QRS durations with evidence of mechanical intraventricular dyssynchrony may benefit from implantation of a CRT device.[9,10] There is substantial variation across Europe both with regard to interpretation of the indications as well as implantation routines and procedures. Specifically, practice varies with regard to decisions concerning device type.[11]

This European CRT survey was initiated by the Heart Failure Association (HFA) and the EHRA of the ESC in order to describe current European practice and routines associated with CRT-P/CRT-D implantations based on a sample of patients enrolled in 13 countries. The data collected following implantation provide information including clinical characteristics, diagnostic criteria, implantation routines and techniques, adverse experience, in-hospital course, discharge status, and assessment of adherence to guideline recommendations. This report details the information captured following successful implantation and entry into the survey. A single follow-up visit at 1 year (9–15 months) will provide patient information and short-term clinical outcomes.

Methods

Objectives

The primary objective of this survey is to describe current European practice based on a broad sampling in 13 countries. The information collected will enable practice between centres and countries to be compared and permit benchmarking with national and international practice. The survey provides valuable quality assurance assessment for individual centres, permits limited economic analyses, and broadly evaluates adherence to guideline recommendations.

Design

The rationale and design of the CRT survey has been published recently.[12] All centres implanting CRT devices (CRT-P, CRT-D, or an upgrade) in the chosen countries were invited to participate. Centres were asked to enrol consecutive patients after successful implantation between 1st November 2008 and 30th June 2009.

Data collection

Data were collected using online internet entry. An electronic case report form (eCRF) was developed by the Scientific Committee (Appendix 1) to capture demographics and clinical characteristics, selection criteria assessed prior to implantation, implantation procedures and techniques, device programming and optimization, adverse experience, hospitalization data, and pharmacological therapy at discharge. The contents of the eCRF are detailed in Appendix 2.

All centres were asked to complete a one-time site questionnaire describing the type and size of the centre, reference area population, facilities, and number of invasive procedures performed. Germany and Sweden have ongoing device registries which include CRTs and capture most of the information contained in the CRT survey eCRF. With permission from both of the Steering Committees, CRT data collected consecutively in these two registries during the time frame were merged into the CRT survey database.

A central database was created at the data management centre, Institut für Herzinfarktforschung in Ludwigshafen an der Universität Heidelberg, Germany, which also maintained and interrogated the database and performed analyses. A web site www.crt-survey.org supported by the ESC Web department provides all the relevant documents and reports the current status.

Participating countries

The following 13 European countries contributed patients to the survey: Austria, Belgium, France, Germany, Ireland, Israel, Italy, the Netherlands, Norway, Spain, Sweden, Switzerland, and UK. Two national co-ordinators, one each from the fields of heart failure and electrophysiology, were selected and given the responsibility of facilitating recruitment in their respective countries (Appendix 1).

Survey population

All consecutive patients successfully implanted with a new CRT-P, CRT-D, or upgrades were eligible. The procedure itself identified the patient as a Survey candidate. A successful implantation was defined as a completed procedure. Patients screened but not successfully implanted were not entered into the Survey. Ethics approval and written informed consent were obtained in countries where required.

Statistical methodology

Percentages are shown for categorical variables to describe the patient population, and medians with inter-quartile range or means with standard deviations for continuous variables. Binary variables were compared between subgroups by Pearson χ^2 test and continuous variables by Mann–Whitney *U* test. Descriptive statistics were calculated for the available cases. A significance level of 0.05 was assumed for the statistical tests and all *P*-values are results of two-tailed tests. The calculations were performed using SAS[a] statistical software, version 9.1 (Cary, North Carolina, USA).

Results

Participating centres

A total of 141 centres in Western Europe participated in the survey and recruited a total of 2438 patients during the 8 month enrolment period; of these 1384 patients were recruited by four countries: Italy (571), Sweden (321), Germany (291), and UK (201) (*Figure 1*).

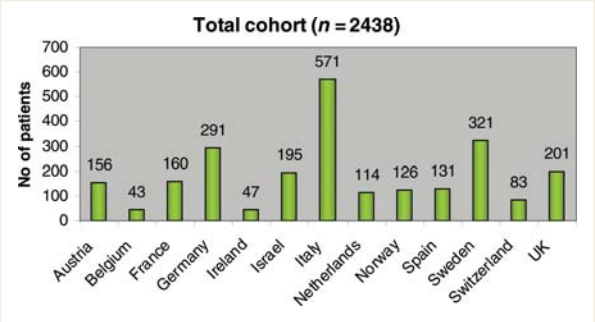

Figure 1 Country distribution of patients included in the CRT Survey.

The median number of inhabitants for the hospital catchment area was 400 000 (range: 25 000–700 000) and 86% of the hospitals covered an area with over 100 000 inhabitants. The median annual number of procedures was as follows: 1650 coronary angiographies, 850 PCI procedures, 200 pacemaker implantations, and 95 ICDs. The average number of invasive/electrophysiology laboratories was 2 (range: 1–6). Out of the total, 86% of hospitals had a heart failure management programme and 89% had a specialized CRT clinic available for follow-up.

Total cohort

Demographics

The median age of patients was 70 (IQR 62–76), 31% were >75 years of age (median of 78 and IQR 76–81), and 24% were women (*Table 1*). It was found that 57% had had an admission to hospital for HF decompensation during the previous year. The aetiology for HF was ischaemic in 51% of patients and non-ischaemic in 40%, while 9% had other aetiology. More men (57%) than women (33%) had ischaemic heart disease ($P < 0.0001$).

Pre-operative evaluation

It was found that 26% of patients had undergone a prior device implantation (pacemaker/ICD) within the last year; 2% of patients were in NYHA functional class I, 20% in II, 70% in III, and 8% in IV (*Table 1*). Concerning rhythm and conduction disturbance, 23% of patients had atrial fibrillation and 68% of patients had left bundle branch block (LBBB); 62% of patients had a QRS duration >150 ms, 18% <130 ms, and 9% <120 ms. The median ejection fraction was of 25 (IQR 20–30) and the average LV end-diastolic diameter was 65 ± 10 mm. It was found that 71% of patients had some degree of mitral insufficiency and 41% of patients had echocardiographic evidence of intraventricular dyssynchrony. The median BNP and NT-pro BNP values were 428 and 1740 pg/mL, respectively, compatible with clinical HF.

Procedure

Out of the total, 82% of patients had an elective planned admission for device implantation (*Table 2*). A CRT-D device was implanted in 73% of patients (75% of men and 67% of women; $P < 0.001$) and CRT-P in 27%. The operator was an electrophysiologist in 76% of cases, invasive cardiologist in 15%, a surgeon in 10%, and an HF physician in 4%. The procedure was performed in EP/catheterization laboratories in 78% of cases; 11% of patients required general anaesthetics; and 94% received prophylactic antibiotics. The median duration of the procedure was 100 min (IQR 66–140) with a median fluoroscopy time of 17 min (IQR 10–28).

It was found that 11% of patients had a peri-procedural complication reported; 3% of these were a pocket hematoma, and 2% phrenic nerve pacing. Coronary sinus dissection occurred in 1% of patients and required intervention in only a single patient. Only successful implantations were entered into this survey and therefore no deaths directly related to the procedure were reported.

The right ventricular (RV) lead was placed in an apical position in 74% of patients and the LV lead was placed in a lateral or posterolateral position in 89% of patients. Positioning was reported by the operator.

Table 1 Pre-implantation evaluation of the total cohort ($n = 2438$)

Demographics	
Age (years)[a]	70 (62–76)
Age ≥ 75 (%)	31
Females (%)	27
BMI (kg/m2)[a]	26 (24–29)
Heart failure aetiology (%)	
Ischaemic	51
Non-ischaemic	40
Other	9
Past History (%)	
Hear Failure hospitalisation during last year	57
Diabetes mellitus	30
Chronic lung disease	17
CABG	23
PCI	26
History of ablation	5
Prior device (PPM, ICD)	26
VF/sustained VT	14
ECG (%)	
Mean heart rate (b.p.m.)	72 ± 15
Sinus rhythm	73
Atrial fibrillation	23
QRS complex (%)	
LBBB	68
RBBB	6
Paced rhythm	19
Mean QRS duration (msec)	157 ± 32
QRS duration < 120 ms	9
QRS duration 120 - 129 ms	10
QRS duration 130 - 149 ms	20
QRS duration ≥ 150 ms	62
Elective admission for CRT-implantation (%)	82
Clinical evaluation (%)	
NYHA I	2
NYHA II	20
NYHA III	70
NYHA IV	8
Mean LV ejection fraction (%)	27 ± 8
<25%	37
25–35%	46
>35%	17
LV end-diastolic diameter (mm)	65 ± 10
LV end-systolic diameter (mm)	54 ± 11
Mitral regurgitation (%)	
Mild	36
Moderate	28
Severe	7

Continued

Table 1 *Continued*

Mechanical dyssynchrony (%)	
Absent/subtle	14
Obvious	25
Marked	16
Not assessed	46
CRT implantation based on (%)	
QRS duration	53
Mechanical dyssynchrony	9
Both	37

[a]Median and interquartile range.

Discharge status

The median duration of hospitalization was 3 days (IQR 2–7). Out of the total, 10 patients died during their hospitalization following implantation (*Table 3*). Device-related complications were recorded in 4% of patients. Lead displacement and phrenic nerve stimulation were observed each in 2%. The mean paced QRS duration after optimization was 133 ± 27 ms, and significantly shorter than the pre-implant spontaneous QRS duration.

Substantial improvement in NYHA functional status was reported ($P < 0.0001$) (*Figure 2*). Prior to implantation 22% of patients were reported to be in NYHA functional classes I–II and at discharge 52% of patients were considered NYHA classes I–II. It should be emphasized that these data were uncontrolled, subjective, and based on investigator evaluation.

Selected populations

Device type

Ischaemic heart disease was more frequent in patients receiving a CRT-D (56 vs. 41%, $P < 0.001$) and previous VF/sustained VT was observed more frequently in the CRT-D group (19 vs. 2%, $P < 0.001$) (*Table 4*). Atrial fibrillation was reported less frequently in the CRT-D group (20 vs. 32%, $P < 0.0001$).

General anaesthetic was required during the procedure more often in the CRT-D group (12 vs. 7%, $P < 0.001$). As expected, the duration of the procedure was longer for CRT-D implantation (110 vs. 90 min, $P < 0.001$). Peri-procedural complication rates were similar. The median duration of hospitalization was longer for patients receiving a CRT-D (4 days (IQR 2–8) vs. 3 days (IQR 1–6), $P < 0.001$).

Age

Out of the total, 31% of the patients were ≥75 years age (*Table 5*). The median age of the older cohort was 78 (IQR 76–81) and the younger cohort (<75 years) 66 (IQR 59–70). Older patients were more likely to have ischaemic heart disease (56 vs. 48%, $P < 0.001$), less likely to have a QRS duration of <130 ms (13 vs. 21%, $P < 0.0005$), and less likely to receive a CRT-D (55 vs. 81%, $P < 0.001$), and the duration of procedure was therefore shorter (90 vs. 110 min, $P < 0.001$). There was no substantial difference between the groups with regard to peri-procedural complications or adverse events during hospitalization.

Table 2 Procedural details of the total cohort ($n = 2438$)

Operator (%)	
Electrophysiologist	76
Heart failure physician	4
Invasive cardiologist	15
Surgeon	11
Location of procedure (%)	
EP/Catheterization lab.	78
Operating room	21
Sedation/anaesthesia (%)	
None	43
IV sedation	47
General anaesthetic	11
Duration of procedure (min)[a]	100 (66–140)
Fluoroscopy time (min)[a]	17 (10–28)
Epicardial approach (%)	3
Prophylactic antibiotics (%)	96
RV lead position (%)	
Basal	10
Middle	15
Apical	74
LV lead position (%)	
Anterior	1
Antero-lateral	9
Lateral	43
Posterolateral	46
Middle cardiac vein	1
Peri-procedural complications (%)	10
Bleeding	1
Pocket haematoma	3
Pneumothorax	1
Pericadial tamponade	0.3
Coronary sinus dissection	1
Phrenic nerve pacing	2
Lead dislocation	3

[a]Median and interquartile range.

Discussion

This CRT Survey recruited 2438 patients from 141 centres in 13 Western European countries. Important information reflecting current clinical practice included description of demographics and clinical characteristics, diagnostic criteria, implantation procedures and techniques, adverse experience, and hospital course. The recent ESC guideline recommendations are largely based on two key studies: COMPANION and CARE-HF. A third trial, REVERSE, was published more recently. *Table 6* reports the key characteristics of the patient cohorts in comparison with the patients included in this survey.[10,13,14] The REVERSE population as well as the population included in the recently concluded

Table 3 Post-implantation details

Hospital mortality (%)	0.5
Device related complications (%)	4
Lead displacement	2
Lead malfunction	0
Phrenic nerve stimulation	2
Clinical evaluation (%)	
NYHA I	3
NYHA II	49
NYHA III	46
NYHA IV	2
CRT programming (%)	
To optimize AV interval	19
To optimize VV interval	22
Both	59
Mean paced QRS duration (msec)	133 ± 27
Device follow-up at implanting centre (%)	93
Hospital periods (days)[a]	
Duration admission –> discharge	3 (2–7)
Duration admission –> procedure	1 (0–3)
Duration procedure –> discharge	2 (1–4)
Medical treatment at discharge (%)	
Diuretic	88
ACE inhibitor	67
ARB	24
Beta blocker	84
Aldosterone antagonist	46
Statin	56
Antiarrhythmic agent	24
Calcium channel antagonist	6
Anticoagulant	45
Platelet inhibitor	50
Laboratory measurements[a]	
Hb (g/dL)	13.0 (11.7–14.3)
Na (mmol/L)	139 (137–141)
K (mmol/L)	4.2 (4.0–4.6)
Creatinine (umol/L)	103 (81–133)
NT-proBNP (pg/mL)	1740 (655–3542)
BNP (pg/mL)	428 (185–911)

[a]Median and interquartile range

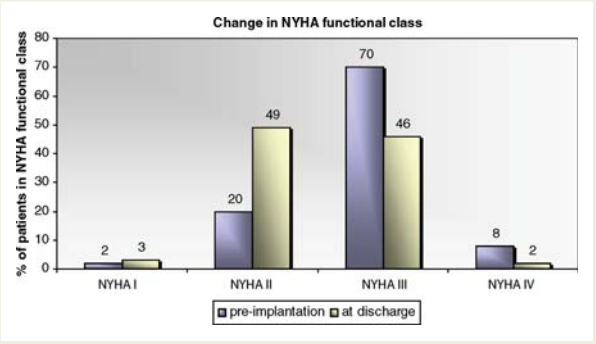

Figure 2 Investigator reported NYHA functional class before implantation and at discharge.

MADIT-CRT[15] trial differ from the other two RCTs in that patients were asymptomatic or mildly symptomatic.

When compared with RCTs, surveys and registries address different types of questions and provide different types of information. Surveys provide a snapshot of current practice, whereas registries entail long-term follow-up. RCTs evaluate new interventions in the populations that are most likely to benefit using a controlled protocol. A positive treatment response should translate into improved outcome, which depends on the primary endpoints of the trial.[16] In contrast, if all patients can be included consecutively, the design of surveys and registries should reflect actual clinical practice. The results demonstrate the degree to which physicians implement the results of RCTs and guideline recommendations. This Survey adheres to the suggested criteria for judging the scientific value of a clinical data registry.[17]

Guidelines recommend CRT for patients in NYHA functional classes III and IV, EF $\leq$ 35%, and QRS duration $\geq$120 ms despite optimal medical treatment. Guidelines are by nature conservative and only consider published clinical trials. The National Institute for Health and Clinical Excellence guidelines suggest that patients in NYHA functional class I/II may be candidates if they had had recent clinical deterioration.[7]

No differentiation is made regarding the choice between CRT-P and CRT-D, except in cases where an ICD is recommended for secondary prevention of near lethal ventricular arrhythmias. Decisions regarding device type are based on clinical judgement as well as resource availability.[4–6] There are obvious differences in patient characteristics, comparing the populations receiving CRT-D with patients receiving CRT-P. The reason for this is multifactorial, but it is clear that demographic and economical factors are taken into consideration. The data demonstrates that younger patients, men, and patients with ischaemic aetiology are more likely to receive a CRT-D device. The reasons for these differences deserve to be investigated.

The target populations and diagnostic investigations that would best select patients likely to respond favourably from intervention have not been identified.[18,19] QRS duration, a measure of electrical dyssynchrony, has formed the basis inclusion criteria in RCTs. Currently, none of the commonly employed echocardiographic measurements appear robust enough to accurately evaluate mechanical dyssynchrony or predict clinical response.[20] Based on clinical experience and intuition, clinicians frequently extrapolate the data from RCTs to wider populations, which is appropriate when clinical evidence is lacking and no opportunity to enrol the patient into a relevant RCT exists. Ongoing trials are also addressing populations previously not considered candidates for CRT.[15,21] It is evident from the description of the patient characteristics of the population included in this Survey that clinicians are actively exploring wider indications.

Table 4 Selected variables by device type (CRT-D vs. CRT-P)

	CRT-D (n = 1694)	CRT-P (n = 620)	P-value
Demographics			
Age (years)[a]	68 (61–74)	75 (68–80)	<0.0001
Age ≥ 75 (%)	21	52	<0.0001
Females (%)	21	30	<0.0001
Heart failure aetiology (%)			
Ischaemic	55	39	<0.0001
Past History (%)			
CABG	24	19	<0.05
PCI	30	16	<0.0001
Prior device (PPM/ICD)	25	30	<0.05
VF/sustained VT	19	2	<0.0001
ECG (%)			
Sinus rhythm	76	65	<0.0001
Atrial fibrillation	20	32	<0.0001
QRS complex (%)			
Paced rhythm	16	25	<0.0001
QRS duration (ms)	157 ± 32	158 ± 31	ns
QRS duration < 120 ms	9	7	ns
QRS duration ≥ 150 ms	62	63	ns
Mean LV ejection fraction (%)	26 ± 7	29 ± 9	<0.0001
<25%	38	34	ns
25–35%	49	34	<0.0001
>35%	13	32	<0.0001
LV end-diastolic diameter (mm)	66 ± 10	63 ± 9	<0.0001
LV end-systolic diameter (mm)	55 ± 10	51 ± 11	<0.0001
CRT implantation based on (%)			
QRS duration	49	64	<0.0001
Mechanical dyssynchrony	10	7	<0.05
Both	41	29	<0.0001
Elective admission for CRT-implantation (%)	82	87	<0.01
Duration of procedure (min)	110 (70–150)	90 (60–120)	<0.0001
Fluoroscopy time (min)	17 (10–30)	15 (9–25)	<0.01
LV lead position (%)			
Lateral	42	47	ns
Posterolateral	48	39	<0.01
Peri-procedural complications (%)	9	12	ns
CRT programming (%)			
To optimize AV interval	18	20	ns
To optimize VV interval	17	39	<0.0001
Both	65	41	<0.0001
Mean paced QRS duration (msec)	132 ± 27	133 ± 25	ns
Device follow-up at implanting centre (%)	94	90	<0.05
Hospital periods (days)[a]			
Duration admission –> discharge	4 (2–8)	3 (1–6)	<0.0001
Duration admission –> procedure	1 (0–3)	0 (0–1)	<0.0001
Duration procedure –> discharge	2 (1–4)	1 (1–3)	<0.0001

[a]Median and interquartile range

Table 5 Selected variables by age

	Age < 75 (n = 1663)	Age ≥ 75 (n = 742)	P-value
Demographics			
Age (years)[a]	66 (59–70)	78 (76–81)	<0.0001
Females (%)	23	24	ns
BMI (kg/m2)	26 (24–28)	27 (24–30)	<0.0001
Heart failure aetiology (%)			
Ischaemic	48	57	<0.001
Non-ischaemic	43	34	<0.0001
ECG (pre-implantation) (%)			
Heart rate (b.p.m.)	73 ± 15	71 ± 15	<0.05
Sinus rhythm	76	67	<0.0001
Atrial fibrillation	21	28	<0.0001
QRS complex (%)			
Paced rhythm	17	23	<0.001
Mean QRS duration (msec)	156 ± 32	160 ± 30	<0.05
QRS duration < 120 ms	10	5	<0.01
QRS duration ≥ 150 ms	61	66	ns
Mean LV ejection fraction (%)	26 ± 8	28 ± 8	<0.001
Laboratory measurements[a]			
Creatinine (umol/L)	99 (80–127)	115 (89–147)	<0.0001
NT-proBNP (pg/mL)	1381 (450–2943)	3127 (1234–4828)	<0.0001
BNP (pg/mL)	378 (165–840)	509 (282–1043)	ns
Device type (%)			
CRT-D	81	55	<0.0001
CRT-P	19	45	<0.0001
Duration of procedure (min)[a]	110 (70–150)	90 (60–125)	<0.0001
Peri-procedural complications (%)	9	12	ns
Hospital mortality (%)	0.6	0.3	ns
Duration admission –> discharge (days)[a]	3 (2–8)	3 (2–7)	ns

[a]Median and interquartile range

NYHA class was improved following CRT implantation most probably reflecting the placebo effect by device implantation,[22] but to some extent also the rapid onset of clinical improvement following CRT implantation. Interestingly, the paced QRS duration became significantly shorter after CRT implantation. A shortened paced QRS duration according to some authors has been shown to be related to a clinical benefit to CRT.[23]

There are several important limitations of this Survey that deserve emphasis and necessitate caution in interpreting the findings. Participation was voluntary and 141 centres were recruited that represent approximately 18% of all potential implantation centres in the 13 countries. Three countries made major contributions (Italy, Sweden, and Germany). Differences in practice between countries, for example regarding choice of device type, can skew the results.[11] Based on the variations in the descriptions of the contributing centres, this Survey appears to have recruited a reasonably representative sample. Although the importance of consecutive inclusion is emphasized repeatedly to all investigators, we cannot confirm that all patients were included consecutively. Similarly, the accuracy of the data will not be audited and the potential for investigator selection bias is obvious. There is considerable variation in the sample size for some of the eCRF variables due to unavailable information, incomplete data entry, and incomplete overlap between the variables collected in the two device registries and this survey. Importantly, only successful implantations defined as a completed procedure were entered into the survey. We have no information regarding patients screened and not implanted or unsuccessful attempts. The contents of the eCRF were necessarily abbreviated and only the most important variables were included. The investigators were not compensated financially and data entry into this survey represented an extra effort in addition to busy clinical practice.

A strength of this survey is the key findings that in contrast to populations from RCTs, our patients were older and a substantial number had a narrow QRS complex. Importantly, RCTs with one exception[24] excluded patients with AF and previous device

Table 6 Comparison between COMPANION, CARE-HF, REVERSE and CRT Survey cohorts

	COMPANION	CARE-HF	REVERSE	CRT Survey
Number of patients	1212	409	419	2438
Patients with a CRT-P (%)	51	100	18	27
Patients with a CRT-D (%)	49	NA	82	73
Previous device (PPM or ICD) (%)	0[a]	0[a]	0[a]	26
Mean age (years)	67	65	63	68
Women (%)	33	27	22	24
Ischaemic heart disease (%)	55	38	56	51
NYHA class III (%)	86	64	0[b]	70
LV ejection fraction (%)	22	26	27	26
LV diastolic diameter (mm)	67	72	69	66
QRS (ms)	160	165	153	160
Atrial fibrillation (%)	0[a]	0[a]	0[a]	23
Heart rate (b.p.m.)	72	70	67	70
Diuretics (%)	95	99	91	88
ARB/ACEI (%)	89	85	96	91
Betablockers (%)	68	72	96	85
Aldosterone antagonists (%)	54	56	NA	46

[a]Previous device implantation and atrial fibrillation were exclusion criteria. [b] NYHA class III/IV were exclusion criteria.

implantation. In our cohort approximately one-fourth had atrial fibrillation and one-fourth had had a device implanted previously. Non-randomized observational studies, however, indicate a similar benefit from CRT as in sinus rhythm patients provided that patients have undergone AV nodal ablation, and CRT therapy delivery thus can be ensured.[25]

Generally our cohort is remarkably similar to the cohorts recruited in RCTs. A consistent finding is the low proportion of women receiving CRTs both in RCTs and this survey. Aggressive medical management was confirmed with high percentages of patients treated with diuretics, ACE inhibitors, ARBs, betablockers, and aldosterone antagonists. Importantly in this real-world population, complication rates were similar to the rates reported in RCTs. On the other hand, the peri-operative complication rate is not negligible and must be weighed against the potential benefits when considering CRT therapy in patients in mild symptoms. A single, follow-up visit at approximately 1 year following implantation will capture relevant clinical information and short-term outcomes.

Clinical implications

This Survey represents a reasonably large sample reflecting current European practice in the use of CRT devices in the management of patients with heart failure. The cohort recruited for this Survey is in many ways remarkably similar to the cohorts included in RCTS. Specifically, there were no substantial differences with regard to QRS width, LVEF, aetiology, gender, NYHA classification, and medical therapy. In contrast, there were major differences with regard to the proportion of elderly patients, patients with atrial fibrillation, or a previous device. Clinicians, researchers, and health care providers should find these data useful in designing future strategies for patient management, trial design, and resource allocation.

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Conflict of interest: K.D. has received speaker's honoraria from Medtronic and Biotronik. S.P. is a member of the speaker's bureau for Medtronic and Boston Scientific. A.A. has received speaker fees from Medtronic, Biotronik, and Sorin; is a consultant to Medtronic and Sorin, and has received grants from Boston Scientific, Medtronic, and Biotronik. J.G.C. was principal investigator for the CARE-HF study and has received honoraria from Medtronic and Biotronik. C.L. has received a research grant and consulting fees from Medtronic and consulting fees from St. Jude. D.J.V. is the principal investigator of the DOT-HF study and has received consultancy fees from Medtronic. J.B. has received research grants from Medtronic, Boston Scientific, Biotronik, Sorin, and St Jude Medical.

Appendix 1

Scientific committee

K.D. (HFA Coordinator), S.P. (EHRA Coordinator), A.A., N.B., J.B., J.G.C., Geneviève Derumeaux, A.G., Daniel Gras, Michel Komajda, T.L., C.L., John Morgan, and D.J.V.

National coordinators

(HF, heart failure; EP, electrophysiology).

Austria: Friedrich Fruhwald HF, Bernhard Strohmer EP; Belgium: Marc Goethals HF, Johan Vijgen EP; France: Jean Noel Trochu HF, Daniel Gras EP; Germany: Michael Kindermann HF, Christoph Stellbrink EP; Ireland: Ken McDonald HF, David Keane EP; Israel: Tuvia Ben Gal HF, Michael Glikson EP; Italy: Marco Metra HF, Maurizio Gasparini EP; Netherlands: Alexander Maass HF, Luc Jordaens EP, Marco Alings EP; Norway: Alf Inge Larsen HF, Svein Færestrand EP; Spain: Juan Delgado HF, Lluis Mont EP; Sweden: Hans Persson HF, Fredrik Gadler EP; Switzerland: Hans Peter Brunner-La Rocca HF, Stefan Osswald EP; and UK: Iain Squire HF, John Morgan EP.

Appendix 2

Contents of electronic case report form

Demographics

✓Date of admission, age, gender, height, weight, elective admission.

HF aetiology

✓Ischemic, non-ischaemic, other.

Past history

✓HF hospitalization during past year, diabetes mellitus, chronic lung disease, previous CABG, previous PCI, previous valvular surgery, history of ablation, previous device implantation, previous VF/sustained VT.

Pre-implant clinical evaluation

✓NYHA functional class.

Pre-implant ECG

✓Heart rate, QRS annotation, PR interval, QRS duration.

Basic Echocardiography

✓LVEF, LV EDD, LV ESD, degree of mitral regurgitation, aortic stenosis, aortic regurgitation and intraventricular dyssynchrony.

Extended Echocardiography (optional)

✓LV end-systolic volume, LV end-diastolic volume, estimated systolic pulmonary arterial pressure, R-R interval, E-velocity, A-velocity, duration of left ventricular ejection, QRS to aortic opening (APET), QRS to pulmonary opening (PPET).

Laboratory measurements

✓Hb, Na, K, BNP, NT-proBNP, Creatinine.

Procedure

✓Date, type of device, device implantation based on (QRS duration, mechanical dyssychrnony, both, neither), operator (electrophysiologist, HF physician, invasive cardiologist, surgeon, other), location of procedure, sedation/anaesthesia, epicardial approach, duration of procedure, prophylactic antibiotics, fluroscopy time, test shock.

Peri-procedural complications

✓Death, bleeding, pocket haematoma, pneumothorax, pericardial tamponade, haemothorax, coronary sinus dissection, phrenic nerve pacing, lead dislocation or displacement.

Post-implant assessment

✓Right and left ventricular lead position, paced QRS duration after optimization, CRT programming.

Discharge status and major adverse events

✓Vital status, date, adverse events after implantation: MI, stroke, infection, decompensation, arrhytmias, other, device related complications: lead displacement, lead malfunction, phrenic nerve stimulation, other, functional class at discharge, centre for of follow-up.

Medical treatment at discharge

✓Diuretic, ACEi, ARB, beta blocker, aldosterone antagonist, statin, anti-arrhythmic agent, calsium channel blocker, anticoagulant, platelet inhibitor.

Appendix 3

List of contributing centres

Austria: A. ö. Landeskrankenhaus – Universitätsklinikum Graz; Landeskrankenhaus-Innsbruck-Universitätskliniken, Innsbruck; Krankenhaus der Elisabethinen, Linz; Landesklinikum Thermenregion, Mödling; Landeskliniken Salzburg - Paracelsus Medizinische Privatuniversität, Salzburg; Landesklinikum St. Pölten; Krankenhaus Hietzing mit Neurologischem Zentrum am Rosenhügel, Wien; Wilhelminenspital der Stadt Wien, Wien; A. ö. Krankenhaus Wiener Neustadt; Kaiser Franz Josef Spital, Wien

Belgium: Clinique St Jean, Brussels; Cliniques Universitaires UCL, Mont Godinne/Brussels; University Hospital, Gent; Virga Jesse Ziekenhuis, Hasselt

France: Hôpital du Bocage, Dijon; Chu, Saint Etienne; Nouvelles Cliniques Nantaises, Nantes; Hôpital Louis Pradel, Lyon Cedex; Hôpital Princesse Grace, Monaco

Germany: Städtisches Klinikum Dessau, Dessau; Städtisches Klinikum Brandenburg GmbH, Brandenburg; Krankenhaus Reinbek; Universitätsklinikum Aachen, Aachen; Klinik Rotes Kreuz, Frankfurt am Main; Saarland-Heilstätten GmbH Kliniken Völklingen; Universitätsklinikum des Saarlandes, Homburg; Kreiskliniken Altötting-Burghausen, Altotting; Klinikum St. Marien, Amberg; Hufeland Krankenhaus GmbH, Bad Langensalza; Städtische Kliniken Frankfurt am Main – Höchst, Frankfurt am Main; Städtisches Klinikum München Bogenhausen, Munchen; Krankenhaus St. Franziskus Mönchengladbach; St. Josefs-Krankenhaus Potsdam; Klinikum Lippe-Detmold; Städtisches Klinikum Bielefeld - Klinikum Mitte, Bielefeld; Städtisches Klinikum München Neuperlach, München; Klinikum der Universität München-Großhadern, München; Universitätsklinikum Heidelberg (Innere Med. Klinik III), Heidelberg; Universitätsklinikum Münster (Kardiologie), Münster; Klinikum Coburg Gmbh, Coburg; Herzzentrum Ludwigshafen, Ludwigshafen; Herzzentrum Brandenburg, Bernau; Allgemeines Krankenhaus Celle, Celle; Klinikum Ernst von Bergmann Potsdam; Herzzentrum Coswig, Coswig

Ireland: Mater Misercordea University Hospital, Dublin; South Infirmary Victoria University Hospital, Cork; St Vincent's University Hospital, Dublin

Israel: Sheba Medical Center, Ramatgan; Barzilai Medical Center, Ashkelon; Wolfson Medical Center, Holon; Kaplan Medical Center, Rehovot; Rabin Medical Center, Petah Tikva; Haemek Medical Center, Afula

Italy: Ospedale Moriggia-Pelascini, Gravedona; Osped. Fatebenefratelli Sgc, Roma; Osp. S. Giovanni di Dio Fatebenefratelli, Napoli; P.O. Frosinone Ceccano, Frosinone; Osped. S. Maria Misericordia-Perugia, Perugia; Presidio Ospedaliero di Rivoli, Rivoli; Ospedale S. Andrea, Verceli; P.O. Genova-Ponente P.A. Micone, Genova-Sestri Ponente; A.O. Osped. S. Gerardo, Monza; Policlinico Di Monza, Monza; Humanitas Mirasole Spa, Rozzano; IRLCS Multimedica, Sesto San Giovani; A.O.Osp.Treviglio Caravaggio Trev, Treviglio; A.O. Desenzano Del Garda, Desenzano Garda; Spedali Civili Di Brescia, Brescia; Fond.ne Poliambulanza Ist. Osp., Brescia; A.O. Maggiore Della Caritá Novara, Novana; Pres.Osped. Di Montebelluna, Montebelluna; Az.Osped.S.Maria Miseric Udine, Udine; Presidio Osp. Di Camposampiero, Camposampiero; Presidio Ospedaliero Di Cittadella, Cittadella; Azienda Ospedaliera Di Padova, Padova; Presidio Ospedaliero Di Vicenza, Vicenza; Osp.Civile Destra Secchia, Pieve di Coriano; Osp.Le S.M. Annunziata Bagno A Rip, Bagno A Ripoli; Stabilimento Di Cisanello, Pisa; Istituto Fisiologia Clinica, Pisa; Pia Fondazione, Tricase; Ospedale S.Maria Di Loreto Mare, Napoli; Az.Osped.S.Giovanni Di Dio, Salerno; Clinica SantÁnna, Catanzaro; Ospedale "Umberto I", Nocera Inferiore; Clinica Mediterranea, Napoli

The Netherlands: Academisch Medisch Centrum, Amsterdam; Amphia Ziekenhuis, Breda; Catharina Ziekenhuis, Eindhoven; Isala Klinieken Zwolle, Zwolle; Medisch Centrum Alkmaar, Alkmar; Medisch Spectrum Twente, Enschede; Erasmus MC, Rotterdam; Kennemer Gasthuis, Haarlem; Universitair Medisch Centrum Groningen, Groningen

Norway: Ålesund Hospital, Ålesund; Haukeland University Hospital, Bergen; Kristiansand Hospital, Kristiansand; Oslo Univesity Hospital, Rikshospitalet, Oslo; Stavanger University Hospital, Stavanger; St. Olavs Hospital, Trondheim; Oslo Univesity Hospital, Ullevål, Oslo

Spain: Hospital De Cruces, Barakaldo; Hospital Gregorio Maranon, Madrid; Hospital Virgen de la Victoria, Malaga; Hospital Universitario De Tenerife, Tenerife; Hospital Dr. Peset - Valencia; Centro Medico Salus Baleares S.l. - Benidorm - Alicante; Hospital Clinic, University of Barcelona, Barcelona; Hospital Sta. Creu Y St. Pau, Barcelona; Hospital General Universitario, De Alicante, Alicante

Sweden: Danderyds Sjukhus AB, Danderyd; Länssjukhuset, Kalmar; Karolinska Universitetssjukhuset, Solna, Stockholm; Akademiska Sjukhuset; Blekingesjukhuset; Centrallasarettet Västerås; Falu lasarett; Hudiksvalls Sjukhus; Kärnsjukhuset Skövde; Lässjukhuset Gävle; Länssjukhuset Kalmar; Norrlands Universitetssjukhus; Sahlgrenska Universitetssjukhuset; St Görans Sjukhus; Sundsvalls Sjukhus; Universitetssjukhuset Örebro; Universitetssjukhuset Lund; Varbergs Sjukhus

Switzerland: Cardiocentro Ticino, Lugano; HCF Hopital Cantonal, Fribourg; Hopitaux Universitaires de Geneve, Chêne-Bourg; Universitatsspital Basel, Basel

UK: Southampton General Hospital, Southampton; Kings College Hospital, London; Queen Elizabeth Hospital, Birmingham; Leeds General Infirmary, Leeds; Hull Royal Infirmary, Kingston Upon Hull; Papworth Hospital, Papworth Everad; University Hospital of Wales, Cardiff

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