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European cardiac resynchronization therapy survey: rationale and design

The CRT Survey Scientific Committee†

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Aims The European cardiac resynchronization therapy (CRT) Survey is a joint initiative taken by the Heart Failure Association (HFA) and European Heart Rhythm Association (EHRA) of the European Society of Cardiology. The primary objective is to describe the current European practice and routines associated with CRT/CRT-D implantations based on a wide range of sampling in 13 countries.

Methods and results The data collected should provide useful information, including demographics and clinical characteristics, diagnostic criteria, implantation routines and techniques, short-term outcomes, adverse experience, and assessment of adherence to guideline recommendations.

Keywords Cardiac resynchronization therapy • Heart failure • Survey • Benchmarking • Adherence to guidelines

Introduction

On the basis of a series of randomized controlled trials (RCTs), the ESC Heart Failure Guidelines,[1,2] the ESC/EHRA Guidelines for Cardiac Pacing,[3] and the ACC/AHA/HRS 2008 Guidelines for Device Therapy[4] provide a class I recommendation with a level of evidence A for implantation of a cardiac resynchronization device with or without a defibrillator function (CRT-D/CRT), for patients with left ventricular systolic dysfunction (ejection fraction $<35\%$), symptomatic heart failure despite optimal medical therapy and a QRS duration of ≥ 120 ms, in order to improve survival and reduce morbidity. However, it is likely that many patients who would benefit from device therapy do not receive it. This reflects lack of expert knowledge and access to the requisite skills in the doctors who care for patients with heart failure, leading to a failure to apply the guidelines.

On the other hand, some patients who receive a CRT/CRT-D do not fulfil all the guideline criteria.[5] To some extent, this reflects the fact that guidelines tend to be conservative in their recommendations, which is usually appropriate. However, recent publications suggest that patients with a left ventricular ejection fraction (LVEF) of up to 40% and with few or no symptoms may benefit from CRT/CRT-D.[6,7] Indeed, the guidelines do not necessarily conform strictly to the entry criteria for clinical trials (for instance, the ESC guidelines do not exclude patients with atrial fibrillation). Substantial variations in implantation routines also exist.

Although RCTs confirm efficacy, the target populations most likely to benefit from intervention have not been reliably identified. No consensus exists among clinicians of the precise measurements from diagnostic investigations that would best identify those patients likely to respond among potential candidates for CRT/CRT-D implantation.[8,9] RCTs have based inclusion criteria on measurements of QRS duration. However, largely based on intuition, clinicians frequently make decisions based on evidence of mechanical dyssynchrony (i.e. myocardial wall motion and TDI measurements). The presence of substantial mitral regurgitation that may be due to papillary muscle dyssynchrony often provides a further argument for device implantation.

Only one randomized trial required evidence of mechanical dyssynchrony measurements in addition to the conventional criteria and then only when the QRS duration was between 120 and 149 ms.[10] Currently, none of the commonly employed echocardiographic measurements appear robust enough to accurately predict response.[11] It is uncertain whether patients with a narrow QRS duration benefit from CRT, since adequate studies have not been undertaken.[12] More evidence of benefit is required in patients with mild symptoms and those with atrial fibrillation,

† For The CRT Survey Scientific Committee, see Appendix 1.

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right bundle branch block, or QRS durations between 120 and 150 ms. Whether to include an ICD in the device (CRT-D) is often a difficult clinical decision, and practice varies widely.[13] There is a lack of comparative data between CRT-P and CRT-D apart from the limited information available from the COMPANION trial.[14] There is a considerable geographical variation in device implantation rates across Europe, which reflects differences in interpretation and implementation of evidence-based recommendations and administrative priorities concerning appropriate allocation of local healthcare resources.[15] The cost of devices and their implantation is substantial but the benefits of treatment can also be great and, therefore, among patients similar to those in the clinical trials, device therapy is highly cost-effective in terms of quality-adjusted life-years.[16] A total of about 32000 devices (CRT-P and CRT-D) were implanted in Western Europe in 2007. *Figures 1* and *2* clearly demonstrate the differences both in implantation rates per million inhabitants and in the ratios of CRT-P vs. CRT-D device implantation.

There is a need to describe routine current clinical practice in Europe more precisely and the adverse experiences associated with implantation. It is also important to relate outcomes and events to operator and implantation centre experience. CRT devices are implanted by electrophysiologists, surgeons, and heart failure physicians, and management of these patients often requires a multidisciplinary approach including non-invasive (echocardiography, MRI) and invasive cardiologists. Practical aspects of the implantation techniques and follow-up procedures routinely employed across Europe should be described and shared as this may help to improve care.

As 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 imply long-term follow-up. By including consecutive patients, the design of surveys and registries should reflect actual clinical practice and partially avoid the selection bias that characterises RCTs[17] which usually restrict the cohort to rigid inclusion criteria.

Methods

Objectives of the CRT Survey

This Survey is a joint initiative taken by the Heart Failure Association (HFA) and European Heart Rhythm Association (EHRA) of the European Society of Cardiology. The primary objective is to describe the current European practice based on a wide range of sampling in 13 countries. All centres implanting CRT-D in these countries have been invited to participate. This large sample should provide representative results. The Survey will capture data from patients receiving either a new CRT-P or CRT-D or an upgrade. The data will be collected using an electronic case report form (eCRF) and include demographics and clinical characteristics, diagnostic criteria assessed prior to implantation, pharmacological therapy at baseline and at follow-up, implantation procedure and techniques, device programming, short- and long-term outcomes, adverse experience, and hospitalization (Appendix 2). This information should permit limited economic analyses and assessment of adherence to guideline recommendations. There will be an abbreviated follow-up visit according to hospital routines.

These data will enable practice between centres and countries to be compared. Importantly, all participating centres will be able to benchmark online with national and international practice, so that participation provides valuable quality assurance assessment data for individual centres. A website www.crt-survey.org, supported by the ESC web department, describes the Survey and permits downloading

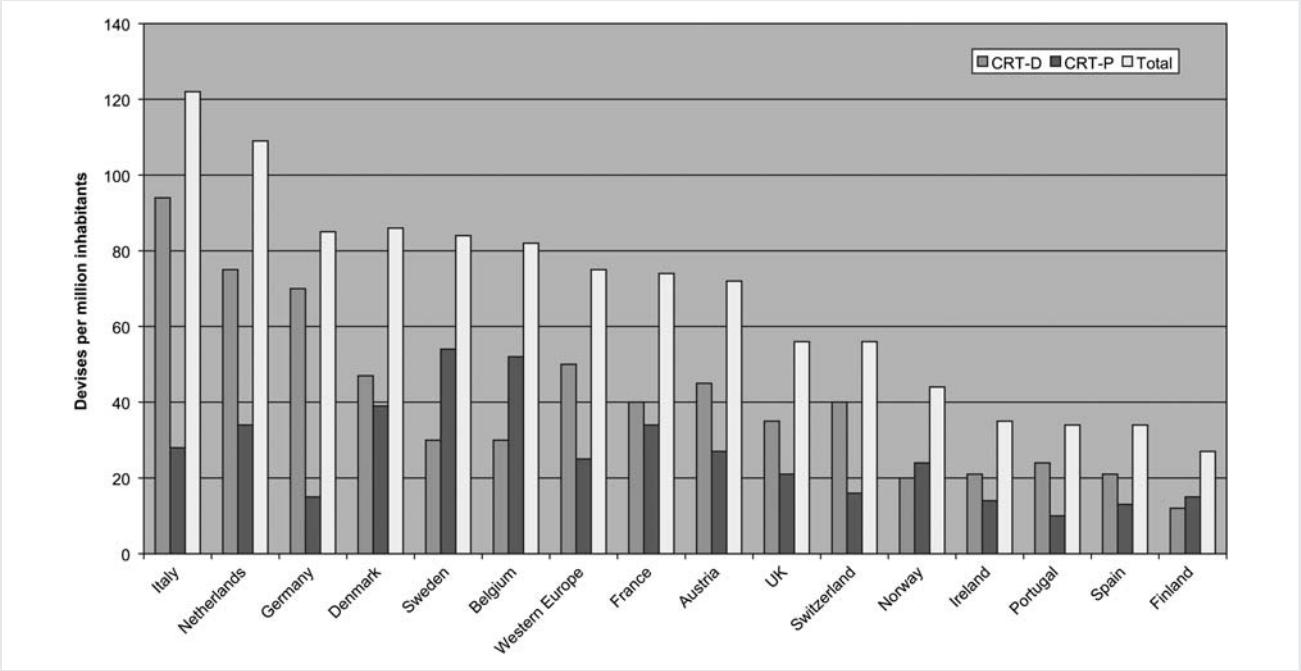

Figure 1 Implantation rates of CRT-D and CRT-P per million inhabitants across Europe in 2006.[15]

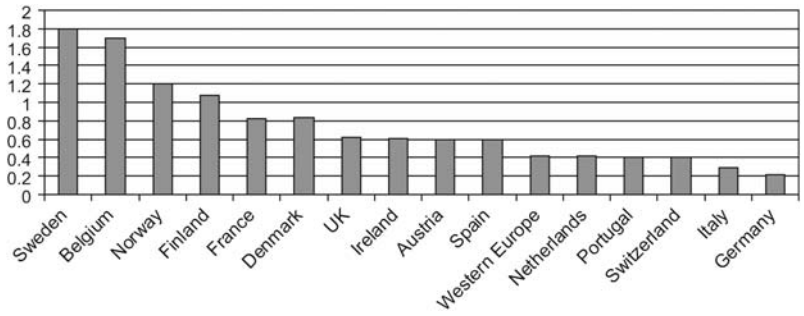

Figure 2 Ratio between implanted CRT-P and CRT-D across Europe in 2006 (modified from Swedberg *et al.*[15]).

of the protocol, eCRF, patient consent form, and site questionnaire. The eCRF can be accessed and completed online. The current status of total recruitment is updated weekly on the site.

Participating countries

The two associations, HFA and EHRA, have invited investigators from the following 13 European Countries with a total of over 500 centres to participate in the survey: Austria, France, Spain, Ireland, Israel, Italy, the Netherlands, Norway, Germany, Switzerland, UK, Belgium, and Sweden. It is estimated that these countries are responsible for over 90% of the implantations in Europe (EUCOMED data on file). The survey may also establish an infrastructure for networking among centres and provide potential for future cooperation in clinical trials.

Two national coordinators have been selected from each of the 13 participating countries, one each from the fields of heart failure and electrophysiology (Appendix 1). A secretariat actively coordinates recruitment and motivates centres to assure rapid inclusion and successful follow-up. The field force supporting implantations from the five industry sponsors (EUCOMED) in participating countries has been informed about this initiative, but have no specific responsibilities in its performance. The survey started on 1 November 2008 and the planned inclusion period is 8 months.

Survey population

All consecutive patients receiving a new CRT-P/CRT-D at a participating centre are eligible for inclusion. The procedure itself identifies the patient as survey candidate. With a conservative estimate of response from 200 of the centres approached and an 8 month recruitment period, ~3000–4000 patients should be included in the survey. Ethics approval has been obtained from countries where needed and written informed consent forms will be completed where required.

Data collection and management

Data will be collected using online internet data entry. The eCRF is streamlined yet collects essential details (Appendix 2). The database has been constructed at the data management centre in the Institut für Herzinfarktforschung, Ludwigshafen an der Universitaet Heidelberg, Germany, which will also maintain and interrogate the data and perform the data analyses.

Summary

The European CRT Survey is a joint initiative by the HFA and EHRA of the European Society of Cardiology. The primary objective is to describe the current European practice and routines associated with CRT/CRT-D implantation based on a wide range of sampling in 13 countries.

Funding

This Survey is supported by an unrestricted grant from the five EUCOMED companies (Biotronik, Boston Scientific, Medtronic, Sorin and St Jude Medical) and Roche Diagnostics Ltd.

Conflict of interest: J.C. was principal investigator for the CARE-HF study and has received honoraria from Medtronic and Biotronik. J.M has received support from Medtronic and St Jude. C.L. has received a research grant and consulting fees from Medtronic and consulting fees from St Jude. D.V. is the principal investigator of the DOT-HF study and has received consultancy fees from Medtronic. 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. S.P. is a member of the speaker's bureau for Medtronic and Boston Scientific.

Appendix 1

Scientific Committee

Kenneth Dickstein (HFA Coordinator), Silvia Priori (EHRA Coordinator), Angelo Auricchio, Josep Brugada Terradellas, John Cleland, Geneviève Derumeaux, Daniel Gras, Michel Komajda, Cecilia Linde, John Morgan, Dirk J. van Veldhuisen, Anselm Gitt, Nigussie Bogale.

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Italy: Marco Metra HF, Maurizio Gasparini EP.
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Germany: Michael Kindermann HF, Christoph Stellbrink EP.
Spain: Juan Delgado HF, Lluis Mont EP.
UK: Ian Squire HF, John Morgan EP.

Appendix 2

Content of eCRF

Demographics

- Date of admission, age, sex, height, weight, elective admission

HF aetiology

- Ischaemic, 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), and 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 dyssynchrony, 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 optimisation, CRT programming

Discharge status and major adverse events

- Vital status, date, adverse events after implantation: MI, stroke, infection, decompensation, arrhythmias, 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, calcium channel blocker, anticoagulant, platelet inhibitor

Follow-up 1 year (9–15 months)

- Date, death: (all-cause, CV death, HF death), hospitalizations: (non-CV, CV related, HF related, device related), global patient assessment, device related complications: (lead displacement, phrenic nerve stimulation, lead malfunction, device replacement, arrhythmias, infection, other serious events), functional class, BP, appropriate and inappropriate shocks, appropriate ATP

ECG 1 year

- Heart rate, QRS annotation, PR interval, QRS duration

Basic echocardiography 1 year

- 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 1 year

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

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