

# Approach to cardiac resynchronization therapy

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## Aims

The purpose of this EP Wire is to compare indications, techniques, implant strategy, and follow-up regarding cardiac resynchronization therapy (CRT) in several countries across Europe.

## Methods and results

Forty-one centres, members of the EHRA-EP Research Network, responded to this survey and completed the questions. Thirty-two per cent of the responding centres always use CRT in heart failure (HF) patients with New York Heart Association functional class II and QRS width  $>120$  ms, and 55% of the responding centres demand additional criteria when indicating CRT, most often QRS width  $>150$  ms (49%) and echocardiographic criteria of asynchrony (34%). Only 10% of centres indicate CRT in all HF patients with QRS  $>120$  ms and right bundle branch block, and 51% demand additional criteria, most frequently echocardiographic asynchrony parameters. The vast majority of centres also indicate CRT in patients with atrial fibrillation and standard criteria for CRT. In 24% of the centres, biventricular pacemaker (CRT-P) is implanted in all situations, unless there is an indication for secondary prevention of sudden cardiac death, while 10% always choose to implant a biventricular defibrillator (CRT-D). There are no clear evidence-based recommendations concerning the implant procedure and follow-up in patients treated with CRT; therefore, the chosen strategies vary widely from one centre to another.

## Conclusion

This EP Wire survey shows a wide variation not only as far as CRT indications are concerned, but especially in techniques, implant strategy, and follow-up across the European countries.

## Introduction

Cardiac resynchronization therapy (CRT) has become a readily available option for patients with moderate/severe heart failure (HF). However, there are still several open issues, and therefore practice regarding the CRT device varies widely between countries.

The purpose of this EP Wire is to compare indications, techniques, implant strategy, and follow-up regarding CRT therapy across the European countries.

## Results

Forty-one centres, members of the EHRA-EP Research Network, responded to this survey and completed the questions. Twenty-nine of them were university hospitals (71%), nine non-university (22%), and three private hospitals (7%). Thirty-one centres (76%) are large-volume centres, with  $>200$  pacemaker implants in the last year, nine centres (22%) have 50–199 pacemaker

implants, and one centre has 25–49 implants. Thirty-two of the responding centres also have a cardiovascular surgery unit.

The current evaluation is representative for the common European practice, despite the rather low number of centres who responded to our questionnaire, considering the fact that their geographical distribution is wide and the economic conditions are quite heterogeneous and balanced (Figure 1).

## Cardiac resynchronization therapy indication

Thirty-two per cent of the responding centres stated that they always use CRT in New York Heart Association (NYHA) functional class II patients on optimal medical therapy with left bundle branch block (LBBB) morphology, QRS complex width  $>120$  ms, and left ventricular ejection fraction (LVEF)  $<35\%$ , while 13% never take this approach. Fifty-five per cent of the responding centres demand additional criteria when indicating CRT, most often QRS width  $>150$  ms (49%) and echocardiographic criteria of asynchrony (34%). A combination of the two

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**Figure 1** Geographical distribution of the responding centres.

criteria is considered necessary in one-third of the patients with QRS complex width  $>150$  ms and half of the patients who have echocardiographic criteria of asynchrony. In only one responding centre, the presence of non-ischaemic dilated cardiomyopathy was considered the single necessary additional criterion for CRT.

Sixty-eight per cent of the responding centres indicate CRT in all patients with LVEF  $<35\%$ , QRS complex width  $>120$  ms, and NYHA functional class III–IV on optimal medical therapy, independent of any other additional criteria. The rest consider that additional criteria are needed and rely, in similar proportions, on QRS width  $>150$  ms, echocardiographic criteria of asynchrony, the absence of significant scars on echo/magnetic resonance imaging, or a combination of those.

Only 10% of the responding centres indicate CRT in all patients with LVEF  $<35\%$ , QRS complex width  $>120$  ms, NYHA functional class III–IV on optimal medical therapy, and right bundle branch block (RBBB), while 39% never use CRT in such conditions. Fifty-one per cent of the responding centres demand additional criteria for indicating CRT in patients with RBBB; the preferred criterion is the presence of echocardiographic asynchrony parameters (considered by 41% of the responding centres), followed by QRS width  $>150$  ms (22%). Moreover, in more than half the cases, both criteria are demanded in order to indicate CRT, and only 7% of the responding centres take into account the presence of non-ischaemic dilated cardiomyopathy as an additional criterion, always associated with at least one of the previous two criteria.

In patients with permanent atrial fibrillation (AF), 54% of the responding centres indicate CRT in patients with, QRS complex width  $>130$  ms, LVEF  $<35\%$ , and NYHA functional class III or

IV, without any additional criteria. In contrast, just 2% of the responding centres never indicate CRT in such patients. All the rest consider CRT in AF patients, but demand additional criteria such as QRS width  $>150$  ms, echocardiographic criteria of asynchrony, or both simultaneously.

In 10 centres (24%) a device without defibrillation capabilities (CRT-P) is implanted in all situations, unless there is an indication for secondary prevention of sudden cardiac death (SCD), while 4 centres (10%) always choose a device with defibrillation capabilities (CRT-D). In the remaining centres, CRT-P is only chosen in patients with severe co-morbidities (26 centres), non-ischaemic dilated cardiomyopathy (9 centres), or with ambulatory functional NYHA class IV.

### Implant strategy

For patients with permanent AF, physicians in 59% of the responding centres choose to implant three leads [right atrial (RA), right ventricular (RV), and left ventricular (LV)], but in only 63% of those sinus rhythm restoration is attempted if there is reverse remodelling, while the others are satisfied with heart rate control, either by using drugs or by atrioventricular (AV) node ablation. In 37% of the centres, biventricular pacing without atrial lead is preferred, with a rate control strategy. Interestingly, in these centres, an overwhelming majority (71%) prefer the initial use of drugs for heart rate control, while only 29% resort to AV node ablation as a first-line approach.

Four centres (11%) consider that a good pacing threshold is the only criterion that should be used during the implant procedure to choose the best site for the LV lead. All other centres use

additional criteria; in 24 responding centres, the preferred criterion for LV lead placement is the radiological position, which should correspond to the zone of maximum mechanical delay on echocardiography; in other 13 centres, the LV lead is implanted using the maximal delay of LV lead electrogram compared with the QRS/RV lead electrogram. Six centres always use a multipolar (i.e. more than two poles) LV lead.

If there are no feasible lateral veins for LV lead implantation via coronary sinus, the first preferred alternative is to implant an epicardial LV lead via thoracotomy (54%) or to place the LV lead in the anterior vein (29%). The endocardial trans-septal approach is used as the first alternative in five centres and dual-site RV stimulation (high septal and apical) in one centre.

## Follow-up

In 10 centres (24%), no initial optimization in timing intervals of the implanted device is used. In 21 centres (51%), the AV interval is optimized first, using either standard, always fixed, interventricular (VV) interval (3 centres), or variable VV depending on clinical/electrocardiogram (ECG) conditions (7 centres); in 11 centres, after AV optimization, the VV interval is also optimized if necessary. Only four centres use VV interval optimization first, and five centres use the company algorithms proposed by the implanted device as the preferred method for optimization.

Several methods are used for optimization of the CRT after implantation: QRS morphology/duration on 12-lead ECG (54%), standard M-Mode/B-Mode/Doppler echocardiography (66%), tissue Doppler imaging (37%), speckle-tracking echocardiography (20%), and 3D echocardiography (10%). The vast majority of centres use most of these techniques for CRT optimization. None of the responding centres describe the use of techniques like invasive  $dp/dt_{max}$  or non-invasive cardiac index measurement by impedance as tools for CRT optimization.

The most important criteria in assessing the response to CRT are considered to be the NYHA class improvement in 37% of centres, the improvement of LVEF in 34%, and the LV volume change evaluated by echocardiography in 15%. Other criteria are improved performance in walking test (8%) and quality-of-life improvement, evaluated by specific questionnaires (6%).

In all centres, the first steps followed in the case of CRT non-responders are the reassessment of drug therapy (46% as a first step) and the optimization of pacing parameters (54% as a first step). Other options such as LV lead repositioning, the use of a multipolar LV lead, or the use of high septal RV stimulation instead of an apex lead are considered as secondary options.

Sixty-eight per cent of the responding centres believe that multipolar (i.e. more than two poles) lead LV pacing will soon become the standard of care for CRT implants. This option is supported by many arguments (fewer CRT lead revisions, more basal pacing options, increased chance of LV pacing with low pacing thresholds, and without phrenic nerve stimulation, fewer CRT non-responders), all considered by the vast majority of the centres.

## Discussion

### Cardiac resynchronization therapy indication

Two recent guidelines provide an update to previous indications of CRT in patients with HF.<sup>1,2</sup> Both guidelines state that CRT is clearly indicated in patients with NYHA functional class III or IV HF, in sinus rhythm, with a QRS width of  $\geq 120$  ms, LBBB QRS morphology, and an EF  $\leq 35\%$ . These indications are supported by evidence from two key randomized clinical trials (RCT), COMPANION and CARE-HF, which have both shown that CRT reduced the risk of death from any cause and the number of hospital admissions for worsening HF.<sup>3,4</sup> In our survey, this indication is accepted by 68% of the responding centres, while the others require further criteria, mainly related to QRS complex duration or echocardiographic parameters of asynchrony. A similar approach was used in the CARE-HF study in which patients who had a QRS width between 120 and 149 ms were only included in the study provided that echocardiographic criteria of asynchrony were also present.<sup>4</sup>

Currently, the indication of CRT in the case of RBBB QRS morphology is still subject to much debate. In a subanalysis of the CARE-HF trial, RBBB was one of the predictors of non-favourable outcome.<sup>5</sup> In our survey, more than half of the responding centres demand additional criteria in order to indicate CRT in such patients, and 29% of the centres never use CRT in RBBB patients.

The results of recent trials show that beneficial effects of CRT in patients with mild HF are very similar to those observed in cohorts of patients with severe HF. Despite this, only one-third of the responding centres indicate CRT in patients with functional class NYHA II, and more than half of these request additional criteria, most often related to QRS width. Moreover, pre-specified subgroup analysis of data collected from the MADIT CRT and REVERSE studies showed that patients in whom QRS width was  $\geq 150$  ms benefited most from CRT.<sup>6,7</sup>

To date, patients with AF have not been adequately studied in large trials. Most key studies that focused on CRT excluded patients with AF. The RAFT study was the only one to include patients with permanent AF or flutter; 229 such patients were admitted in the study and heart rate control was attempted either by using drugs or by AV ablation. However, this subgroup only represented a small minority in the study cohort.<sup>8</sup> Nevertheless, in our survey, most of the responding centres indicate CRT in patients with AF.

### Implant strategy and follow-up

Some patients with permanent AF may resume sinus rhythm during CRT or following successful left atrial ablation.<sup>9</sup> Therefore, implanting an atrial lead may be justified even in patients with AF. However, there is consensus that a robust ventricular capture is mandatory in order to maximize clinical benefit and improve prognosis in patients with permanent AF.<sup>10</sup> This often requires the induction of complete heart block by AV node ablation, although, surprisingly, most centres prefer to attempt heart rate control by using drugs as a first-line approach.

The choice of CRT-D over CRT-P is supported by one large meta-analysis.<sup>11</sup> In the COMPANION trial, CRT-D was associated with significant decrease in all-cause mortality, while the relative risk reduction in mortality associated with CRT-P was barely statistically significant. However, the superiority of one CRT strategy over the other could not be demonstrated, as the comparison between CRT-D and CRT-P was not pre-specified.<sup>3</sup> In our survey, just 10% of the responding centres stated that they implanted CRT-D devices on a regular basis, whenever CRT is recommended, while a quarter of the centres only use CRT-D for the secondary prevention of SCD. It is very likely that this decision is influenced by clinical and economical factors alike.

There are no clear recommendations concerning the implant strategy and post-procedural management in patients treated with CRT. It seems that the basal position of the LV lead improves results when compared with the apical placement of the LV lead.<sup>12</sup> Radiological positioning of the LV lead concordant with the zone of maximal mechanic delay on echocardiography is associated with a better prognosis.<sup>13</sup> The timing of the LV electrogram was also proved to lead to acute haemodynamic improvement, but long-term results concerning the impact on remodelling, symptoms and prognosis have not yet been obtained.<sup>14</sup> Each of these concepts is applied in variable proportions in the responding centres; therefore, the chosen strategies vary widely from one centre to another.

Numerous methods for CRT optimization have been suggested so far, many based on echocardiographic parameters. However, further RCTs with long-term clinical endpoints comparing methods are needed. Despite limited validation, optimization was included in some landmark clinical trials and is inherent in evidence-based practice.<sup>15</sup>

## Conclusions

This EP Wire survey shows a wide variation not only as far as CRT indications are concerned, but also especially in techniques, implant strategy, and follow-up across the European countries.

**Conflict of interest:** none declared.

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