

## Cardiac resynchronisation therapy in Europe: are Swiss CRT recipients different?

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Cardiac resynchronisation therapy (CRT) on top of optimal heart failure medication has a proven benefit on long-term clinical outcome in symptomatic patients with reduced left ventricular ejection fraction (LVEF) and electrical dyssynchrony. The first prospective randomised trial to show a significant mortality reduction in patients with heart failure of New York Heart Association (NYHA) class III and IV was the landmark trial CARE-HF [1]. Of note, in that study CRT pacemakers (CRT-P), but not CRT defibrillators (CRT-D) were implanted. Thereafter, the addition of CRT to an implantable cardioverter-defibrillator (ICD) in patients with milder NYHA class II or III heart failure, a wide QRS complex and left ventricular systolic dysfunction showed reduced rates of death and hospitalisation for heart failure [2]. This evidence is reflected in the current guidelines of the European Society of Cardiology (ESC) on cardiac pacing and CRT published in 2013 [3]. CRT is recommended in chronic heart failure patients with LVEF  $\leq 35\%$ , who remain in NYHA functional class II, III or ambulatory IV despite adequate medical treatment, and in patients with left bundle-branch block (LBBB) and QRS duration  $>150$  ms (class I indication with level of evidence A). For patients with LBBB and a QRS duration of 120 to 150 ms a class I indication with level of evidence B is given. Patients without LBBB and with QRS duration  $>150$  ms represented a class IIa indication with a level of evidence B.

Whether CRT is beneficial in patients with systolic heart failure and a QRS duration of less than 130 ms but evidence of dyssynchrony on echocardiography was studied in the EchoCRT trial [4]. CRT in these patients, however, did not reduce the rate of death or hospitalisation for heart failure and even showed increased mortality. In contrast, for patients with atrioventricular block and a pacing indication, a moderately reduced LVEF of  $<50\%$  and NYHA class I–III heart failure, biventricular pacing was superior to conventional right ventricular pacing [5].

Randomised controlled trials (RCTs) form the basis for recommendations and guidelines. However, one disadvantage of RCTs is the exclusion of high-risk patients [6]. Therefore, surveys and registries without exclusion criteria may provide interesting and important data on daily clinical practice.

The European CRT Survey II included more than 11,000 CRT patients within 42 ESC member countries between October 2015 and December 2016, with the aim to collect real-life data on contemporary patient selection, implantation and follow-up practice [7]. This survey permits assessment of guideline adherence and demonstrates variations among different countries.

Currently in *Swiss Medical Weekly*, Zeljkovic and co-workers compare the characteristics of Swiss CRT recipients with the overall European CRT population in the European CRT Survey II [8]. They found that Swiss CRT patients are older (71 vs 68.5 years), less symptomatic and suffer more often from comorbidities including more chronic kidney disease. Most often CRT-D systems were implanted (in two thirds), but Swiss patients more often received CRT-P systems than their European counterparts. A strength of this survey and the comparison is the high number of patients included (overall 11,088 patients from 42 countries, including 320 patients from Switzerland) and the timely inclusion period between 2015 and 2016, which allow reflection on the adherence to the current guidelines published in 2013.

The higher rate of patients implanted with CRT-P systems may be explained by the older age of the patients and the higher rate of competing risk factors for death, where the effect of an additional defibrillator function may be minimal or even absent. Therefore, evidence seems to guide the decision as to which device should be implanted, but not the fact that the reimbursement system in Switzerland allows for easy access to all technologies. Whether different attitudes of the patients to the mode of death may play a role is speculative and deserves further investigation. Although Swiss patients were older and had more comorbidities, they were less often hospitalised for heart failure before implantation, reflecting a better access to ambulatory healthcare services. Easy access to the latest technologies and medication is also reflected by the fact that a higher proportion of Swiss patients were implanted with quadripolar leads and that they received novel oral anticoagulants (NOACs), if anticoagulation was indicated, more often than patients in other European countries. Swiss patients less often had the classical indication of heart failure with a wide QRS complex, and less often complete LBBB, but more often a higher degree atrioventricular-block with

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CRTs employed for expected dyssynchrony due to a high amount of right ventricular pacing. An explanation may be faster transition of recent evidence into current practice, and a reimbursement system that allows faster adoption of new evidence. It will be interesting to see whether newest evidence from the DANISH trial will translate into current practice in a similar way [9]. In that study, prophylactic ICD implantation in patients with symptomatic systolic heart failure not caused by coronary artery disease was not associated with a significantly lower long-term rate of death from any cause than was usual clinical care.

Finally, there are also some similarities between Switzerland and the other European countries. In both, women were underrepresented (24 vs 24%), despite the fact that women, including those with narrower QRS (130–150 ms), seem to have a higher benefit from CRT [10]. The undertreatment of women in the field of cardiovascular diseases is known, but not fully understood and should be addressed in further research.

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#### References

- Cleland JG, Daubert JC, Erdmann E, Freemantle N, Gras D, Kappenberger L, et al.; Cardiac Resynchronization-Heart Failure (CARE-HF) Study Investigators. The effect of cardiac resynchronization on morbidity and mortality in heart failure. *N Engl J Med*. 2005;352(15):1539–49. doi: <http://dx.doi.org/10.1056/NEJMoa050496>. PubMed.
- Tang AS, Wells GA, Talajic M, Arnold MO, Sheldon R, Connolly S, et al.; Resynchronization-Defibrillation for Ambulatory Heart Failure Trial Investigators. Cardiac-resynchronization therapy for mild-to-moderate heart failure. *N Engl J Med*. 2010;363(25):2385–95. doi: <http://dx.doi.org/10.1056/NEJMoa1009540>. PubMed.
- Brignole M, Auricchio A, Baron-Esquivias G, Bordachar P, Boriani G, Breithardt OA, et al.; European Society of Cardiology (ESC); European Heart Rhythm Association (EHRA). 2013 ESC guidelines on cardiac pacing and cardiac resynchronization therapy: the task force on cardiac pacing and resynchronization therapy of the European Society of Cardiology (ESC). Developed in collaboration with the European Heart Rhythm Association (EHRA). *Europace*. 2013;15(8):1070–118. doi: <http://dx.doi.org/10.1093/europace/eut206>. PubMed.
- Ruschitzka F, Abraham WT, Singh JP, Bax JJ, Borer JS, Brugada J, et al.; EchoCRT Study Group. Cardiac-resynchronization therapy in heart failure with a narrow QRS complex. *N Engl J Med*. 2013;369(15):1395–405. doi: <http://dx.doi.org/10.1056/NEJMoa1306687>. PubMed.
- Curtis AB, Worley SJ, Adamson PB, Chung ES, Niazi I, Sherfese L, et al.; Biventricular versus Right Ventricular Pacing in Heart Failure Patients with Atrioventricular Block (BLOCK HF) Trial Investigators. Biventricular pacing for atrioventricular block and systolic dysfunction. *N Engl J Med*. 2013;368(17):1585–93. doi: <http://dx.doi.org/10.1056/NEJMoa1210356>. PubMed.
- Masoudi FA, Havranek EP, Wolfe P, Gross CP, Rathore SS, Steiner JF, et al. Most hospitalized older persons do not meet the enrollment criteria for clinical trials in heart failure. *Am Heart J*. 2003;146(2):250–7. doi: [http://dx.doi.org/10.1016/S0002-8703\(03\)00189-3](http://dx.doi.org/10.1016/S0002-8703(03)00189-3). PubMed.
- Dickstein K, Normand C, Auricchio A, Bogale N, Cleland JG, Gitt AK, et al. CRT Survey II: a European Society of Cardiology survey of cardiac resynchronization therapy in 11 088 patients—who is doing what to whom and how? *Eur J Heart Fail*. 2018;20(6):1039–51. doi: <http://dx.doi.org/10.1002/ejhf.1142>. PubMed.
- Zeljko I, Burri H, Breitenstein A, Amman P, Mueller A, Auricchio A, et al. Cardiac Resynchronization Therapy (CRT) II Survey: CRT implantation in Europe and in Switzerland. *Swiss Med Wkly*. 2018;148:w14643. doi: <http://dx.doi.org/10.4414/smw.2018.14643>. PubMed.
- Køber L, Thune JJ, Nielsen JC, Haarlo J, Videbæk L, Korup E, et al.; DANISH Investigators. Defibrillator Implantation in Patients with Non-ischemic Systolic Heart Failure. *N Engl J Med*. 2016;375(13):1221–30. doi: <http://dx.doi.org/10.1056/NEJMoa1608029>. PubMed.
- Zusterzeel R, Selzman KA, Sanders WE, Caños DA, O'Callaghan KM, Carpenter JL, et al. Cardiac resynchronization therapy in women: US Food and Drug Administration meta-analysis of patient-level data. *JAMA Intern Med*. 2014;174(8):1340–8. doi: <http://dx.doi.org/10.1001/jamainternmed.2014.2717>. PubMed.