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REVIEW

What determines who gets cardiac resynchronization therapy in Europe? A comparison between ESC-HF-LT registry, SwedeHF registry, and ESC-CRT Survey II

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Aims Cardiac resynchronization therapy (CRT) is effective in heart failure with reduced ejection fraction (HFrEF) and dyssynchrony but is underutilized. In a cohort study, we identified clinical, organizational, and level of care factors linked to CRT implantation.

Methods and results We included HFrEF patients fulfilling study criteria in the ESC-HF-Long Term Registry (ESC-HF-LT, $n = 1031$), the Swedish Heart Failure Registry (SwedeHF) ($n = 5008$), and the ESC-CRT Survey II ($n = 11\,088$). In ESC-HF-LT, 36% had a CRT indication of which 47% had CRT, 53% had indication but no CRT, and the remaining 54% had no indication and no CRT. In SwedeHF, these percentages were 30, 25, 75, and 70%. Median age of patients with CRT indication and CRT present vs. absent was 68 vs. 65 years with 24% vs. 22% women in ESC-HF-LT, 76 vs. 74 years with 26% vs. 26% women in SwedeHF, and 70 years with 24% women in CRT Survey II (all had CRT). For ESC-HF-LT, independent predictors of having CRT were guideline-directed medical therapy (GDMT), atrial fibrillation (AF), prior HF hospitalization, and NYHA class. For SwedeHF, they were GDMT, age, AF, previous myocardial infarction, lower NYHA class, enrolment at university hospital, and follow-up at HF centre/Hospital. In SwedeHF, above median income and higher education level were also independently associated with having CRT. In the ESC-CRT Survey II ($n = 11\,088$), all patients received CRT but with differences in the clinical characteristics between countries.

Conclusion CRT was used in a minority of eligible patients and more used in ESC-HF-LT than in SwedeHF.

Keywords Heart failure • Cardiac resynchronization therapy • Epidemiology • Registry • Survey • Implementation

Introduction

Over recent decades, treatment for heart failure with reduced ejection fraction (HFrEF) has improved dramatically.[1] However, outcomes have not improved in a commensurate way.[2,3] Numerous studies from Europe and the USA suggest that the lack of a meaningful improvement in outcomes may be due to poor implementation of evidence-based and guideline-directed medical and device therapy.[3–5]

Cardiac resynchronization therapy (CRT) improves outcomes and physical function in patients with HFrEF and electrical dyssynchrony. However, while the implementation of evidence-based medical therapies is poor, it may be even worse for more specialized interventions such as CRT.[6–9]

Previous assessments of CRT utilization within cohorts and between different data sources report large variations in the use of CRT between and within countries and regions.[3,10–12] However, there

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are no direct *patient-level* comparisons of CRT utilization between different care settings. The European Society of Cardiology (ESC) and its subspecialty associations the Heart Failure Association (HFA) and European Heart Rhythm Association (EHRA) have collected data on HF in the ESC-HF-LT Registry and on CRT implantation in the ESC-CRT Survey II. The Swedish Heart Failure Registry (SwedeHF) is a national HF quality registry, which continuously enrols patients with HF.

We compared demographic, clinical, organizational, and level of care factors between these three cohorts with different HF care settings and characterized the extent of and underlying reasons for CRT underutilization.

Methods

Sources

The ESC-CRT Survey II initiated by HFA and EHRA was designed to reflect the clinical practice of CRT implantation and was conducted at 288 electrophysiology centres in 42 ESC-member countries implanting CRT between October 2015 and December 2016.[13] Consecutive patients undergoing CRT implantation either as *de novo* or upgrades from a previous implantable cardioverter defibrillator (ICD) or pacemaker were included. Patient characteristics at implantation, diagnostic workups, CRT indication, implant procedures, in-hospital complications, medications at discharge, and the planned follow-up whether at an electrophysiology clinic, HF clinic, or elsewhere (more than one could be given) were collected. There were no socio-economic data and no follow-up.[14] There was also one-time site-specific data collection describing hospital resources.

The ESC-HF-LT Registry was initiated by HFA in 2013 and enrolled patients with HF in 33 countries from 337 centres and was managed by the EURObservational Research Programme. Participating centres enrolled out- and in-HF patients on a one-day-per-week basis and recorded information on demographics, medical history, comorbidities, laboratory and diagnostic parameters, HF medication, and devices (with no information on time of implantation). Data on subsequent hospital admissions and mortality were obtained at 12 months and have previously been published.[4]

The SwedeHF is a continuous quality registry created in 2003. Patients with clinician-judged HF are included. In 2019, the coverage of SwedeHF was 30.4% of the prevalent HF population in Sweden, and 84% of all hospitals entered data into the registry.[15] Approximately 80 variables, including demography, comorbidity, diagnostic procedures, clinical and laboratory data, and medication, are recorded at discharge from the hospital or during outpatient visits. Data can be entered by cardiologists, nurses at nurses-leading HF clinics, internal medicine specialists, and general practitioners at in- and out-hospital settings.[16] Using the unique identifier available to all Swedish citizens, SwedeHF was linked to the Longitudinal Integrated Database for Health Insurance and Labour Market Studies in order to obtain socio-economic information and the National Patient Register to obtain additional information on comorbidities using ICD-10 codes. More information on the linkage between registries, initial selection criteria, and specification for ICD codes can be found at https://kiheartfailure.github.io/shfdb3/.

To compare clinical data during the same time period in all three cohorts, we applied the following time frame: January 2013 to December 2016 to the ESC-HF-LT registry and the SwedeHF registry that includes the ESC-CRT Survey II enrolment time (October 2015 to December 2016). Patients with missing data on left ventricular (LV) ejection fraction (EF), with HF duration <6 months, missing data on devices, QRS duration and left bundle branch block morphology (LBBB), and New York Heart Association (NYHA) class were excluded (*Figure 1*).

Data, included demographics, clinical characteristics, NYHA class, LVEF, guideline-directed medical therapy (GDMT),[17] and other medical therapy. Organizational and logistical factors were collected when available. We used the Meta-Analysis Global Group in Chronic HF (MAGGIC) risk score[18,19] to further evaluate HF disease severity and prognosis. Habitation status, offspring, level of education, and income were available from national registries linked to SwedeHF,[16] and habitation status (living alone) in the ESC-HF-LT registry. Hospital type and details of planned follow-up were retrieved from SwedeHF and ESC-HF-LT registries and from ESC-CRT Survey II.

Cardiac resynchronization therapy indications according to 2013 ESC guidelines on cardiac pacing and cardiac resynchronization therapy

In all cohorts, patients with CRT were assumed to have met indications for CRT. Among patients without CRT in ESC-HF-LT and SwedeHF, we defined CRT indication based on class I–IIa recommendations in the 2013 ESC-EHRA guidelines,[20] which were available when ESC-CRT Survey II was conducted. Indications included Class I: sinus rhythm, LBBB, and QRS duration $\geq$ 120 ms, EF $\leq$ 35%, and NYHA class $\geq$ II. Class IIa: non-LBBB with QRS duration $>$ 150 ms, EF $\leq$ 35%, and NYHA class $\geq$ II, or atrial fibrillation (AF), QRS $\geq$ 120 ms, EF $\leq$ 35%, and NYHA class III–IV.[20]

Study design

We performed a cross-sectional cohort study. Firstly, patient characteristics in the ESC-CRT Survey II were compared with patients with CRT (and presumed indication) and with indication in the two registries. Secondly, predictors of CRT use were determined from the variables in the ESC-HF-LT and SwedeHF registries.

A sensitivity analysis to compare the baseline characteristics in the ESC-CRT Survey II vs. ESC-HF-LT and SwedeHF registries was also conducted considering only the overlapping countries between ESC-CRT Survey II and ESC-HF-LT (Supplementary material online, *Table S3*).

Statistical analysis

Categorical variables were presented with the absolute number (%) and continuous variables with the median (interquartile range). Differences across study groups for patient characteristics are reported by standardized mean difference (SMD),[21] which is less influenced by the differences in sample sizes. SMD 0.0–0.2 was considered non-significant and SMD >0.2 as significant.

In patients with CRT or with indication, the association between pre-specified clinical variables and CRT use was modelled using univariable and multivariable logistic regressions separately in the ESC-HF-LT registry and SwedeHF. The selection of variables was based on clinical judgement. Fewer variables were selected for model from the ESC-HF-LT registry due to the limited number of subjects in this registry. Therefore, two regression models were performed for the SwedeHF, where one only contained the same variables as in the ESC-HF-LT registry model. Information on analysis with more extensive pre-specified variables is given in Supplementary material online, *Table S1*. Details of MAGGIC score calculation are given in Supplementary material online, *Table S5*.

Outliers were investigated with Cook's distance and multicollinearity with the variance inflation factor, and no corrective action was deemed necessary (see Supplementary material online, Figure *S2 and Table S6*).

Missing data were handled using multiple imputations ($n = 10$) with mice.[22] Variables included in the model are the same as are included in the logistic regression models. Imputation was done separately for the two registries. All analyses were performed using R version 4.0.2 (2020-06-22) (R Core Team 2019). The level of significance is set to 5%, two-sided. The R code used to perform the analyses is found at https://github.com/KIHeartFailure/crt.

Results

The ESC-CRT Survey II included 11 088 patients (*Figure 1*). There were 24 countries overlapping in the ESC-CRT Survey II and ESC-HF-LT

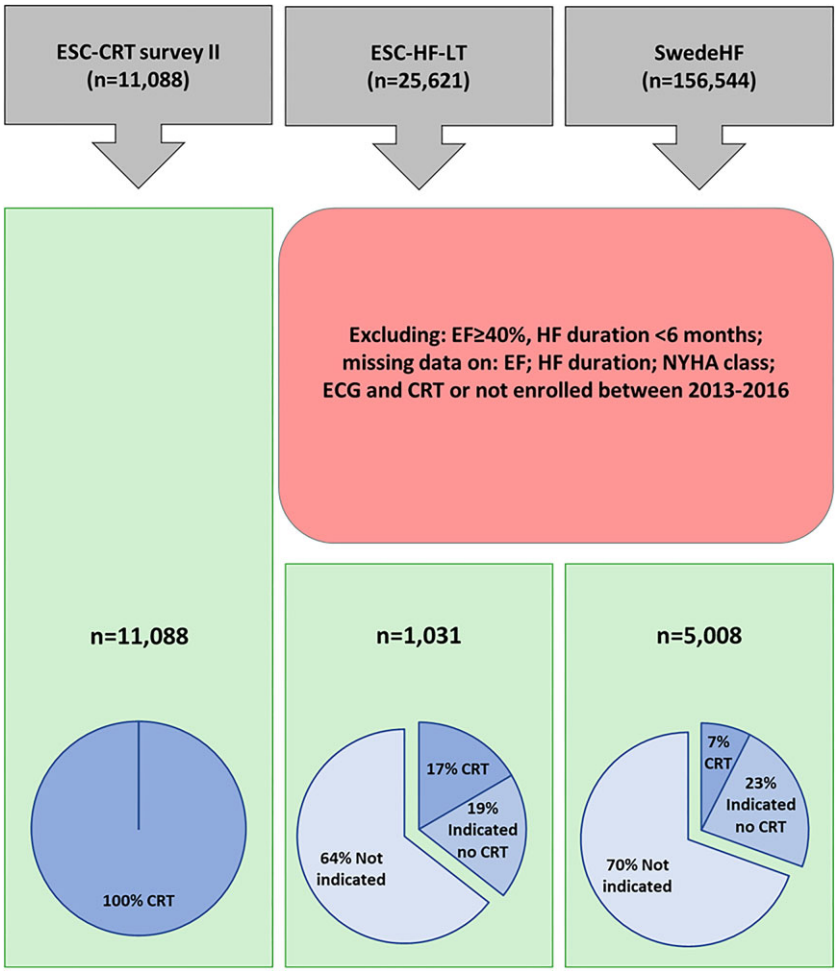

Figure 1 Flow chart of patient selection from the three cohorts the ESC-CRT survey II, ESC-HF-LT, and SwedeHF. The total number (*n*) of patients is given in grey boxes. The exclusion criteria applied to ESC-HF-LT and SwedeHF are given in the red box. The green box indicates the final number of patients in this study. The proportion of patients indicated for CRT in ESC-HF-LT and SwedeHF, implanted with CRT or not implanted are given in the pies chart. CRT, cardiac resynchronization therapy; ECG, electrocardiography; EF, Ejection fraction (EF); ESC, European Society of Cardiology; HF, heart failure; LT, long term; NYHA, New York Heart Association class.

registry (Supplementary material online, *Table S2*). The ESC-HF-LT registry included a total of 25 621 patients. SwedeHF conducted only in Sweden had a total of 156 544 patients. Reasons for exclusion after applying selection criteria are given in *Figure 1*. Our final study population thus included 11 088 (CRT Survey II), 1031 (ESC-HF-LT registry), and 5008 (SwedeHF) (*Figure 1*). Patients in overlapping countries were 8151 in CRT Survey II and 857 in ESC-HF-LT.

Patient characteristics

In the ESC-HF-LT registry, 367 (36%) were considered guideline-indicated for CRT. Of those, 171/367 (47%) already had a CRT device and 196/367 (53%) did not. Amongst reasons for non-CRT use were patients' declining (19%), costs (6%), or logistical issues (9%) (Supplementary material online, *Figure S1*). In SwedeHF, 1529 (30%) patients had indications for CRT. Of those, 374/1529 (25%) had CRT, and 1155/1529 (75%) did not (*Figure 1*). The reasons for non-CRT use were not collected in this registry. None of the registries indicated if CRT implantation was planned in the future, but all patients had HF duration of 6 months or longer, suggesting there had been time for GDMT optimization and potentially improvement of EF, NYHA class, and/or electrical dyssynchrony.

We compared patients with an indication for CRT (including those who had CRT) in the two registries to ESC-CRT Survey II (in which all received CRT and had a presumed indication) (*Table 1*). Key data from the ESC-CRT Survey II, ESC-HF-LT, and SwedeHF were as follows: age 70 vs. 68 vs. 76 years, female 24% vs. 24% vs. 26%, history of myocardial infarction 36% vs. 47% vs. 52%, AF 41% vs. 31% vs. 54%, diabetes 31% vs. 38% vs. 37%, NYHA III-IV 59% vs. 38% vs. 62%, EF 30–39% (vs. <30%) 40% vs. 59% vs. 60%, and NT-proBNP 2400 vs. 1490 vs. 2820 pmol/L. The proportion of CRT-D vs. CRT-P was 83% vs. 79% vs. 69%. Results on key clinical characteristics in overlapping countries (Supplementary material online, *Table S3*) were consistent in the sensitivity analysis except for AF that was significantly higher in the ESC-CRT Survey II compared to the ESC-HF-LT.

Organization of care

Most patients included in the ESC-CRT Survey II and ESC-HF-LT were from university centres, whereas this number was only 30%

Table 1 Clinical characteristics of patients with CRT or with an indication for CRT but not implanted in ESC CRT survey II and the ESC-HF-LT and SwedeHF registries

	ESC-CRT Survey II	ESC-HF-LT		SwedeHF	
	CRT	CRT/indication		CRT/indication	
	11 088	367	SMD[a]	1529	SMD[b]
Female	2686 (24)	87 (24)		392 (26)	
Age, years	70 [62, 76]	68 [59, 75]		76 [69, 82]	0.56
Non-ischaemic aetiology	6078 (55)	179 (49)		647 (48)	
Myocardial infarction	3957 (36)	171 (47)	0.21	788 (52)	0.31
Hypertension	6962 (64)	208 (57)		1053 (69)	
Atrial fibrillation	4459 (41)	113 (31)	0.21	819 (54)	0.26
COPD	1315 (12)	62 (17)		231 (15)	
Diabetes	3428 (31)	141 (38)		562 (37)	
Chronic kidney disease	2532 (42)	155 (47)		798 (53)	0.22
Ejection fraction, %			0.45		0.46
<30%	5425 (51)	217 (59)		917 (60)	
30–39%	4326 (40)	150 (41)		612 (40)	
LVEDD, mm	63 [58, 69]	66 [60, 72]	0.29		
LBBB[c]	7861 (73)	190 (52)	0.44	1071 (70)	
QRS,[c] ms	160 [140, 174]	154 [138, 170]		156 [142, 170]	
NYHA (III–IV)	6395 (59)	140 (38)	0.43	946 (62)	0.06
Sys. BP, mmHg	122 [110, 137]	120 [109, 130]	0.21	120 [108, 130]	0.23
Dia. BP, mmHg	72 [66, 80]	70 [64, 80]		70 [60, 80]	0.3
NT-proBNP, pg/mL	2400 [1050, 5513]	1490 [718, 3034]	0.38	2820 [1239, 6214]	
HF hospitalization < 12 months	5078 (47)	179 (49)		881 (58)	0.22
MAGGIC score	25 [20, 29]	23 [19, 28]		28 [23, 32]	0.46
Loop diuretic	8621 (81)	326 (89)	0.22	1254 (82)	
RASI	9163 (86)	322 (88)		1387 (91)	
MRA	6682 (63)	286 (78)	0.33	719 (47)	0.32
BB	9472 (89)	340 (93)		1436 (94)	
Digoxin	1100 (10)	72 (20)	0.26	168 (11)	
Anticoagulants	4928 (47)	151 (41)		778 (51)	
Antiplatelets	4846 (44)	206 (56)	0.25	635 (42)	
CRT-D	8443 (83)	135 (79)		259 (69)	
CRT-P	1703 (17)	36 (21)		115 (31)	
PM or ICD		67 (34)		190 (16)	

Categorical variables are presented with number (*n*) [percentage (%)] and continuous variables with median [first and third quartile (q1–q3)]. SMD is considered significative if >0.2.

BB, Beta-blockers; CRT-D, cardiac resynchronization therapy with defibrillator; CRT-P, cardiac resynchronization therapy without defibrillator; COPD, chronic obstructive pulmonary disease; Dia. BP, diastolic blood pressure; LBBB, left bundle branch block; LVEDD, left ventricle diastolic diameter; MRA, mineralocorticoid receptor antagonists; NT-proBNP, N-terminal pro-B-type natriuretic peptide; RASI, renin–angiotensin system inhibitors; Sys. BP, systolic blood pressure; PM, pacemaker; ICD, implantable cardioverter defibrillator.

[a] Standard mean difference (SMD) between the European Society of Cardiology (ESC) cardiac resynchronization therapy (CRT) Survey II (ESC-CRT Survey II) vs. patients with CRT or indication for CRT but not implanted in the ESC heart failure (HF) long-term registry (ESC-HF-LT).

[b] SMD between the ESC-CRT Survey II vs. patients with CRT or indication for CRT but not implanted in the Sweden HF Registry (SwedeHF).

[c] Intrinsic in the ESC-CRT Survey II. Including paced QRS in the ESC-HF-LT and SwedeHF.

in SwedeHF. In the ESC-CRT Survey II, only 25% were referred for CRT implantation and the remainder were patients already cared for in the respective CRT-implanting centres. Whereas ESC-CRT Survey II was solely conducted at CRT implanting centres, 86 and 46% of patients were enrolled at hospitals with CRT implantation possibilities in ESC-HF-LT and SwedeHF, respectively (*Figure 2*).

Regarding follow-up for ESC-CRT Survey II, among 288 centres, follow-up at implantation centres was available at 93% of centres, and a HF clinic was available at 68% of centres.[13] Elective admissions for CRT implantation were 77%, and 86% were planned to be followed at the implanting centre and 10% in a specialized CRT clinic. In contrast, only 3% were planned to be followed at an HF clinic despite high availability. In the registries, follow-up at an HF clinic was 89% in ESC-HF-LT and 74% in SwedeHF (*Figure 2*).

Predictors of CRT utilization in patients with CRT indication in ESC-HF-LT and SwedeHF (*Figure 3* and Supplementary material online, *Table S4*).

Independent predictors of CRT use that were common for ESC-HF-LT and SwedeHF were AF, milder HF (NYHA I-II rather than III-IV), and greater use of GDMT. Additionally, in ESC-HF-LT, a prior

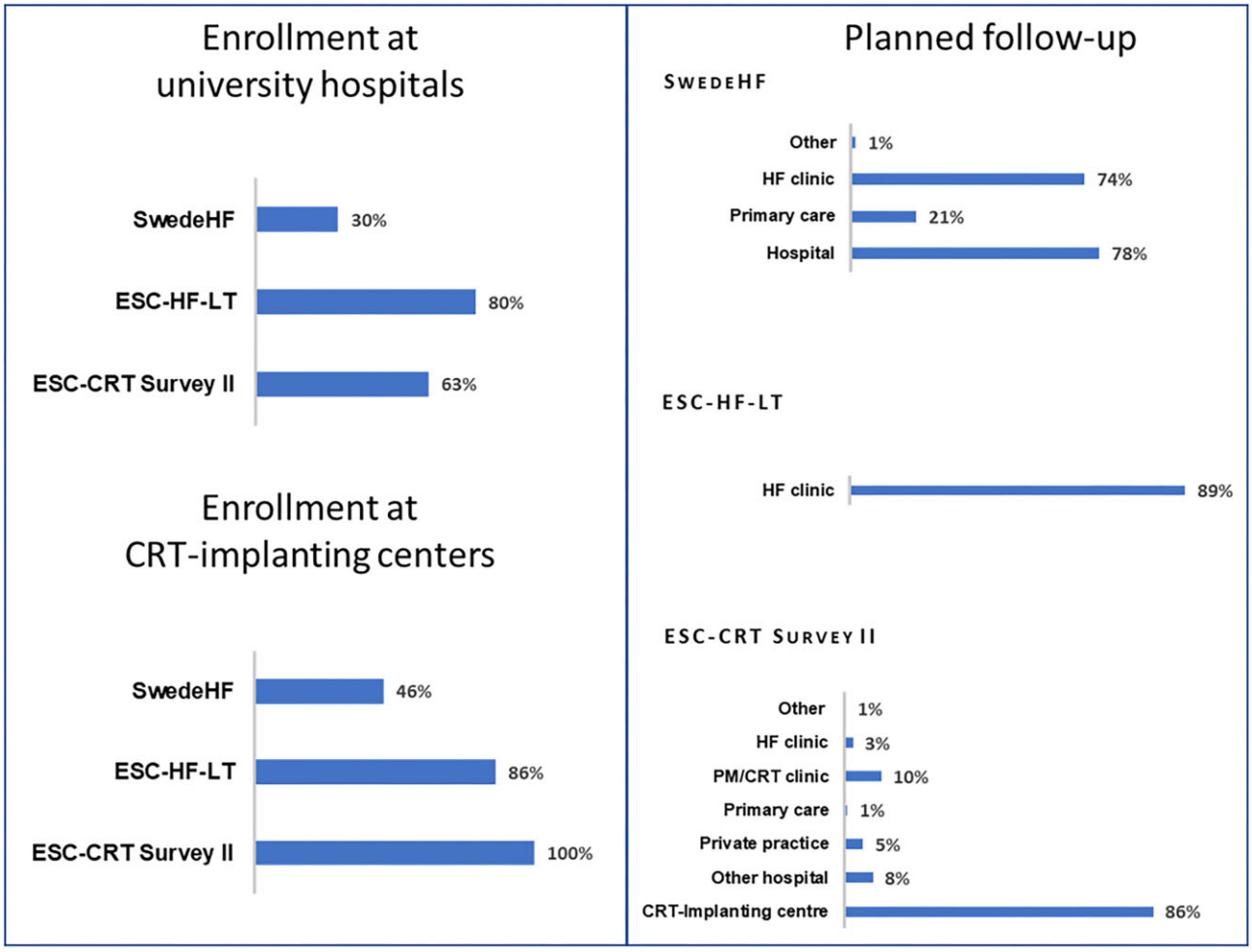

Figure 2 Proportion of patients enrolled at university hospitals and at centres preforming CRT implantation in SwedeHF, ESC-HF-LT, and ESC-CRT Survey II (right side). Proportion of patients with planned follow-up according to options given in each cohort (left side). More than one alternative can be given. PM, pacemaker; for other abbreviations, please see legend to *Figure 1*.

HF hospitalization predicted CRT. In SwedeHF, independent predictors were also age <75 years, history of MI, higher income, higher education level, non-smoking, care at university hospital, and planned follow-up in specialist rather than primary care but not follow-up in a nurse-based HF unit.

Discussion

To the best of our knowledge, this is the first patient-level comparison of CRT use and predictors in three large HF cohorts in different clinical settings. CRT was underused, with 47% of patients with an indication having CRT in ESC-HF-LT and 25% in SwedeHF. There were differences in clinical settings and in clinical characteristics between cohorts, smaller proportions in university hospitals or CRT implanting centres, and higher age and more severe HF in SwedeHF, but similar proportions women. Both clinical, demographic and access to care were factors affecting CRT use. We and others have previously shown large underuse of CRT and ICD therapy in indicated patients.[3,6,7,23–25]

Our study illustrates the difficulties in analysing 'real-world' HF practice. The patients in ESC-HF-LT registry were largely from university hospitals. These patients were a median of 65–68 years and thus were younger than most patients with HF seen in clinical practice. Patients in SwedeHF were more representative for age (median age 74–76 years old) and recruited over the entire care system and with greater proportion in NYHA class III-IV (62%) than in ESC-HF-LT (38%). HF medication was best in ESC-CRT Survey II and better in ESC-HF-LT registry than in SwedeHF. Nonetheless, there was substantial underuse of CRT in ESC-HF-LT and even worse in SwedeHF with a broader variety of healthcare givers. The reason for CRT underuse is not obvious. We believe awareness of CRT therapy contributed to CRT underuse. In SwedeHF, general cardiologists and HF nurses and even primary care physicians entered data and were responsible for care which means that their awareness of device therapy, including CRT and ICD, was less than for the HF specialists in ESC-LT-HF. Somewhat surprisingly, the lack of CRT implantation services (*Figure 2*) was not the reason for CRT underuse since such services were available at many centres in both registries (ESC-HF-LT; 86% and SwedeHF; 50%). Our results suggest internal referral challenges within centres. Moreover, we do not know to which proportion lack of external referrals was a contributing factor since we do not have such information except for ESC-CRT Survey II in which it was 25%. In conclusion, our results illustrate the lack of completeness of both

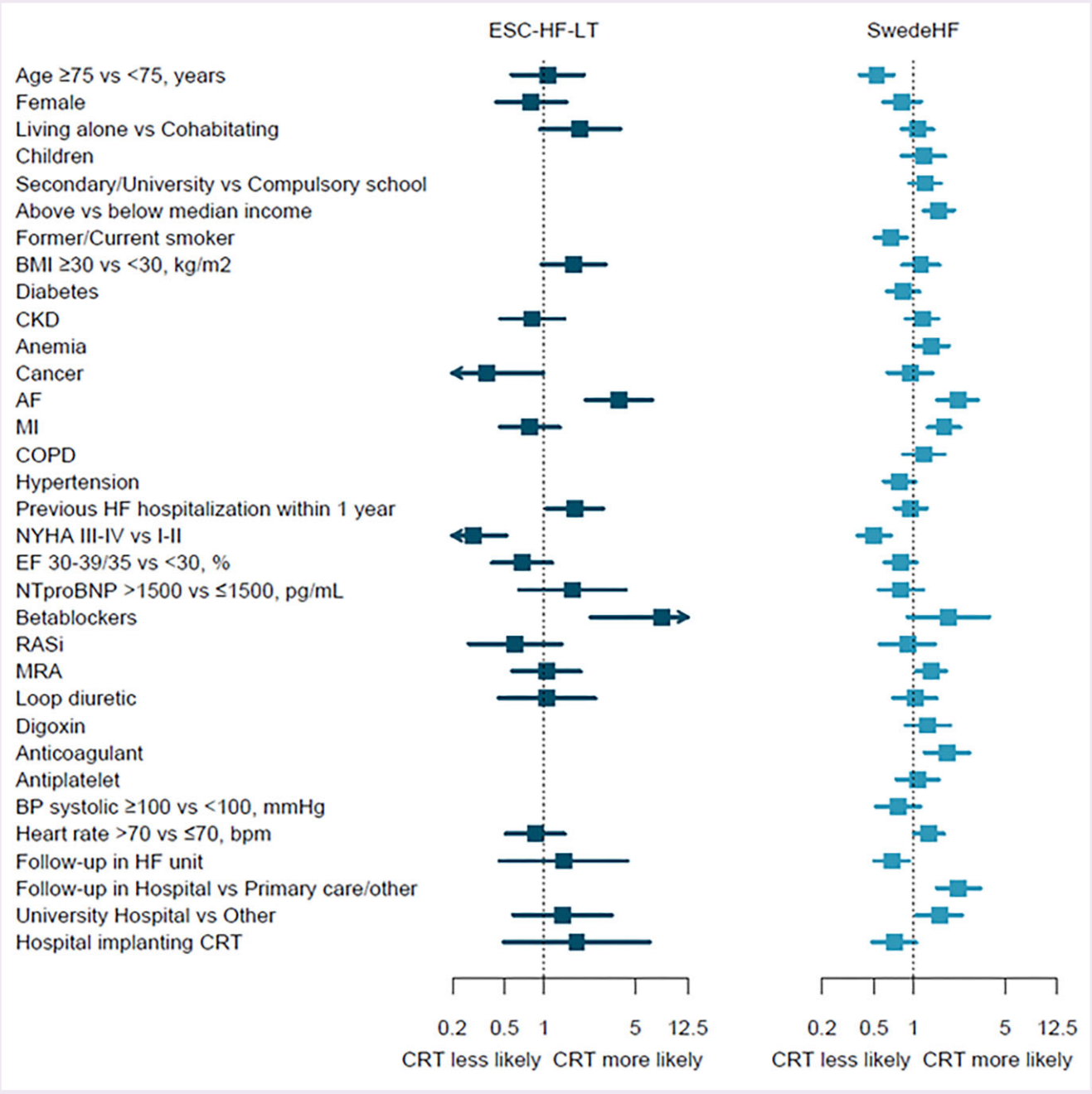

Figure 3 Predictors of CRT use in ESC-HF-LT registry and SwedeHF registry. Adjusted odds ratios for CRT by clinical characteristics in ESC-HF-LT and SwedeHF. AF, atrial fibrillation, BP, blood pressure; BMI, body mass index; CI, confidence intervals; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; EF, ejection fraction; MRA, mineralocorticoid receptor antagonists; MI, myocardial infarction; NYHA, New York Heart Association class; NT-proBNP, N-terminal pro B-type natriuretic peptide (NT-proBNP); RASi, renin–angiotensin system inhibitors.

in-house and external referral patterns as well as the lack of awareness of CRT therapy.

Predictors of cardiac resynchronization therapy implantation

Although NYHA III-IV in our analysis was associated with *less CRT* use we do not know if CRT was planned at the time of data entry or merely reflects that such patients more often are treated at HF centres. Moreover, even in the presence of CRT, CRT treatment time was unknown, which affects both NYHA class, LVEF and NT-pro-BNP. Hence, data on disease severity and therapy, such as CRT, are difficult to study since we did not have information on the CRT implantation date in our registries nor if a CRT implantation was planned.

Somewhat surprisingly, we found that a history of AF was a predictor of CRT utilization both in ESC-HF-LT and SwedeHF despite weaker scientific evidence for CRT benefit in this population.[23] In the ESC-CRT Survey II, 23.2% of CRT implantations were upgrades from a previous pacemaker or ICD, and many patients had AV nodal ablation planned or performed. In our registries, we do not know if a CRT was

implanted in preparation for such an intervention. Still, we believe that the conviction of the HF physician that CRT is beneficial also in AF patients was a more common reason despite lack of strong guidelines indications. Similar findings were also demonstrated in the CRT Survey I.[26]

In SwedeHF, the presence of a history of myocardial infarction was associated with higher utilization of CRT, suggesting, as for AF, that patients with a previous cardiovascular disease may have been treated at more specialized health care units (cardiology and HF specialist). CRT in HF patients with ischaemic aetiology erroneously has been linked to lower response.[27] We do not believe that this is the main explanation for underuse of CRT. On the contrary, many of them may have had a primary preventive ICD indication and as such would have been suitable for CRT-D. In our analysis, most CRT-treated patients were indeed implanted with a CRT-D, with a somewhat larger proportion in the ESC-CRT Survey II and ESC-HF-LT than in the SwedeHF.[6,24,28]

We have previously reported that factors besides clinical characteristics determine the implementation of CRT[6] and that participation in a patient registry, as opposed to not, is associated with better management and outcome, including CRT utilization.[6,29–31] In this study, we found that income higher than median and higher educational level were associated with more CRT. Social class may facilitate doctor–patient communication and enable discussion on relative risks and benefits of device therapy, including CRT.[32] Such patients may also by themselves have voiced a request for CRT therapy. Surprisingly, follow-up in specialized nurse-led HF units was associated with *less* likelihood of CRT implantation. Although we do not have a solid explanation for this, we cannot rule out that CRT was planned but not accomplished at the data entry. The alternative explanation is that nurse-led clinics focus on HF medication and patient education but miss out on device recommendations.

Taken together, our data mostly reflect enrolment at motivated centres. We, therefore, believe that the quality of HF care, including consideration for CRT, may have been *even worse* for the general HF patient population outside such centres. In addition, our study results stress the importance of smooth referral patterns from primary care to HF teams and/or implantation centres for CRT implantation. Such referral recommendations were helpful in achieving better implementation of HF care as previously reported by us.

Limitations

This study has several important limitations. Firstly, the number of patients was relatively small especially as regards the ESC-HF-LT registry. The ESC-CRT Survey II only included patients at CRT Implanting centres and mostly from university or teaching hospitals. Only 25% of patients were referred from other hospitals. In the ESC-HF-LT registry, enrolling centres were HF centres and mostly university hospitals reflecting the HFA initiative. Even if SwedeHF to date the largest HF registry in the world, coverage of this registry is 30%, and enrolment at primary care centres is low. Furthermore, there are obvious limitations to comparing different patient cohorts. We tried to minimize difficulties by using the same time period for all three cohorts and by using the ESC guidelines recommendations for CRT indications. However, in those already implanted with a CRT, we could not assess which criteria were used as indication. We are aware of the most recent 2021 ESC guidelines on cardiac pacing and CRT,[33] which had not been published at the study time of this cohort study. We do not believe that the adaptation of them would have influenced our results. Moreover, we cannot rule out that survival is a source of bias. But we can speculate that if we did have information on survival, this might have led to an overestimate of the proportion of patients having vs. non-having a CRT since those who were very sick (and died) might not have gotten a CRT, and therefore those who did get a CRT might have had longer life expectancy at the implantation but also longer lives because of the CRT. This potential bias leads to consider that the rates of underuse are even higher.

The observational design of the current study implies that causality cannot be extrapolated. Potential residual and unknown confounders despite a large adjustment cannot be ruled out. Since the exclusion by protocol of patients without information on QRS, LBBB, EF, and devices, the underutilization might be underestimated and thorough information collected in the registry may be a marker of better care.

It was assumed that indication criteria for CRT implantation were fulfilled at the time of implantation, although the presence of CRT implantations that do not meet the indication criteria cannot be ruled out. The definition of CRT indication and the characteristics were extrapolated by the available variables, and misclassification cannot be completely excluded but, since the expected relative low numbers in this category and the quality of the data sources, this should not have a substantial impact on our results. The selection of a specific time frame was used to minimize the heterogeneity regarding the general knowledge among clinicians of CRT indications during the study period. Our sources allow only a time-point extrapolation of the data, and changes in characteristics and CRT implantation and indication status cannot be properly addressed over time. The chosen level of 0.2 for detecting a significant difference between characteristics was adopted based on previous studies,[21] but results may differ considering different thresholds. Differences due to regional variation should be accounted and a sensitivity analysis with only overlapping countries in ESC-CRT survey II and ESC-HF-LT registry was conducted.

Conclusion

CRT, despite its proven efficacy, is still underutilized. Our results indicate that besides clinical findings such as high age, income, and educational level, access to HF care and type of follow-up are associated with CRT use. These associations, if confirmed, should lead to a rethinking of the organization of referral of HFrEF patients and stress the importance that patients with potential indications for CRT are screened and followed in qualified centres.

Supplementary material

Supplementary material is available at *European Heart Journal—Quality of Care and Clinical Outcomes* online.

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Data availability

Data cannot be shared for ethical/privacy reasons.

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