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SECOND EUROPEAN CARDIAC RESYNCHRONISATION THERAPY SURVEY (CRT SURVEY II): LATVIAN DATA COMPARED TO EUROPE

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The cardiac resynchronisation therapy (CRT) survey II is a joint initiative between the European Heart Rhythm Association and the Heart Failure Association. It compiles real world data about cardiac resynchronisation therapy in European Society of Cardiology member states. 11 088 patients assigned to implantation of CRT with pacemaker function (CRT-P) or CRT with an incorporated defibrillator (CRT-D) were enrolled in the survey starting 1 October 2015 till 31 December 2016 and for each patient, an electronic case report form (eCRF) was completed. Each participating country had each eCRF data-point benchmarked against the total cohort. In total, 79 patients were included from Latvia. The mean age of patients was 68.1, similar to the total cohort of other ESC member states, and 21.8% of patients were female. Latvian patients compared to other countries more often had permanent atrial fibrillation, NYHA class III and IV, ejection fraction 35 %. CRT-Ds and multipolar lead implantation rates were higher. Peri-procedural complication rates were similarly low in both groups. At discharge, prescribed medication rates were similar but more frequently MRAs, ivabradine and calcium channel blockers were prescribed and slightly less frequently ACE inhibitors/ARBs were prescribed. The CRT survey II is a valuable resource that describes ongoing practice of cardiac resynchronisation therapy around Europe and benchmarking against the total cohort is nationally significant for each participating country.

Key words: *demographic, medication therapy, heart failure.*

INTRODUCTION

One of the major cardiovascular health problems is heart failure, affecting around 26 million people worldwide, and its prevalence is increasing (Savarese and Lund, 2017). In the United States heart failure-related deaths was 89.5 per 100 000 population in 2009 and 96.9 in 2014 (Ni and Xu, 2015).

Conduction delays and dyssynchrony of regional contractility are associated with further deterioration of ventricular function, and therefore cardiac resynchronisation therapy (CRT) is used to restore myocardial contraction sequence.

Along with optimal medical treatment for selected patients, CRT is recommended with a high level of evidence (Ponikowski *et al*., 2016).

CRT has shown improvement in symptoms, exercise tolerance, ventricular function and reduction of mortality (Cazeau *et al*., 2001; Abraham *et al*., 2002; Cleland *et al*., 2005; Moss *et al*., 2009). It has been suggested that approximately 10% of hospitalised heart failure patients would meet criteria for CRT (Farwell *et al*., 2000). Mostly evidence for recommendations of CRT comes from randomised controlled trials (RCT) with selected patient groups, while patient groups like elderly with more comorbidities are not widely represented (Dickstein *et al*., 2015).

The first European CRT survey was launched in 2008–2009 by the Heart Failure Association (HFA) and the European Heart Rhythm Association (EHRA of the European Society of Cardiology (ESC). It compiled real-life data of 13 ESC countries and demonstrated that the patient population receiving CRT was broader than that recommended by guidelines and it showed that a significant fraction of patients of those groups were not well represented in RCTs (Dickstein *et al*., 2009).

On the basis of the CRT survey, HFA and EHRA initiated the CRT survey II in 2015. It collected broader data compared to the first survey, as well as represented trends of changes in the CRT receiving population, since new guidelines were presented during the period between the two surveys. All 47 ESC member states (ESCMS) were invited to participate in the CRT survey and 42 of them agreed to participate and actively included patients (Dickstein *et al*., 2018).

The aim of this article is to compare CRT implantation data in Pauls Stradiņš Clinical University Hospital with data from other ESCMS.

MATERIALS AND METHODS

The survey was designed as a joint initiative between the EHRA and HFA. The design and rationale were published previously (Dickstein *et al*., 2015).

Of the 47 invited ESCMS, 42 participated in the CRT survey II and overall 288 centres actively included patients. The study was designed to include all patients assigned to *de-novo* implantation of CRT with pacemaker function (CRT-P), CRT with an incorporated defibrillator (CRT-D), an upgrade from a permanent pacemaker (PPM) or an implantable cardioverter defibrillator (ICD). Initially, patient inclusion period was planned nine months starting from 1 October 2015, but was extended by six months till 31 December 2016 to increase the sample size.

Each implanting centre completed a one-time site questionnaire that represented hospital infrastructure, population served, and details of CRT device implantation routines. For each consecutive patient survey, an investigator completed an electronic case report form (eCRF). ECRF included information about patient demographics, past medical history and major comorbidities, pre-implantation clinical evaluation, implant procedure, complications and adverse events during index hospitalisation.

No further follow-up data collection was planned, patient anonymity was strictly provided and eCRT was reviewed by ESC data protection consultants. Taking this into consideration, the RSU Research Ethics Committee was informed and no informed consents or approval from Ethics Committee were necessary.

The daily survey process was monitored by Tessa Baak at Stavanger University Hospital, University of Bergen, Norway. Data management and statistical analyses was conducted by Institut für Herzinfarktforschung Ludwigshafen, Germany. Each participating country had each eCRF datapoint benchmarked against the total cohort. Categorical variables were displayed as absolute numbers and percentages and continuous variables were displayed as means with standard deviations or medians with interquartile range. To detect statistical significance between groups, the Mann–Whitney–Wilcoxon test was used for continuous variables and Chi-squared test for categorical variables.

RESULTS

During the 15-month enrolling period (October 2015 to December 2016) there were 11 088 patients included in CRT Survey II from 288 centres in 42 ESC countries. 79 patients were enrolled in Pauls Stradiņš Clinical University Hospital.

Patient characteristics. The results of patient demographic characteristics and data of past medical history are presented in Table 1. In Latvia, the mean age of patients was 68.1 years, which was similar to other countries. 21.8% of CRT receivers were females compared to 24.3% in other countries. Heart failure with ischaemic origin in both patient groups was similar (42.3% vs 44.5%, OR 0.91, 95% CI 0.58–1.43). Thereby prior history of revascularisation and myocardial infarction also were without major difference. There were several differences in other major comorbidities. Latvian patients receiving cardiac resynchronisation therapy more often had atrial fibrillation (55.1% vs 40.7%, $p = 0.01$, OR 1.79, CI 95% 1.14–2.80) and 58.1% of them had permanent form compared to 42.2% in patients of other countries (OR 1.90, CI 95% 1.03–3.50). Furthermore, anaemia was more frequent in Latvian patients. On the other hand, they suffered less from diabetes hypertension and obstructive lung disease.

Clinical evaluation. More patients assigned to cardiac resynchronisation therapy were in the New York Heart Association (NYHA) functional class III or IV in Latvia than in other ESC countries (Table 2). While both groups had similar systolic blood pressure measurement, Latvian patients had slightly higher diastolic blood pressure (76.2 ± 9.1 vs

Table 1. Patient demographic characteristics and past history

Parameters	Latvia, n = 77	All other countries, n = 10962	*p*-value	OR (95%-CI)
Age, years	68.1 ± 9.3	68.5 ± 10.8	0.341	
Median (1. quartile, 3. quartile)	68 (62, 75)	70 (62, 76)		
5th and 95th percentile	53 , 83 (VIG)	49 , 84 (VIG)		
Age < 65	33.8% (26/77)	31.5% (3452/10962)		1.11 (0.69–1.78)
65 ≤ Age < 75	40.3% (31/77)	36.4% (3994/10962)		1.18 (0.74–1.86)
Age ≥ 75	26.0% (20/77)	32.1% (3516/10962)		0.74 (0.45–1.24)
Gender			0.604	
Male	78.2% (61/78)	75.7% (8305/10974)		1.15 (0.67–1.98)
Female	21.8% (17/78)	24.3% (2669/10974)		0.87 (0.51–1.49)
Elective admission	88.5% (69/78)	76.9% (8353/10868)	0.015	2.31 (1.15–4.63)
Referral from another centre	3.8% (3/78)	25.5% (2767/10860)	0	0.12 (0.04–0.37
Primary HF aetiology				
Ischaemic	42.3% (33/78)	44.5% (4842/10875)		0.91 (0.58–1.43)
Non-ischaemic	44.9% (35/78)	49.8% (5418/10875)		0.82 (0.52–1.28)
Other	12.8% (10/78)	5.7% (615/10875)		2.45 (1.26–4.79)
Myocardial infarction	39.7% (31/78)	36.2% (3926/10848)	0.515	1.16 (0.74–1.83)
Prior revascularisation	41.0% (32/78)	38.8% (4213/10846)	0.694	1.10 (0.70–1.72)
Hypertension	39.7 % (31/78)	64.0% (6931/10822)	0	0.37 (0.23–0.58)
Atrial fibrillation	55.1% (43/78)	40.7% (4416/10842)	0.010	1.79 (1.14–2.80)
Paroxysmal	27.9% (12/43)	34.8% (1536/4416)		0.73 (0.37–1.42)
Persistent	11.6% (5/43)	22.4% (989/4416)		0.46 (0.18–1.16)
Permanent	58.1% (25/43)	42.2% (1864/4416)		1.90 (1.03–3.50)
Obstructive lung disease	6.4% (5/78)	12.1% (1310/10844)	0.125	0.50 (0.20–1.24)
Diabetes	17.9% (14/78)	31.5% (3414/10843)	0.010	0.48 (0.27–0.85)
Anaemia	23.1% (18/78)	15.0% (1622/10838)	0.046	1.70 (1.00–2.89)
Chronic kidney disease (GFR 60)	30.8% (24/78)	31.1% (3371/10829)	0.945	0.98 (0.61–1.59)

HF, heart failure; GFR, glomerular filtration rate, OR, odds ratio; *p*-value, statistical significance of difference between Latvian and other ESC mamber state data, significant considered if < 0.05

73.6 ± 11.5, $p = 0.014$). Several differences were observed in pre-implantation ECG. Latvian patients displayed longer PR interval (204 ± 51 vs 189 ± 50, $p = 0.017$) and QRS duration (168 ± 31 vs 157 ± 27, $p = 0.001$). There was slightly more left bundle brunch block (LBBB) and less right bundle brunch block (RBBB) in Latvian patients, although not reaching statistical significance. Latvian patients presented with a better left ventricle (LV) ejection fraction (EF) than other patients (31.6 ± 10.6 vs 28.4 ± 8.1, $p = 0.022$) and consequently a higher percentage of patients had ejection fraction > 35% (Table 3). However, end diastolic diameter (EDD) was significantly wider in the Latvian population (67.0 ± 8.4 vs 63.5 ± 9.1, $p = 0.001$) and 50% had at least moderate mitral regurgitation.

CRT implantation procedure, complications. All CRT implantation procedures during the inclusion period were successful in Latvia (Table 4). Mean duration was significantly longer than in other countries (131.8 ± 48.9 vs 99.6 ± 46.2, $p < 0.0001$) but there was no difference in fluoroscopy time. In contrast to other countries, CRT-Ds were implanted more than CRT-Ps in Latvia and a multipolar LV lead was chosen more frequently. Complication rates were similar in both groups — in total 5.1% Latvian patients and 5.6% patients of other ESC countries had peri-operative complications.

Discharge status. There were no deaths or major adverse events (myocardial infarction, stroke, infection, worsening heart failure, worsening renal function, arrhythmias) during hospitalisation in the Latvian patient group. On the other hand, these events occurred in 4.8% of patients in other ESC member states ($p = 0.046$).

In post-implant ECG, mean QRS duration in the Latvian patient group was 155 ± 28 ms compared to 138 ± 24 ms in the other patient group ($p < 0.0001$). The QRS width distribution is presented in Figure 1.

The CRT survey II also compiled data on recommended medications at discharge. There were several statistically significant differences between Latvian patients and the total cohort (Table 5). Angiotensin converting enzyme inhibitors (ACEi) or angiotensin receptor blockers (ARBs) were prescribed in 78.2% of Latvian patients compared to 86.5% of patients in other ESC countries ($p = 0.034$, OR 0.56, CI 95% 0.33–0.96); also beta-blockers were prescribed less often although without reaching statistical significance. Latvian patients more often had mineralocorticoid receptor an-

Table 2. Clinical evaluation

Parameters	Latvia	All other countries	*p*-value	OR (95%-CI)
NYHA class			< 0.0001	
I	0% (0/78)	3.4% (370/10770)		
II	19.2% (15/78)	37.8% (4068/10770)		0.39 (0.22–0.69)
III	73.1% (57/78)	54.3% (5852/10770)		2.28 (1.38–3.77)
IV	7.7% (6/78)	4.5% (480/10770)		1.79 (0.77–4.13)
BMI, kg/m²	29.9 ± 6.4, n = 13	27.9 ± 4.9, n = 10461	0.288	
Diastolic blood pressure, mmHg	76.2 ± 9.1, n = 77	73.6 ± 11.5, n = 10625	0.014	
Systolic blood pressure, mmHg	126.8 ± 15.3, n = 77	124.7 ± 18.9, n = 10628	0.127	
Pre-implant ECG				
Heart rate, bpm	70 ± 16, n = 77	72 ± 17, n = 10645	0.082	
Atrial rhythm			0.094	
Sinus	59.0% (46/78)	69.3% (7450/10758)		0.64 (0.41–1.00)
Atrial fibrillation	38.5% (30/78)	25.5% (2748/10758)		1.82 (1.15–2.88)
Atrial paced	2.6% (2/78)	2.8% (301/10758)		0.91 (0.22–3.74)
PR interval, ms	204 ± 51, n = 43	189 ± 50, n = 7231	0.017	
AV block II/III	18.2% (14/77)	18.9% (2012/10623)	0.866	0.95 (0.53–1.70)
Intrinsic QRS duration, ms	168 ± 31, n = 78	157 ± 27, n = 9457	0.001	
LBBB	80.8% (42/52)	75.2% (7796/10365)	0.355	1.38 (0.69–2.76)
RBBB	3.8% (2/52)	6.6% (686/10365)	0.422	0.56 (0.14–2.32)
Other	15.4% (8/52)	18.2% (1883/10365)	0.604	0.82 (0.38–1.74)
AV node ablation for pat with AF	23.3% (7/30)	30.4% (827/2720)	0.402	0.70 (0.30–1.63)
Performed	85.7% (6/7)	22.6% (187/827)		20.53 (2.46–171.64)
Planned	14.3% (1/7)	77.4% (640/827)		0.05 (0.01–0.41)

AF, atrial fibrillation; AV, atrioventricular; BMI, body mass index; NYHA, New York Heart Association; ECG, electrocardiogram; LBBB, left bundle brunch block; RBBB, right bundle brunch block; *p*-value, statistical significance of difference between Latvian and other ESC mamber state data, significant considered if < 0.05

Table 3. Echo data prior implantation

Echo parameters	Latvia	All other countries	*p*-value	OR (95%-CI)
LVEF, %	31.6 ± 10.6, n = 74	28.4 ± 8.1, n = 10731	0.022	
LVEF, % < 25	21.6% (16/74)	27.6% (2963/10731)		0.72 (0.42–1.26)
25 ≤ LVEF, % ≤ 35	58.1% (43/74)	59.5% (6383/10731)		0.94 (0.59–1.50)
LVEF, % > 35	20.3% (15/74)	12.9% (1385/10731)		1.72 (0.97–3.03)
LVEDD by Echo, mm	67.0 ± 8.4, n = 68	63.5 ± 9.1, n = 8569	0.001	
Mitral regurgitation			0.339	
Mild	21.7% (13/60)	46.6% (4631/9940)		0.32 (0.17–0.59)
Moderate	43.3% (26/60)	26.4% (2620/9940)		2.14 (1.28–3.57)
Severe	6.7% (4/60)	6.9% (686/9940)		0.96 (0.35–2.67)
None	28.3% (17/60)	20.2% (2003/9940)		1.57 (0.89–2.75)

LVEDD, left ventricle end diastolic diameter; LVEF, left ventricle ejection fraction; *p*-value, statistical significance of difference between Latvian and other ESC mamber state data, significant considered if < 0.05

tagonists and calcium channel blockers prescribed and significantly greater percentage of ivabradine (25.6% vs 5.5%, $p < 0.0001$, OR 5.95, CI 95% 3.56–9.96).

DISCUSSION

The CRT survey II is a valuable resource describing the "real world" CRT receiver population. Although the Latvian sample size is not large, it clearly describes the demographics of patients and post-implantation care after receiving a CRT device. Moreover, it is an interesting tool to compare data from a single implanting centre — Pauls Stradiņš Clinical University Hospital — benchmarked against a cohort of all other ESC member states.

Mean age of patients included in the survey was similar in Latvia and other ESC countries. Usually, females in CRT

Table 4. Procedure related parameters and complications

Parameters	Latvia	All other countries	*p*-value	OR (95%-CI)
Admission to implantation, day	2.4 ± 2.4, n = 80	3.9 ± 9.4, n = 10907	0.533	
Type of device			0.010	
CRT-P	16.9% (13/77)	30.3% (3243/10692)		0.47 (0.26–0.85)
CRT-D	83.1% (64/77)	69.7% (7449/10692)		2.14 (1.18–3.90)
Duration, min	131.8 ± 48.9, n = 80	99.6 ± 46.2, n = 10347	0	
Fluoroscopy time, min	17.5 ± 16.7, n = 71	17.8 ± 17.1, n = 10271	0.324	
LV lead placement successful	98.2% (54/55)	99.4% (10479/10539)	0.222	0.31 (0.04–2.27)
Lead placement epicardially	7.4% (4/54)	9.2% (963/10479)		0.79 (0.28–2.19)
LV lead type			0.024	
Unipolar	0% (0/62)	0.7% (77/10539)		
Bipolar	29.0% (18/62)	42.3% (4460/10539)		
Multipolar	71.0% (44/62)	57.0% (6002/10539)		
Complication	5.1% (4/79)	5.6% (620/11009)	0.827	0.89 (0.33–2.45)
Death	0% (0/79)	0.1% (8/11009)	0.811	
Bleeding	1.3% (1/79)	1.0% (107/11009)	0.791	1.31 (0.18–9.48)
Requiring intervention	0% (0/79)	0.3% (35/11009)	0.616	
Pocket haematoma	1.3% (1/79)	0.8% (84/11009)	0.610	1.67 (0.23–12.13)
Pneumothorax	1.3% (1/79)	1.0% (111/11009)	0.820	1.26 (0.17–9.13)
Haemothorax	0% (0/79)	0.1% (9/11009)	0.799	
Coronary sinus dissection	0% (0/79)	1.9% (214/11009)	0.211	
Pericardial tamponade	0% (0/79)	0.3% (28/11009)	0.654	
Other	2.5% (2/79)	1.5% (170/11009)	0.479	1.66 (0.40–6.80)

CRT-D, cardiac resyhchronization therapy with incooperaed defibrilaor, CRT-P, cardiac resynchronization therapy with pacemaker function; LV, left ventricle

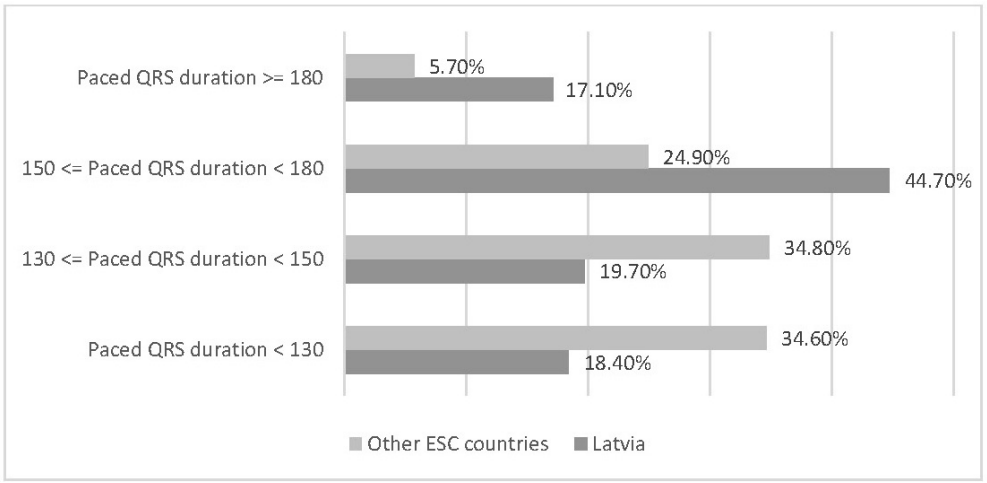

Fig. 1. Post – implant QRS

trials form a significantly lower proportion of the study population, which is true also in the CRT survey II, although female gender is one of the factors predicting better response to CRT. If we look at other major factors that are associated with greater benefit from CRT (LBBB, wider QRS than 150 ms, non-ischemic genesis of heart failure), then also the CRT survey II showed that CRT receiving patients fulfil those criteria both in Latvia and other ESC countries. However, there are patients who are not in the zone that predicts greatest benefit of CRT (narrower QRS, LVEF ≥ 35%, ischaemic HF genesis, non-LBBB). Latvian patients more often had LVEF ≥35%, although mean EF was not much different to other countries. Reduced LVEF, being one of the main criteria for CRT device implantation, is also a slightly dynamic parameter affected by patient clinical status at the time of examination, action of heart failure compensatory mechanisms, and also inter-observer variability for LVEF measured by two dimensional echocardiography is quite significant. CRT in patients with LVEF > 35% is still an important question for discussion, which is too complicated to be proved through large randomised trials. (Linde *et al*., 2016). However, it has been shown that patients with NYHA class III–IV status, and QRS > 130 ms appear to derive clinical and structural benefit from CRT (Chung *et al*., 2010). Moreover, in the presence of EF 36%–50%, left bundle brunch block is related to worse clin-

Table 5. Drug therapy at discharge

Drugs	Latvia	All other countires	*p*-value	OR (95%-CI)
Loop diuretic	79.5% (62/78)	81.1% (8559/10557)	0.722	0.90 (0.52–1.57)
ACE inhibitor/ARB	78.2% (61/78)	86.5% (9102/10525)	0.034	0.56 (0.33–0.96)
MRA (aldosterone antagonist)	76.6% (59/77)	63.1% (6623/10496)	0.014	1.92 (1.13–3.25)
Betablocker	83.3% (65/78)	89.0% (9407/10570)	0.112	0.62 (0.34–1.12)
Ivabradine	25.6% (20/78)	5.5% (573/10465)	0	5.95 (3.56–9.96)
Digoxin	9.0% (7/78)	10.4% (1093/10466)	0.672	0.85 (0.39–1.84)
Calcium channel blocker	15.4% (12/78)	8.9% (934/10453)	0.047	1.85 (1.00–3.44)
Amiodarone	12.8% (10/78)	17.3% (1815/10469)	0.293	0.70 (0.36–1.36)
Other anti-arrhythmic agent	5.1% (4/78)	1.7% (177/10453)		3.14 (1.13–8.68)
Oral anticoagulant	50.0% (39/78)	46.6% (4889/10499)	0.545	1.15 (0.73–1.79)
Warfarin (Coumadin)	79.5% (31/39)	70.2% (3432/4889)	0.206	1.65 (0.75–3.59)
Dabigatran	10.3% (4/39)	6.6% (323/4889)	0.362	1.62 (0.57–4.57)
Rivaroxaban	10.3% (4/39)	12.4% (607/4889)	0.684	0.81 (0.29–2.28)
Apixaban	0% (0/39)	10.4% (509/4889)	0.033	
Edoxaban	0% (0/39)	0.4% (18/4889)	0.704	
No oral anticoagulant	50.0% (39/78)	53.4% (5610/10499)	0.545	0.87 (0.56–1.36)
Anti-platelet agent	39.2% (31/79)	43.7% (4815/11009)	0.422	0.83 (0.53–1.31)
Aspirin	33.3% (26/78)	41.4% (4331/10469)	0.151	0.71 (0.44–1.14)
Clopidogrel	9.0% (7/78)	12.4% (1297/10469)	0.361	0.70 (0.32–1.52)
Ticagrelor	1.3% (1/78)	1.3% (135/10469)	0.995	0.99 (0.14–7.20)
Prasugrel	0% (0/78)	0.3% (31/10469)	0.630	
Dual anti-platlet therapy	3.8% (3/78)	9.3% (978/10469)	0.096	0.39 (0.12–1.23)
Oral anticoagulation and P2Y12 Inhibitor	5.1% (4/78)	4.1% (436/10542)	0.661	1.25 (0.46–3.44)
Triple Therapy	1.3% (1/78)	2.1% (217/10543)	0.630	0.62 (0.09–4.46)

ACE, angiotensin converting enzyme; ARB angiotensin receptor blocker; MRA, mineralocorticoid receptor antagonist

ical outcomes than for no conduction abnormality (Witt *et al*., 2016). Considering that more Latvian patients had NYHA class III-IV and LBBB, it seems that patient clinical status and possibility of LVEF dynamic worsening in near future play important roles in decisions for CRT implantation. This may reflect that CRT implanters mostly adhere to guidelines, and their implanting centre experience may also play an important role in deciding if patients need cardiac resynchronisation therapy.

Significantly more patients in Latvia had atrial fibrillation, with almost 70% having either the persistent or permanent form. Since 2013, CRT is a IIa recommendation in patients with atrial fibrillation if strict rate control can be provided (Bringole *et al*., 2013). High atrial rates is one of the main reasons for loss of biventricular pacing and significant reduction in mortality has been observed when biventricular pacing is more than 98% (Hayes *et al*., 2011). In 23.3% of LV patients with permanent atrial fibrillation AV nodal ablation was done or planned without statistically significant differences from other ESCMS. The results of cardiac resynchronisation in patients with atrial fibrillation could be an important question to study further, also locally.

Differences were observed also in the rates of other comorbidities. Latvian patients presented with less diabetes, hypertension and obstructive lung disease, while another study describing the Latvian CRT receiver population showed that more than 70% of them had a previous history of smoking. This also could show gaps in chronic disease diagnostics at the primary care setting. More notably, more comorbidities have not been shown to reduce the response to CRT (Zeitler *et al*., 2017; Barra *et al*., 2017).

Regarding the devices used in cardiac resynchronisation therapy, a CRT-D ratio to CRT-P was higher in Latvia than in other ESCMS. This ratio may reflect good guideline adherence as patients with an EF ≤ 35% have a guideline indication for a device with defibrillator function (Ponikowski *et al*., 2016). Furthermore, multipolar left ventricular leads were more often used in the Latvian population. Multipolar LV leads compared to bipolar LV leads allow lower LV pacing threshold and decrease the possibility of phrenic nerve stimulation (Gurevitz *et al*., 2005).

Furthermore, together with the indications for CRT of EF < 35% and wide QRS, patients also should be symptomatic despite optimal medical treatment. Although the CRT survey II did not include questions about medical treatment prior to the implantation, data about drug therapy at discharge were compiled. There were some statistically significant differences observed. An important finding was slightly lower ACI/ARB prescription rates in the LV population. 78.2% of Latvian patients received ACI/ARBs compared to 86.5% in other countries ($p = 0.034$). Furthermore, the percentage of ACI/ARBs receivers with reduced ejec-

tion fraction in the ESC-HF Long-Term Registry was 92.2% (Maggioni *et al*., 2013). This could be another important question for further investigation, because the indication for angiotensin receptor neprilysin inhibitor was included in the HF guidelines during the patient inclusion period in the CRT survey II. In contrast, MRAs was prescribed significantly more often in Latvian population.

An interesting finding was that ivabradine was prescribed almost five times more in Latvian patients. Regarding the prescription rate of beta-blockers, there was a statistically non-significant lower prescription rate in the Latvian patients. Although the CRT survey II did not collect data about medication dosage, we might speculate that probably we do not reach target doses of beta blockers in Latvia andthat this led to more frequent prescription of ivabradine. Although the main beta-blocker trials are designed to reach target doses of beta-blockers, it has been shown that beta-blocker usage at any dose and reaching the target heart rate might be more important than a maximal beta-blocker dose (Cullington *et al*., 2012; Swedberg *et al*., 2012). In ESC Heart failure guidelines, 2016 ivabradine is recommended if a patient with HFrEF and sinus rhythm is still symptomatic after using ACIs, MRAs, Betablockers in maximal tolerated doses and heart rate ≥ 70 x/min. In the SHIFT study, where ivabradine was compared to a placebo for patients with HFrEF, the ivabradine group had reduced rates of morbidity and mortality due to heart failure (Swedberg *et al*., 2010).

Thus, CRT II shows not only the particulars of patient selection for CRT and with implantation procedure related data but also insights into overall heart failure medication therapy in Latvia and in other ESC member states.

CONCLUSION

The CRT survey II enrolled 11 088 patients that received cardiac resynchronisation therapy in ESC member states and there were 79 patients included in the Pauls Stradiņš Clinical University Hospital. Compared to other countries, Latvian patients more often had atrial fibrillation and especially a permanent form, more were in NYHA classes III and IV. Similarly, the majority of patients had complete LBBB, but Latvian patients more often had EF > 35%, although EDD was wider in the Latvian population. Latvian patients more frequently received CRT-Ds and quadripolar leads, peri-procedural complication rates were similarly low and post-implantation QRS was wider in LV patients. The CRT survey II also demonstrated differences in heart failure drug therapy between both patient groups. For example, Latvian patients received more MRAs, ivabradine and CCB and less ACE inhibitors. In summary, the majority of patients fulfil the recommendations of guidelines, but a significant number of patients who receive a CRT device receive it, without strong background of evidence from randomised controlled trials, and the CRT survey II is a valuable source for further research in those groups.

REFERENCES

Abraham, W. T., Fisher, W. G., Smith, A. L., Delurgio, D. B., Leon, A. R., Loh, E., Kocovic, D. Z., Packer, M., Clavell, A. L., Hayes, D. L *et al.* (2002). Cardiac resynchronization in chronic heart failure. *New Engl. J. Med*., **346** (24), 1845–1853.

Barra, S., Providźncia, R., Agarwal, S., Marijon, E., Boveda, S. (2017). The benefit of cardiac resynchronization therapy is not hindered by the number of comorbidities. *J. Amer. Coll. Cardiol.*, **70** (16), 2096–2097.

Brignole, M., Auricchio, A., Baron-Esquivias, G., Bordachar, P., Boriani, G, Breithardt, O. A., Cleland, J., Deharo, J. C, Delgado, V., Elliott, P. M. *et al*. (2013). 2013 ESC Guidelines on cardiac pacing and cardiacresynchronization therapy. *Eur. Heart J.,* **34**, 2281–2329.

Cazeau, S., Leclercq, C., Lavergne, T., Walker, S., Varma, C., Linde, C., Garrigue, S., Kappenberger, L., Haywood, G. A., Santini, M., Bailleul, C., Daubert, J. C., Multisite Stimulation in Cardiomyopathies (MUSTIC) Study Investigators (2001). Effects of multisite biventricular pacing in patients with heart failure and intraventricular conduction delay. *New Engl. J. Med.,* **344** (12), 873–880.

Chung, E. S., Katra, R. P., Ghio, S., Bax, J., Gerritse, B., Hilpisch, K., Peterson, B. J., Feldman, D. S., Abraham, W. T. (2010). Cardiac resynchronization therapy may benefit patients with left ventricular ejection fraction 35%: a PROSPECT trial substudy. *Eur. J. Heart Failure,* **12** (6), 581–587.

Cleland, J. G. F., Daubert, J.-C., Erdmann, E., Freemantle, N., Gras, D., Kappenberger, L., Tavazzi, L. (2005). The effect of cardiac resynchronization on morbidity and mortality in heart failure. *New Engl. J. Med*., **352**, 1539–1549.

Cullington, D., Goode, K. M., Clark, A. L., Cleland, J. G. (2012), Heart rate achieved or beta-blocker dose in patients with chronic heart failure: Which is the better target? *Eur. J. Heart Failure*, **14**, 737–747.

Dickstein, K., Bogale, N., Priori, S., Auricchio, A., Cleland, J. G., Gitt, A., Limbourg, T., Linde, C., van Veldhuisen, D. J., Brugada, J., Scientific Committee, National Coordinators (2009). The European cardiac resynchronization therapy survey. *Eur. Heart J.,* **30** (20), 2450–2460.

Dickstein, K., Normand, C., Anker, S. D., Auricchio, A., Blomström-Lundqvist, C., Bogale, N., Cleland, J., Filippatos, G., Gasparini, M., Gitt, A., Hindricks, G., Kuck, K.H., Ponikowski, P., Stellbrink, C., Ruschitzka, F., Linde, C. (2015). European Cardiac Resynchronization Therapy Survey II: rationale and design. *EP Europace*, **17** (1), 137–141.

Dickstein, K., Normand, C., Auricchio, A., Bogale, N., Cleland, J. G., Gitt, A. K., Stellbrink, C., Anker, S. D., Filippatos, G., Gasparini, M. *et al.* (2018). CRT Survey II: a European Society of Cardiology survey of cardiac resynchronisation therapy in 11 088 patients — who is doing what to whom and how? *Eur. J. Heart Failure*, **20**, 1039–1051.

Farwell, D., Patel, N. R., Hall, A., Ralph, S., Sulke, A. N. (2000). How many people with heart failure are appropriate for biventricular resynchronization? *Eur. Heart J.,* **21** (15), 1246–1250.

Gurevitz, O., Nof, E., Carasso, S., Luria, D., Bar-Lev, D., Tanami, N., Eldar, M., Glikson, M. (2005). Programmable multiple pacing configurations help to overcome high left ventricular pacing thresholds and avoid phrenic nerve stimulation. *Pacing Clin. Electrophysiol., PACE*, **28** (12), 1255–1259.

Hayes, D. L., Boehmer, J. P., Day, J. D., Gilliam, F. R., 3rd, Heidenreich, P. A., Seth, M., Jones, P. W., Saxon, L. A. (2011). Cardiac resynchronization therapy and the relationship of percent biventricular pacing to symptoms and survival. *Heart Rhythm*, **8** (9), 1469–1475.

Linde, C., Curtis, A. B., Fonarow, G. C., Lee, K., Little, W., Tang, A., Levya, F., Momomura, S., Manrodt, C., Bergemann, T., Cowie, M. R. (2016). Cardiac resynchronization therapy in chronic heart failure with moderately reduced left ventricular ejection fraction: Lessons from the Multicenter InSync Randomized Clinical Evaluation MIRACLE EF study. *Int. J. Cardiol.,* **202**, 349–355.

Maggioni, A.P., Anker, S.D., Dahlström, U., Filippatos, G., Ponikowski, P., Zannad, F., Amir, O., Chioncel, O., Leiro, M.C., Drozdz, J., Erglis, A. *et al.* (2013). Are hospitalized or ambulatory patients with heart failure treated in

accordance with European Society of Cardiology guidelines? Evidence from 12 440 patients of the ESC Heart Failure Long-Term Registry. *Eur. J. Heart Failure*, **15**, 1173–1184.

Moss, A. J., Hall, W. J., Cannom, D. S., Klein, H., Brown, M. W., Daubert, J. P., Estes, N. A. 3rd, Foster, E., Greenberg, H., Higgins, S. L., Pfeffer, M. A., Solomon, S. D., Wilber, D., Zareba, W. (2009). Cardiac-resynchronization therapy for the prevention of heart-failure events. *New Engl. J. Med.,* **361**, 1329–1338.

Ni, H., Xu, J. (2015). Recent trends in heart failure-related mortality: United States, 2000–2014. *NCHS data brief*, (231), 1–8.

Ponikowski, P., Voors, A. A., Anker, S. D., Bueno, H., Cleland, J. G. H., Coats, A. J. S., Falk, V., González-Juanatey, J. R., Harjola, V. P., Jankowska, E. A. *et al.* (2016). 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur. J. Heart Failure*, **18** (8), 891–975.

Savarese, G., Lund, L. H. (2017). Global public health burden of heart failure. *Cardiac Failure Rev*., **3** (1), 7–11.

Swedberg, K., Komajda, M., Böhm, M., Borer, J. S., Ford, I., Dubost-Brama, A., Lerebours, G., Tavazzi, L., SHIFT Investigators (2010). Ivabradine and outcomes in chronic heart failure (SHIFT): A randomised placebo-controlled study. *Lancet,* **376** (9744), 875–885.

Swedberg, K., Komajda, M., Böhm, M., Borer, J., Robertson, M., Tavazzi, L., Ford, I., SHIFT Investigators (2012). Effects on outcomes of heart rate reduction by ivabradine in patients with congestive heart failure: Is there an influence of beta-blocker dose? *J. Amer. Coll. Cardiol.,* **59** (22), 1938–1945.

Witt, C. M., Wu, G., Yang, D., Hodge, D. O., Roger, V. L., Cha, Y. M. (2016). Outcomes with left bundle branch block and mildly to moderately reduced left ventricular function. *JACC. Heart Failure*, **4** (11), 897–903.

Zeitler, E. P., Friedman, D. J., Daubert, J. P., Al-Khatib, S. M., Solomon, S. D., Biton, Y., McNitt, S., Zareba, W., Moss, A. J., Kutyifa, V. (2017). Multiple comorbidities and response to cardiac resynchronization therapy: MADIT-CRT long-term follow-up. *J. Amer. Coll.Cardiol.,* **69** (19), 2369–2379.

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OTRĀ EIROPAS SIRDS RESINHONIZĀCIJAS TERAPIJAS APTAUJA (*CRT SURVEY II):* LATVIJAS UN EIROPAS DATU SALĪDZINĀJUMS

CRT survey II ir Eiropas Sirds ritma asociācijas *(Europian Heart Rhythm Association (EHRA)* un Sirds Mazspējas asociācijas *(Heart Failure Association (HFA))* kopīga iniciatīva. Šī aptauja apkopo "reālās dzīves" datus par sirds resinhronizācijas terapiju Eiropas Kardiologu biedrības dalībvalstīs. Laika posmā no 2015. gada 1. oktobra līdz 2016. gada 31. decembrim tika iekļauti 11 088 pacienti, kuriem tika implantēta sirds resinhronizācijas ierīce ar stimulatora funkciju (CRT-P) vai sirds resinhronizācijas ierīce ar defibrilatora funkciju (CRT-D), un par katru pacientu tika aizpildīta elektroniska klīniskā gadījuma forma. Visas dalībvalstis saņēma analīzi par katru elektroniskās formas parametru, kas tika salīdzināts ar kopējo kohortu. Līdzīgi citu valstu datiem vidējais Latvijas pacientu vecums bija 68,1 gads, un 21,8% bija sievietes. Latvijas pacientiem salīdzinoši biežāk bija diagnosticēta ātriju fibrilācija, viņiem bija sirds mazspējas III un IV NYHA funkcionālā klase un izsviedes frakcija 35%. Biežāk tika implantēti CRT-D un lietoti multipolāri elektrodi. Līdzīgi kā kopējā Eiropas valstu kohortā, periprocedurālas komplikācijas bija sastopamas reti. Līdzīgi rādītāji bija arī izrakstītajiem medikamentiem, izrakstoties no stacionāra, bet biežāk latviešu pacienti saņēma minerālkortikoīdu receptoru antagonistus, ivabradīnu un kalcija kanālu blokatorus, savukārt nedaudz retāk tika izrakstīti angiotensīna konvertējošā enzīma inhibitori vai angiotensīna receptoru blokatori. *CRT survey II* ir vērtīgs apkopojums par pašreizējo praksi Eiropā sirds resinhronizācijas terapijas pielietošanā, kā arī lokāli nozīmīga katrai valstij bija tās datu salīzināšana ar kopējo Eiropas kohortu.