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ORIGINAL ARTICLE

Risk stratification in patients with cardiac resynchronisation therapy: the AL-FINE CRT risk score

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Abstract

Background: Mortality and morbidity in patients with cardiac resynchronisation therapy (CRT) remain very high. Prognostic evaluation of CRT candidates might be useful for the assessment of CRT indications, directing further therapy, counselling, etc.

Aim: Our goal was to assess the prognostic value of various parameters in order to construct a risk score that could predict long-term mortality and morbidity during the initial evaluation of CRT candidates.

Methods: This was a retrospective, single-centre, large cohort study involving consecutive heart failure patients who underwent CRT device implantation. In order to build a prediction model, 28 parameters were analysed using uni- and multivariate Cox models and Kaplan-Meier survival curves.

Results: Data from 552 patients were used for the long-term outcome assessment. During nine years of follow-up, 232 patients met the primary endpoint of death and 128 patients were hospitalised for heart failure. The strongest and clinically most relevant predictors were selected as the final model. AL-FINE is the acronym for these six predictors: **A**ge (> 75 years), non-**L**eft bundle branch block morphology (according to Strauss criteria), **F**urosemide dose (> 80 mg), **I**schaemic aetiology, **N**ew York Heart Association class (> III), and left ventricular **E**jection fraction (< 20%). Depending on the number of AL-FINE score points, overall mortality at seven years was in the range of 28% (0–1 points) to 74% (3–6 points).

Conclusions: A novel, multiparametric CRT risk score was constructed on the basis of simple and recognised clinical, electrocardiographic, and echocardiographic parameters that show a significant add-on effect on mortality in this specific population.

Key words: cardiac resynchronisation therapy, heart failure, long-term mortality, risk score, Strauss criteria

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INTRODUCTION

Cardiac resynchronisation therapy (CRT) improves the survival in patients with moderate and advanced heart failure (HF). Despite this fact, mortality and morbidity in CRT patients remain very high; different CRT trials and studies have indicated the 5–7-year mortality to be around 20% to 70%, with a median survival after device implantation of approximately five years [1–7]. Although many factors that predict the outcome have been identified in patients with HF, few variables enable to predict it consistently. Moreover, in HF patients with CRT, certain prognostic factors might play a greater role, while the impact of others might be minimised by this interventional therapy. The add-on effects of independent prognostic factors warrant the construction of a multiparametric risk score to improve the prediction of outcomes.

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Risk stratification scores applicable for other patient populations, like euroSCORE for coronary heart disease patients, SCORE risk chart for the general cardiovascular risk stratification [8], or CHA_2DS_2-VASc score for atrial fibrillation patients, have been accepted as very useful. Similar prognostic evaluation of CRT patients would have obvious potential applications for the assessment of CRT indications, guiding further therapy, counselling, and other purposes.

Our goal was to assess the prognostic value of various clinical parameters in order to construct a simple risk score that could help in predicting long-term mortality and morbidity at the time of initial evaluation of candidates for CRT device implantation.

METHODS

Patient population

This was a retrospective, single-centre, large cohort study including consecutive HF patients who underwent CRT device implantation in our institution (a university/teaching hospital), from February 2006 to December 2014. CRT devices were implanted according to recognised indications and using standard transvenous techniques, as described previously [9].

Variables analysed

In order to build a predictive model, several relevant parameters useful in predicting mortality in CRT patients were gathered. These included:

- basic clinical data: age, sex, and body mass index;
- major comorbidities: diabetes mellitus, permanent atrial fibrillation, and hypertension;
- HF aetiology: categorised as ischaemic or non-ischaemic. Ischaemic aetiology was defined as a history of myocardial infarction or any significant stenotic lesions in coronary angiography;
- New York Heart Association (NYHA) functional class; the highest class assigned in medical records was used;
- electrocardiographic (ECG) data including: (i) baseline QRS morphology, categorised as left bundle branch block (LBBB), according to the Strauss definition (requirement for a mid-QRS notch in at least two left ventricular (LV) leads and longer QRS duration), or non-LBBB; and (ii) preimplantation QRS duration, assessed according to the global QRS method, i.e. from the earliest onset of the QRS of 12 simultaneously recorded standard ECG leads to the last observable QRS component in any of these leads, as recommended by the American Heart Association and the World Health Organization [10]. For ECG assessment, the digital recording system (EP Lab System PRO, Boston Scientific, Boston, MA, USA) and digital callipers were used with high paper speed (100 ms/s) and appropriately adjusted with respect to amplitude augmentation;
- echocardiographic data: pre-implantation LV ejection fraction (EF), LV end-diastolic diameter (LVEDD), and the severity of mitral regurgitation;
- biochemical data: sodium plasma concentration, haemoglobin concentration, presence of hypercholesterolaemia, and alanine aminotransferase level;
- glomerular filtration rate (GFR) measured according to the Modification of Diet in Renal Disease formula: GFR (mL/min/1.73 m^2) = 175 × (serum creatinine)$^{-1.154}$ × (age)$^{-0.203}$ × (0.742 if female);
- use of cardiovascular drugs: diuretics, β-blockers, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, aldosterone antagonists, and acetylsalicylic acid;
- dose of furosemide; in patients taking torasemide, the dose was calculated using the conversion of 1 mg torsemide to 2 mg of furosemide;
- procedure-related data: upgrade or de novo implantation of a CRT-pacing or CRT-defibrillation device.

Measures of clinical outcome

The primary endpoint was all-cause mortality, and the secondary endpoint was all-cause mortality and HF-related hospitalisations. Data concerning mortality and hospitalisations were collected through medical records from our outpatient department (where most CRT patients were followed regularly at six- to ten-month intervals) as well as through the analysis of all available medical documentation and phone interviews with patients and their relatives. In the absence of any contact with a patient or their family, the survival status was determined from the national Polish PESEL registry. Urgent heart transplantation was classified as death.

Statistical analysis

Continuous variables are presented as means and standard deviations, and categorical variables as numbers and percentages. Survival time distribution was visualised using the Kaplan-Meier curves. The risk score was constructed from multivariate Cox proportional hazards (CPH) model (more methodological details are given in the results section). There were no significant violations of the proportionality assumption that underlies the CPH method. The discriminative power of the Cox model was measured using Harrell's C-statistic. All statistical analyses were performed using R 3.4 software, with p-values < 0.05 considered significant.

RESULTS

During the study, 590 patients underwent CRT device implantation procedures. Of these, 38 were excluded due to the following reasons: unsuccessful LV lead implantation (15 patients; success rate of 97.5%), incomplete medical records (eight patients), late LV lead repositioning/loss of CRT (five patients), upgrade to triple site pacing (two LV

Table 1. Basic patient characteristics

Basic clinical data and comorbidities:	
Age [years]	67.8 ± 10.4
Male sex	451 (81.7)
BMI [kg/m^2]	28.3 ± 3.9
Permanent atrial fibrillation	156 (28.3)
Diabetes mellitus	243 (44.0)
Hypertension	406 (73.6)
Heart failure-related data:	
Ischaemic aetiology	349 (63.2)
NYHA functional class:	
Class II	47 (8.5)
Class III	434 (78.6)
Class IV	71 (12.9)
Electrocardiographic and echocardiographic data:	
LBBB (Strauss)	226 (40.9)
QRS duration [ms]	172.7 ± 33.1
LVEF [%]	24.3 ± 6.8
LVEDD [mm]	69.4 ± 9.4
Mitral regurgitation grade > 3	52 (9.4)
Biochemical data:	
Sodium [mmol/L]	138.6 ± 3.54
ALAT [U/L]	29.0 ± 18.9
Hypercholesterolaemia	355 (64.3)
Haemoglobin [g/dL]	13.7 ± 1.6
Pharmacological therapy:	
ACEI/ARB	479 (86.6)
β-blocker	524 (94.9)
Aldosterone	362 (65.6)
ASA	426 (77.2)
Loop diuretic	511 (92.6)
Furosemide dose [mg]	73.2 ± 63.4
Procedure-related data:	
Device upgrade	145 (26.3)
CRT-P device	247 (44.7)

Data are presented as number (percentage) or mean ± standard deviation. ACEI/ARB — angiotensin converting enzyme inhibitor/angiotensin receptor blocker; ALAT — alanine aminotransferase; ASA — acetylsalicylic acid; BMI — body mass index; CRT-P — cardiac resynchronisation therapy-pacing; LBBB — left bundle branch block; LVEF — left ventricular ejection fraction; LVEDD — left ventricular end-diastolic diameter; NYHA — New York Heart Association

leads; seven patients), and implementation of a non-standard resynchronisation type (direct His bundle pacing, dual-site right ventricular pacing; three patients). Thus, data from 552 patients were used for the long-term outcome assessment. Baseline characteristics of these patients are presented in Table 1.

During the nine years of observation (average follow-up time of 46 ± 28 months), 232 patients met the primary endpoint of death from any cause or urgent heart transplantation. There were 101 deaths due to HF worsening, and 23 sudden deaths, with four patients undergoing urgent heart transplantations. Eighteen deaths were classified as non-HF cardiac in nature and 44 as non-cardiac. The cause of death could not be determined in the remaining 42 patients. The survival rates at the end of years 1–7 were 89.7%, 80.7%, 70.6%, 63.6%, 57.2%, 52.7%, and 46.9%, respectively. During the same time period, 128 patients required unplanned hospitalisation for HF-related reasons, 132 were hospitalised for other cardiac-related reasons, and 107 were hospitalised for non-cardiac reasons. Of the 128 patients suddenly hospitalised for HF-related reasons, 68 patients eventually died. Thus, 292 patients met the composite endpoint of all-cause death or hospitalisation for HF.

Outcome predictors and the AL-FINE CRT risk score construction

Several of the analysed variables had prognostic value. Results of the univariate and multivariate Cox analyses for the all-cause mortality and all-cause mortality or HF hospitalisation are presented in Tables 2 and 3. The predictive model including all variables had a C-statistic of 0.716 for all-cause mortality and 0.693 for the secondary endpoint. Initially, in order to build a new risk score, we calculated Cox models with all possible subsets of two to six predictors. The resulting models with predictive abilities similar to the full model were then assessed using clinical knowledge. The model with both high C index (0.713 for and 0.682 for the primary and secondary endpoints, respectively) and clinically most meaningful/practical predictors was selected as the final one. AL-FINE is the acronym for the six predictors included in the final model: **A**ge, non-**L**BBB morphology, **F**urosemide dose, **I**schaemic aetiology, **N**YHA class, and left ventricular **E**F. These were the variables responsible for 99.6% of the prognostic power of the model (for all-cause mortality) that included all variables. To further simplify the risk assessment, continuous predictors incorporated in the model were transformed into categorical variables using arbitrary cut-off points. Kaplan-Meier survival curves for all-cause mortality for all six variables are presented in Figure 1. Each of these unfavourable characteristics was then assigned one AL-FINE CRT risk score point. This resulted in a major simplification at a minimal cost to the predictive power as shown by C-statistics of 0.701 and 0.661 for the primary and secondary endpoints, respectively (Table 4). All-cause mortality increased with the accumulation of the risk factors. Hazard ratio for 2 or 3–6 AL-FINE score points (calculated vs. 0–1 points) was 2.45 (95% confidence interval [CI] 1.66–3.61, $p < 0.001$), and 4.72 (95% CI 3.28–6.80, $p < 0.001$), respectively. Depending on the number of AL-FINE score points, overall mortality at

Table 2. Predictors of all-cause mortality and all-cause mortality or heart failure-related hospitalisation in univariate Cox analysis

Predictor	All-cause mortality		All-cause mortality/HF hospitalisation	
	HR (95% CI)	p	HR (05% CI)	p
LBBB (Strauss)	0.84 (0.65–1.09)	0.197	0.53 (0.41–0.68)	< 0.001
Age (per 10 years)	1.31 (1.14–1.49)	< 0.001	1.17 (1.04–1.31)	0.010
Male sex	1.13 (0.79–1.63)	0.494	1.04 (0.76–1.42)	0.823
Ischaemic aetiology	1.51 (1.14–1.99)	0.004	1.34 (1.05–1.70)	0.019
NYHA class > 3	2.48 (1.88–3.28)	< 0.001	2.06 (1.60–2.64)	< 0.001
Persistent AF	0.90 (0.67–1.21)	0.472	1.09 (0.84–1.40)	0.519
LVEF (per 10%)	0.72 (0.59–0.88)	0.001	0.79 (0.67–0.95)	0.010
LVEDD (per 10 mm)	1.08 (0.94–1.24)	0.290	1.07 (0.94–1.21)	0.315
Severe mitral insufficiency	1.17 (1.02–1.35)	0.030	1.25 (1.10–1.42)	0.001
Diabetes mellitus	1.30 (1.00–1.68)	0.048	1.36 (1.08–1.71)	0.008
eGFR (per 10 mL/min/1.73 m^2)	0.92 (0.87–0.98)	0.011	0.91 (0.86–0.96)	0.001
Hypercholesterolaemia	0.80 (0.62–1.05)	0.111	0.85 (0.67–1.08)	0.172
BMI (per 5 kg/m^2)	0.78 (0.67–0.91)	0.001	0.93 (0.82–1.06)	0.269
Hypertension	0.92 (0.69–1.22)	0.562	1.20 (0.92–1.56)	0.169
Preimplantation QRS (per 50 ms)	0.98 (0.80–1.19)	0.828	0.88 (0.73–1.05)	0.149
Furosemide daily dose (per 50 mg)	1.42 (1.31–1.54)	< 0.001	1.41 (1.31–1.52)	< 0.001
Haemoglobin (per 1 g/dL)	0.94 (0.87–1.02)	0.148	0.94 (0.87–1.01)	0.074
Sodium (per 5 mmol/L)	0.72 (0.60–0.86)	< 0.001	0.77 (0.66–0.90)	0.001
ALAT (per 10 IU/L)	1.05 (0.98–1.12)	0.173	1.07 (1.01–1.14)	0.028
ASA	1.22 (0.87–1.69)	0.249	0.97 (0.73–1.28)	0.827
ARB	0.76 (0.45–1.29)	0.308	0.70 (0.44–1.13)	0.147
ACEI	0.93 (0.68–1.27)	0.633	0.94 (0.71–1.25)	0.685
β-blocker	0.45 (0.27–0.74)	0.002	0.61 (0.38–0.98)	0.040
Diuretic	3.75 (1.77–7.98)	0.001	5.14 (2.42–10.89)	< 0.001
Aldosterone antagonist	1.02 (0.77–1.35)	0.872	0.98 (0.76–1.25)	0.863
Device upgrade	1.35 (1.02–1.79)	0.036	1.33 (1.03–1.71)	0.027
CRT-P	0.84 (0.65–1.09)	0.192	0.89 (0.70–1.12)	0.308

AF — atrial fibrillation; CI — confidence interval; EF — ejection fraction; eGFR — estimated glomerular filtration rate; HF — heart failure; HR — hazard ratio; other abbreviations — see Table 1

Table 3. Significant predictors of all-cause mortality and all-cause mortality or heart failure-related hospitalisation in multivariate Cox analysis

Predictor*	All-cause mortality		All-cause mortality or HF hospitalisation	
	HR (95% CI)	p	HR (95% CI)	p
LBBB (Strauss)	0.67 (0.48–0.94)	0.019	0.66 (0.49–0.89)	0.007
Age (per 10 years)	1.41 (1.19–1.67)	< 0.001	1.10 (0.95–1.28)	0.203
NYHA class > 3	1.90 (1.41–2.58)	< 0.001	1.56 (1.19–2.05)	0.001
Persistent AF	0.63 (0.45–0.87)	0.006	0.75 (0.57–1.00)	0.046
LVEF (per 10%)	0.75 (0.60–0.95)	0.016	0.82 (0.67–1.00)	0.054
Preimplantation QRS (per 50 ms)	0.78 (0.60–1.00)	0.047	0.76 (0.61–0.94)	0.012
Furosemide daily dose (per 50 mg)	1.25 (1.12–1.39)	< 0.001	1.21 (1.10–1.33)	< 0.001
Sodium (per 5 mmol/L)	0.82 (0.69–0.98)	0.032	0.86 (0.73–1.01)	0.070
β-blocker	0.50 (0.29–0.87)	0.013	0.79 (0.47–1.33)	0.377
Loop diuretic	2.13 (0.97–4.70)	0.060	3.10 (1.43–6.75)	0.004

*Multivariate Cox model included all predictors listed in Table 2; abbreviations — see Tables 1 and 2

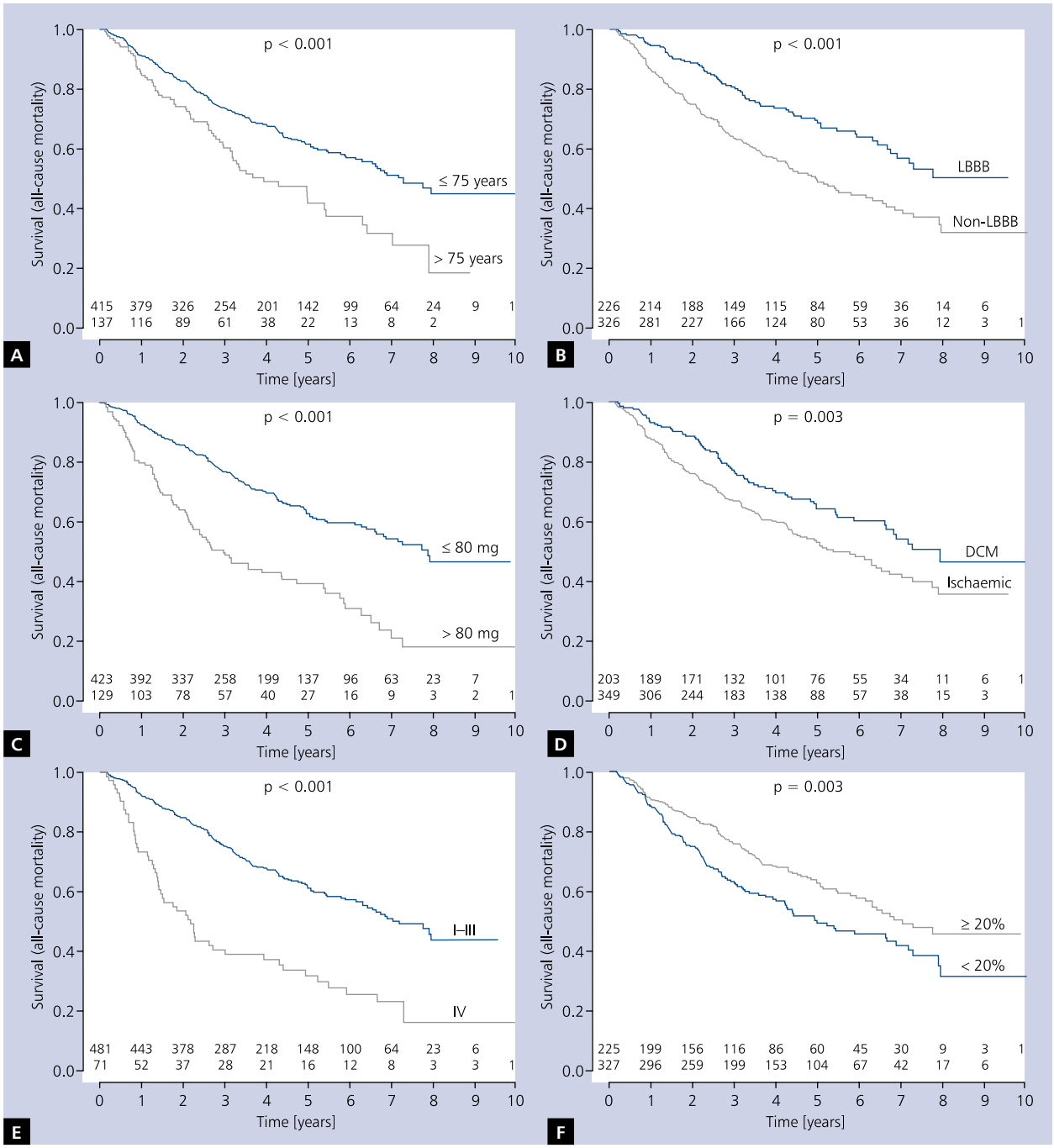

Figure 1. Kaplan-Meier survival curves for all-cause mortality. The six variables selected for the AL-FINE CRT score: **A**ge, non-**L**BBB morphology, **F**urosemide dose, **I**schaemic aetiology, **N**YHA class, and left ventricular **E**F. **A.** Age; **B.** Left bundle branch block (LBBB; Strauss); **C.** Furosemide dose; **D.** Aetiology; **E.** New York Heart Association class; **F.** Left ventricular ejection fraction; DCM — dilated cardiomyopathy

seven years was within the range of 28% to 74%. Similarly, for the secondary endpoint, the risk also increased with the number of AL-FINE CRT risk score points: HR of 2.21 (95% CI 1.60–3.06, $p < 0.001$) and 3.41 (95% CI 2.51–4.64, $p < 0.001$), for 2 or 3–6 AL-FINE score points, respectively. Figures 2 and 3 demonstrate Kaplan-Meier survival curves for 0–1, 2, and 3–6 AL-FINE score points for all-cause mortality and all-cause mortality or HF-related hospitalisation, respectively. Additionally, a Kaplan-Meier survival curve for the preimplantation QRS duration > 150 ms was calculated (**Suppl. Fig. 1 — see journal website**) because this is a widely recognised prognostic parameter in CRT patients.

Table 4. AL-FINE CRT risk score predictors in multivariate Cox analysis

Predictor	All-cause mortality		All-cause mortality or HF hospitalisation	
	HR (95% CI)	p	HR (95% CI)	p
Age > 75 years	1.68 (1.25–2.25)	0.001	1.30 (0.99–1.71)	0.056
Non-**L**BBB (Strauss)	1.62 (1.22–2.16)	0.001	1.76 (1.37–2.27)	< 0.001
Furosemide dose > 80 mg/day	2.01 (1.50–2.69)	< 0.001	2.03 (1.56–2.65)	< 0.001
Ischaemic aetiology	1.40 (1.04–1.88)	0.025	1.19 (0.92–1.54)	0.184
NYHA class 4	1.95 (1.40–2.73)	< 0.001	1.58 (1.15–2.16)	0.004
EF < 20%	1.60 (1.19–2.14)	0.002	1.37 (1.04–1.79)	0.023

Abbreviations — see Tables 1 and 2

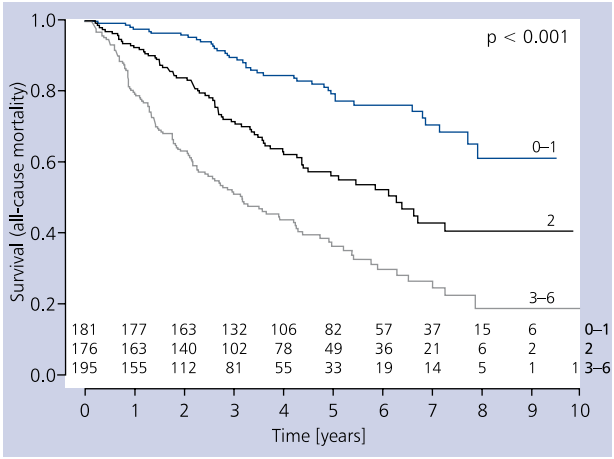

Figure 2. Kaplan-Meier survival curves for all-cause mortality based on the number of AL-FINE CRT score points

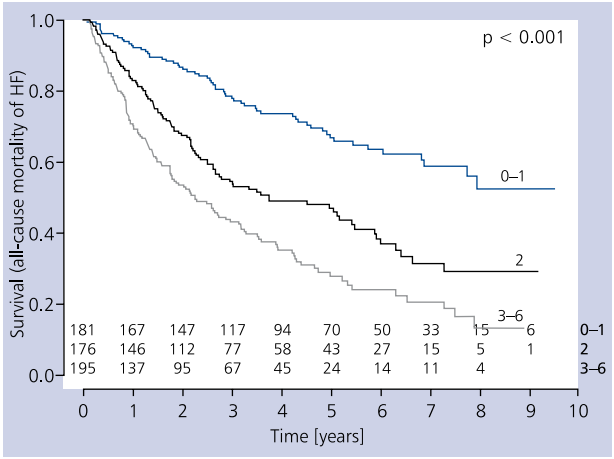

Figure 3. Kaplan-Meier survival curves for all-cause mortality or heart failure (HF)-related hospitalisation based on the number of AL-FINE CRT score points

DISCUSSION

The major finding of the current study was that the constructed prognostic AL-FINE CRT score was based on simple, readily available clinical variables and was capable of predicting prognosis in CRT patients at the preimplantation stage. This allows stratification of patients into those with good (seven-year survival rate: 72%), intermediate, and poor prognosis (seven-year survival rate: 26%).

Predictors of mortality used in the AL-FINE CRT score

Age

Age is a recognised prognostic factor in HF. In the ESC-HF Long-Term Registry, mortality rates in patients > 75 years old were over two times higher than in patients < 65 years old [11]. In the MADIT-CRT cohort, which included patients with mild HF, patients > 74 years old did not benefit from CRT in terms of lower mortality in a long-term observation [12]. In the current study, age > 75 years significantly and independently predicted a worse survival. In patients with more advanced HF or more comorbidities, the impact of age might be even more pronounced. The combination of older age and any two other high-risk characteristics in our study placed patients in the group with the lowest survival rate.

LBBB

Left bundle branch block is considered a major prognostic factor in HF patients [13, 14]. However, while LBBB is a marker of a worse prognosis in patients not treated with CRT, in CRT patients, the presence of LBBB is associated with better prognosis. This reflects the specificity of resynchronisation therapy, which is based on correcting asynchronous contraction caused by LBBB, and, in its essence, it is aimed at "curing" LBBB. For this to occur, LBBB needs to be present. Of note, LBBB was a better prognostic factor than preimplantation QRS duration > 150 ms (**Suppl. Fig. 1 — see journal website**). However, not all studies confirm the importance of LBBB morphology. We believe that this is related to the differences in LBBB definitions, precision in ECG assessment, and differences in acute outcome of the procedure (presence

of acute QRS narrowing, i.e. correction of LBBB). It was recently shown by us and others that long-term survival in CRT patients depends greatly on the applied LBBB definition [13, 15]. Various LBBB definitions result in diagnosing LBBB in significantly different groups of patients, and this leads to different prognostic values. It is unfortunate that some studies aimed at the construction of a CRT score did not even specify the definition used for diagnostic or prognostic purposes in their study [2, 5]. It seems that the recently proposed Strauss criteria are the best method for identification of patients with a true LBBB, i.e. those with baseline potential to favourably respond to biventricular pacing. In the current study, the lack of LBBB morphology according to the Strauss criteria plus any other two disadvantageous characteristics at the preimplantation stage identified patients with a high mortality risk, perhaps because CRT cannot influence the natural course of HF in such patients.

Heart failure aetiology

Several studies found that ischaemic aetiology of HF is related to a lesser benefit from CRT in terms of reverse remodelling when compared to patients with idiopathic cardiomyopathy [16, 17]. Conversely, non-ischaemic aetiology was among the strongest factors associated with reverse remodelling following CRT in the MADIT-CRT cohort [18]. When known relationships between reverse remodelling and mortality are taken into consideration, it is not surprising that ischaemic aetiology is associated with worse survival. Such a relationship was present in the current study and was reported previously by others. Notably, a meta-analysis based on five randomised CRT trials reported HR of 1.64 for all-cause mortality for ischaemic aetiology [19]. The negative impact of ischaemic aetiology on CRT outcomes might reflect the fact that the presence of post-myocardial infarction scarring results in some degree of non-reversible asynchrony or lower contribution of asynchrony to the systolic dysfunction of the left ventricle. Myocardial scarring is also probably linked with ineffective biventricular pacing (e.g. latency and the resulting wide LV-paced QRS complexes with ensuing small contributions of LV activation to the biventricular QRS complex and LV contraction) [20, 21].

NYHA functional class IV

Despite the fact that the NYHA functional class is a rather crude and subjective assessment of symptoms, it was shown to predict mortality in chronic HF in several studies [22, 23]. The impact of the NYHA functional class on mortality in CRT patients was less thoroughly investigated; however, it can be easily appreciated when mortality in CRT trials that included NYHA class III–IV patients (COMPANION, MIRACLE, CARE-HF) and trials that predominantly included patients in NYHA class I–II (MADIT-CRT, RAFT) is compared. Moreover, in three of the previous CRT scores, NYHA class was the strongest predictor of mortality in multivariate analysis [2, 5, 24]. Similarly, in the current study the highest assigned NYHA class was on par with the furosemide dose as the strongest predictor of long-term mortality and morbidity.

LVEF

Studies involving general HF patients showed contradictory results with regard to the prognostic value of echocardiographic LVEF. This might reflect the inaccuracy of measuring EF by echocardiography [25]. However, in CRT cohorts, the prognostic importance of LVEF was confirmed by several studies [2, 5, 7, 24, 26], and our results are concordant with these in this respect. Hypothetically, EF might be prognostically more important in CRT patients due to the fact that in patients with a low EF, the magnitude of correctable dyssynchrony might be smaller, resulting in a markedly worse response to CRT.

Dose of loop diuretic

Loop diuretics are commonly used in symptomatic patients with HF to prevent fluid retention and to control symptoms. The current guidelines assigned class I recommendations for such treatment in patients with signs or symptoms of hypervolaemia. A meta-analysis has shown that in patients with chronic HF, diuretics reduce the risk of death [27]. However, several studies have shown that higher diuretic doses are associated with worse survival [28–30], suggesting that the furosemide dose might be a potent prognostic factor that is rarely considered or reported. We believe that the prognostic value of a loop diuretic dose comes from it being a marker of HF severity and from the higher prevalence of concomitant illnesses, as some studies have suggested [31]. However, a reverse association was also discussed: diuretics could worsen the HF course by activating neuroendocrine systems, renin-angiotensin-aldosterone, and renal dysfunction that together facilitate disease progression [32]. A cut-off dose of 80 mg furosemide per day to define a high and low loop diuretic dose, used for prognostic purposes in the current study, was already proposed and was associated with a worse outcome in previous studies [32–34]. Our study is the first to show the prognostic importance of the furosemide dose in CRT patients. Of note, in every potential CRT candidate, this variable is easy to obtain at no extra cost.

Other multiparametric CRT scores

Most previous CRT studies have focused on isolated risk factors such as HF aetiology or QRS morphology, and only a few recent studies proposed multiparametric risk scores dedicated to the assessment of CRT patients (EAARN, VALID-CRT, CRT-SCORE, and L_2ANDS_2). Only two of these scores (EAARN and CRT-SCORE) are applicable, like the AL-FINE CRT score, for preimplantation assessment of long-term (i.e. > five years) overall mortality risk. Also, some general prognostic scores can be used for CRT patients, e.g. the Seattle Heart Failure Model. However, with the exception of the EAARN score, they are rather complicated and therefore less practical for everyday

application because they include up to 23 parameters (and/or some require dedicated applications or calculators for score determination). Despite simplification, the predictive power of our score (Harrel C-statistic of 0.701) does not seem to be inferior to the other scores. The VALID-CRT score reported a C-statistic of 0.70, the CRT-SCORE had an area under the curve (AUC) of 0.748, and the AUC of the Seattle Heart Failure Model equalled 0.64 [2, 35]. Apart from simplicity, another distinct feature of our score is the attention to pre-implantation QRS morphology. It is the unique study that applied the new, more precise definition of LBBB (Strauss criteria), which is known to impact long-term prognosis by identifying patients with the greatest potential for response to biventricular pacing.

Clinical application

In order to enhance the implementation in clinical practice, the proposed risk score was simplified to include as few as six readily available and straightforward variables. These variables have been shown to be related with a poor outcome in other studies and were also included in other more complex CRT scores [2, 5, 35], which strongly suggests their universal applicability to other CRT populations. We believe that the AL-FINE CRT risk score may positively impact the management of CRT patients at all stages of care. At the preimplantation stage, patient selection is of the utmost importance. Regarding the cost-effectiveness and complication burden, CRT should preferentially be proposed to potential responders. An AL-FINE score of 0 points was related to a seven-year survival rate of 72%, while in patients with high-risk characteristics (two or more points) the survival rate at seven years was only 26%. Estimation of life expectancy after a CRT procedure is part of the initial assessment at the preimplantation stage. A high-risk score should alert both the physician and the patient to assess the long-term benefit of the procedure more realistically. High-risk scores could also be useful later, at the implantation stage, to identify "special care" patients, in whom the implantation procedure could require more experienced implanters in order to maximise the benefit. Achievement of technically correct LV capture might not be an adequate endpoint of the procedure in such patients. Perhaps extra measures should be implemented on an obligatory basis in order to improve the outcome. This could include more meticulous LV lead positioning guided by local delay mapping, LV-paced QRS morphology assessment, and acute QRS shortening.

At the postimplantation stage, a high AL-FINE CRT score might identify patients that require more frequent follow-up visits and also, perhaps, early revision of the pacing strategy in case of a lack of response, i.e. echocardiographic optimisation of pacing parameters, upgrade to His bundle pacing, or deactivation of the BiV pacing in patients with persistent QRS prolongation (presumed desynchronisation effect).

The retrospective nature of the study and inclusion of patients at a single centre may have introduced bias. However, our cohort was representative of patients who underwent CRT implantation in different studies, and the mortality rate was within the expected range.

In conclusion, a novel, multiparametric CRT risk score was constructed on the basis of simple and recognised clinical, electrocardiographic, and echocardiographic parameters that show a significant add-on effect on mortality in this specific population. Clinical application of the AL-FINE risk score might be beneficial and warrants validation in other CRT cohorts.

Conflict of interest: *none declared*

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WHAT IS NEW?

The paper presents the design and assessment of the AL-FINE CRT score, a novel multiparametric prognostic score for the estimation of the risk of all-cause death and the combined endpoint of death and heart failure hospitalisation in cardiac resynchronisation therapy (CRT) patients. It is based on six simple and easily available parameters that cover major clinical and physiological domains known to have an impact on heart failure morbidity and overall mortality in this population. It is one of the few scoring systems enabling the assessment of CRT patients at the preimplantation stage and the only one that includes two powerful prognostic predictors: the presence of true left bundle branch block according to the Strauss criteria and the use of high-dose loop diuretics. This is the only CRT score that was built and assessed on the basis of a Polish CRT cohort.