Risk Factors for Short-Term Versus Long-Term Mortality in Patients Who Underwent Cardiac Resynchronization Therapy

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Cardiac resynchronization therapy (CRT) is an effective therapy in selected patients with advanced heart failure that reduces all-cause mortality at short-term follow-up. However, data regarding long-term mortality after CRT implantation are scarce, with no separate analysis available of the covariates associated with respectively short-term and long-term outcomes. Accordingly, the present study evaluated the risk factors associated with short-term (2-year follow-up) versus long-term (10-year follow-up) mortality after CRT implantation. Patients who underwent CRT implantation and had echocardiographic evaluation before implantation were included in the present study. The primary end point was all-cause mortality, and independent associates of short-term (2-year follow-up) and long-term (10-year follow-up) mortality were compared. In total, 894 patients (mean age 66 ± 10 years, 76% males) who underwent CRT implantation were included in the present study. The cumulative overall survival rates for the total population were 91%, 71%, and 45% at 2-, 5- and 10-year follow-up, respectively. Multivariable Cox regression analysis showed that short-term mortality was associated with both clinical and echocardiographic variables at the moment of CRT implantation; whereas long-term mortality was predominantly associated with baseline clinical parameters and was less strongly associated with baseline echocardiographic parameters. In conclusion, at long-term (10-year) follow-up, a significant proportion (45%) of patients with advanced heart failure who underwent CRT implantation were still alive. Importantly, the risk assessment for short-term (2-year follow-up) and long-term (10-year follow-up) mortality differ considerably, which may influence clinical decision making. **(Am J Cardiol 2023;197:34−41)**

Introduction

Patients diagnosed with heart failure (HF) and severe left ventricular (LV) systolic dysfunction (LV ejection fraction [LVEF] ≤35%) and prolonged QRS duration ≥130 ms, who remain symptomatic despite optimal medical therapy (New York Heart Association [NYHA] functional class II, III, and ambulatory IV), benefit from cardiac resynchronization therapy (CRT).[1] Several randomized controlled trials have shown that, in these well-selected patients, CRT results in improved exercise capacity, a better quality of life, and echocardiographic reverse remodeling, which is associated with better overall survival.[1−4] When evaluating outcomes, clinical trials have mainly focused on short-term outcomes after CRT implantation and identifying predictors of survival at 2- or 3-year follow-up.[4,5] The COMPANION (Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure) trial showed that QRS duration, left bundle branch block, and an ischemic etiology of HF was associated with all-cause mortality at short-term follow-up.[5] Furthermore, the MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial−Cardiac Resynchronization Therapy) trial has shown that, even in mildly symptomatic patients, over an average follow-up of 2.4 years, women and patients with a longer QRS duration experienced a greater benefit of CRT in combination with an implantable defibrillator (CRT-D).[6] However, limited data exist on long-term outcomes after CRT implantation. Accordingly, the aims of this study were 1) to assess long-term all-cause mortality (up to 10 years) in patients who underwent CRT implantation; and 2) to evaluate the

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baseline clinical and echocardiographic covariates associated with long-term versus short-term overall survival.

Methods

Patients diagnosed with HF who received CRT (de novo or upgrade), between 1999 and 2014, according to prevailing guidelines[1] and with a QRS duration ≥130 ms, were included in a single-center registry of the Leiden University Medical Center (Leiden, The Netherlands). Demographic and clinical data were retrospectively collected from the Departmental Cardiology Information System (EPD-Vision, Leiden University Medical Center). This retrospective analysis was approved by the institutional review board of the Leiden University Medical Center and they waived the need for patient written informed consent. The study complies with the Declaration of Helsinki, as revised in 2013.

Demographic, clinical, and laboratory variables were evaluated before CRT implantation. Demographic characteristics included age, gender, and body mass index. Clinical characteristics included cardiovascular risk factors, relevant medical history and co-morbidities, functional status (NYHA class), and HF medication. Ischemic etiology of HF was defined as significant coronary artery disease on invasive coronary angiography.

All patients underwent complete transthoracic echocardiography before CRT implantation. Transthoracic echocardiographic data were acquired at rest, according to current guidelines, using commercially available equipment (Vivid 7, E9, and E95 systems, GE-Vingmed, Horten, Norway) and images were digitally stored for offline analysis (EchoPAC versions 113.0.3, 202 and 203; GE-Vingmed).[7–9] ECG-triggered M-mode, 2-dimensional, and Doppler data were acquired at rest, according to current guidelines. From the apical 4-chamber and 2-chamber views, LV volumes were measured and LVEF was quantified using the biplane Simpson's method.[8] Left atrial volume was measured using the biplane method at end-systole on the apical 4-chamber and 2-chamber views and indexed for body surface area.[8] Right ventricular systolic function was evaluated by the tricuspid annular plane systolic excursion, measured on M-mode recordings of the lateral tricuspid annulus. Furthermore, integrative assessment of mitral and tricuspid regurgitation severity was performed through a multiparametric approach including qualitative, semiquantitative, and quantitative parameters evaluated on color, continuous, and pulsed wave Doppler data and was graded according to current guidelines.[7,9] Systolic pulmonary artery pressure was estimated from the tricuspid regurgitation peak velocity, applying Bernoulli's equation and adding right atrial pressure.[7]

Implantation of the CRT device was performed according to a standard approach; insertion of the right atrial and ventricular leads by way of the subclavian or cephalic veins. The LV pacing lead was introduced into the coronary sinus through an 8 Fr guiding catheter, and positioned in a posterior or posterolateral vein, if possible. Posterior or lateral position was achieved in 654 patients (87%) with information available on lead placement. All leads were connected to a dual-chamber, CRT without an implantable defibrillator (CRT-P), or CRT-D device. CRT recipients were followed up at regular intervals at the outpatient HF clinic. After implantation, atrioventricular and interventricular delays were empirically set at 120 to 140 ms and 0 ms, respectively. CRT optimization was performed during follow-up visits at the discretion of the treating physician.

The primary end point of the study was all-cause mortality. Outcomes were analyzed from the time of baseline echocardiography until death or last follow-up in April 2021. Additionally, all-cause mortality was analyzed at 2 time points: after 2-year follow-up (short-term outcomes) and after 10-year follow-up (long-term outcomes). Survival data were ascertained from the departmental Cardiology Information System linked to the Social Security Death Index and were completed for all patients.

Continuous variables are presented as mean ± SD when normally distributed and as median and interquartile range (IQR) when not normally distributed. Categorical variables are presented as frequencies and percentages.

The Kaplan-Meier survival analysis was performed to estimate survival rates. To investigate the association between different clinical and echocardiographic variables with all-cause mortality, univariable and multivariable Cox proportional hazards regression models were performed for short-term (2-year follow-up) and long-term mortality (10-year follow-up). Variables with a $p < 0.10$ on the univariable analysis were included in the multivariable model. Furthermore, the number of missing values of the variables included in the multivariable regression analysis did not exceed 10% of the total study population. The low number of events for short-term mortality limited the number of variables that could potentially be included to avoid overfitting the multivariable model. Therefore, 3 different models were created: (1) clinical variables that were significant on univariable analysis; (2) echocardiographic variables that were significant on univariable analysis; (3) a combination of clinical and echocardiographic variables that were significant in Models 1 or 2. Hazard ratios with 95% confidence intervals (CI) were calculated and results were presented as forest plots. All statistical tests were 2-sided, and a $p < 0.05$ was considered statistically significant. All data were analyzed using SPSS for Windows, version 23.0 (SPSS Inc, IBM Corp, Armonk, New York).

Results

A total of 894 patients (mean age 66 ± 10 years, 76% men) were included in the current analysis. Clinical and echocardiographic characteristics of the overall population are listed in Tables 1 and 2. Overall, 500 patients (56%) had an ischemic etiology of HF and 621 patients (70%) were in NYHA III to IV. A total of 622 patients (70%) had sinus rhythm and mean QRS duration was 168 ± 26 ms, with 543 patients (61%) having left bundle branch block. Most patients (850 [95%]) received CRT-D. The mean LVEF was 26 ± 8%, with a mildly dilated left atrium, borderline-normal pulmonary artery systolic pressure, and preserved right ventricular systolic function. Moreover, 345 patients (42%) had moderate-to-severe mitral regurgitation and 174 patients (25%) had moderate-to-severe tricuspid regurgitation.

Table 1
Baseline clinical variables of the overall population

	Overall population (n=894)
Demographic characteristics	
Age, years	66±10
Male gender, n	680 (76%)
Body mass index, kg/m^2	26.5±4.3
Medical history	
Arterial hypertension, n	401 (45%)
Diabetes mellitus, n	180 (20%)
Dyslipidemia, n	361 (40%)
Smoking, n	371 (42%)
Ischemic etiology, n	500 (56%)
NYHA III, n	621 (70%)
History of ventricular tachycardia, n	128 (14%)
ECG characteristics prior to CRT implantation	
Rhythm, n	
Sinus rhythm	622 (70%)
Atrial fibrillation	147 (16%)
Atrial pacing	125 (14%)
QRS morphology, n	
Left bundle branch block	543 (61%)
Right bundle branch block	103 (12%)
Intra-ventricular conduction delay	70 (8%)
Ventricular pacing	178 (20%)
QRS duration, ms	168±26
Laboratory values	
Hemoglobin, g/100 ml	13.4±1.6
eGFR - MDRD, ml/min/1.73 m^2	65.1±23.9
Medication	
Loop diuretic, n	724 (81%)
MRA, n	397 (44%)
β-blocker, n	650 (73%)
RAAS-inh, n	793 (89%)
Statin, n	530 (59%)

Values are mean ± SD, median (IQR), or n (%).
eGFR-MDRD = estimated glomerular filtration rate − modification of diet in renal disease; IQR = interquartile range; MRA = mineralocorticoid receptor antagonist; NYHA = New York Heart Association; RAAS-inh = renin-angiotensin-aldosterone system inhibitor.

Table 2
Baseline echocardiographic variables of the overall population

	Overall population (n=894)
Left-sided echocardiographic variables	
Left ventricular end-diastolic volume - indexed, ml/m^2	107±39
Left ventricular end-systolic volume - indexed, ml/m^2	79±35
Left ventricular ejection fraction, %	26±8
Left atrial volume indexed, ml/m^2	41 (31−53)
Moderate or severe mitral regurgitation, n	345 (42%)
Right-sided echocardiographic variables	
Right ventricular basal diameter, mm	42±9
Tricuspid annular plane systolic excursion, mm	16±5
Right atrial maximum area - indexed, cm^2/m^2	9 (7−12)
Moderate or severe tricuspid regurgitation, n	164 (23%)
Pulmonary artery systolic pressure, mm Hg	33 (26−43)

Values are mean ± SD, median (IQR), or n (%).
IQR = interquartile range.

After a median follow-up of 94 months (IQR: 52 to 143), 563 patients (63%) died. The Kaplan-Meier curve for the 10-year overall survival is shown in Figure 1. At 2-, 5- and 10-year follow-up, there were respectively 80 deaths (9%), 259 deaths (29%), and 484 deaths (54%). A landmark analysis was performed of all patients who were still alive 5 years after CRT (Figure 1), showing 10- and 15-year cumulative survival rates of 63.6% and 43.1%, respectively.

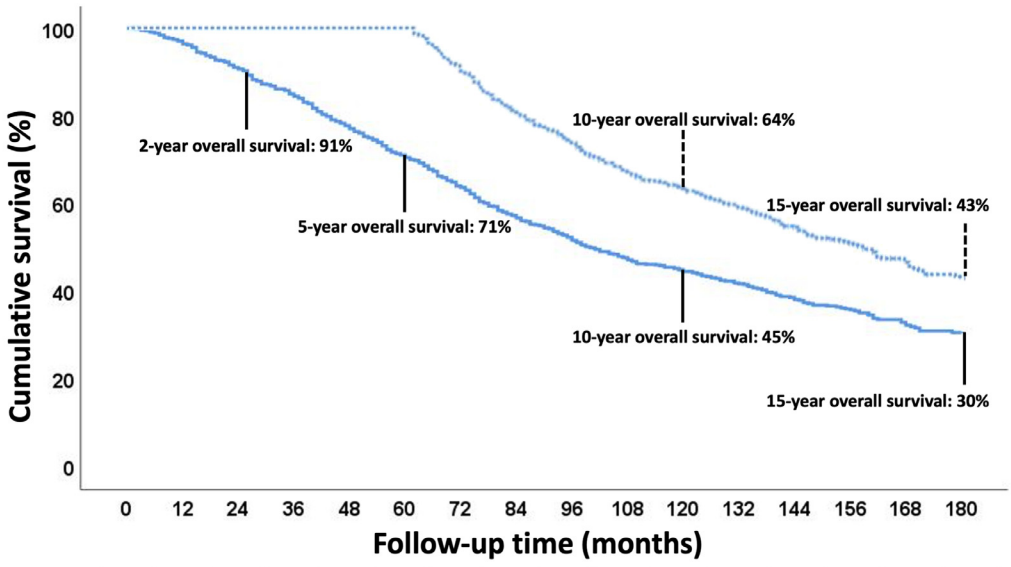
Univariable and multivariable Cox regression analyses for short-term and long-term all-cause mortality are presented in Figure 2, Tables 3 and 4. Multivariable Cox regression analysis for short-term all-cause mortality (describing the clinical variables, model 1) showed that an ischemic etiology of HF, NYHA III or IV, atrial fibrillation, shorter QRS duration, and more impaired renal function was independently associated with all-cause mortality. The following echocardiographic variables (model 2) were independently associated with all-cause mortality: larger LV end-systolic volume, larger right ventricular basal diameter, larger maximal right atrial area, and the presence of moderate or severe tricuspid regurgitation. The combination (model 3) of significant clinical (model 1) and echocardiographic (model 2) variables showed that an ischemic etiology of HF, shorter QRS duration, more impaired renal function, larger LV end-systolic volume, larger right ventricular basal diameter, and a larger maximal right atrial area remained independently associated with all-cause mortality at short-term follow-up.

Multivariable Cox regression analysis for long-term all-cause mortality showed an independent association for older age, lower body mass index, diabetes mellitus, an ischemic etiology of HF or NYHA III or IV, a history of ventricular tachycardia, shorter QRS duration, more impaired renal function, larger LV end-systolic volume, and impaired right ventricular systolic function with all-cause mortality.

Discussion

The main findings of the present study are: (1) the 10-year overall survival rate of patients who underwent CRT implantation is 45%; (2) short-term survival (2-year follow-up) is related to both clinical and echocardiographic parameters (ischemic etiology of HF, shorter QRS duration, more impaired renal function, and larger LV, right ventricular, and right atrial size) at the time of CRT implantation. Conversely, long-term survival (10-year follow-up) is predominantly associated with clinical factors and cardiovascular co-morbidities, and less strongly associated with baseline echocardiographic parameters (older age, lower body mass index, presence of diabetes mellitus, ischemic etiology of HF, NYHA III or IV, a history of ventricular tachycardia, shorter QRS duration, more impaired renal function, larger LV end-systolic volume, and impaired right ventricular function).

HF prevalence in developed countries is estimated at 1% to 2% of the general population with almost 12% in patients ≥65 years.[10] Moreover, HF prevalence is still rising because of population growth, aging of the population and improved survival of patients with coronary artery disease.[10] A recent meta-analysis by Jones et al[11] showed



Patients at risk	0m	12m	24m	36m	48m	60m	72m	84m	96m	108m	120m	132m	144m	156m	168m	180m
CRT recipients	894	868	813	759	694	634	571	505	437	373	323	271	219	157	102	77

Figure 1. Kaplan-Meier estimates for all-cause mortality in cardiac resynchronization therapy recipients. The solid line displays the overall survival of the total population, and the dotted line shows the overall survival of patients who survived at least 5 years (landmark analysis at 60 months).

survival rates in chronic HF patients of 86.5%, 72.6%, 56.7%, and 34.9% at 1-, 2-, 5-, and 10 years, respectively. Of note, this meta-analysis included studies from 1980 until 2018, with significant heterogeneity in the survival rates related to important differences in patient populations. Nevertheless, a clear trend toward improved 1- and 5-year survival rates was noted for each decade since the 1980s.[11] The present study showed survival rates at 1-, 2-, 5-, and 10 years of 97.1%, 91.0%, 71.0%, and 44.8%, respectively, which were superior compared with the results in the meta-analysis.[11] As discussed by Jones et al[11], mortality was lowest in studies conducted in secondary care settings, because of higher reported prescription rates of HF medication. The superior outcomes in the present study, stemming from a tertiary referral center with augmented HF medication prescription rates, highlight the benefit in the long-term

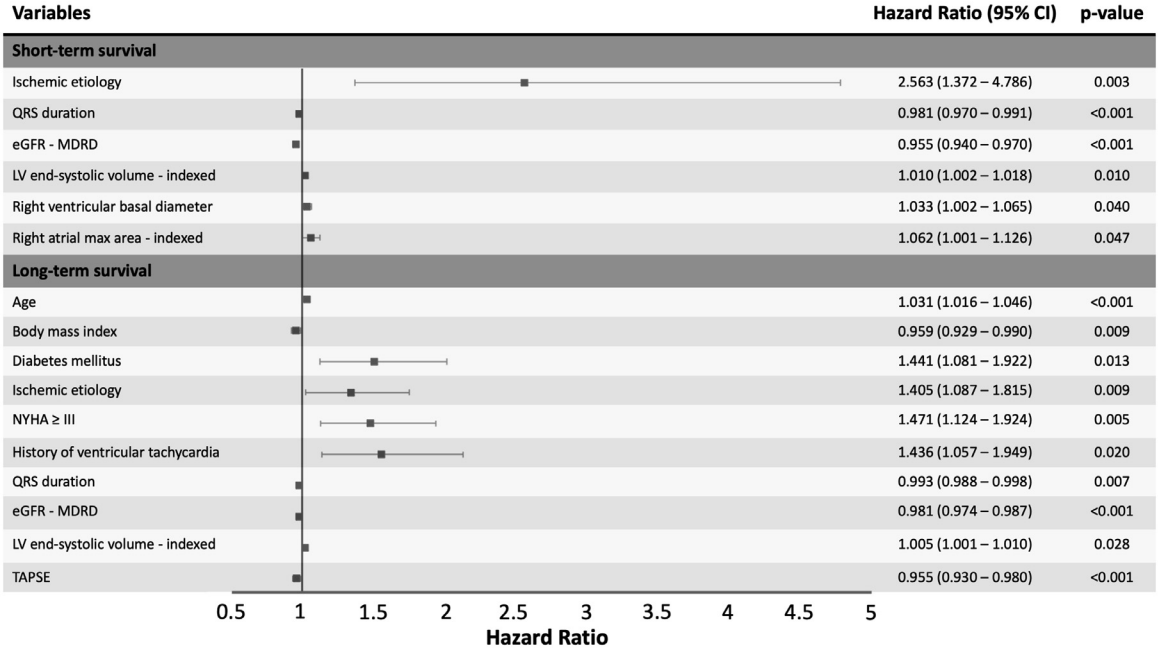


Figure 2. Forest plot for short-term (2-year follow-up) and long-term (10-year follow-up) all-cause mortality in cardiac resynchronization therapy recipients. eGFR-MDRD = estimated glomerular filtration rate-modification of diet in renal disease; TAPSE = tricuspid annular plane systolic excursion.

Table 3
Univariable and multivariable Cox regression analyses for short-term (2-year follow-up) all-cause mortality

	Univariable model		Multivariable model 1 clinical variables		Multivariable model 2 echocardiographic variables		Multivariable model 3 combined	
	Hazard ratio (95%CI)	p Value	Hazard ratio (95%CI)	p Value	Hazard ratio (95%CI)	p Value	Hazard ratio (95%CI)	p Value
Demographic characteristics								
Age, years	1.041 (1.016−1.068)	**0.001**	1.009 (0.982−1.036)	0.537				
Male gender	1.086 (0.643−1.835)	0.758						
Body mass index, kg/m^2	0.949 (0.898−1.004)	0.066	0.961 (0.907−1.018)	0.174				
Medical history								
Arterial hypertension	0.984 (0.624−1.550)	0.943						
Diabetes mellitus	1.235 (0.738−2.066)	0.422						
Dyslipidemia	1.123 (0.712−1.771)	0.619						
Smoking	0.931 (0.595−1.455)	0.752						
Ischemic etiology	2.028 (1.250−3.291)	**0.004**	1.866 (1.099−3.167)	**0.021**			2.563 (1.372−4.786)	**0.003**
NYHA III	3.337 (1.667−6.680)	**0.001**	2.135 (1.044−4.365)	**0.038**			1.631 (0.712−3.737)	0.247
History of ventricular tachycardia	1.523 (0.881−2.634)	0.132						
ECG characteristics								
Atrial fibrillation	2.468 (1.538−3.960)	**<0.001**	2.151 (1.289−3.591)	**0.003**			1.401 (0.734−2.673)	0.306
Left bundle branch block	0.658 (0.424−1.020)	0.061	0.811 (0.507−1.297)	0.383				
QRS duration, ms	0.990 (0.981−0.999)	**0.038**	0.988 (0.979−0.998)	**0.015**			0.981 (0.970−0.991)	**<0.001**
Device characteristics								
CRT-D vs CRT-P	1.601 (0.697−3.680)	0.267						
Laboratory values								
Hemoglobin, g/100 ml	0.841 (0.730−0.968)	**0.016**	1.002 (0.860−1.167)	0.981				
eGFR - MDRD, ml/min/1.73 m^2	0.963 (0.953−0.974)	**<0.001**	0.968 (0.956−0.981)	**<0.001**			0.955 (0.940−0.970)	**<0.001**
Echocardiographic variables								
LV end-systolic volume - indexed, ml/m^2	1.007 (1.001−1.012)	**0.016**			1.009 (1.001−1.017)	**0.027**	1.010 (1.002−1.018)	**0.010**
LV ejection fraction, %	0.983 (0.957−1.011)	0.229						
Left atrial volume indexed, ml/m^2	1.016 (1.007−1.025)	**0.001**			0.992 (0.977−1.007)	0.275		
Moderate or severe mitral regurgitation	1.708 (1.063−2.744)	**0.027**			1.291 (0.703−2.371)	0.409		
RV basal diameter, mm	1.063 (1.039−1.088)	**<0.001**			1.039 (1.007−1.072)	**0.016**	1.033 (1.002−1.065)	**0.040**
TAPSE, mm	0.933 (0.890−0.979)	**0.004**			0.951 (0.894−1.011)	0.106		
Right atrial maximum area - indexed, cm^2/m^2	1.071 (1.039−1.103)	**<0.001**			1.063 (1.006−1.122)	**0.029**	1.062 (1.001−1.126)	**0.047**
Moderate or severe TR	3.156 (1.900−5.241)	**<0.001**			2.234 (1.140−4.379)	**0.019**	1.673 (0.933−2.999)	0.084
PASP, mm Hg	1.040 (1.026−1.054)	**<0.001**						

CI = confidence interval; CRT-D = cardiac resynchronization therapy in combination with an implantable defibrillator; CRT-P = cardiac resynchronization therapy without implantable defibrillator; eGFR-MDRD = estimated glomerular filtration rate − modification of diet in renal disease; LV = left ventricle; NYHA = New York Heart Association; PASP = pulmonary artery systolic pressure; RV = right ventricle; TAPSE = tricuspid annular plane systolic excursion; TR = tricuspid regurgitation.

Table 4
Univariable and multivariable Cox regression models for long-term (10-year follow-up) all-cause mortality

	Univariable model		Multivariable model	
	Hazard ratio (95%CI)	p Value	Hazard ratio (95%CI)	p Value
Demographic characteristics				
Age, years	1.045 (1.035−1.056)	**<0.001**	1.031 (1.016−1.047)	**<0.001**
Male gender	1.418 (1.134−1.773)	**0.002**	1.171 (0.851−1.610)	0.333
Body mass index, kg/m^2	0.969 (0.948−0.991)	**0.005**	0.955 (0.925−0.986)	**0.005**
Medical history				
Arterial hypertension	1.018 (0.850−1.220)	0.844		
Diabetes mellitus	1.528 (1.242−1.881)	**<0.001**	1.505 (1.123−2.018)	**0.006**
Dyslipidemia	1.171 (0.976−1.404)	0.089	0.921 (0.717−1.184)	0.520
Smoking	1.063 (0.887−1.273)	0.508		
Ischemic etiology	1.762 (1.461−2.125)	**<0.001**	1.341 (1.025−1.754)	**0.032**
NYHA III	1.729 (1.393−2.146)	**<0.001**	1.478 (1.127−1.938)	**0.005**
History of ventricular tachycardia	1.422 (1.121−1.804)	**0.004**	1.558 (1.139−2.133)	**0.006**
ECG characteristics				
Atrial fibrillation	1.700 (1.366−2.115)	**<0.001**	1.215 (0.887−1.666)	0.225
Left bundle branch block	0.674 (0.564−0.807)	**<0.001**	0.878 (0.676−1.140)	0.328
QRS duration, ms	0.997 (0.994−1.000)	0.088	0.993 (0.988−0.998)	**0.007**
Device characteristics				
CRT-D vs CRT-P	1.240 (0.835−1.841)	0.286		
Laboratory values				
Hemoglobin, g/100 ml	0.877 (0.827−0.930)	**<0.001**	1.005 (0.928−1.088)	0.905
eGFR - MDRD, ml/min/1.73 m^2	0.976 (0.972−0.980)	**<0.001**	0.980 (0.973−0.986)	**<0.001**
Echocardiographic variables				
LV end-systolic volume - indexed, ml/m^2	1.005 (1.002−1.007)	**<0.001**	1.006 (1.001−1.011)	**0.013**
LV ejection fraction, %	0.988 (0.977−0.999)	**0.031**	1.007 (0.987−1.027)	0.487
Left atrial volume indexed, ml/m^2	1.012 (1.007−1.016)	**<0.001**	0.996 (0.990−1.003)	0.232
Moderate or severe mitral regurgitation	1.326 (1.099−1.601)	**0.003**	1.057 (0.825−1.353)	0.662
RV basal diameter, mm	1.029 (1.018−1.039)	**<0.001**	1.010 (0.995−1.025)	0.180
TAPSE, mm	0.940 (0.921−0.958)	**<0.001**	0.960 (0.935−0.986)	**0.003**
Right atrial maximum area - indexed, cm^2/m^2	1.052 (1.035−1.069)	**<0.001**	1.020 (0.992−1.049)	0.164
Moderate or severe TR	1.731 (1.385−2.162)	**<0.001**	1.225 (0.903−1.660)	0.192
PASP, mm Hg*	1.031 (1.024−1.039)	**<0.001**		

* PASP was not included in the multivariable model because of >10% missing values.

CI = confidence interval; CRT-D = cardiac resynchronization therapy in combination with an implantable defibrillator; CRT-P = cardiac resynchronization therapy without implantable defibrillator; eGFR-MDRD = estimated glomerular filtration rate − modification of diet in renal disease; LV = left ventricle; NYHA = New York Heart Association; PASP = pulmonary artery systolic pressure; RV = right ventricle; TAPSE = tricuspid annular plane systolic excursion; and TR = tricuspid regurgitation.

survival of systematic HF medication prescription, which can be even further improved by guideline-directed CRT implantation.[12,13] Furthermore, few studies have focused on the long-term survival benefit of CRT in HF patients.[14] Patel et al[15] reported a 10-year survival after CRT implantation of 32.7%, which is lower compared with the 44.8% 10-year survival in the present study, possibly related to the lower LVEF and more extensive cardiovascular disease as compared with the current patient population.[15−17] Moreover, a landmark analysis in the present study, of patients who survived at least 5 years after CRT implantation, showed continued benefit in survival rates at 10- and 15-year follow-ups of 64% and 43%, respectively.

Estimation of survival in CRT recipients remains challenging because of the heterogeneity of the patient population. Nevertheless, several baseline demographical, clinical, and laboratory variables, and echocardiographic variables, have been identified that influence short-term and mid-term survival. Even a small number of multiparametric prognostic risk scores have been developed to estimate the overall (short-term) survival after CRT implantation.[18−21] The current results regarding short-term survival are agrees with previous studies, indicating that both baseline clinical and echocardiographic variables are associated with short-term outcomes. In addition to these known variables, the present study revealed that right ventricular size and function and right atrial size are important for short-term outcomes and underscore detailed assessment of the right-sided echocardiographic parameters in CRT recipients. Additionally, few published data exist on long-term CRT outcomes: Patel et al[15] identified age, gender, the presence of an ischemic etiology of HF, QRS duration, atrial fibrillation, brain natriuretic peptides levels, creatinine levels, and LV end-diastolic diameter at the time of CRT implantation as significant predictors of 10-year survival. Of note, only 1 echocardiographic variable at the moment of CRT implantation remained significantly associated with long-term outcomes. The present study underscores the importance of clinical variables for

long-term outcomes, in contrast to echocardiographic variables, which are important for short-term outcomes.

The current results underscore that in well-selected patients with advanced HF, treated with guideline-directed medical therapy, CRT should be considered as a complementary therapy to improve clinical response and survival because a large proportion of these patients experience long-term, continued benefit. However, risk assessment for short-term and long-term mortality differs considerably. Short-term mortality is associated with both clinical and echocardiographic variables before CRT implantation, whereas long-term mortality is mainly associated with the clinical condition of the patient and co-morbidities at the time of CRT implantation.

First, this study is limited by its retrospective design from a single tertiary center. Second, cardiac HF biomarkers (particularly brain natriuretic peptide or N-terminal pro-brain natriuretic peptide) were not systematically available. Third, the study inclusion period covers a broad time frame in which several advances in devices, leads, and programming has been made, which may have influenced outcomes. However, dividing the cohort into 'early inclusion' and 'late inclusion' groups showed nonsignificant p values in the Kaplan-Meier curves analysis, and on the univariable Cox regression analysis, for 10-year overall survival (data available in the supplementary material, Supplementary Figure 1, Supplementary Table 1). Fourth, only 5% of the population received CRT-P and therefore the present study cannot provide an accurate evaluation of the prognostic implications of CRT-D versus CRT-P. Finally, only data on all-cause mortality were available and no distinction between cardiac and noncardiac death could be made.

In conclusion, CRT implantation is an effective therapy in patients with advanced HF, with a significant survival rate at 10-year follow-up. The risk evaluation for short-term (2-year follow-up) versus long-term (10-year follow-up) survival shows considerable differences. Short-term survival is mainly dependent on both baseline clinical and echocardiographic parameters; whereas long-term survival is predominantly dependent on the clinical status of the patient and associated co-morbidities at the time of CRT implantation.

Disclosures

Dr. Delgado received speaker fees from Abbott Vascular, Edwards Lifesciences, GE Healthcare, Medtronic, Merck Sharp & Dohme, and Novartis. Dr. Ajmone Marsan received speaker fees from Abbott Vascular and GE Healthcare. Dr. Bax received speaker fees from Abbott Vascular and Edwards Lifesciences. The remaining authors have no conflicts of interest to declare.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2023.03.026.

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