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Long-term outcome, mortality predictors and cardiac-device related infective endocarditis in patients with surgically corrected valvular versus non-valvular heart failure treated with cardiac resynchronization therapy

Short title: Cardiac resynchronization therapy after valvular surgery

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WHAT'S NEW?

In a real-world registry, about 7% of patients receiving cardiac resynchronization therapy (CRT) had valvular heart failure that had been previously corrected surgically. The long-term prognosis of CRT recipients with valvular etiology of heart failure is similar to that of other patients undergoing cardiac resynchronization therapy. Mortality rates in CRT subjects with valvular etiology of heart failure reach 50% within 4.5 years. The independent mortality

predictor in patients with valvular heart failure and subsequent CRT implantation is advanced age. Procedural duration and fluoroscopy time is similar in valvular versus non-valvular CRT recipients. The risk of device-related infective endocarditis is not higher in CRT patients with valvular compared with non-valvular heart failure.

ABSTRACT

Background: Little is known about the prognosis in patients with valvular etiology of heart failure (HF) after cardiac surgery treated with cardiac resynchronization therapy (CRT).

Aims: To assess the long-term outcome, mortality predictors, and the risk of cardiac device-related infective endocarditis (CDRIE) in patients with valvular etiology of HF after cardiac surgery treated with CRT.

Methods: The study population consisted of 1059 consecutive patients with CRT implanted between 2002 and 2019 in a tertiary care university hospital in Poland.

Results: The studied population was divided into two groups: 1) valvular group (n = 74; 7.0%) in patients with HF after cardiac surgery treated with CRT, and 2) non-valvular group (control group, n = 985; 93.0%) that comprised all other CRT recipients. During the median follow-up of 1661 days (815–2792), all-cause mortality of CRT recipients with valvular versus non-valvular HF did not differ significantly (50% vs. 54.4%; $P = 0.46$). Also, the risk of CDRIE was not different (2.7% vs. 5.7%; $P = 0.28$). On multivariable regression analysis, only older age (HR, 1.04; 95% CI, 1.01–1.07, $P = 0.02$) was identified as an independent predictor of higher mortality in patients with valvular HF treated with CRT.

Conclusions: CRT recipients with valvular HF that had been corrected surgically have similar long-term mortality to CRT patients with non-valvular HF etiologies. In both, death rates reach 50% within 4.5 years. The risk of CDRIE is not higher in the valvular versus non-valvular group of CRT recipients, and advanced age appeared to be the only independent mortality predictor in patients with CRT implanted for valvular HF.

Key words: cardiac device-related infective endocarditis; cardiac resynchronization therapy; cardiac surgery; heart failure; valvular heart failure

INTRODUCTION

Cardiac resynchronization therapy (CRT) has been a proven therapy in patients with symptomatic heart failure (HF) with reduced left ventricular ejection fraction (LVEF) and

prolonged QRS duration [1–3]. Many studies on CRT have identified factors associated with reverse remodeling and positive response to resynchronization. These include QRS duration, female sex, left bundle branch block, and non-ischemic cardiomyopathy [4–7]. Nevertheless, the non-ischemic etiology of HF is a broad concept and includes post-inflammatory, dilated, hypertrophic, tachyarrhythmic cardiomyopathy as well as HF caused by valvular diseases. Despite surgical correction of the valvular disease-causing heart failure, some patients still require CRT implantation. Importantly, such patients have never been studied separately in randomized trials on CRT, and there is scarce data on the long-term effects of resynchronization in this group. It seems reasonable to assess separately and specifically the response of valvular HF to resynchronization because of a different remodeling pattern compared to other etiologies of HF. For example, some valvular diseases, such as stenosis, cause hypertrophy, while others, such as valve regurgitation, cause dilatation. There is also little data on the risk of infective endocarditis in this group, and it may be increased because of two invasive procedures, that is, valve surgery and CRT implantation, respectively. Thus, our study aimed to assess the long-term outcome, mortality predictors, and the risk of cardiac device-related infective endocarditis (CDRIE) in patients with valvular etiology of HF after cardiac surgery treated with CRT.

METHODS

Study population

All consecutive patients with CRT implanted between 2002 and 2019 in a high-volume, tertiary care university hospital in a densely inhabited urban region of Poland were included in the study. Subjects were qualified for CRT implantation in line with the respective European Society of Cardiology (ESC) guidelines. The inclusion criteria were: age ≥18 years old, informed consent, symptomatic HF in New York Heart Association (NYHA) class II, III, or ambulatory class IV (despite optimal medical treatment), LVEF ≤35%, and prolonged QRS duration according to the current ESC guidelines. Each patient was informed about the procedure and potential complications and signed an informed written consent. The study complied with international standards, i.e., the Declaration of Helsinki. The number of the Institutional Review Board is KNW/0022/KB/139/17.

The procedure of CRT implantation was performed according to current standards. An intravenous prophylactic dose of antibiotic (cefazolin single dose intravenous; or clindamycin single dose intravenous in case of allergy to cephalosporins) was given to all subjects before the procedure.

Follow-up

All patients were assessed during scheduled (one week, one month, and every 6 months afterward) and unscheduled visits throughout the observation period. Hospital records, outpatient notes, telephone calls, insurer's records, and death certificates directly from patients and relatives were also used for data collection. Patients were followed from CRT implantation until March 2021.

Statistical analysis

The categorical variables were expressed as numbers and percentages, whereas numerical parameters were expressed as median with interquartile ranges (IQR) according to the parameters' distribution. The groups were compared using the χ^2, Yates corrected χ^2, or Mann–Whitney U tests as appropriate. Survival was analyzed using the Kaplan–Meier estimator. Multivariable Cox regression tests were used to identify independent risk factors for mortality. The multivariable regression model was constructed to assess the predictors of mortality and included baseline confoundings that differentiated alive and deceased patients in the studied population with a *P*-value of <0.05, except for redundant variables. Results were expressed as hazard ratio (HR) with 95 percent confidence intervals (95% CI).

The *P*-value of less than 0.05 was considered statistically significant. All statistical analyses were performed using the Statistica software package (version 6.0, StatSoft Inc., Tulsa, OK, US, and version 10.0).

RESULTS

Study population

The study population consisted of 1059 consecutive patients with CRT implanted between 2002 and 2019 in a tertiary care university hospital in a densely inhabited, urban region of Poland (949 subjects [89.6%] with CRT-D; 110 patients with CRT-P [10.4%]). The median LVEF in the whole population was 25% (IQR 20%–29%), with a median age of 65 years (58–72), 78.6% of males (n = 832), and a median QRS duration was 163 msec (150–181).

The studied population was divided into two groups according to the etiology of HF: 1) the valvular group (n = 74; 7.0%) in patients with HF after cardiac surgery before CRT implantation and 2) the non-valvular group (control group, n = 985; 93.0%) that comprised all other CRT recipients. Patients with valvular versus non-valvular HF did differ with respect to age (64 [53–70] vs. 65 [58–72] years; *P* = 0.005), coronary artery disease (20.3 vs. 58%; *P* <0.001), permanent atrial fibrillation (36.5 vs. 20.4%; *P* = 0.001), previously implanted

pacemaker (41.9% vs 12.7%, P<0.001), diabetes (21.6 vs 35.6%, P=0.01), and C-reactive protein level before CRT implantation (3.01 [1.7–8.1] vs. 3.2 [1.3–7.9] mg/l; *P* = 0.04). The procedural duration and fluoroscopy time were similar in both groups. The baseline characteristics of the whole population and study groups are shown in Table 1.

In the group of valvular HF patients, 28 subjects (37.8%) had aortic valve surgery, 23 (31.1%) mitral valve surgery, 11 (14.9%) aortic and mitral valve exchange, 7 (9.5%) mitral and tricuspid valve procedure, 2 (2.7%) only tricuspid valve surgery, and 3 (4.1%) aortic, mitral and tricuspid valve surgery.

In the non-valvular group, 128 patients (12.9%) had moderate to severe secondary mitral regurgitation, and optimal medical treatment, including cardiac resynchronization therapy, was initially implemented. Twelve of these subjects had MitraClip implanted during follow-up due to persistent severe secondary mitral regurgitation after the CRT procedure.

Outcomes

During the median follow-up of 1661 days (815–2792 days), 54.3% of patients died (n = 575). A comparative analysis of survival in the whole CRT population concerning vital status is presented in Table 2. Survivors versus deceased patients with valvular HF treated with cardiac surgery before CRT implantation differed with regard to the following variables: age (61 [59–68] vs. 67 [58–73] years; *P* = 0.02), NYHA class (2.5 [2–3] vs. 3 [2–4]; *P* = 0.005), and left ventricular end-systolic diameter before CRT (59 [46–63] vs. 53 [47–60] mm; *P* = 0.04) (Table 3).

On multivariable regression analysis, only older age (HR, 1.04; 95% CI, 1.01–1.07; *P* = 0.02) was identified as an independent predictor of higher mortality in patients with valvular HF after cardiac surgery treated with CRT (Table 4).

During the follow-up, 37 (50%) and 536 (54.4%) patients died in the valvular and control group, respectively (*P* = 0.46). Figure 1 shows Kaplan–Meier curves of survival in the study groups.

The risk of CDRIE was non-different in patients with valvular *versus* non-valvular HF (n = 2; 2.7% vs. n = 56; 5.7%; *P* = 0.28). In the first group, CDRIE occurred in 1 patient in the first 12 months following the procedure and 1 >12 months after device implantation. In both patients, vegetations were identified on CRT electrodes, and no vegetations were observed within the implanted valves. One subject had the device removed, whereas the other one did not. Despite treatment, both patients died of CDRIE after a median of 74 days of hospitalization.

DISCUSSION

The main findings of our study are as follows: 1) in a real-world registry, about 7% of patients receiving CRT had valvular HF that had been previously corrected surgically; 2) long-term prognosis of CRT patients with valvular etiology of HF is similar to other patients undergoing resynchronization; 3) mortality rates in valvular HF patients treated with CRT reach 50% within 4.5 years; 4) procedural duration and fluoroscopy time is similar in valvular *versus* non-valvular CRT recipients; 5) risk of device-related infective endocarditis is not higher in CRT patients with valvular compared with non-valvular heart failure; 6) independent mortality predictor in patients with valvular HF and subsequent CRT implantation is advanced age.

Outcome

Only a few studies assessed response to CRT and outcomes in patients with prior valvular cardiomyopathy and subsequent cardiac surgery followed by CRT implantation [8–11]. Such patients were usually excluded from randomized trials on CRT or represented a minority of enrolled subjects. For example, in the CARE-HF study, the valvular etiology of HF was at 2% (19 patients) of all patients, making any subgroup analysis futile [2]. Nonetheless, regardless of the underrepresentation of those patients from RCTs, they still do have indications for CRT [8]. In our study, 6.9% of all patients being qualified for CRT had previous valvular heart surgery with subsequent development of HF, which is in line with previously published data, e.g., from The InSYnc/InSync ICD Italian Registry with 5.9% of such patients [8].

Our study showed a similar prognosis of patients with surgically corrected valvular *versus* non-valvular HF and subsequent CRT. Similar outcomes have also been reported on a smaller population and in a shorter follow-up [10]. In that study, the composite outcome of all-cause mortality, heart transplantation, and left ventricular assist device occurred in 26% of patients during 3 years of follow-up. In contrast, in our analysis, all-cause mortality within 4.5 years reached 50%. Another two studies showed long-term outcome of valvular cardiomyopathy treated with cardiac surgery and subsequent CRT comparable to the outcome of ischemic HF and worse than in dilated cardiomyopathy [8, 9], with mortality reaching 71% during a median follow-up of 4.5 years. That is higher than we report here. The difference between previously published studies and our analysis of the mortality rate is simple to explain. In these studies, made about 10 years ago, a significantly lower number of patients received recommended pharmacotherapy (52% of patients on β-blockers, 57% of subjects on aldosterone receptor antagonists), and most patients received CRT-pacing rather than CRT-defibrillator [9].

Valvular HF may be of different pathophysiology. For example, heart remodelling caused by valvular defect leads to hypertrophy in aortic stenosis, whereas regurgitation causes dilatation, myocardial injury, and conduction abnormalities [9]. In addition, a higher number of patients with valvular disease develop atrial fibrillation. For example, in our study, permanent atrial fibrillation was present in more than 1/3 of subjects compared with only 1/5 in other aetiologies of HF [8, 9]. Importantly, atrial fibrillation is a well-known comorbidity that decreases the percentage of responders to CRT and worsens outcomes in CRT subjects [12, 13]. Another important factor would be the need for chronic anticoagulation following valvular cardiac surgery, which inevitably increases the risk of bleeding, further procedure-related complications, etc. [14, 15]. All these factors combined may increase complication rate and deteriorate outcome in patients with valvular HF after cardiac surgery treated with CRT compared to other CRT recipients. Moreover, awareness of these risks could result in less frequent qualification of such patients for CRT. Thus, our analysis adds new, important data on this population, which, despite hazards, should be considered for CRT procedures as per current guidelines.

Procedural data and CDRIE

The duration of CRT implantation and fluoroscopy time assessed in our study was similar in patients with valvular *versus* non-valvular HF. In addition, we also focused on one of the most serious and deleterious cardiac implantable electronic device complications, which is device-related infective endocarditis. We observed CDRIE namely in 2.7% valvular CRT and 5.7% non-valvular CRT recipients ($P = 0.28$). To the best of our knowledge, it is the first study that delivers such data. Infective complications following valve surgery and subsequent CRT implantation are of utmost importance as each of the procedures increases the risk of infective endocarditis [16]. In the POL-ENDO registry, cardiac implantable devices were present in 21% of patients with infective endocarditis, and 3.2% of subjects had cardiac resynchronization therapy. However, no observations of CDRIE have been reported in patients after valve implantation [17]. Despite additional invasive procedures, such as CRT implantation, and the presence of other artificial elements, such as device can, and in particular intravascular electrodes, surprisingly, we did not observe any excess in CDRIE incidence in the vascular CRT group. The reasons for that are unclear and may be partially explained by a limited number of patients. Also, infective endocarditis prophylaxis, which is very strictly implemented after each cardiac surgery, may have played a role. In addition, during CRT implantation, operators may pay more attention to the maintenance of sterile conditions as post-cardiac surgery patients

are relatively rare and well-known to be at particular risk of infectious complications. Thus, usually, more experienced operators perform such procedures. Finally, various physicians, being aware of the risks in patients with artificial valves, seem to pay special attention to infection prophylaxis, e.g., general practitioners, dentists, and others.

Of note, we have assessed specifically the risks and outcomes of CDRIE in the CRT population in another study [18, 19]. Indeed, we found in one statistical model that up-grade from ICD to CRT and higher baseline NYHA class were independently associated with increased risk of CDRIE, whereas the second model showed up-grade from ICD, higher NYHA class, hypertrophic cardiomyopathy, lower baseline hemoglobin level, and chronic obstructive pulmonary disease were all independently associated with a higher risk of CDRIE [19]. Of all etiologies, only hypertrophic cardiomyopathy was associated with CDRIE.

Mortality predictors

In our study, only advanced age was an independent mortality predictor in patients with valvular HF and subsequent CRT. Independent predictors of poor outcome in this group of patients are difficult to assess. The only study on this issue showed that only chronic atrial fibrillation, not treated with atrioventricular node ablation, was an independent mortality predictor, whereas age was near to statistical significance [8]. A relatively small study group may partially explain this. This issue undoubtedly requires further observation and studies. However, advanced age was described as an independent predictor of mortality in patients with valvular diseases before and after cardiac surgery [20–22]. Our data may thus suggest that age plays a crucial role for patients scheduled for valvular cardiac surgery who may need inevitably subsequent resynchronization. Consequently, we may speculate further, that two invasive procedures, that is cardiac surgery and subsequent CRT implantation may be a real burden for elderly patients. Thus, one could consider perhaps less invasive valve procedures in such patients, e.g., transcatheter aortic valve implantation, MITRA-CLIP before CRT implantation. Nevertheless., such hypothesis would need to be verified in a prospective randomized trial.

Study limitations and strengths

A single-center study design is an obvious limitation of our observations. A relatively small group of patients is another one, but on the other hand, the number of patients was sufficient for statistical purposes.

Data regarding left ventricle function before cardiac surgery was incomplete. Analysis with respect to specific valve defects was not performed due to a limited number of cases, which would make reliable subanalyses impossible.

CONCLUSIONS

CRT recipients with valvular HF that had been corrected surgically have similar long-term mortality to CRT patients with non-valvular HF etiologies. In both, death rates reach 50% within 4.5 years. The risk of device-related infective endocarditis is not higher in subjects with valvular versus non-valvular HF treated with CRT, and advanced age appeared to have been the only independent mortality predictor in patients with CRT implanted for valvular HF.

Article information

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Conflict of interest

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Table 1. Baseline characteristics of the whole population, patients with valvular heart failure treated with cardiac surgery, and control group

	Whole population (n = 1059)	**CRT patients with valvular HF (n = 74)**	**Control group (n = 985)**	***P*-value**
Age (years)	65 (58–72)	64 (53–70)	65 (58–72)	0.005
Male	832 (78.6)	57 (77)	775 (78.7)	0.74
NYHA class	3 (2–3)	3 (2–3)	3 (2–3)	0.19
LVEF (%)	25 (20–29)	25 (20–30)	25 (20–29)	0.32
LVESD before CRT (mm)	57 (49–64)	56 (49–61)	57 (49–64)	0.39
LVEDD before CRT (mm)	68 (61–74)	66 (60–74)	68 (61–74)	0.48
Primary prevention of SCD	895 (84.5)	61 (82.4)	834 (84.7)	0.61

Previous ICD	197 (18.6)	16 (21.6)	181 (18.4)	0.49
Previous pacemaker	156 (14.7)	31 (41.9)	125 (12.7)	<0.001
CRT-P	110 (10.4)	11 (14.9)	99 (10.1)	0.19
Coronary artery disease	591 (55.8)	15 (20.3)	571 (58)	<0.001
Previous myocardial infarction	481 (45.4)	0	481 (48.8)	<0.001
Hypertension	667 (63)	40 (54.1)	627 (63.7)	0.09
Paroxysmal and presistent AF	230 (21.7)	19 (25.7)	211 (21.4)	0.39
Permanent AF	228 (21.5)	27 (36.5)	201 (20.4)	0.001
Diabetes	367 (34.7)	16 (21.6)	351 (35.6)	0.01
Creatinine before CRT (umol/ L)	96 (79–118)	91 (74–114)	96 (80–119)	0.26
NTproBNP before CRT (pg/mL)	2131 (961–4358)	2236 (1683–4389)	2110 (940–4343)	0.57
CRP before CRT (mg/L)	3.2 (1.3–8)	3.01 (1.7–8.1)	3.2 (1.3–7.9)	0.04
QRS duration at CRT implantation (msec)	163 (150–181)	170 (157–190)	162 (150–180)	0.34
Procedure time (min)	120 (105–157)	120 (110–150)	122 (105–160)	0.32
Fluoroscopy time (min)	17 (11–28)	14 (11–27)	17 (11–28)	0.48
Follow-up time (days)	1661 (815–2792)	1534 (822–2560)	1669 (815–2826)	0.61
Medications at discharge				
β-blocker	1031 (97.4)	73 (98.6)	958 (97.3)	0.47
ACEI/ARB	955 (90.2)	64 (86.5)	891 (90.5)	0.27

Loop diuretics	885 (83.6)	60 (81.1)	825 (83.8)	0.55
Aldosterone antagonist	929 (87.7)	64 (86.5)	865 (87.8)	0.74
ARNI	32 (3.0)	4 (5.4)	28 (2.8)	0.37
SGLT-2 inhibitor	27 (2.5)	2 (2.7)	25 (2.5)	0.77

Numerical variables are presented as median (IQRs), and categorical variables as numbers (percentages)

**P* — for comparison of patients with valvular heart failure treated with cardiac surgery, and control group

Abbreviations: ACEI, angiotensin-converting-enzyme inhibitors; AF, atrial fibrillation; ARB, angiotensin receptor blockers; ARNI, angiotensin receptor/neprilysin inhibitor; CRP, C-reactive protein level; CRT, cardiac resynchronization therapy; HF, heart failure; ICD, implantable cardioverter-defibrillator; LVEDD, left ventricle end-diastolic diameter; LVEF, left ventricular ejection fraction; LVESD, left ventricle end-systolic diameter; SCD, sudden cardiac death; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association classification; SGLT-2, sodium-glucose cotransporter-2

Table 2. Baseline characteristics of the whole population in relation to vital status

Patients	**Alive (n = 484)**	**Deceased (n = 575)**	***P*-value**
Age, years	64 (55–71)	66 (59–73)	<0.001
Male	359 (77.2)	473 (82.3)	0.001
NYHA class	3 (2–3)	3 (2–4)	<0.001
LVEF, %	26 (22–30)	24 (20–28)	<0.001
LVESD before CRT, mm	55 (46–62)	59 (52–66)	<0.001
LVEDD before CRT, mm	65 (59–71)	69 (64–76)	<0.001
Primary prevention of SCD	434 (89.7)	461 (80.2)	<0.001
Previous ICD	85 (17.6)	112 (19.5)	0.42

Previous pacemaker	84 (17.4)	72 (12.5)	0.03
CRT-P	47 (9.7)	63 (11)	0.51
Coronary artery disease	222 (45.9)	369 (64.2)	<0.001
Previous myocardial infarction	171 (35.3)	310 (53.9)	<0.001
Hypertension	305 (63)	362 (63)	0.98
Paroxysmal and persistent AF	91 (18.8)	139 (24.2)	0.03
Permanent AF	108 (22.3)	120 (20.9)	0.57
Diabetes	140 (28.9)	227 (39.5)	<0.001
Creatinine before CRT implantation, umol/l	90 (73–108)	106 (85–133)	<0.001
NTproBNP before CRT, pg/ml	1213 (566–2603)	2900 (1584–5184)	<0.001
CRP before CRT, mg/l	2.3 (1.1–5.4)	4.4 (1.9–10.3)	<0.001
QRS duration at CRT implantation, msec	165 (150–180)	161 (146–183)	0.89
Procedure time, min	125 (105–160)	120 (100–155)	0.66
Fluoroscopy time, min	16 (10–29)	17 (11–28)	0.54
Medications at discharge			
β-blocker	474 (97.9)	557 (96.9)	0.28
ACEI/ARB	447 (92.4)	508 (88.3)	0.03
Loop diuretics	360 (74.4)	525 (91.3)	<0.001
Aldosterone antagonist	430 (88.8)	499 (86.8)	0.31
ARNI	17 (3.5)	15 (2.6)	0.39
SGLT-2 inhibitor	10 (2.1)	17 (2.9)	0.36

Numerical variables are presented as median (interquartile ranges), categorical variables as numbers (percentages)

Abbreviations: see Table 1

Table 3. Baseline characteristics of patients with valvular HF and control group in relation to vital status

	CRT patients with valvular HF and cardiac surgery before CRT (n=74)			**Control group (n=985)**		
Patients	**Alive n = 37 50%**	**Deceased n = 37 50%**	***P*-value**	**Alive n = 447 45.4%**	**Deceased n = 538 54.6%**	***P*-value**
Age, years	61 (59–68)	67 (58–73)	0.02	64 (55–72)	66 (59–73)	<0.001
Male	30 (81.1)	27 (73)	0.41	329 (73.6)	446 (82.9)	<0.001
NYHA class	2.5 (2–3)	3 (2–4)	0.005	3 (2–3)	3 (2–4)	<0.001
LVEF, %	25 (20–29)	26 (20–31)	0.32	26 (22–30)	23 (20–28)	<0.001
LVESD before CRT, mm	59 (56–63)	53 (47–60)	0.04	54 (46–62)	69 (52–67)	<0.001
LVEDD before CRT, mm	68 (64–74)	64 (57–72)	0.06	65 (59–71)	70 (64–76)	<0.001
Primary prevention of SCD	32 (86.5)	29 (78.4)	0.36	402 (90)	432 (80.3)	<0.001
Previous ICD	9 (24.3)	7 (18.9)	0.57	76 (17)	105 (19.5)	0.31
Previous pacemaker	17 (45.9)	14 (37.8)	0.48	67 (14.9)	58 (10.8)	0.04
CRT-P	6 (16.2)	5 (13.5)	0.74	41 (9.2)	58 (10.8)	0.4

Coronary artery disease	5 (13.5)	10 (27)	0.15	217 (48.5)	359 (66.7)	<0.001
Hypertension	20 (54.1)	20 (54.1)	1.0	285 (63.8)	342 (63.6)	0.95
Paroxysmal and persistent AF	8 (21.6)	11 (29.7)	0.42	83 (18.6)	128 (23.8)	0.046
Permanent AF	16 (43.2)	11 (29.7)	0.23	92 (20.6)	109 (20.3)	0.90
Diabetes	8 (21.6)	8 (21.6)	1.0	132 (29.5)	219 (40.7)	<0.001
Creatinine before CRT implantation, umol/l	86 (73–99)	98 (78–127)	0.09	90 (73–109)	106 (86–133)	<0.001
NTproBNP before CRT, pg/ml	2049 (961–4079)	2996 (1683–4628)	0.91	1162 (564–2449)	2884 (1562–5218)	<0.001
CRP before CRT, mg/l	2.3 (1–4.6)	4.9 (2.4–9.6)	0.07	2.3 (1.1–5.6)	4.4 (1.9–10.3)	<0.001
QRS duration at CRT implantation, msec	170 (152–190)	170 (160–190)	0.62	165 (150–180)	161 (145–183)	0.98
Procedure time, min	120 (110–150)	120 (110–135)	0.29	125 (105–160)	120 (100–160)	0.78
Fluoroscopy time, min	14 (12–29)	14 (11–26)	0.63	16 (10–29)	17 (11–28)	0.49
Medications at discharge						
β-blocker	37 (100)	36 (97.3)	0.31	437 (97.8)	521 (96.8)	0.38
ACEI/ARB	34 (91.9)	30 (81.1)	0.17	413 (92.4)	478 (88.8)	0.06
Loop diuretics	28 (75.7)	32 (86.5)	0.24	332 (74.3)	493 (91.6)	<0.001
Aldosterone antagonist	35 (94.6)	29 (78.4)	0.04	395 (88.4)	470 (87.4)	0.63

ARNI	3	1	0.61	14	14	0.62
SGLT2	2	0	0.47	8	17	0.17

Numerical variables are presented as median (IQRs), categorical variables as numbers (percentages)

**P* — for comparison of survivals vs. non-survivals

Abbreviations: see Table 1

Table 4. Multivariable Cox regression models for mortality prediction in patients with valvular HF after cardiac surgery treated with CRT and non-valvular HF patients with CRT

Valvular HF patients after cardiac surgery treated with CRT		
Variable	**HR (95% CI)**	***P*-value**
Age	1.04 (1.01–1.07)	0.02
NYHA class before CRT	1.49 (0.87–2.56)	0.15
LVESD before CRT	0.97 (0.94–1.02)	0.22
Non-valvular HF patients treated with CRT		
Variable	**HR (95% CI)**	***P*-value**
Male	1.22 (0.96–1.55)	0.1
Age	1.02 (1.01–1.03)	<0.001

Primary prevention of SCD	0.69 (0.55–0.85)	<0.001
Ischaemic HF	1.5 (1.24–1.82)	<0.001
Diabetes	1.28 (1.07–1.54)	0.006
Paroxysmal and persistent AF	1.28 (1.04–1.57)	0.02
NYHA class before CRT	1.42 (1.2–1.67)	<0.001
LVESD before CRT	1.03 (1.02–1.04)	<0.001
NTproBNP before CRT, pg/ml	1.001 (1.00–1.002)	<0.001
Creatinine before CRT implantation	1.004 (1.002–1.005)	<0.001

Abbreviations: CI, confidence interval; HR, hazard ratio, other — see Table 1

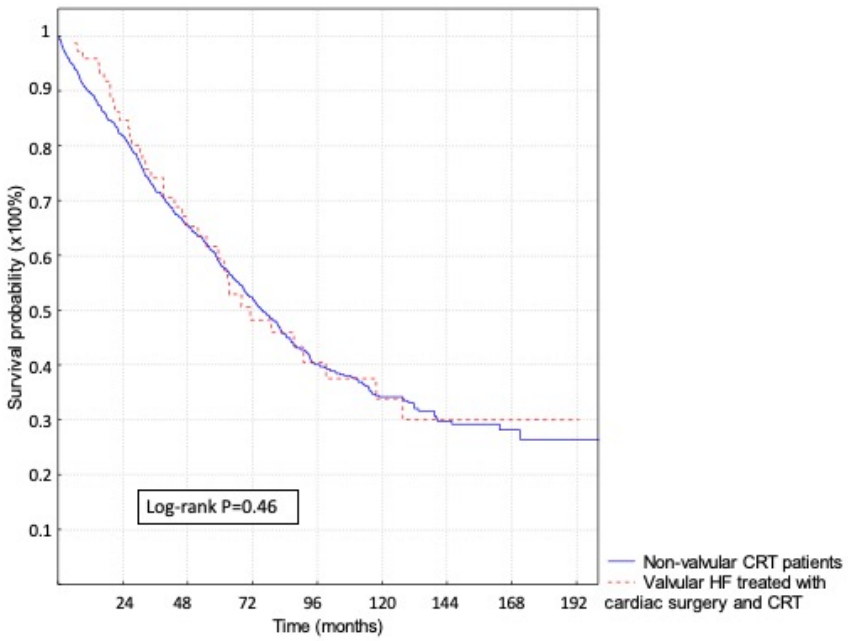

Figure 1. Kaplan–Meier curves of survival in patients with valvular HF after cardiac surgery vs control group

Abbreviations: CRT, cardiac resynchronization therapy; HF, heart failure