Cardiology Journal

VIA MEDICA

ORIGINAL ARTICLE

DOI: 10.5603/CJ.a2022.0057

ISSN 1897–5593
eISSN 1898–018X

Complications of cardiac resynchronization therapy implantation: De novo implants versus upgrades

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Abstract

Background: *Cardiac resynchronization therapy (CRT) is a well-established treatment of patients with advanced heart failure and electrical dyssynchrony. Implantation of those devices is in some cases associated with intervention on a formerly implanted system. The aim of this analysis was to compare the rate and type of complications of de novo implants and upgrades to CRT-D.*

Methods: *Retrospective data were collected from medical records, including 326 patients treated with CRT-D between 2015 and 2020. The following data were analyzed: procedure data including complications, demographics, co-morbidities, pharmacotherapy, and laboratory tests. The primary endpoint of the study was all-cause mortality.*

Results: *A total of 326 procedure were included, of which 53% (n = 172) were de novo implants and 47% (n = 154) were upgrades. Groups did not differ in the incidence of complications: in the de novo group: 25.5% (n = 44); in the upgrade group: 30.5% (n = 47), p = 0.78. The incidence of complications was also similar in respect of the following: early (p = 0.98) and late (p = 0.45), infectious (p = 0.38) and non-infectious (p = 0.82), surgical (p = 0.38) and device or lead related (p = 0.6). The most common complication in the upgrade group was pocket hematoma (n = 9, 5.8%) and in the de novo group pneumothorax (n = 8, 4.7%).*

Conclusions: *Upgrade procedures are not associated with a higher percentage of complications than de novo implantations of CRT-D. Previously implanted cardiac implantable electronic device should not limit implantation of CRT-Ds.* (Cardiol J)

Key words: cardiac resynchronization therapy, upgrade, de novo implantation, complications

Introduction

Cardiac resynchronization therapy (CRT) is a well-established treatment of advanced heart failure with reduced ejection fraction (HFrEF) and electrical dyssynchrony [1, 2]. Implantation of such devices is recommended for symptomatic patients with wide QRS complexes mainly of left bundle branch block morphology and substantially reduced left ventricular ejection fraction (LVEF) [3]. Indication for upgrading an existing cardiac implantable electronic device (CIED) to CRT-D also include high percentage of right ventricular pacing together with LVEF ≤ 35% and symptoms of heart failure, because right ventricular pacing increases mortality in patients with heart failure [4, 5]. Resynchronization therapy has proven to carry many advantages for patients with HFrEF, such as improving survival and LVEF, reducing the incidence of ventricular arrhythmias as well as decreasing symptoms [6]. CRT can be implanted de novo — in patients without CIED, as well as

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Received: 22.02.2022 Accepted: 27.05.2022 Early publication date: 15.06.2022

in patients who already have a device, the latter procedures are associated with intervention on a formerly implanted system. Of note, according to a European survey, it is estimated that more than 25% of CRT implantations are upgrade procedures [7]. Such operations are more complex because they are associated with existing device replacement, lead extraction or implantation of a new lead to a previously existing device; this runs the risk of higher procedural complications and possibility of i.a. venous occlusive disease, hematoma, pneumothorax or infection [8, 9]. Previous data concerning procedural complications are conflicting. Some studies have shown that upgrade procedures carry a higher risk of procedural complications and even higher short-term mortality, as compared to de novo CRT implantations [10, 11]. On the other hand, some research (including European surveys) resulted in similar rates of complications regardless of the type of procedure [12–15]. Moreover, little is known about the differences in the types of complications between those surgeries.

Aim of the study was an evaluation of the following: 1) whether procedures of CIED upgrade to CRT-D are associated with higher rates of short- and long-term complications, than de novo implantations; 2) whether any subgroups of complications are more common in a certain type of procedure.

Methods

Medical documentation was analyzed to compare the rate and type of complications of CRT implantation. We took into consideration records of patients who received CRT between January 2015 and September 2020 at the 1st Department of Cardiology in University Hospital of Lord's Transfiguration of Poznan University of Medical Sciences, Poland. All surgeries were performed by experienced operators. The study included all de novo implantations of CRT-D in addition to upgrades of pacemakers, CRT-P and implantable cardioverter-defibrillators to CRT-D. Revision interventions of CRT devices and pulse generator replacements were excluded. Prior to the procedure all patients were eligible for implantation of CRT and met current guidelines at the time of implant [4]. Patients provided written informed consent before all procedures of implantation.

Analyzed data

Medical histories of 326 patients were analyzed. Collected data included basic demographic data – gender, age; and clinical data such as – medical history, pharmacotherapy (including anticoagulation therapy), etiology to heart failure, and comorbidities. Data related to the procedure were as follows: type of procedure (i.e., upgrade or de novo implantation), necessity of electrode removal, exposure time, operation time, contrast consumption and complications. Complications were divided into the following: early (occurring to 30 days after the procedure) and late (occurring after 30 days after the procedure), infectious (fever, sepsis, infective endocarditis, decubitus) and non-infectious, as well as surgical and device or lead related; the division into groups is shown in Table 1. Moreover, before CRT implantation, the following data were obtained: ejection fraction estimated by experienced echocardiographers and parameters from laboratory tests i.a.: peripheral blood smear, lipid panel, electrolytes, C-reactive protein, glycemia, creatinine.

Table 1. Division of complications into surgical and device or lead related.

Device or lead related	Surgical
Lead dysfunction	Pneumothorax
Lead dislocation	Hemothorax
	Pericardial effusion
	Tamponade
	Mediastinal effusion
	Intraprocedural pocket bleeding
Ruptured lead insulation	Pocket hematoma
Right ventricular perforation	Subclavian artery rupture
	Subclavian vein rupture
	Coronary sinus dissection

Follow-up

Patients were followed until July 2021, taking into consideration all-cause mortality. Mortality data were collected form the National Health Insurer. Information about deaths and dates were obtained from government records.

Statistical analyzes

Statistical analyzes comprised descriptive statistics and assessment of significance level, which were performed using STATISTICA 13, TIBCO Software Inc. The distribution of the collected data was assessed using the Shapiro-Wilk test, and groups were compared with the Mann–Whitney U

Table 2. Baseline characteristics of patients.

	De novo (n = 172, 52.8%)	Upgrade (n = 154, 47.2%)	P
Age [years]	64.1 ± 12.9	65.3 ± 11.3	0.70
Gender (%male)	72% (n = 124)	84% (n = 130)	0.01
Weight [kg]	81.5 ± 16.3	85.9 ± 16	0.02
Height [m]	1.71 ± 0.1	1.73 ± 0.1	0.02
Ischemic CHF etiology	86 (50%)	93 (60.39%)	0.06
Dilated CHF etiology	57 (33.14%)	36 (23.38%)	0.05
Valvular heart disease CHF etiology	10 (5.81%)	9 (5.84%)	0.99
Pacing-induced CHF etiology	1 (0.58%)	10 (6.49%)	< 0.01
Atrial fibrillation	61 (35.47%)	68 (44.16%)	0.11
Coronary artery disease	93 (54.07%)	101 (65.58%)	0.03
Valvular heart disease	29 (16.86%)	32 (20.78%)	0.37
Post-mitral clipping	1 (0.58%)	7 (4.55%)	0.02
Post TAVI	1 (0.58%)	1 (0.65%)	0.94
Diabetes mellitus	57 (33.14%)	48 (31.17%)	0.70
Malignancy in the past	13 (7.56%)	4 (2.6%)	0.04
Ventricular arrhythmia	24 (13.95%)	63 (40.91%)	< 0.01
Anticoagulants	72 (41.86%)	84 (54.55%)	0.02
Vitamin K antagonists	42 (24.42%)	45 (29.22%)	0.33
Oral anticoagulants	30 (17.44%)	41 (26.62%)	0.04
Antiplatelets	74 (43.02%)	65 (42.21%)	0.88
Dual antiplatelet therapy	21 (12.21%)	13 (8.44%)	0.27
ACEI/ARB	154 (89.53%)	130 (84.42%)	0.17
Beta-blockers	161 (93.6%)	147 (95.45%)	0.47
Aldosterone antagonists	132 (76.74%)	131 (85.06%)	0.06
Antibiotic therapy after implantation	22 (12.79%)	18 (11.69%)	0.76

ACEI/ARB — angiotensin–converting enzyme inhibitors/angiotensin receptor blockers; CHF — congestive heart failure; TAVI — transcatheter aortic valve implantation

test. Dependencies between variables were calculated using the following tests: Spearman's ρ, Kendall's τ coefficient, and chi-squared. Differences were statistically significant if $p < 0.05$.

The study was approved by the head of the local Ethics Committee.

Results

Between January 2015 and September 2020, 326 implantations of CRT-D were performed, of which 172 (52,8%) were de novo implantations and 154 (47.2%) were upgrades. From the upgrade group 70 (45%) operations were associated with lead extraction. Preimplantation data (demographic, most common congestive heart failure etiology, selected morbidity, and pharmacotherapy) are shown in Table 2.

The groups differed in terms of frequency of dilated cardiomyopathy and pacing-induced cardiomyopathy. New York Heart Association classes did not differ significantly in both groups. Differences between the groups in comorbidities comprised: incidence of coronary artery disease, malignancies, ventricular arrhythmia, and mitral clipping implantation before CRT implantation. The pharmacotherapy of heart failure and coronary artery disease were similar in both groups. Of note, patients in the upgrade group were more often on oral anticoagulation, but this fact was not correlated with the incidence of hemorrhages. Anticoagulants were withdrawn 24 hours before surgery and resumed 48 hours after the procedure; bridging was not used. Post-procedural antibiotic therapy was used similarly often in both groups, which is important in view of subsequent infectious complications.

Table 3. Procedures data.

	De novo (n = 172, 52.8%)	Upgrade (n = 154, 47.2%)	P
Operation time [min]	48.5 ± 12.9	59.6 ± 32.4	0.26
Exposure time [s]	627.4 ± 562.5	688 ± 592.4	0.41
Volume of contrast [mL]	146 ± 61.8	151.5 ± 82.2	0.35
Radiation dose [Gy]	75.1 ± 230.7	91.3 ± 165.5	0.02

Data are shown as mean ± standard deviation

Procedures and complications

The operation time, exposure time, and volume of contrast used were similar in both groups, but the radiation dose was higher in the upgrade group, because the upgrade procedures are more complicated and often associated with lead extraction (Table 3).

In total we noticed 91 complications in 74 (22.7%) patients; the maximum number of complications in one patient was 3. Complications requiring reintervention or longer hospital stay occurred in 14% (n = 24) in the de novo group and in 16% (n = 25) in the upgrade group (p = 0.57). The most common complication in the general population was pocket hematoma (n = 14, 4.3%); in the upgrade group also pocket hematoma (n = 9, 5.8%); and in the de novo group — pneumothorax (n = 8, 4.7%). None of the pocket hematomas required surgical intervention, whereas 2.4% (n = 8) of the pneumothorax required drainage. Detailed data concerning complications are given in Table 4.

Categories of complications are shown in Figure 1. We did not notice significant differences between groups taking into consideration the following complications: early (p = 0.98) and late (p = 0.45), infectious (p = 0.38) and non-infectious (p = 0.,82), surgical (p = 0.38) and device or lead related (p = 0.6).

Survival

The mean follow-up was 39 and 34 months in the de novo and upgrade group, respectively (p = 0.05); during this time the all-cause mortality in both groups was similar, reaching 25.6% and 31.8%, respectively (p = 0.21). None of analyzed categories of complications was associated with worse survival. The only complication that caused worse survival was intraprocedural pocket bleeding (p = 0.02).

Discussion

The principal findings of this study are as follows: 1) procedures of upgrade to CRT-D and de novo implantations have similar rates of complications of about 27% in a mean 3-year follow-up; 2) we did not notice differences in incidence of any category of complications in the study groups; and 3) both populations had similar survival in a 3-year follow-up, and most complications did not affect survival.

The percentages of complications of CRT implantation vary in previous studies, from 4% to 27%, dependent on the analyzed population, timing of complication occurrence, and type of procedure [16, 17]. Some authors note more adverse events after de novo implants than after upgrades, which is very interesting because the latter are more complex and associated with mechanical as well as infectious complications [12, 16]. However, it seems that most studies, including this one, show similar rates of complications after de novo as well as upgrade procedures [13, 15, 18].

The percentage of complications noted in our study can be compared to the Replace registry, which showed 22.9% of complications in the upgrade group, including minor and major, in a 6-month follow-up [8]. Similarities in rates of complications are a result of longer follow-up in the Replace registry, because most studies record only periprocedural complications whereas our analysis involved a 3-year follow-up. Another study — a subanalysis of the RAFT study, in which CRT procedure complications were analyzed — showed percentages of complications of 19% and 26% in upgrades and de novo implants, respectively [16]. De novo group in the RAFT study showed a similar percentage of complications to ours, which might be a result not only of longer follow-up, but also of the similar categories of complications recorded in ours and in the RAFT study. Of particular interest is a comparison to a Dutch study that included a similar number of patients of congruous characteristics (etiology of congestive heart failure, comorbidities); their results are similar to ours: procedures of upgrade and de novo implants

Table 4. Complications.

Complications	Total (n = 326)	De novo (n = 172, 52.8%)	Upgrade (n = 154, 47.2%)	P
Pocket hematoma	14 (4.3%)	5 (2.9%)	9 (5.8%)	0.19
Pneumothorax	12 (3.7%)	8 (4.7%)	4 (2.6%)	0.33
Pneumothorax requiring intervention	8 (2.4%)	5 (2.9%)	3 (2%)	**0.59**
LV lead dislocation	9 (2.8%)	5 (2.9%)	4 (2.6%)	0.86
RA lead dislocation	7 (2.1%)	5 (2.9%)	2 (1.3%)	0.32
Decubitus	5 (1.5%)	1 (0.6%)	4 (2.6%)	0.14
Tamponade	4 (1.2%)	2 (1.2%)	2 (1.3%)	0.91
Pericardial effusion	4 (1.2%)	2 (1.2%)	2 (1.3%)	0.91
LV lead dysfunction	4 (1.2%)	2 (1.2%)	2 (1.3%)	0.91
Right ventricular perforation	3 (0.9%)	2 (1.2%)	1 (0.7%)	0.63
Intraprocedural pocket bleeding	3 (0.9%)	2 (1.2%)	1 (0.7%)	0.63
RV lead dislocation	3 (0.9%)	1 (0.6%)	2 (1.3%)	0.50
RV lead dysfunction	3 (0.9%)	1 (0.6%)	2 (1.3%)	0.50
Subclavian vein rupture	2 (0.6%)	0 (0%)	2 (1.3%)	0.13
Coronary sinus dissection	2 (0.6%)	1 (0.6%)	1 (0.7%)	0.94
Subclavian artery rupture	2 (0.6%)	2 (1.2%)	0 (0%)	0.18
Left arm thrombosis	2 (0.6%)	1 (0.6%)	1 (0.7%)	0.94
Ventricular fibrillation	2 (0.6%)	0 (0%)	2 (1.3%)	0.13
Mesenteric artery embolism	1 (0.3%)	0 (0%)	1 (0.7%)	0.29
Left arm edema	1 (0.3%)	1 (0.6%)	0 (0%)	0.34
RA lead dysfunction	1 (0.3%)	0 (0%)	1 (0.7%)	0.29
Mediastinal effusion	1 (0.3%)	0 (0%)	1 (0.7%)	0.29
Ruptured lead insulation	1 (0.3%)	0 (0%)	1 (0.7%)	0.29
Death	1 (0.3%)	0 (0%)	1 (0.7%)	0.29
Fever	1 (0.3%)	0 (0%)	1 (0.7%)	0.29
Sepsis	1 (0.3%)	1 (0.6%)	0 (0%)	0.34
Infective endocarditis	1 (0.3%)	1 (0.6%)	0 (0%)	0.34
Hemothorax	1 (0.3%)	1 (0.6%)	0 (0%)	0.34
Total	91 (27.9%)	44 (25.5%)	47 (30.5%)	0.78

LV — left ventricle; RA — right atrium; RV — right ventricle

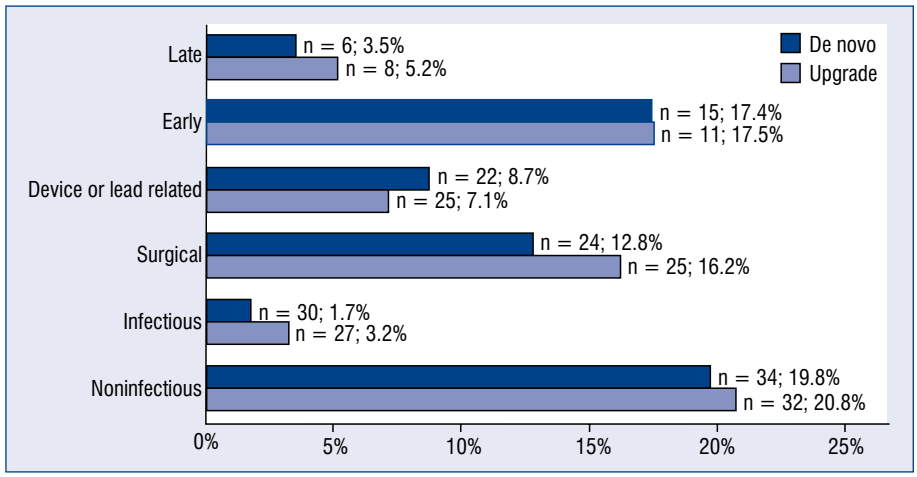

Figure 1. Complications divided into: late (more than 30 days after the procedure) and early; infectious and noninfectious; surgical and device related.

had similar rates of complications, with a total percentage of more than 20% [12].

On the other hand, in a European survey concerning CRT, published by Bogale et al. [7], the percentage of complications of de novo implants and upgrades was similar and substantially lower than in our center. This difference may be because we considered much more categories of complications, which were not included in the survey, and a longer follow-up. Although we analyzed early complications (30-days) in our center as opposed to periprocedural in the survey, the numbers are similar. When considering several complications, the percentages are similar in respect of most common ones, i.e., bleeding or tamponade; nevertheless, we noticed more cases of, e.g., pneumothorax, but fewer of coronary sinus dissection [7].

The results of a large American registry showed a much smaller percentage of upgrade procedures than in our study (4% vs. 47%). In terms of specific complications, we noticed a minor percentage of periprocedural deaths: only 0.7% in the upgrade group compared to 1.9% in the registry. Similarly, the percentage of cardiac perforation was lower in our cohort, but for, e.g., pneumothorax the tendency was opposite [11]. What is more, the registry of Cheung et al. [11] shows that upgrade procedures are associated with higher rates of procedural complications than de novo implants. This was explained by the fact that upgrade procedures are more complicated; however, we did not notice this tendency despite the fact that 45% of our upgrades were associated with lead extraction. The difference in percentage of procedural complications may be a result of the different methodologies of those studies (we included more categories of complications) and different proportion of upgrades vs. de novo implants.

Most studies analyze only limited categories of complications, such as the following: bleeding, pocket hematoma, pneumothorax, tamponade, coronary sinus dissection, and lead dislocation [7, 11], i.e., periprocedural complications recorded only acutely after the procedure. The longer follow-up in our study led to a higher percentage of complications, and in more than 3 years we were able to notice complications such as decubitus, chronic pericardial effusion (which was detected at in-patient visits), arm thrombosis, or infective endocarditis. What is more, a relatively high percentage (more than 45%) of lead removal was associated with the incidence of complications that can occur only in those procedures, for example reptured lead insulation. An analysis by Nemer et al. [13] included, apart from the most common complications, deep vein thrombosis; occurrence of this event reached 1% and was similar in the de novo and upgrade groups. In this aspect, our results are comparable.

Taking into consideration the mortality rate in our population (more than 20% in 3-year follow-up), those results are similar to previously reported [19]. We noted only one case of death directly associated with the procedure of CRT implantation, which occurred in the upgrade group. What is more, no type of procedure was associated with increased mortality, and the only complication that led to higher mortality was intraprocedural pocket bleeding.

Conclusions

This study revealed that procedures of upgrade to CRT-D are not associated with higher rate of complications than de novo implantations. The types and categories of complications were as common in the de novo group as in the upgrade group, despite a substantial percentage of the latter being associated with lead removal. The presence of any CIED should not be a limiting factor for CRT-D implantation. Caution during the procedure as well as the active search for complications, even rare ones, is mandatory. Database maintenance is crucial because it allows us to monitor the number of complications.

Conflict of interest: None declared

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