An urgent in-hospital upgrade to resynchronization therapy is associated with lower likelihood of survival as compared to planned procedures

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INTRODUCTION

Cardiac resynchronization therapy (CRT) is known to reduce mortality and symptoms of heart failure (HF) and improve the quality of life in carefully selected patients [1–4].

According to the European CRT Survey, upgrades from previously implanted pacemakers or implantable cardioverter-defibrillators constitute close to a quarter of all CRT implantations [5]. As stated in the European Society of Cardiology (ESC) Guidelines, CRT is a treatment option for patients with reduced left ventricular ejection fraction (LVEF) ≤35% and QRS duration ≥130 ms, with the highest class of recommendation for patients with QRS ≥150 ms of left bundle branch block morphology [6]. An upgrade to CRT should be considered in patients with a high percentage of right ventricular pacing and worsening of HF symptoms despite optimal medical therapy [6].

Despite these guidelines, there are reports of successful off-label *de novo* CRT implantations in inotropy-dependent patients or on mechanical support [7, 8]. However, there are only limited data on off-label CRT upgrades [9, 10]. Our study aimed to analyze the frequency and follow-up of patients who underwent an upgrade to CRT that was not fully in accordance with the current guidelines.

METHODS

Between January 2010 and December 2014 in the National Institute of Cardiology, 94 consecutive CRT upgrade procedures were performed. We retrospectively analyzed indications for those CRT upgrades, medical characteristics, and follow-up of these patients.

The study group consisted of 24 patients who underwent procedures that were assigned as "urgent" and were performed due to acute cardiac decompensation (non-ambulatory New York Heart Association [NYHA] class IV) or an electrical storm, which implies that these upgrades were not performed following the current guidelines. The group of 70 patients who underwent scheduled upgrade CRT implantation served as a control group. Patient survival was defined as the time from CRT implantation to all-cause mortality. The data on mortality and heart transplantation were sourced from the national databases provided by the Ministry of Digital Affairs and POLTRANSPLANT. Follow-up was limited to 60 months.

The study was approved by the Bioethics Committee of the National Institute of Cardiology (IK-NPIA-0021-98/1677/17).

Statistical analysis

Statistical analysis was performed with R software. The Shapiro-Wilk test indicated that the sample data was not normally distributed. Continuous data were presented as median (interquartile range [IQR]). Categorical data were presented as the absolute number and percentage of patients in each group. *P*-values <0.05 were considered statistically significant. The Mann-Whitney U test for continuous variables and the χ^2 test for nominal variables were used. Survival was estimated with the Kaplan-Meier curve. The plots were compared

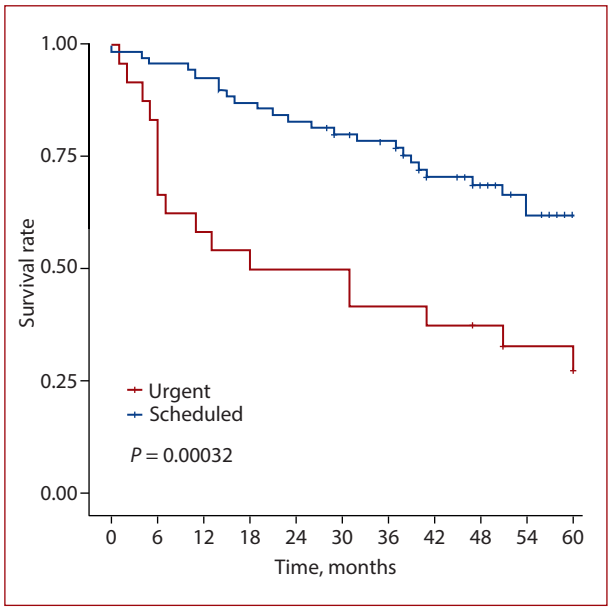

Figure 1. Survival in urgent versus scheduled cardiac resynchronization therapy upgrade

using the log-rank test. A univariate Cox regression analysis was used to evaluate factors affecting survival.

RESULTS AND DISCUSSION

In the study group, acute cardiac decompensation was an indication for 19 procedures and an electrical storm in 5 cases.

There were no significant differences between the two groups in age, sex, LVEF, presence of AF, diabetes or pacing dependency, and history of myocardial infarction. (Supplementary material, *Table S1*). The only statistically significant difference was found in HF etiology (non-ischemic cardiomyopathy was present in 67% of patients in the study group and 40% of patients in the control group) and NYHA class at baseline. The median follow-up in the study group was 29 (6–53) months while in the control group 44 (33–60) months, and the difference in the length of follow-up was statistically significant. Survival was found to be worse in patients that underwent a CRT upgrade in an urgent mode compared with planned procedures (hazard ratio 3.3 with 95% confidence interval [CI], 1.9–5.9, P <0.001) (Figure 1).

Ten patients (42%) died within the first year after the upgrade, and only 6 patients (25%) survived five years after the procedure. Three patients survived until cardiac transplantation.

Multivariable Cox-regression analyses showed that among all patients the urgent mode of the procedure along with the absence of a high RV pacing burden were associated with worse survival (Supplementary material, *Table S2*). However, no statistically significant predictor of poor prognosis was found in the study group (Supplementary material, *Table S3*).

Six patients were dependent on continuous intravenous inotropic therapy, which was defined as the inability to withdraw or decrease the dose of drugs without the occurrence of hypotension — systolic blood pressure <90 mm Hg, oliguria <20 ml/h and/or hypoxemia. The median time to complete withdrawal of inotrope support was 6 (1.25–13.75) days. Four patients did not survive the first year of follow-up, and one underwent cardiac transplantation.

Nine patients (38%) in the study group had indications for CRT during the previous implantation or device replacement. That group consisted of patients referred from centers that did not consider CRT at the time of previous intervention or their attempt to perform a CRT implantation was unsuccessful.

Patients with end-stage HF are poorly represented in clinical trials on CRT. According to an article by Nisha et al. [11], the current guidelines were based on studies that consisted of only 5% of NYHA class IV individuals. Nonetheless, the ESC guidelines do not exclude NYHA class IV patients from being candidates for CRT [6]. The treatment alternatives for HF patients who do not respond to medical therapy are mechanical circulatory support devices and heart transplantation [6].

Our research showed that patients who underwent an urgent CRT upgrade have a higher risk of death than those who had a scheduled procedure. Forty-one percent of patients from the study group died in the first year of follow-up. In comparison, only 7% of patients from the control group died in the same period. Only 25% of patients from the study group survived 5 years, two of them after heart transplantation.

The worst outcomes were observed among inotropy-dependent patients. Only two out of six patients survived the first year of follow-up after an upgrade procedure. However, few studies showed a beneficial effect of CRT *de novo* implantation in inotropy-dependent end-stage heart failure patients. Sokal et al. [7] reported 100% success in weaning from inotropes in eleven individuals after a CRT implantation. In a meta-analysis by Hernandez et al. [8], weaning from inotropes was successful in 93% of patients, and the 1-year survival rate was 69% after CRT *de novo* implantation.

Given the unfavorable outcomes presented in our study, it must be underlined that patients with end-stage heart disease had initially poor prognosis, and a CRT upgrade served as a rescue therapy or "bridge-to--transplant" for these individuals, especially considering the time of the investigation when not many alternative treatment options were available [12]. Considering that in some studies upgrades constitute almost half of all CRT procedures [13], it would be valuable to identify the factors for poor response in this group. It is also important to make careful clinical assessment of patients during implantation or exchange of devices to avoid delaying initiation of CRT therapy as had happened in 38% of patients in the study group.

Supplementary material

Supplementary material is available at https://journals.viamedica.pl/kardiologia_polska

Article information

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REFERENCES

1. Cazeau S, Leclercq C, Lavergne T, et al. Effects of multisite biventricular pacing in patients with heart failure and intraventricular conduction delay. N Engl J Med. 2001; 344(12): 873–880, doi: 10.1056/NEJM200103223441202, indexed in Pubmed: 11259720.
2. Cleland J, Daubert JC, Erdmann E, et al. The CARE-HF study (CArdiac REsynchronisation in Heart Failure study): rationale, design and end-points. Eur J Heart Fail. 2001; 3(4): 481–489, doi: 10.1016/s1388-9842(01)00176-3.
3. Lenarczyk R, Jędrzejczyk-Patej E, Mazurek M, et al. Quality of life in cardiac resynchronization recipients: association with response and impact on outcome. Pacing Clin Electrophysiol. 2015; 38(1): 8–17, doi: 10.1111/pace.12523, indexed in Pubmed: 25319879.
4. Cleland JGF, Daubert JC, Erdmann E, et al. The effect of cardiac resynchronization on morbidity and mortality in heart failure. N Engl J Med. 2005; 352(15): 1539–1549, doi: 10.1056/NEJMoa050496, indexed in Pubmed: 15753115.
5. Dickstein K, Normand C, Auricchio A, et al. CRT Survey II: a European Society of Cardiology survey of cardiac resynchronisation therapy in 11 088 patients-who is doing what to whom and how? Eur J Heart Fail. 2018; 20(6): 1039–1051, doi: 10.1002/ejhf.1142, indexed in Pubmed: 29457358.
6. McDonagh TA, Metra M, Adamo M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2021; 42(36): 3599–3726, doi: 10.1093/eurheartj/ehab368, indexed in Pubmed: 34447992.
7. Sokal A, Jędrzejczyk E, Lenarczyk R, et al. Efficacy of cardiac resynchronisation therapy in the treatment of end-stage inotrope-dependent heart failure patients. Kardiol Pol. 2014; 72(9): 777–782, doi: 10.5603/KP.a2014.0090, indexed in Pubmed: 24846358.
8. Hernandez GA, Blumer V, Arcay L, et al. Cardiac resynchronization therapy in Inotrope-Dependent heart failure patients: a systematic review and meta-analysis. JACC Heart Fail. 2018; 6(9): 734–742, doi: 10.1016/j.jchf.2018.02.016, indexed in Pubmed: 30098968.
9. Michael KA, Paisey JR, Mayosi BM, et al. A hybrid form of cardiac resynchronisation therapy in patients with failing systemic right ventricles. J Interv Card Electrophysiol. 2008; 23(3): 229–233, doi: 10.1007/s10840-008-9296-0, indexed in Pubmed: 18836823.
10. Mörtsell D, Thilén U, Tydén P, et al. Transvenous interventional implantation of CRT-D in a critically ill Mustard patient waiting for heart transplant. Clin Case Rep. 2019; 7(7): 1415–1418, doi: 10.1002/ccr3.2183, indexed in Pubmed: 31360501.
11. Almeida ND, Suarthana E, Dendukuri N, et al. Cardiac resynchronization therapy in heart failure: do evidence-based guidelines follow the evidence? Circ Cardiovasc Qual Outcomes. 2017; 10(12), doi: 10.1161/CIRCOUTCOMES.117.003554, indexed in Pubmed: 29222164.
12. Actuarial risk of sudden death while awaiting cardiac transplantation in patients with atherosclerotic heart disease. Am J Cardiol. 1991; 68(5): 545–546, doi: 10.1016/0002-9149(91)90796-n.
13. Grymuza M, Katarzyńska-Szymańska A, Chmielewska-Michalak L, et al. Follow-up and characteristics of recipients of cardiac resynchronization therapy with and without a defibrillator. Kardiol Pol. 2022; 80(7-8): 806–812, doi: 10.33963/KP.a2022.0125, indexed in Pubmed: 35545837.