

## Case Report

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# Upgrade from ICD to CRT-D: clinical and haemodynamic impact of biventricular pacing in a patient with acquired long QT syndrome

**Abstract:** Long QT syndrome (LQTS) is characterised by both the depolarisation and repolarisation disorder of cardiac muscle cells. Cardiac resynchronising therapy (CRT) is an important treatment option for patients with chronic heart failure (CHF) when echocardiographic and electrocardiographic criteria are met. Although CRT was introduced in clinical practice 10 years ago, doubts related to application of this treatment method persist because of its potential proarrhythmogenic effect. This is a case describing a 66-year-old Caucasian female with LQTS coexisting with a left bundle branch block (LBBB) and an implantable single-cavity cardioverter-defibrillator (ICD VR), who had repeated appropriate high-energy treatments. The upgrade to resynchronisation therapy defibrillator (CRT-D) significantly reduced frequency of ventricular tachycardia and the need for electrical therapies. The normalisation of the left ventricle size, as seen on echo examination, and the improvement of heart failure symptoms were also observed.

**Keywords:** long QT syndrome (LQTS), cardiac resynchronising therapy (CRT), resynchronisation therapy defibrillator (CRT-D), implantable cardioverter-defibrillator (ICD), polymorphic ventricular tachycardia, Torsade de Pointes (TdP), heart failure (HF)

DOI 10.1515/med-2015-0023

Received: May 23, 2013; accepted: December 11, 2014

## 1 Introduction

Long QT syndrome (LQTS) is described as a depolarisation and repolarisation cardiac muscle cell disorder. LQTS can be of genetic or iatrogenic origin [1]. Electrocardiographically, it is characterized by a prolonged QT interval ( $\geq 450$  ms in women,  $\geq 460$  ms in men and  $\geq 500$  ms in bundle branch blocks or ventricular pacing) [4]. LQTS manifests through attacks of polymorphic ventricular tachycardia, also called Torsades de Pointes (TdP). Clinically it may lead to syncope, cardiac arrest, or sudden death. To date, no effective methods are available for treating patients with LQTS.

LQTS is an indication for the implantable cardioverter-defibrillator (ICD) in patients using beta-blockers, with previous cardiac arrests and who have a reasonable expectation of survival with a good functional status of more than 1 year [2].

Cardiac resynchronising therapy (CRT) has a recognised significance in treatment of patients with chronic heart failure (CHF) and left ventricular ejection fraction (LVEF)  $\leq 35\%$ , where a broadening of the QRS complex  $\geq 120$  ms is seen with the morphology of a left bundle branch block (LBBB), and in functional class II-IV according to the New York Heart Association (NYHA) classification system despite adequate medical treatment [3]. Although CRT was introduced to the clinical practice 10 years ago, doubts related to the application of this treatment persist due to the potential proarrhythmogenic effect.

This is the case of successful application of cardiac resynchronisation therapy defibrillator (CRT-D) in a patient with LQTS coexisting with a LBBB and an

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implantable single-cavity cardioverter-defibrillator (ICD VR) who experienced repeated high-energy therapies mainly caused by TdP.

## 2 Case description

A 66-year-old woman with an ICD VR was transferred to our department at the Medical University of Silesia in Katowice from a peripheral hospital for further management of an electrical storm, which occurred the day before. The information provided by the referring physician included the history of recurrent electrical storms and details of the administered medications; the patient required not only a correction of hypokalaemia/hypomagnesemia and administration of metoprolol, amiodarone and lidocaine but also a sedation with midazolam to cessate the arrhythmia.

The patient was known from the implantation of an ICD VR 15 months earlier at another centre due to repeated episodes of TdP (with subsequent losses of consciousness). Each episode of TdP was preceded by the prolongation of the QT interval. A transthoracic echocardiogram (TTE) performed at that time showed a normal-sized left ventricle: end-diastolic diameter (EDD), 47 mm; end-systolic diameter (ESD) 37 mm; end-diastolic volume (EDV) 79 ml; end-systolic volume (ESV) 43 ml; slightly impaired systolic left ventricle function with an ejection fraction (EF) of 45%. Coronary angiography performed before the implantation of the ICD VR did not indicate any changes in the epicardial coronary arteries. In the ECG, typical features of a LBBB were seen with a widened QRS complex to 130 ms.

The patient was admitted to the Intensive Cardiac Care Unit in stable circulatory and respiratory condition and heart failure classified as a functional NYHA class III. Within 1 day preceding the indexed admission, numerous high-energy therapies for ventricular tachycardias were recorded in the memory of the ICD VR (202 adequate therapies, including 149 high-energy therapies) (Figure 1). Moreover, the exhausted battery message occurred. The ECG showed prolonged corrected QT interval of 0,61 s (Bazett's formula) with a LBBB and widened QRS complex of 160 ms (Figure 2).

A control TTE examination in comparison with the previous one revealed a slight enlargement of left ventricle (EDD 48 mm, ESD 42 mm, EDV 95 ml, ESV 65 ml) with more severe global left ventricle systolic dysfunction (LVEF 31%) and atrioventricular, inter- and intraventricular dyssynchrony. The diastolic filling time (DFT) was 327

ms – 33% of cardiac cycle duration (RR), left ventricular pre-ejection period (LVPEP) was 177 ms, right ventricular pre-ejection period (RVPEP) was 85 ms, intraventricular delay (IVD) was 92 ms, and septal-to-posterior wall motion delay (SPWMD) was 250 ms.

Serum potassium, calcium and magnesium concentrations remained within normal limits. Moreover, a significant hypothyroidism (iatrogenic, most likely from amiodarone) was found with a thyroid stimulating hormone (TSH) concentration of 58 mU/l in blood serum. Amiodarone therapy, originally applied for 12 months, was discontinued. L-thyroxine was introduced with the goal of lowering the TSH concentration fivefold after a few weeks.

The patient was qualified for the CRT-D implantation procedure on the basis of the clinical heart failure (NYHA class III), electrocardiographic (LBBB, QRS 160 ms), and echocardiographic (EF 31%, dyssynchrony of the left ventricle systole) criteria for resynchronisation therapy. After the procedure, no complex ventricular cardiac disorders were observed in the patient during a five-week hospitalisation.

In the genetic analysis no changes in the coding sequence of the *HERG* and *KCNQ1* genes were detected.

The patient was discharged with the recommendation to take the following medications: metoprolol succinate 50 mg daily; L-thyroxine 100 µg daily; spironolactone 100 mg daily; ramipril 5 mg daily; potassium losartan 100 mg daily; lacidipinum 4 mg daily; simvastatinum 20 mg daily; acetylsalicylic acid 75 mg daily and potassium substitution.

In the six-month follow-up, the symptoms of heart failure significantly improved from NYHA class III to class I and remained stable in time during next 12 months. In ECGs, a narrowing of QRS complexes to 120 ms was seen (Figure 3).

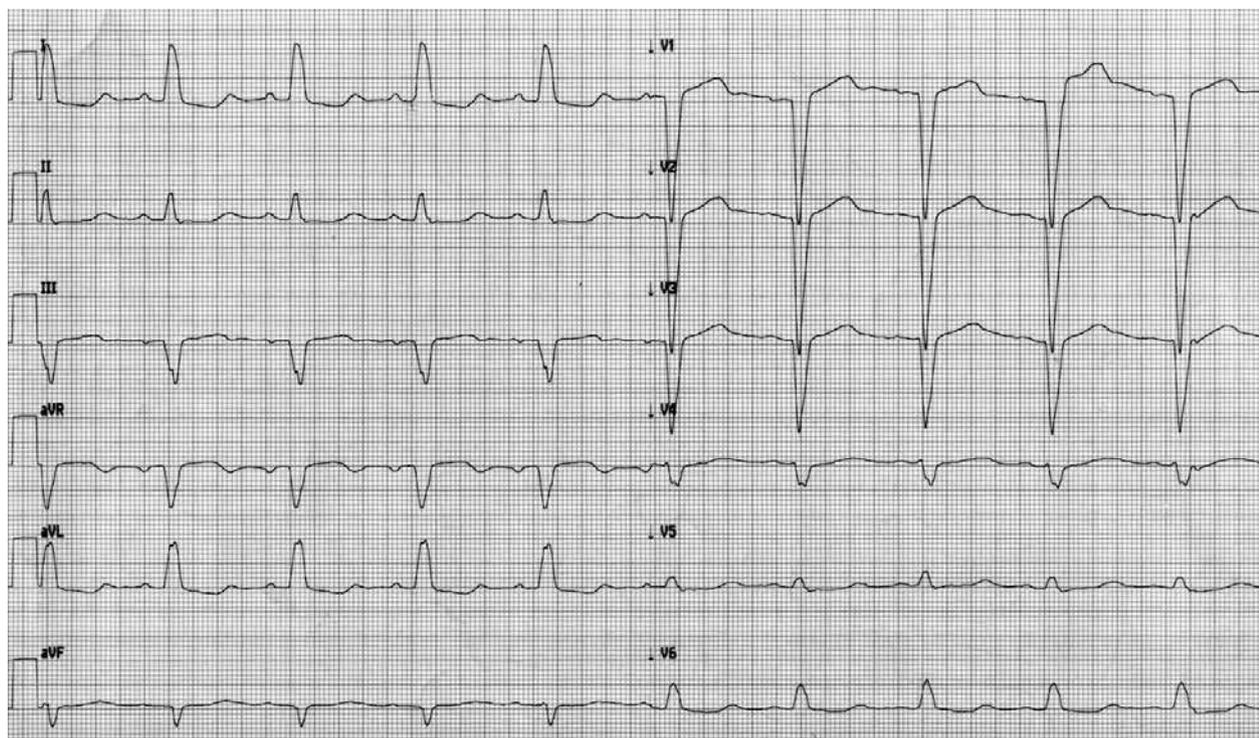
The TTE performed at 3, 6 and 18 months after CRT-D implantation showed a gradual improvement of all parameters with final normalization of left ventricle size (EDD 46 mm; ESD 32 mm; EDV 65 ml; ESV 32 ml), left ventricle contractility (EF 50%) and met criteria for synchrony (DFT 362 ms – 48% of RR, LVPEP 89 ms RVPEP 89 ms, IVD 0 ms). An euthyroid state was reached with a TSH level of 5,20 µIU/ml.

Over a period of 18 months, only four episodes of spontaneous complex ventricular rhythm disorders were found: two TdP and two VF successfully treated with a high-energy therapy.

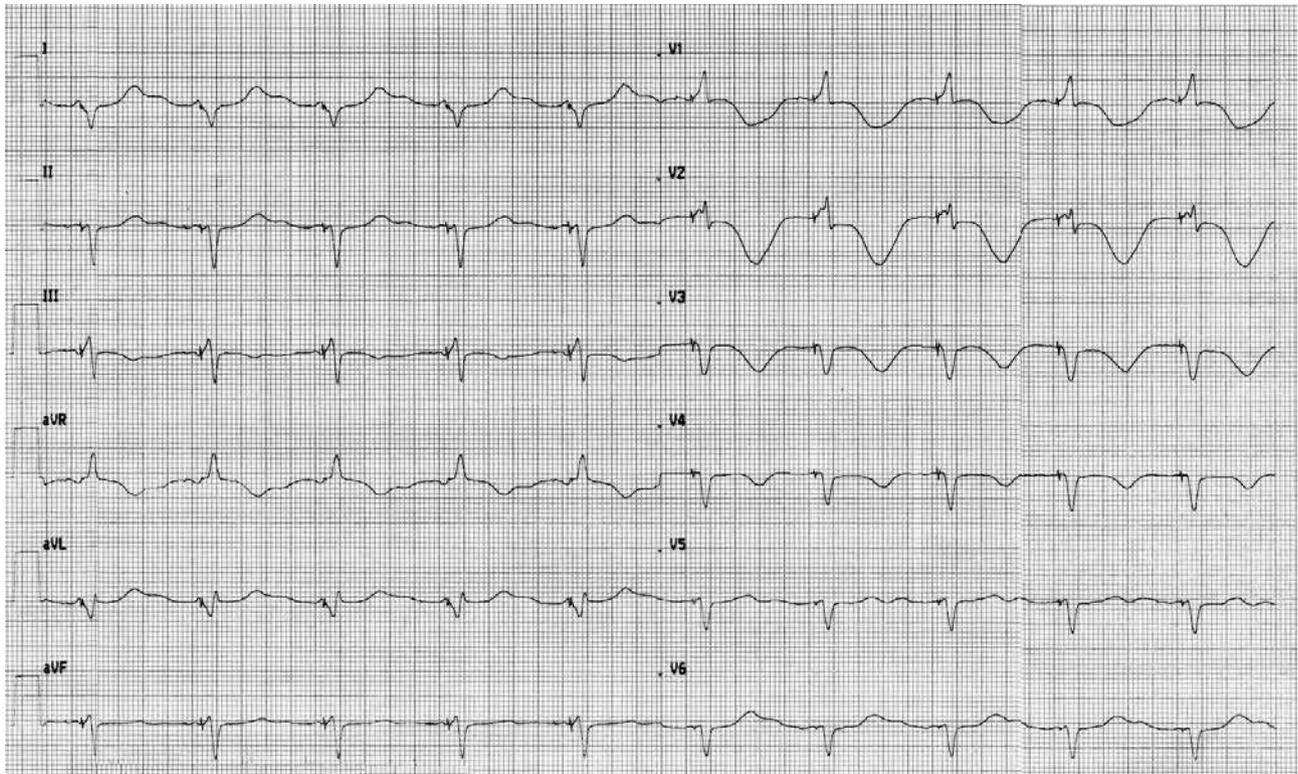
During subsequent follow-ups, an immediate occurrence of ventricular arrhythmia (presence of ventricular extrasystolic beats, including ventricular pairs and



**Figure 1:** Internal electrocardiogram retrieved from ICD memory showing one of the TdP episodes. Report of the number of the TdP and VF episodes.



**Figure 2:** ECG on admission. LBBB with broadening of the QRS complex to 160 ms. Elongated corrected QT interval (Bazett's formula) to 0,61 s.



**Figure 3:** Follow-up ECG. Narrowed QRS complexes to 120 ms and shortened corrected QT interval to 480 ms.

salves) was noted each time the resynchronising pacing was turned off (Figure 4).

**Ethical approval:** The research related to human use has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration, and has been approved by the authors' institutional review board or equivalent committee.

**Informed consent:** Informed consent has been obtained from all individuals included in this study.

### 3 Discussion

CRT has become a recognised addition to the optimal pharmacological treatment of patients with advanced CHF, impaired left ventricular function and intraventricular conduction disorders.

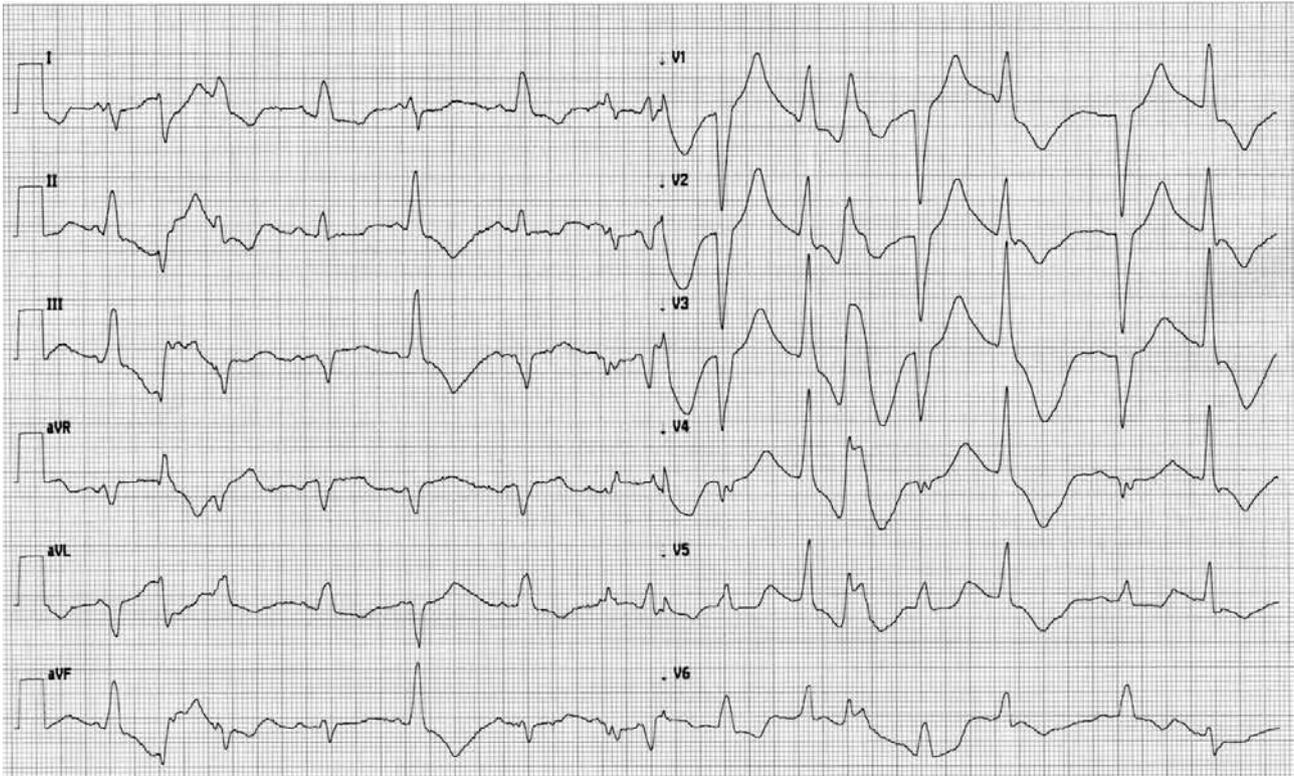
More and more patients with an implantable ICD may develop indications for upgrade to a CRT-D during follow-up. Numerous papers have shown that isolated right ventricular pacing not only leads to the development of pacing cardiomyopathy but also has a proarrhythmic effect [5,6]. Gardiwal A. *et al.* showed that right ventricular

pacing of more than 2% is an independent risk factor for ventricular arrhythmias in patients with left ventricular ejection fraction below 40% and with an ICD used as a secondary prevention [5]. The probability of ventricular tachyarrhythmias increases as LVEF decreases [7].

In the presented patient, 30% of pacing of the right ventricle was found. Together with LQTS and LBBB, it could lead to a significant disorder in myocardium electrical activity. Furthermore, a significant decrease in LVEF in the patient when compared with the initial examination was found (45% vs. 31%). This decrease likely results from the cardiac muscle stunning caused by numerous ICD discharges from recurring polymorphic ventricular tachycardias. However, the additive to LQTS arrhythmogenic action of amiodarone therapy cannot be excluded. Even normal baseline ECG does not exclude the drug-dependent repolarization prolonging leading to proarrhythmic events during therapy and the onset of TdP. Nevertheless, after discontinuation of this therapy and partial normalization of thyroid gland function ventricular arrhythmias still persisted.

A genetic examination did not reveal any mutations in the sequence of the HERG and KCNQ1 genes. Mutations in those genes are responsible for 70-90% of cases of congenital LQTS [1].

Subsequent application of biventricular stimulation resulted in a decreased frequency of TdP occurrence in the



**Figure 4:** Follow-up ECG. Noticeable ventricular arrhythmia (ventricular pairs) just after switching-off of resynchronizing pacing.

patient described, which is comparable to the research of Ermis et al. They found that CRT reduces the frequency of ventricular tachycardia (VT) and ventricular fibrillation (VF) and thereby reduces CRT-D interventions when compared with ICD in patients with cardiac insufficiency [6]. Those outcomes are in line with CONTAK-CD [8] and MIRACLE-ICD [9] studies. However, investigators analysed the ICD group and the CRT-D group separately. Many other clinical studies also demonstrate that biventricular pacing significantly reduces the frequency of ventricular arrhythmias [7,10,11]. The underlying mechanism is complex and poorly understood. The most probable hypothesis of anti-arrhythmogenic effect of biventricular pacing is that the anatomical remodelling, both left and right ventricle, after implementation of CRT therapy in responders leads to mechanical remodelling and thereby to the reduction of ventricular arrhythmic episodes. Moreover, the more pronounced the anatomical remodelling, the stronger the reduction in ventricular arrhythmias [10,12,13]. Recent studies gave new insights in this field showing that the reduction in VT/VF is more significant in patients with ventricular conduction disorders (LBBB) prior to CRT implantation, in whom the improvement in dyssynchrony with CRT is more visible [14,15].

On the contrary, recent reports suggest that the application of CRT-D therapy may have a proarrhythmic effect by inverting the direction of the left ventricle activation, elongating the duration of myocardial repolarization and delaying the transmural conduction during biventricular stimulation. These adverse episodes were recorded only in very short-term after implantation and were suppressed in the long term [16,17].

The antiarrhythmic effect of biventricular pacing, as observed in presented patient, is likely related to the improvement in synchrony of both electrical (elimination of intraventricular conduction disorders resulting not only from the LBBB) and mechanical (DFT, IVD, SPWMD) activity of the left ventricle. It was confirmed by the immediate occurrence of ventricular arrhythmias once the pacing was turned off.

## 4 Conclusion

The presented case report describing a patient with LQTS, LBBB, CHF and electrical storms in anamnesis shows that the final therapeutic success of almost total reduction of ventricular arrhythmias was the effect of parallel actions:

firstly, the conversion from an ICD to a CRT-D, and secondly, the implementation of optimal pharmacological treatment.

**Acknowledgements:** We thank Prof. Anna Latos-Bieleńska, Dr Agata Józefiak and Mgr Marcin Straburzyński from the Center for Medical Genetics “GENESIS” in Poznań for performing the genetic tests in the patient. We also thank the staff of the American Journal Experts for English language editing of the manuscript.

**Conflict of interest statement:** Authors state no conflict of interest

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