

Implantable cardioverter-defibrillator therapy in patients with congenital long QT syndrome: do we know what we need to know?

Gerold Mönig¹, Virgilijus Ziukas², Matthias Koopmann¹

¹Department of Cardiology, Schuechtermann-Klinik, Bad Rothenfelde, Germany

²Department of Cardiac Surgery, Schuechtermann-Klinik, Bad Rothenfelde, Germany

Article Zienciuk-Krajka et al., see p. 1687

INTRODUCTION

There is an ongoing debate about device-based prevention of sudden cardiac death (SCD) in general, as well as the use of devices in the primary prevention in long QT syndrome (LQTS) subjects. Implantable cardioverter-defibrillators (ICDs) have a proven efficacy in the prevention of SCD due to life-threatening arrhythmias in a plethora of cardiac diseases [1]. However, controversy exists regarding their use in subjects with congenital arrhythmogenic disorders and an increased risk of potentially fatal arrhythmias, such as LQTS. This has stimulated research, and recently we have witnessed major strides in the detection of such channelopathies. Consequently, it has led to an increasing awareness in the clinical arena, which resulted in a growing number of young individuals who received an ICD. Especially in LQTS subjects, an early ICD implantation may lead to specific problems in the long term. LQTS patients are particularly at risk of ICD discharge, as well as device-related complications. Device programming to prevent both adequate and inadequate shocks is of utmost importance because of the possibility of spontaneous termination of torsade de pointes (TdP) arrhythmias. Device-related complications are mostly associated with transvenous leads. In fact, the dilemma of increased arrhythmia risk in conjunction with device-induced harm leads to a struggle for clinical cardiologists dealing with this challenging patient population. Thus, because ICD therapy might be life-saving, the indications should be based on a solid risk-benefit ratio to avoid complications.

There is a lack of randomised, controlled trials in LQTS patients with ICDs, therefore our knowledge is largely based on observational studies and registries. In a direct response to the paucity of available data, in this issue Zienciuk-Krajka et

al. [2] report on the multicentre Polish experience in 67 LQTS patients followed up for 48 months. This retrospective study identifies risk factors for ICD discharge and supports the results of many single-centre experiences [3] as well as multicentre registries [4–6]. It is still of special interest because clinical management of LQTS patients with ICD has to consider many specific aspects that can be concluded only from these retrospective experiences.

CONCOMITANT THERAPY

The importance of continuous β -blocking therapy even after ICD implantation is further supported by this LQTS cohort [2]. Noncompliance to β -blockers was associated with increased risk for adequate ICD therapy. Furthermore, the high rate of inappropriate shocks caused by sinus- and supraventricular tachycardia (SVT) points to the need for ongoing β -blockade in this young population. However, nowadays β -blocker medication to prevent ICD interventions seems to be a more accepted therapy with better adherence compared to past cohorts.

RISK FOR ICD SHOCKS

Another fact we can learn from this study is the long-term incidence of shocks, both appropriate and inappropriate. Even after event-free survival for several years, there is still a risk of malignant arrhythmia and SCD in LQTS patients. This might be of importance in the decision regarding ICD explantation in this young population after one or two event-free battery cycles. Furthermore, older LQTS patients might still be at risk of sudden cardiac arrest, as demonstrated by an ICD intervention after six decades in one patient in this cohort [2]. Conversely, the risk of inadequate ICD discharge is highest in the first two years after implantation. Although there is no definite

Address for correspondence:

Prof. Gerold Mönig, Kardiologie, Schüchtermann Klinik, Ulmenallee 5-11, D-49214 Bad Rothenfelde, Germany, tel: +49-5424 641-826, fax: +49-5424 641-829, e-mail: gmoennig@schuechtermann-klinik.de

Kardiologia Polska Copyright © Polish Cardiac Society 2018

Note: The opinions expressed by the authors are not necessarily those of the journal editors, Polish Cardiac Society or publisher.

explanation for this observation, it might be speculated that reprogramming of ventricular tachycardia (VT) detection, upgrading to dual-chamber systems, or intensifying β -blocking therapy is beneficial in preventing inappropriate discharge.

In this Polish cohort, a history of cardiac arrest is the predominant indication. This might explain the higher intervention rate of 45% compared to other populations [2].

SHOCK CLUSTER IN LQTS

In the Polish cohort there were only 9% of patients with clustered ICD therapy. In LQTS shocks might trigger clusters of TdP. Therefore, we would like to stress the importance of implementing long detection times to allow TdP to terminate. Additionally, β -blocker adherence and antibradycardia pacing are known factors suppressing appropriate ICD discharges, which might be implemented in this contemporary LQTS cohort. A dual-chamber system may be particularly useful in patients with a severe phenotype or multiple episodes despite the above-mentioned management. Notably, a DDD-ICD upgrade was performed in four of the Polish LQTS patients [2].

CHOICE OF DEVICE

Dual-chamber devices seem to reduce the rate of inappropriate interventions. This might be due to antibradycardia pacing or better differentiation of SVT from ventricular arrhythmia. It is known that atrial tachyarrhythmias are more frequent in LQTS patients compared to the general population [7], due to prolonged atrial repolarisation [8]. In this regard, 75% of the atrial fibrillation-induced inappropriate discharges in the Polish cohort occurred in LQTS patients with single-chamber systems [2]. Therefore, it is intriguing to speculate that supraventricular arrhythmias could be prevented by atrial stimulation through decreasing atrial repolarisation.

Because all subjects in this cohort received a transvenous ICD we would like to stress the role of a subcutaneous defibrillator (S-ICD) in this context. In the EFFORTLESS study [9] 20.2% of the patients with channelopathies as a primary cardiac disease received an S-ICD. Channelopathy included the Brugada syndrome, catecholaminergic polymorphic VT, LQTS, short QT syndrome, idiopathic ventricular fibrillation (VF), and TdP. In fact, the most likely index arrhythmia in LQTS is TdP or VF, thus, in combination with young age, it would favour an S-ICD. On the other hand, T-wave oversensing may occur due to changes in T-wave morphology as well as the lack of antibradycardia pacing, rate smoothing, and post-shock pacing, which are major disadvantages of this system. This may raise the risk for inappropriate device discharge and result in the absence of preventive pacing algorithms. Thus, a thorough preimplantation screening is of utmost importance in this setting. Nevertheless, the clinician should have this option in mind for selected LQTS patients.

PRIMARY PREVENTION IN LQTS

The most challenging problem in LQTS is to identify patients at "high risk" for primary prevention. In this context, it is undoubted that a family history of SCD is a weak predictor without other risk factors. From our experience, even syncope under β -blocking therapy is not necessarily a class I indication for ICD. QTc interval seems to be the best predictor of long QT-associated symptoms and arrhythmia in electrocardiographic risk stratification [10]. In a subgroup of primary prevention patients [2], the intervention rate was as high as 33% compared to 22% in an eight-year follow-up study of 212 LQTS patients [5]. In that study QTc > 550 ms and syncope on β -blocker therapy were predictive of appropriate shocks. However, in the Polish cohort LQTS patients were more efficiently identified as "high risk", and previous pacemaker therapy was identified as a risk factor for ICD intervention.

CONCLUSIONS

Controversy remains regarding the optimal management of LQTS patients with respect to ICD therapy, especially in the setting of primary prevention of SCD. Nevertheless, we support the authors' hope that the presented data might improve the management of LQTS patients scheduled for primary prevention ICD implantation, especially when evaluating the risks (short- and long-term) and benefits individually.

Although speculative, the following suggestions regarding ICD therapy in LQTS patients might be derived and could be seen as a basis for further discussion or research projects:

- strict indication for ICD implantation should be present;
- β -blocking medication should be continued following ICD implantation and intensified whenever possible;
- dual-chamber systems might be preferred *a priori*;
- VVI 40 backup pacing might trigger TdP by short-long-short sequences and should thus be avoided;
- identifying high-risk LQTS patients in primary prevention is an unsolved problem:
 - I) QTc > 550 ms is the most robust predictor on the surface electrocardiogram,
 - II) syncope on β -blocker therapy might be a predictor,
 - III) symptoms during pacemaker therapy might be a predictor,
 - IV) positive family history for SCD is not, or is a weak, predictor;
- prolonged detection time in the VT zone might reduce shocks by allowing arrhythmia to terminate spontaneously;
- SVT inhibition criteria should be activated because atrial arrhythmias are more frequent in LQTS patients, which could lead to inappropriate device discharge;
- S-ICD might be an option in highly select LQTS patients.

Conflict of interest: none declared

References

1. Priori SG, Blomström-Lundqvist C, Mazzanti A, et al. 2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: The Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC). Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC). *Eur Heart J*. 2015; 36(41): 2793–2867, doi: [10.1093/eurheartj/ehv316](https://doi.org/10.1093/eurheartj/ehv316), indexed in Pubmed: [26320108](https://pubmed.ncbi.nlm.nih.gov/26320108/).
2. Zienciuk-Krajka A, Sterliński M, Filipecki A, et al. Implantable cardioverter-defibrillators in patients with long QT syndrome: a multicentre study. *Kardiol Pol*. 76(12): 1687–1696, doi: [10.5603/KP.a2018.0177](https://doi.org/10.5603/KP.a2018.0177), indexed in Pubmed: [30251242](https://pubmed.ncbi.nlm.nih.gov/30251242/).
3. Mönnig G, Köbe J, Löher A, et al. Implantable cardioverter-defibrillator therapy in patients with congenital long-QT syndrome: a long-term follow-up. *Heart Rhythm*. 2005; 2(5): 497–504, doi: [10.1016/j.hrthm.2005.02.008](https://doi.org/10.1016/j.hrthm.2005.02.008), indexed in Pubmed: [15840474](https://pubmed.ncbi.nlm.nih.gov/15840474/).
4. Schwartz PJ, Spazzolini C, Priori SG, et al. Who are the long-QT syndrome patients who receive an implantable cardioverter-defibrillator and what happens to them?: data from the European Long-QT Syndrome Implantable Cardioverter-Defibrillator (LQTS ICD) Registry. *Circulation*. 2010; 122(13): 1272–1282, doi: [10.1161/CIRCULATIONAHA.110.950147](https://doi.org/10.1161/CIRCULATIONAHA.110.950147), indexed in Pubmed: [20837891](https://pubmed.ncbi.nlm.nih.gov/20837891/).
5. Biton Y, Rosero S, Moss AJ, et al. Primary prevention with the implantable cardioverter-defibrillator in high-risk long-QT syndrome patients. *Europace*. 2018 [Epub ahead of print], doi: [10.1093/europace/euy149](https://doi.org/10.1093/europace/euy149), indexed in Pubmed: [29947754](https://pubmed.ncbi.nlm.nih.gov/29947754/).
6. Sundström E, Jensen SM, Diamant UB, et al. Implantable cardioverter defibrillator treatment in long QT syndrome patients: a national study on adherence to international guidelines. *Scand Cardiovasc J*. 2017; 51(2): 88–94, doi: [10.1080/14017431.2016.1270463](https://doi.org/10.1080/14017431.2016.1270463), indexed in Pubmed: [27936942](https://pubmed.ncbi.nlm.nih.gov/27936942/).
7. Zellerhoff S, Pistulli R, Mönnig G, et al. Atrial arrhythmias in long-QT syndrome under daily life conditions: a nested case control study. *J Cardiovasc Electrophysiol*. 2009; 20(4): 401–407, doi: [10.1111/j.1540-8167.2008.01339.x](https://doi.org/10.1111/j.1540-8167.2008.01339.x), indexed in Pubmed: [19017345](https://pubmed.ncbi.nlm.nih.gov/19017345/).
8. Kirchhof P, Eckardt L, Franz MR, et al. Prolonged atrial action potential durations and polymorphic atrial tachyarrhythmias in patients with long QT syndrome. *J Cardiovasc Electrophysiol*. 2003; 14(10): 1027–1033, indexed in Pubmed: [14521653](https://pubmed.ncbi.nlm.nih.gov/14521653/).
9. Boersma L, Barr C, Knops R, et al. EFFORTLESS Investigator Group. Implant and Midterm Outcomes of the Subcutaneous Implantable Cardioverter-Defibrillator Registry: The EFFORTLESS Study. *J Am Coll Cardiol*. 2017; 70(7): 830–841, doi: [10.1016/j.jacc.2017.06.040](https://doi.org/10.1016/j.jacc.2017.06.040), indexed in Pubmed: [28797351](https://pubmed.ncbi.nlm.nih.gov/28797351/).
10. Mönnig G, Eckardt L, Wedekind H, et al. Electrocardiographic risk stratification in families with congenital long QT syndrome. *Eur Heart J*. 2006; 27(17): 2074–2080, doi: [10.1093/eurheartj/ehl1159](https://doi.org/10.1093/eurheartj/ehl1159), indexed in Pubmed: [16882679](https://pubmed.ncbi.nlm.nih.gov/16882679/).