Review Article

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Lifestyle modification and medical treatment of long QT syndrome

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ABSTRACT

Studies have shown that many manifestations can be observed for patients suffering from long QT syndrome (LQTS), as it is a common cause of syncope and mortality among younger patients, in addition to convulsions. Many management modalities for LQTS have been described in the literature including medical treatment modalities and lifestyle modification approaches. However, evidence regarding the outcomes of these approaches is continuously updating. In this study, we have reviewed findings from the current studies in the literature about the medical treatment and lifestyle modifications for patients suffering from LQTS. Furthermore, studies have shown that β -blockers are effective modalities and should be used at a maximum dose. However, the potential side events should be considered and adequately managed and patient compliance should be maintained along the course of treatment. Implantable cardioverter-defibrillator (ICD) implantation and LCSD were also discussed in the present study with their favorable indications. Additionally, lifestyle modifications were also important and have been reported with favorable events and therefore, these should be considered in such situations. However, evidence regarding some approaches as limiting competitive exercises is still conflicting, indicating the need for future investigations.

Keywords: Cardiac, Treatment, LQTS, Lifestyle, Pharmacological

INTRODUCTION

Prolonged QT interval on ECG with absent structural heart diseases and no history of relevant drug administration implies the diagnosis of LQTS.¹⁻³ In addition, studies have shown that many manifestations can be observed for these patients, as it is a common

cause of syncope and mortality among younger patients, in addition to convulsions. 4,5 The disease is characterized by channelopathy and usually leads to the development of severe ventricular arrhythmias. 6 Estimates show that LQTS is prevalent among 1:5,000 to 1:2,500 individuals. Ventricular fibrillation, torsades de pointes and polymorphic ventricular tachycardias that are associated

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with this syndrome are mainly attributable to the heterogenous repolarization and early afterdepolarizations (Figure 1). The onset of the disease usually occurs at a mean age of 12 years old and it has been observed that diseases with earlier onsets are observed with more severe forms and increased risk of morbidity and mortality. Many management modalities for LQTS have been described in the literature, including medical

treatment modalities and lifestyle modification approaches. However, evidence regarding the outcomes of these approaches is continuously updating. Thus, we aimed to conduct the present study to discuss the medical treatment and lifestyle modification approaches for managing LQTS, based on evidence from the current studies in the literature.

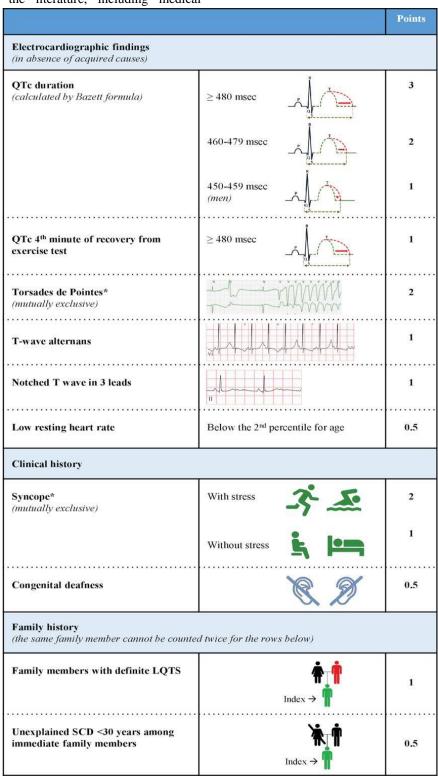


Figure 1: Diagnostic criteria for LQTS.⁵¹

METHODS

This literature review was based on an extensive literature search of the Medline, Cochrane and EMBASE databases which was performed on 1 August 2021 using the medical subject headings (MeSH) or a combination of all possible related terms. ^{8,9} This was followed by the manual search for papers in Google Scholar with the reference lists of the initially included papers. ^{10,11} Papers discussing the medical treatment and lifestyle modification approaches for managing LQTS were screened for relevant information, with no limitation on date, language, age of participants or publication type.

DISCUSSION

Medical treatment

The administration of β-blockers has been reported with many favorable events since they were first reported in the mid-1970s. 4,12,13 It has been estimated that the risk of cardiac events significantly decreases following the administration of β-blockers among LQTS patients.¹⁴ Besides, studies showed that more favorable events with β-blockers were more frequent in LQT1 patients than others with LOT2 or LOT3 probands. 5,15,16 Additionally, in 2014, a European study showed that most of the included centers still consider β-blockers as the first-line therapy. 14 However, it was also reported that regardless of the administration of β -blockers, cardiac events were still observed among LQTS patients particularly those suffering from asymptomatic course of the disease as it was also reported that at least one cardiac event per 5 years will occur in 32% of symptomatic patients and a recurrence of cardiac arrest will also affect 14% of patients that suffered from a previous similar event.¹⁴ Although the efficacy of β -blockers had been validated by many studies, several life-threatening events have been reported, which were probably attributable to patients' non-compliance to the treatment plan and the administration of QT interval-prolonging medications. Accordingly, clinicians should differentiate between patient failure and \(\beta \)-blocker failure to decide the right management modality. 15,17

β-blockers were mainly effective in reducing the risk of exercise-related cardiac events, while they were not very useful against arousal, rest or sleep-related cardiac events. 18,19 However, the administration of these modalities should still be considered in all cases because patients might unintentionally be subjected to exercise-related events. 18 It should also be considered that β-blockers were transmitted through the mothers' milk to their infants. However, the administration of the modalities should not be affected as the risk on these infants is not significant as compared to the benefits to the mothers in reducing the cardiac events. 20 Some side effects of β-blockers should be considered as bradycardia, fatigue, depression, weight gain and asthma aggravation. 17 Hypoglycemia in children might also

develop, especially in cases of LQT2 while no reason for absolute contraindication of asthma has been reported in the literature. ^21,22 It was recommended that β -blockers should be administered at a maximum dose. Nevertheless, abrupt discontinuation should be avoided. Furthermore, some studies have reported that the different β -blockers drugs were not equally effective. ^12,23 However, others have reported that they have similar efficacies. ^24 The reason behind such conflicting findings was not clear and was probably attributable to the different characteristics of the included patients.

ICD devices were described within the literature and were indicated in cases of syncope (despite the adequate administration of β -blockers and left cardiac sympathetic denervation), in patients that have survived cardiac arrest events, patients presenting with electrical instability and others with very prolonged QTc intervals (>550 ms). 25,26 ICD implantation was not recommended in patients with an asymptomatic course of the disease. however, it can be considered in some cases, including prolonged QTc >500 ms in LOT2 women; LOT2 and LOT3 patients with OTc >550 ms; previous family history of LQTS and in cases of an established diagnosis of Jervell and Lange-Nielsen syndrome.3 ICD implantations were not recommended for patients with acquired LQTS, however, a 7 year follow up investigation showed that it might be beneficial in such cases.²⁷ Young active patients might suffer from some adverse events as lead issues, shocks, infections, vascular occlusions, social discrimination and psychological disturbances.²⁸ However, Hocini et al reported that pharmacological therapy and ICD implantation have been recommended as the first-line management modalities for 19% of the included European centers.¹⁴ Findings from recent investigations indicated that ICD implantation rates were increasing, especially for LQT3 patients and the most favorable events were reported with high-risk LQT2 women.²⁹ In addition, a recent study also showed that dual-chamber ICD implantation should not be recommended to avoid lead complications because implanting a dual-chamber ICD did not significantly reduce the rate of inappropriate shocks.30

Although left cardiac sympathetic denervation (LCSD) was not usually performed, studies have shown that it was usually effective. 14 The favorable anti-fibrillatory events of the modality had been reported to be maximum for LQT1 patients followed by LQT2 and LQT3.31,32 Ackerman reported that not a single cardiac event was observed among his LQT1 patients after applying LCSD. Besides, he also reported that the associated comorbidities and adverse events were more frequent in patients with ICD implantation than others with LCSD.³³ The favorable events of the modality are mainly attributable to reducing the ventricular levels of norepinephrine and alleviating the threshold ventricular fibrillation without a significant impact on the cardiac contractility properties.³⁴ A previous larger 8 year follow up study showed that 91% of patients that received

LCSD approaches did not have any potential cardiac events.³² The introduction of videoscopic LCSD had also aided the efficacy of the modality, leading to reduced morbidities and hospital stay. Besides, LCSD was strongly recommended in cases of recurrence of cardiac events in patients receiving β-blockers. Intolerance and β-blockers were compliance to also recommendations for LCSD, with a proven improvement in the quality of life for these patients. 31,32 However, some sympathetic complications might develop and some studies even reported that some high-risk patients might develop cardiac events. Therefore, LCSD should not be used as a curative approach that can replace other modalities.³⁵ In another context, some studies had demonstrated the favorable effects of potassium supplementation in QTc shortening and correction of repolarization in LQT2 patients.36,37 However, it should be cautiously approached because of the risk of hyperkalemia and gynecomastia that was not adequately investigated by studies in the literature. Furthermore, in LQT3 patients and others with recurrent cardiac arrests despite β-blockers administration, sodium channel blockers as flecainide, mexiletine and ranolazine were recommended.^{3,5} However, these modalities should only be used in mutation-specific cases, in patients with minimal response to the aforementioned modalities, the unavailability of long-term data and the observation of irrelevant electrical changes to the clinical efficacies.

Lifestyle modifications

Evidence in the literature from previous studies indicated the importance of lifestyle modifications to achieve adequate management of patients with LQTS. For instance, LQT1 patients were suggested to avoid stressinducing exercises like water sports and swimming. Additionally, LQT2 patients were suggested to avoid disturbing very loud noises as phone ringing and alarm clocks. In the same context, it was also suggested that all LQTS patients should not administer drugs that might potentially prolong QT interval. 15,26 According to recent guidelines for the management of symptomatic LQTS patients, it had been suggested that the physical activities of these patients were ought to be restricted to class 1A exercises like hiking, brisk walking, skating, bowling and golf.³⁸ On the other hand, symptomatic patients with phenotyping negativity/genotyping positivity allowed to practice competitive sporting modalities, apart from swimming in patients with LQT1 because the risk of mortality in these patients was not 0.38 On the other hand, it had been recommended by the European society of cardiology that all patients suffering from any form of LQTS should be restricted from practicing the different types of competitive sporting activities being symptomatic or not, according to the QTc cutoff points, being >460 ms in females and >440 ms in males.³⁹

Evidence in the current literature about whether LQTS patients were allowed to practice competitive sporting activities or not was conflicting among the different

studies, especially in cases with phenotyping negativity/genotyping positivity. In a previous study, it had been demonstrated that the guidelines that prohibited all forms of competitive exercises were excessive and these patients might safely practice these sports.⁴⁰ In the same context, recent recommendations indicated that these patients might be allowed to practice some competitive sporting modalities, on condition that they received the appropriate management modalities and interventional approaches as adequately knowing the baseline life support measures and automatic external defibrillations, particularly among patients negativity/genotyping positivity.⁴⁰ phenotyping addition, studies in the literature have demonstrated that all individuals with ICDs including patients suffering from LQTS, might be able to safely practice excessive competitive sporting activities with no significant impact on the morbidities or death of these patients.⁴¹ Having a previous experience of exercising was also important because it had been previously demonstrated that with phenotype negative/genotype positive patients with fewer previous activities should limited their sporting activities. 42 Besides, it had been previously demonstrated that the risk of morbidity or mortality during sexual exercises was also significantly low.⁴³ Sudden exposure to visual and auditory stimuli and emotional stress were the main causes that attribute to developing non-favorable cardiovascular complications in LQT2 patients. Noises from alarm clocks, telephones, crying babies should be away from these patients. 15,44

Adequate care should also be provided for the serum potassium levels because it might have a significant role in the QTc interval and might impact the prognosis of LQT2 patients. Postpartum care should also be provided because it was previously reported that these women have an increased risk of cardiac events during the first nine months in the postpartum period. 15,20 Furthermore, it had been demonstrated that this period was associated with a 2.7 and 4.1 folds increase in cardiac and life-threatening events, respectively. Accordingly, mothers of infants should avoid crying babies and adequate care should be provided by other family members for these babies.⁴⁵ In another context, asthma might be co-morbidity for patients suffering from LQTS. However, it had been demonstrated that it can be significantly managed after the induction of the β-blocker therapy, reducing the risk of cardiac events. 46 On other hand, the administration of β2-agonists might be associated with an increased risk of cardiac events.⁴⁷ Additionally, the presence of asthma in these patients might be a significant predictor for severe genetic mutations that is responsible for the secretion of chloride within the epithelial cells of the trachea.⁴⁸ Accordingly, it was recommended that the administration of intravenous salbutamol and aminophylline should be avoided and inhaled corticosteroids and anticholinergic medications, leukotriene-receptor agonists and intravenous magnesium should be alternatively administered.49 Other drugs that prolong QT interval and herbal medications as grapefruit and liquorice should be

avoided, while the impact of contraceptive pills had been reported to be non-significant.⁵⁰

CONCLUSION

Studies have shown that β -blockers are effective modalities and should be used at a maximum dose. However, the potential side events should be considered and adequately managed, and patient compliance should be maintained along the course of treatment. ICD implantation and LCSD are also discussed in the present study with their favorable indications. Lifestyle modifications are also important and have been reported with favorable events. Therefore, these should be considered in such situations. However, evidence regarding some approaches, as limiting competitive exercises, is still conflicting, indicating the need for future investigations.

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