JACC: CLINICAL ELECTROPHYSIOLOGY VOL. ■, NO. ■, 2025

PUBLISHED BY ELSEVIER

LETTERS

RESEARCH LETTER

Risk of Cardiac Events During the Postpartum Period Among Women With Treated Type 2 Long QT Syndrome

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In patients with long QT syndrome type 2 (LQT2) the postpartum period is considered a high-risk window for arrhythmias[1] with the first 9 months postpartum associated with 2.7- to 4.1-fold increased risk of experiencing a cardiac event (CE) when compared with preconception time.[1] Therefore, the postpartum period has generated anxiety and fear of pregnancy for these patients.

In this Mayo Clinic Institutional Review Board-approved study, we reviewed patients evaluated between July 2000 and December 2023 to identify women with LQT2 who went through their pregnancy and postpartum period (first 9 months after delivery) followed at in our clinic, to describe their management and outcomes.

Patients were risk stratified during pregnancy using previously established long QT syndrome (LQTS) risk stratification models.[2] Patients were classified as low, intermediate, or high risk for the postpartum period based on QTc and symptomatic status (**Figure 1A**).

A retrospective analysis of 581 LQT2 patients identified 30 pregnancies in 22 women, diagnosed before their first pregnancy (mean diagnosis age: 23 ± 8 years; mean age at childbirth: 30 ± 6 years) (**Figure 1B**). Pre-emptive treatment intensification during pregnancy was guided by individualized risk assessment and shared decision-making. Preventive measures emphasized avoiding QT-prolonging drugs, maintaining electrolyte balance, managing fevers, and ensuring medication adherence. For those without an implantable cardioverter-defibrillator (ICD), a home automatic external defibrillator was advised (**Figure 1A**).

Among 13 low-risk postpartum periods (10 women), 4 pregnancies maintained the same treatment postpartum—1 woman remained off therapy and 3 continued the same beta-blocker (BB) dose. For 9 pregnancies, treatment was intensified: 3 women initiated nadolol, and 6 had increased BB doses. Three of the 10 women (30%) had an ICD. For the 9 intermediate-risk postpartum periods (7 women), 1 patient remained on ICD monotherapy due to BB intolerance. Nadolol was added in 2 cases: 1 to ICD monotherapy, the other to a combination of atrial pacing (AP) and left cardiac sympathetic denervation (LCSD). Five women had optimized BB doses, LCSD was performed in 1 woman, and 2 patients used a life vest. One of the 7 women had an ICD before pregnancy. Eight postpartum periods (8 women) were classified as high risk. Five women had prior CE. Treatment strategies included

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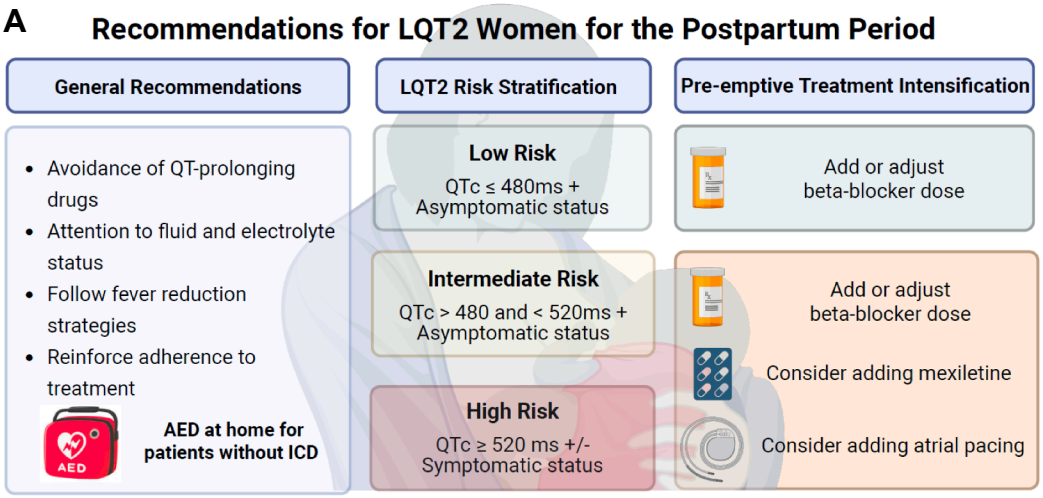
The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received May 6, 2025; revised manuscript received June 4, 2025, accepted June 18, 2025.

ISSN 2405-500X/$36.00 https://doi.org/10.1016/j.jacep.2025.06.023

FIGURE 1 Recommendations and Management of Postpartum Period in LQT2

A



B

Number of female patients, n	22
Number of pregnancies, n	30
Mean age at delivery, years ± SD	30 ± 6
Average QTc during pregnancy, ms ± SD	489 ± 34
ICD, n (%)	10 (45)
Cardiac events prior to the first postpartum period, n (%)	5 (23)
Treatment Intensification for Postpartum Period	
Low risk postpartum, n (%)	**13 (43)**
Kept on the same treatment	4 (31)
BB initiated or dose increased (1.5-2 mg/kg)	9 (69)
Intermediate risk postpartum, n (%)	**9 (30)**
Kept on the same treatment	1 (11)
BB initiated or dose increased (1.5-2 mg/kg)	7 (88)
LCSD	1 (11)
High risk postpartum, n (%)	**8 (27)**
Kept on the same treatment	1 (12)
BB initiated or dose increased (1.5-2 mg/kg)	4 (50)
Mexiletine	2 (25)
Atrial pacing	2 (25)
Cardiac Events during Postpartum Period	
Average QTc during postpartum period, ms ± SD	490 ± 34
BCE during postpartum period, n (%)	1 (3)

(A) The overall recommendations for the postpartum period in women with long QT syndrome type 2 (LQT2). (B) Demographics and pre-emptive treatment intensifications for women with LQT2 during the postpartum period. AED = automatic external defibrillator; BB = beta-blockers; BCE = breakthrough cardiac events; ICD = implantable cardioverter-defibrillator; LCSD = left cardiac sympathetic denervation.

continued triple therapy (nadolol, AP, LCSD) in 1 case, initiation/dose adjustment of nadolol in 4 postpartum periods, addition of mexiletine in 2, and initiation of AP in 2. Seven women had ICDs before pregnancy. One declined ICD placement and was managed with nadolol and mexiletine.

Across all 30 pregnancies and postpartum periods, only 1 CE occurred—an ICD shock in a 21-year-old

high-risk patient during the second postpartum month. No CE occurred during labor/delivery, which proceeded based on obstetrical indications. Cesarean sections were not mandated solely for LQT2, and all patients were encouraged to breastfeed. QTc intervals remained stable (489 ± 34 ms during pregnancy vs 490 ± 34 ms during the 9 months of postpartum; $P = 0.90$; paired t-test). Two postpartum QTc values were missing and excluded from analysis. After the postpartum period, treatment was de-escalated in 20 of intensified cases (83%), returning to prepregnancy regimens. Four patients maintained intensified therapy based on updated risk assessments and personal preference.

Although most women with LQTS have a reduced risk for arrhythmias during pregnancy, the risk dramatically increases during the 9-month postpartum period for women with LQT2.[1] Importantly, unlike the postpartum period for LQT2 patients, pregnancy and labor do not increase risk for patients with LQTS in general.[1] Therefore, pregnancy, labor, and delivery should be navigated according to obstetrical criteria without adjustments due to a LQTS diagnosis. Moreover, all strategies for pain relief, from natural to epidural, during labor/delivery are "QT acceptable" for treated LQTS patients. In fact, in this cohort, there were no CEs during pregnancy or labor/delivery.

Focusing on the postpartum period, this study provides valuable insights into the management and outcomes in this population. Herein, we showed different treatment options that can be pursued for these patients, including BB optimization, initiation of adjunctive therapies, which have proven to be effective for LQT2, such as the addition of mexiletine and/or AP for moderate- to high-risk patients.[3] Based on this, for most of these women, their LQT2-directed therapies were escalated to provide an additional layer of protection during the LQT2 arrhythmic risk period. Of note, the use of BB (nadolol or propranolol) and mexiletine during pregnancy and breastfeeding are not expected to cause any adverse effects in fetal or breastfed infants.[4,5] Treatment adherence and breastfeeding should therefore be encouraged in LQT2 women.

Although the postpartum period is traditionally regarded as a "high risk" window for women with LQT2, when contemporary therapies and preemptive treatment intensification are appropriately implemented, the actual risk of a LQT2-triggered CE is very low. These findings highlight the critical importance of regular risk assessment in LQTS patients, enabling clinicians to anticipate potential risks and optimize treatment strategies to ensure safe postpartum outcomes for women with LQT2. These data should reduce unnecessary anxiety surrounding pregnancy and the postpartum period for these women.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

This work was supported by the Mayo Clinic Windland Smith Rice Comprehensive Sudden Cardiac Death Program (MJA) and the Mayo Clinic Center for Translational Science Activities (CTSA) through grant number UL1TR002377 from the National Center for Advancing Translational Sciences (NCATS), a component of the National Institutes of Health (NIH). Dr Ackerman is a consultant for Abbott, BioMarin Pharmaceutical, Boston Scientific, Bristol Myers Squibb, Illumina, Invitae, Medtronic, Tenaya Therapeutics, and UpToDate. Dr. Ackerman and Mayo Clinic are/were involved in an equity/intellectual property/royalty relationship with AliveCor, Anumana, ARMGO Pharma, Prolaio, Solid Biosciences, and Thryv Therapeutics. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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KEY WORDS long QT syndrome type 2, postpartum, sudden cardiac arrest, sudden cardiac death