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CASE REPORT

ADVANCED

CLINICAL CASE

Application of Electromechanical Window Negativity as an Arrhythmia Risk Correlate in Acquired Long QT Syndrome

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ABSTRACT

Long QT syndrome is a congenital or acquired condition associated with life-threatening cardiac arrhythmias. Risk stratification measures are paramount to providing life-saving therapy. We present a case of a 30-year-old man with syncope and polymorphic ventricular tachycardia from drug-induced QTc prolongation. Electromechanical window negativity correlated with arrhythmia risk and risk predictors. (**Level of Difficulty: Advanced.**) (J Am Coll Cardiol Case Rep 2021;3:1427–1433) © 2021 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

INTRODUCTION

A 30-year-old man with a history of opioid abuse but no structural heart disease presented to the emergency department due to an episode of syncope while at work. He reported dizziness and diaphoresis before collapsing. In the emergency department, he was hemodynamically stable, but an electrocardiogram (ECG) showed sinus rhythm with an atypical left bundle branch block (LBBB) pattern with a wide QRS of 220 ms (**Figure 1**).

Physical examination revealed an alert man in no acute distress with a pulse of 88 beats/min and blood pressure of 142/86 mm Hg. His head was atraumatic, and pupils were equal and reactive to light. There was no jugular venous distention, and the lungs were clear. The heart revealed a regular rhythm without murmurs or gallops. He was cooperative and without tremors or neurologic deficits.

LEARNING OBJECTIVES

- To recognize that loperamide, ingested in high doses, has euphoric effects and is associated with QTc prolongation and TdP.
- To define the normal QTc cut point in patients with polymorphic VT and a wide baseline QRS complex.
- To associate EMW negativity as a risk factor for TdP in acquired LQTS.
- To recognize that application of EMW negativity in patients with suspected LQTS may facilitate the diagnosis of TdP and management of polymorphic VT.

PAST MEDICAL HISTORY

The patient's medical history was pertinent for opioid abuse.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis included polymorphic ventricular tachycardia (VT), monomorphic VT, accelerated ventricular rhythm, and vasovagal syncope.

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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.

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ABBREVIATIONS AND ACRONYMS

ECG = electrocardiogram

EMW = electromechanical window

LBBB = left bundle branch block

LQTS = long QT syndrome

TdP = torsades de pointes

VT = ventricular tachycardia

INVESTIGATIONS

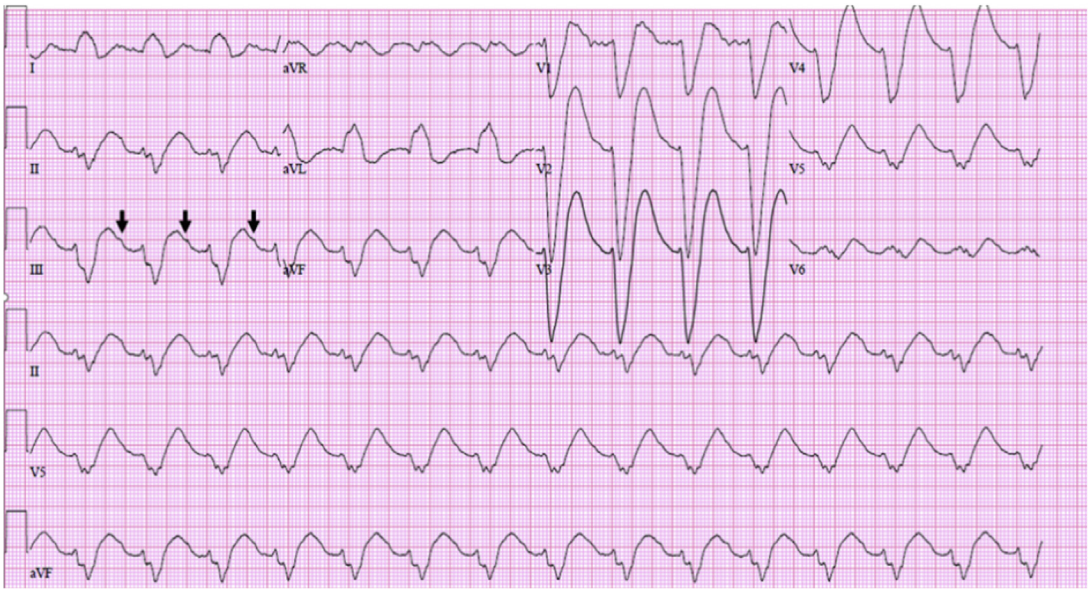
The patient's initial ECG showed sinus rhythm at 88 beats/min with an atypical LBBB with wide QRS and QT/QTc intervals of 220 and 480/581 ms, respectively. He had no previous ECGs for comparison. Initial laboratory test results revealed hypokalemia (serum potassium level of 3.0 mEq/L) and elevated blood urea nitrogen and creatinine of 17 and 1.96 mg/dL, respectively. A repeat ECG 6 h later showed sinus rhythm and shortening of the QRS and QT/QTc intervals (Figure 2). A 2-dimensional echocardiogram revealed a dilated chamber with globally reduced left ventricular ejection fraction of 30% to 35% and no other abnormalities. The urine drug screen was positive for fentanyl and buprenorphine, although he denied recent narcotic use. Later he admitted to ingesting 20 mg of loperamide daily for several days and 40 mg on the day of admission. Loperamide was allegedly used to treat diarrhea.

Several hours later, telemetry strips revealed episodes of torsades de pointes (TdP) and T-wave alternans (Figures 3 and 4).

MANAGEMENT

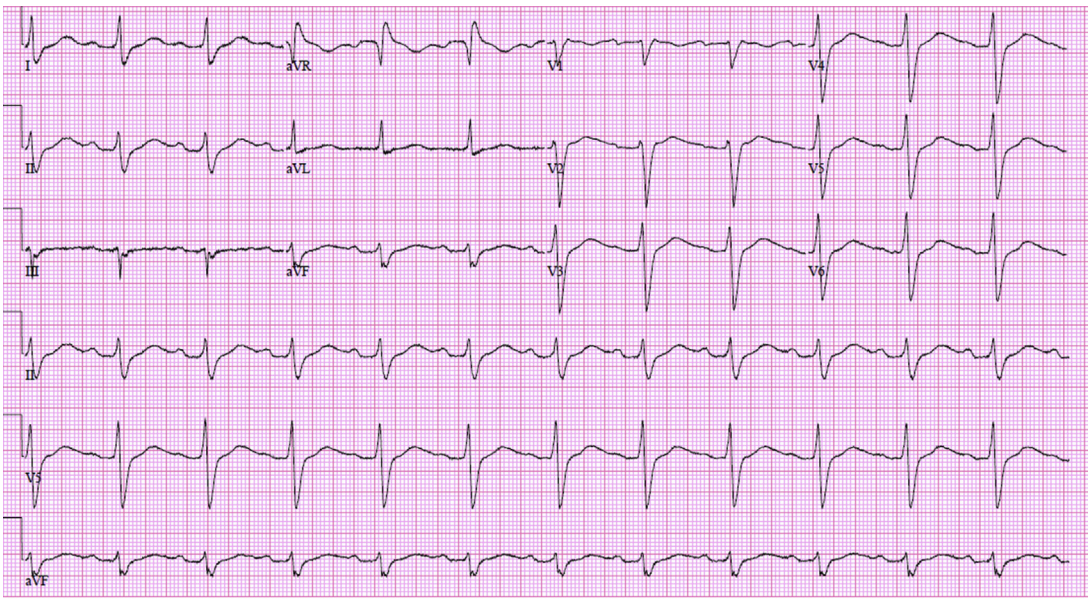
The patient's serum potassium level was repleted, and intravenous fluids normalized his renal function. Beta-blocker therapy was initiated in conjunction with the diagnosis of dilated cardiomyopathy. When VT became incessant, he was treated with boluses of lidocaine and amiodarone, as the primary team perceived that he had an acceptable QTc of 520 ms in the presence of an intraventricular conduction delay. An implantable cardioverter-defibrillator was placed as primary prevention therapy for a dilated cardiomyopathy but episodes of TdP subsequently occurred. He received boluses of intravenous magnesium despite normal levels and was then intubated and sedated. Over the next couple of days, the patient's QRS and QTc intervals began to normalize. The episodes of polymorphic VT were attributed to QTc interval prolongation secondary to loperamide overdose. He was diagnosed with acquired long QT syndrome (LQTS) pending genetic test results. Loperamide is a dose-dependent potassium-channel blocker that has sodium channel-blocking effects; the latter explains the QRS widening. The echocardiogram revealed an electromechanical window (EMW)

FIGURE 1 Initial 12-Lead Electrocardiogram



The tracing revealed sinus rhythm at 88 beats/min, prolonged PR interval, with QRS and QT/QTc intervals of 220 and 480/581 ms, respectively. An atypical left bundle branch block conduction pattern is noted with an uncharacteristically small R-wave in V_1 and a small Q-wave in lead I. **Arrows** indicate sinus P waves.

FIGURE 2 Electrocardiogram Obtained 6 h Later



This tracing revealed sinus rhythm with prolonged PR, QRS, and QT/QTc intervals of 280, 180, and 500/520 ms, respectively.

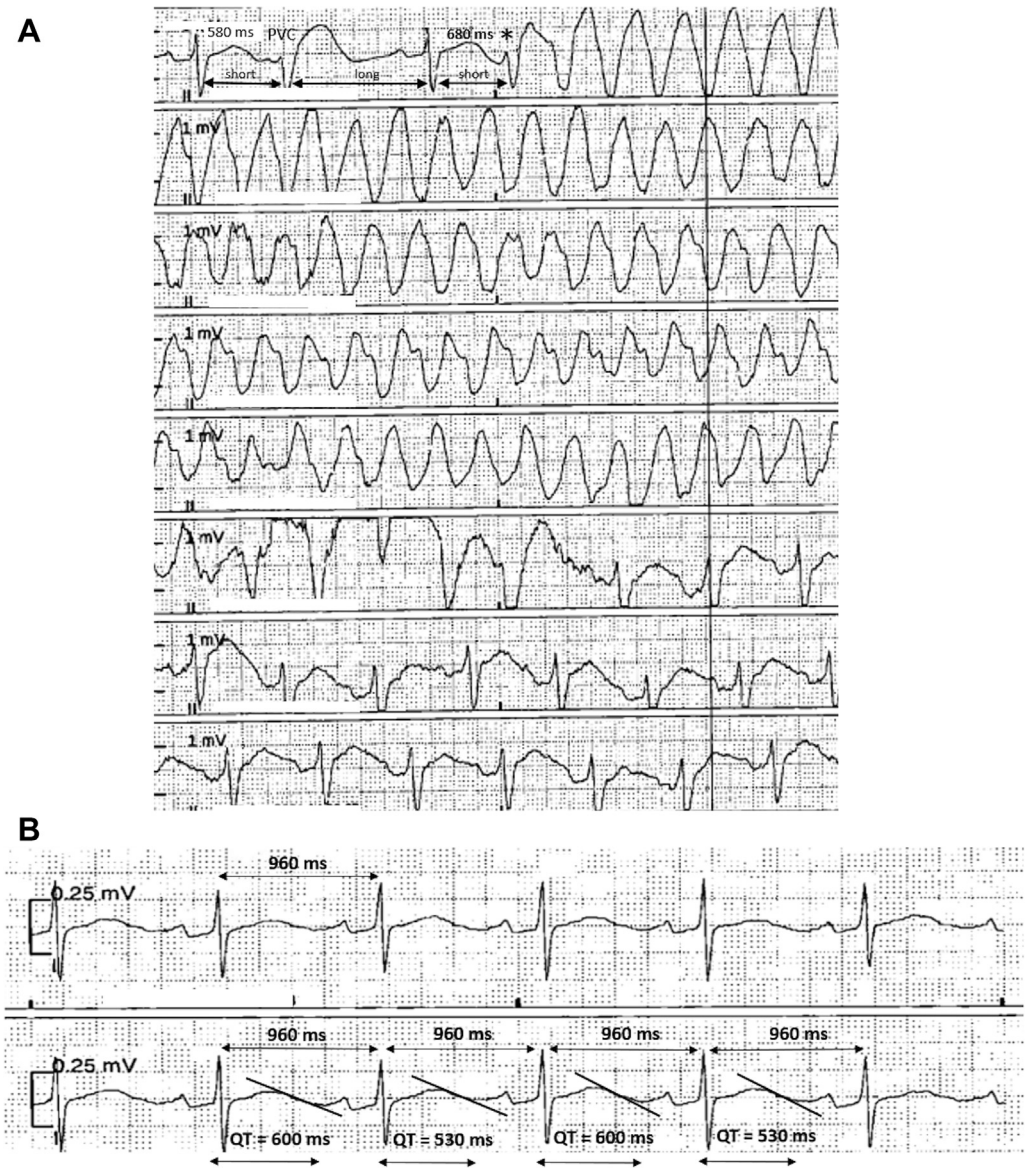
negativity value of -190 ms (Figure 5). The ECG upon discharge (Figure 6) revealed sinus bradyarrhythmia at 49 beats/min and QT/QTc of 600/542 ms. Genetic test results showed that he was genotype-negative for the most common channel mutations associated with LQTS (AKAP9, ANK2, CACNA1C, CAV3, KNE1, KCNH2, KCNJ2 KCNJ5, KCN01, SCN4B, SNC5A, and SNTA1).

DISCUSSION

We report an uncommon case of TdP caused by drug-induced QTc prolongation associated with loperamide overdose (1,2). Loperamide overdose likely occurred due to its euphoric effects experienced when ingested at high doses. The patient's initial ECG showed a wide QRS with an atypical LBBB conduction pattern and indeterminate QT/QTc intervals that complicated recognition of TdP. He exhibited classic R on T phenomenon and T-wave alternans, a predictor of TdP. The patient's urine drug screen revealed buprenorphine, which is a human ether-a-go-go-related gene channel blocker not known to prolong the QTc or cause TdP (3). EMW negativity was associated with T-wave alternans and TdP, and was markedly abnormal relative to values in patients with congenital LQTS (4). Implantable cardioverter-defibrillator therapy was undertaken as primary prevention for a dilated cardiomyopathy, as initial treatment of patients with acquired LQTS generally entails removal of the offending agent and electrolyte replacement.

Recently, Sugrue et al (4) validated EMW negativity as a risk predictor for serious arrhythmias in patients with genetically proven LQTS compared with LQTS patients without arrhythmias. EMW negativity outperformed the QTc interval as a risk predictor (-52 $\pm$ 38 ms vs -18 $\pm$ 29 ms; odds ratio of 1.37 for each 10-ms decrease in EMW, $P = 0.0001$). To our knowledge, this case represents the first report of application of this index in a patient with acquired LQTS. Furthermore, in the presence of a wide QRS, the normal QTc value often is unclear, thus producing a knowledge gap that limits application of QTc cut points to patients with a normal QRS duration. EMW negativity will have no such limitation. The value of EMW in patients with a wide QRS or ventricular-paced rhythm warrants investigation. EMW negativity was associated with T-wave alternans, a predictor of TdP (5). EMW is calculated as the difference between the interval from the onset of the QRS in lead II to aortic valve closure minus the QT interval in the same ventricular beat. A negative EMW is strongly predictive of adverse events and associated with increased

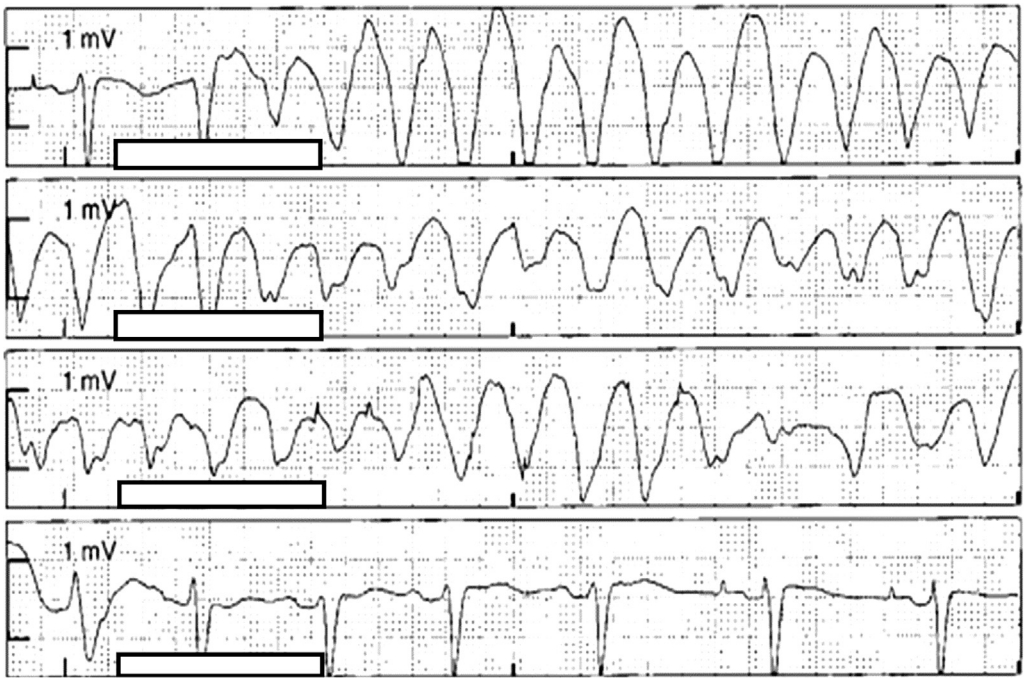
FIGURE 3 Initiation of TdP and T-Wave Alternans



(A) Initiation of torsades de pointes with R on T premature ventricular complex (PVC). The **top strip** shows a sinus conducted QRS complex with a QT interval of 580 ms followed by a PVC resulting in a compensatory pause and rate-related QT prolongation of the subsequent QT interval that measured 680 ms, then an R on T PVC **(asterisk)** initiating = torsades de pointes lasting 30 s. **(B)** Rhythm strip showing T-wave alternans. Sinus rhythm at 63 beats/min (cycle length: 960 ms) is shown in the **top strip**. The **bottom strip** illustrates QT interval measurements using the tangential line method (8). Both strips show T-wave alternans as shown by the intersection of the tangent line with the baseline. Alternating QT interval of 600 and 530 ms is evident. T-wave alternans is a cyclical cardiac repolarization abnormality associated with torsades de pointes.

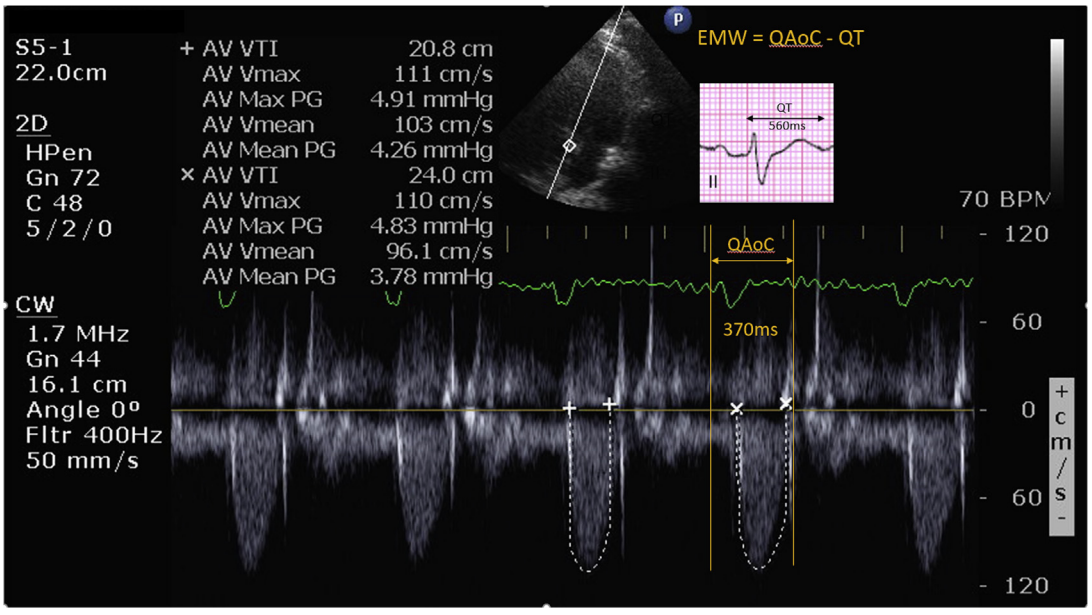
risk of TdP (6). Normally, the end of electrical systole occurs before the end of mechanical systole, resulting in a positive EMW. A negative EMW occurs when there is a mismatch between electrical and mechanical systole from either a lengthening of electrical systole or shortening of mechanical systole or both. In this case (in which QAoC indicates the interval from QRS onset to aortic valve closure), the EMW (EMW = QAoC - QT = 370 - 560 = -190 ms) was found to be extremely negative.

FIGURE 4 Self-Limiting Episode of TdP



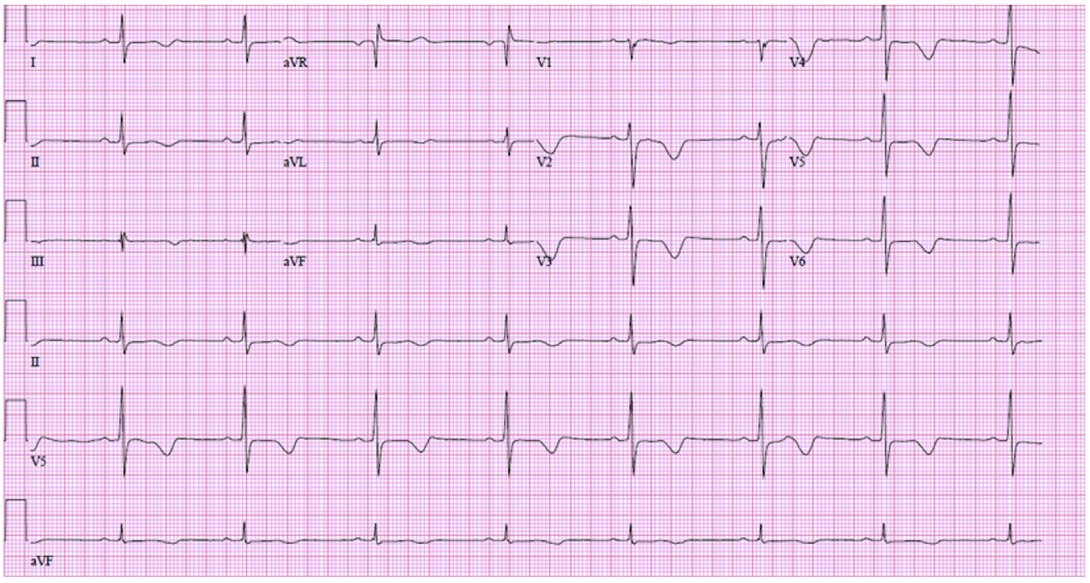
During sinus rhythm a spontaneous episode of torsades de pointes (TdP) lasting 16 s is shown.

FIGURE 5 2-Dimensional Echocardiogram With Continuous-Wave Doppler Showing Calculation of the EMW



Calculation of the electromechanical window (EMW) (apical 5-chamber view) using a concurrent superimposed electrocardiogram (ECG) is shown (EMW = QAoC – QT = 370 – 560 = -190 ms), where QAoC indicates the interval from QRS onset to aortic valve closure. The recording artifact from the echocardiogram ECG tracing necessitated obtaining a lead II tracing, whereby an accurate assessment of the QT interval was obtained. Details are given in the text.

FIGURE 6 Electrocardiogram at Hospital Discharge



This electrocardiogram shows sinus bradycardia at 49 beats/min and prolonged QT/QTc in a genotype-negative patient with acquired long QT syndrome.

Ter Bekke et al (6) reported that patients with LQTS had a negative EMW compared with healthy control subjects whose values were positive. Symptomatic patients with genotype-positive LQTS had a mean EMW of -67 ± 42 ms compared with -27 ± 41 ms in those with LQTS who were event-free ($P = 0.0001$).

EMW was recently validated as a risk predictor in congenital LQTS, and we found it useful in acquired LQTS. EMW assessment may be helpful when a wide QRS influences QTc calculation or there is uncertainty regarding application of correction formulas or method of QT measurement (7,8). EMW may be predictive of arrhythmia risk irrespective of QRS duration.

FOLLOW-UP

The patient will follow-up in the arrhythmia clinic for check of the implantable cardioverter-defibrillator and a repeat echocardiogram.

CONCLUSIONS

Loperamide overdose is associated with QTc prolongation and TdP. EMW negativity is associated with life-threatening arrhythmic events in drug-induced QTc prolongation. It is also useful in the presence of a wide QRS where normal values for QT/QTc are not apparent.

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The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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