



HAL
open science

Wearable electrocardiogram devices in patients with congenital long QT syndrome: The SMART-QT study

Antoine Delinière, Francis Bessière, Leslie Placide, Jean-Luc Pasquié, Christelle Haddad, Solenn Tirel, Hajira Mokhtar, Elodie Morel, Kevin Gardey, Arnaud Dulac, et al.

► To cite this version:

Antoine Delinière, Francis Bessière, Leslie Placide, Jean-Luc Pasquié, Christelle Haddad, et al.. Wearable electrocardiogram devices in patients with congenital long QT syndrome: The SMART-QT study. Archives of cardiovascular diseases, In press, 10.1016/j.acvd.2024.02.010 . hal-04561476

HAL Id: hal-04561476

<https://hal.science/hal-04561476>

Submitted on 6 May 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Wearable electrocardiogram devices in patients with congenital long QT syndrome: The SMART-QT study

Antoine Delinière ¹, Francis Bessière ², Leslie Placide ³, Jean-Luc Pasquié ⁴, Christelle Haddad ⁵, Solenn Tirel ⁶, Hajira Mokhtar ⁶, Elodie Morel ⁶, Kevin Gardey ⁵, Arnaud Dulac ⁵, Geoffroy Ditac ⁵, Frédéric Sacher ⁷, Isabelle Denjoy ⁸, Philippe Chevalier ⁹

¹ National Reference Centre for Inherited Arrhythmia of Lyon (CERA), Hôpital Cardiologique Louis Pradel, Hospices Civils de Lyon, 69500 Bron, France; Electrophysiology Unit, Hôpital Cardiologique Louis Pradel, Hospices Civils de Lyon, 69500 Bron, France; Université Claude-Bernard Lyon-1, MeLiS, CNRS UMR 5284, INSERM U1314, Institut NeuroMyoGène, 69008 Lyon, France; European Reference Network for Rare and Low Prevalence Complex Diseases of the Heart (ERN GUARD-Heart).

² Electrophysiology Unit, Hôpital Cardiologique Louis Pradel, Hospices Civils de Lyon, 69500 Bron, France; Paediatric and Congenital Heart Disease Medico-Surgical Unit, Hôpital Cardiologique Louis Pradel, Hospices Civils de Lyon, 69500 Bron, France; Université Claude-Bernard Lyon-1, LabTau, Inserm, 69003 Lyon, France.

³ Service de Cardiologie, Centre de Compétence des Troubles du Rythme Cardiaque d'Origine Héritaire, Hôpital Arnaud-de-Villeneuve, CHU de Montpellier, 34295 Montpellier, France.

⁴ Service de Cardiologie, Centre de Compétence des Troubles du Rythme Cardiaque d'Origine Héritaire, Hôpital Arnaud-de-Villeneuve, CHU de Montpellier, 34295 Montpellier, France; CNRS UMR9214, Inserm U1046, PHYMEDEXP, Université de Montpellier, 34295 Montpellier, France.

⁵ Electrophysiology Unit, Hôpital Cardiologique Louis Pradel, Hospices Civils de Lyon, 69500 Bron, France.

⁶ National Reference Centre for Inherited Arrhythmia of Lyon (CERA), Hôpital Cardiologique Louis Pradel, Hospices Civils de Lyon, 69500 Bron, France.

⁷ European Reference Network for Rare and Low Prevalence Complex Diseases of the Heart (ERN GUARD-Heart); Institut LIRYC, Centre de référence des MALadies RYthmiques héréditaires (CMARY), Bordeaux University Hospital, 33000 Bordeaux, France; Université de Bordeaux, Inserm, CRCTB, U1045, 33000 Bordeaux, France.

⁸ European Reference Network for Rare and Low Prevalence Complex Diseases of the Heart (ERN GUARD-Heart); Service de Cardiologie, Centre de Référence des Troubles du Rythme Cardiaque d'Origine Héritaire, Hôpital Bichat-Claude-Bernard, AP-HP, 75018 Paris, France.

⁹ National Reference Centre for Inherited Arrhythmia of Lyon (CERA), Hôpital Cardiologique Louis Pradel, Hospices Civils de Lyon, 69500 Bron, France; Electrophysiology Unit, Hôpital Cardiologique Louis Pradel, Hospices Civils de Lyon, 69500 Bron, France;

Université Claude-Bernard Lyon-1, MeLiS, CNRS UMR 5284, INSERM U1314, Institut NeuroMyoGène, 69008 Lyon, France; European Reference Network for Rare and Low Prevalence Complex Diseases of the Heart (ERN GUARD-Heart).

Electronic address: philippe.chevalier@chu-lyon.fr.

Keywords:

Digital health; Long QT syndrome; QT interval; Remote monitoring; Smartwatch.

Abstract

Background:

In patients with congenital long QT syndrome (LQTS), the risk of ventricular arrhythmia is correlated with the duration of the corrected QT interval and the changes in the ST-T wave pattern on the 12-lead surface electrocardiogram (12L-ECG). Remote monitoring of these variables could be useful.

Aim:

To evaluate the abilities of two wearable electrocardiogram devices (Apple Watch and KardiaMobile 6L) to provide reliable electrocardiograms in terms of corrected QT interval and ST-T wave patterns in patients with LQTS.

Methods:

In a prospective multicentre study (ClinicalTrials.gov identifier: [NCT04728100](#)), a 12L-ECG, a 6-lead KardiaMobile 6L electrocardiogram and two single-lead Apple Watch electrocardiograms were recorded in patients with LQTS. The corrected QT interval and ST-T wave patterns were evaluated manually.

Results:

Overall, 98 patients with LQTS were included; 12.2% were children and 92.8% had a pathogenic variant in an LQTS gene. The main genotypes were LQTS type 1 (40.8%), LQTS type 2 (36.7%) and LQTS type 3 (7.1%); rarer genotypes were also represented. When comparing the ST-T wave patterns obtained with the 12L-ECG, the level of agreement was moderate with the Apple Watch ($k=0.593$) and substantial with the KardiaMobile 6L ($k=0.651$). Regarding the corrected QT interval, the correlation with 12L-ECG was strong for the Apple Watch ($r=0.703$ in lead II) and moderate for the KardiaMobile 6L ($r=0.593$). There was a slight overestimation of corrected QT interval with the Apple Watch and a subtle underestimation with the KardiaMobile 6L.

Conclusions: In patients with LQTS, the corrected QT interval and ST-T wave patterns obtained with the Apple Watch and the KardiaMobile 6L correlated with the 12L-ECG. Although wearable electrocardiogram devices cannot replace the 12L-ECG for the follow-up of these patients, they could be interesting additional monitoring tools.

Abbreviations

12L-ECG 12-lead surface electrocardiogram; AW Apple Watch; CI confidence interval; K6L KardiaMobile 6L; LQTS congenital long QT syndrome; LQT1 (. . . 2, 3, 5, 8) long QT syndrome type 1 (. . . 2, 3, 5, 8); QTc corrected QT interval.

1. Background

Congenital long QT syndrome (LQTS) is a rare inherited heart disease leading to a risk of sudden cardiac death from ventricular arrhythmia in young patients. The genotype-phenotype correlation is strong in LQTS between the ST-T wave patterns on the 12-lead surface electrocardiogram (12L-ECG) and the triggers of ventricular arrhythmia [1, 2]. While awaiting the results of the genetic analysis in a patient newly diagnosed with LQTS, a meticulous analysis of the ST-T wave pattern on the 12L-ECG often helps to determine the gene involved, and thus enables genotype-specific preventive strategies to be initiated. The electrocardiogram fluctuates highly over time in patients with LQTS, depending on intrinsic and extrinsic modulators. The short-term risk of ventricular arrhythmia is closely correlated to the size of the corrected QT interval (QTc) increment (it increases by 15% for each 10 ms of QTc prolongation in the three more common genotypes [3]) as well as to changes in ST-T wave morphology (e.g. giant T-U waves are often the harbinger of a torsade de pointes in patients with LQTS [4]).

As it allows determination of ST-T wave patterns and the duration of the QTc, the 12L-ECG is an essential tool for the follow-up of patients with LQTS. However, it is not suitable for remote monitoring, which can be very useful in the event of an acute phenomenon that is likely to transiently lengthen the duration of repolarization. Wearable electrocardiogram devices connected to smartphones have been developed recently, with the initial aim of screening for atrial fibrillation. Some studies have shown that the quality of electrocardiograms obtained with the Apple Watch (AW; Apple Inc., Cupertino, CA, USA) and the KardiaMobile 6L (K6L; Alive Cor Inc., Mountain View, CA, USA) allows reliable measurement of the QTc in the general population [5–7]. As assessment of the QTc is more complex in patients with LQTS [8], an evaluation of the performance of these devices in the different genotypes of LQTS is mandatory before they can be used in clinical practice. Initial single-centre studies carried out with the AW [9] and the K6L [10] have shown that the QTc duration obtained with these devices is potentially close to that obtained with the 12 L-ECG in patients with LQTS, paving the way for studies comparing the two devices in this disease.

In this multicentre study, we sought to evaluate the ability of two wearable electrocardiogram devices (AW and K6L) to obtain reliable electrocardiograms, in terms of QTc duration and ST-T wave pattern, in a large cohort of patients with LQTS.

2.Methods

2.1. Study population

The SMART-QT study was a prospective multicentre study. Children and adult patients with LQTS were enrolled from four French university centres (Lyon, Paris, Bordeaux and Montpellier) between March 2021 and May 2023. LQTS had to be diagnosed with at least one of the following criteria: (1) QTc \geq 480 ms in repeated 12L-ECGs in the absence of secondary causes of QT prolongation; (2) Fig. 1. Method for the measurement of the QT interval and the calculation of the corrected QT (QTc; Bazett's formula). The electrocardiogram shown as an example is obtained with the Apple Watch (lead II) in a patient with long QT syndrome type 1. Measurements were performed manually using a digital caliper (EP Caliper). RR:RR interval. a pathogenic (or likely pathogenic) variant in an LQTS gene according to the American College of Medical Genetics and Genomics /American Association of Molecular Pathology (ACMG/AMP) criteria [11]; and (3) QTc \geq 460 ms in repeated 12L-ECGs in patients with presumed arrhythmic syncope in the absence of secondary causes of QT prolongation. The quality of the 12L-ECG obtained on the day of the recordings had to be sufficient to allow determination of the duration of the QTc and the ST-T wave pattern. The three recordings (12L-ECG, AW and K6L) had to be made during the same visit. All the patients (and, for children, their legal representatives) gave informed consent. The study was approved by the Île-de-France IV Institutional Review Board (IRB 00003835).

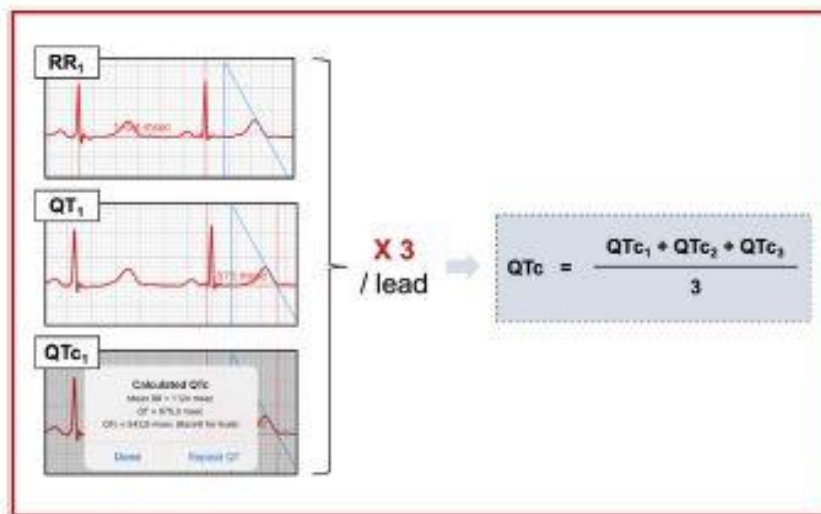


Fig. 1. Method for the measurement of the QT interval and the calculation of the corrected QT (QTc; Bazett's formula). The electrocardiogram shown as an example is obtained with the Apple Watch (lead II) in a patient with long QT syndrome type 1. Measurements were performed manually using a digital caliper (EP Caliper). RR: RR interval.

2.2. Electrocardiogram acquisitions

A 12L-ECG was first recorded while supine, with a paper speed of 25 mm/s. Next, an AW Series 6 was used to record two consecutive 30-second 1-lead electrocardiograms (leads II and V5) while supine, by moving the AW [7,12] (for lead II: AW in left lower abdomen with right finger on the crown; for lead V5: AW in anterior axillary line at the fifth intercostal space with right finger on the crown). Then, a K6L was used to record a 30-second 6-lead electrocardiogram while sitting (thumbs on the top electrode, and left knee or ankle on bottom electrode; leads I and II were recorded directly by the device, whereas the four remaining peripheral leads were reconstructed). All acquisitions were made during the same visit and supervised by a specialized nurse. All the electrocardiograms were recorded digitally.

2.3. QTc assessment and ST-T wave pattern evaluations

All electrocardiogram evaluations were centralized, and were performed by a specialist in inherited arrhythmia syndromes (A.D.), who was blinded at the time of analysis to the genotype of the patients and to the data obtained on the other devices. Measurements were performed manually using a digital caliper (EPCaliper; EP Studios, Inc., Louisville, KY, USA). The measurements were obtained from lead II in the electrocardiograms performed with the three devices, and from lead V5 in the electrocardiograms performed with the 12L-ECG and the AW. The QT interval was measured using the tangent method, and corrected to the previous RR interval using Bazett's formula (Fig. 1), according to the usual standards [13]. When the quality of the recording was sufficient, three consecutive QTcs were calculated and averaged. The ST-T wave patterns were classified according to the criteria established by Zhang et al. [2,14], as follows: LQTS type 1 (LQT1) patterns (broad-based T wave, infantile ST-T wave, late-onset of normal-appearing T wave, normal-appearing T wave); LQT2 patterns (obvious bifid T wave, subtle bifid T wave, low-amplitude and widely split bifid T wave); LQT3/8 patterns (late-onset peaked/biphasic T wave, asymmetrical peaked T wave); and Andersen-Tawil pattern (prominent U wave). Abnormal ST-T wave morphologies not corresponding to the above categories were classified as non-specific patterns. In order to assess the reproducibility of the evaluations, a cardiac electrophysiologist (F.B.) analysed the electrocardiogram obtained with the three devices in a random subset of 10 (10.2%) patients (i.e. 50 QTc duration measurements and 30 ST-T wave pattern assessments). There was a good level of agreement between the two specialists (QTc duration: concordance correlation coefficient 0.800; ST-T wave pattern categorization: 83% of agreement, $k = 0.664$, 95% confidence interval [CI] 0.416–0.911), which supported a reproducible and reliable assessment of ventricular repolarization [8].

Table 1
Clinical characteristics of the patients (n = 98).

Female sex	65 (66.3)
Age (years)	35.3 ± 16.6 (6–76)
Children	12 (12.2)
Proband	59 (60.2)
Symptomatic status	
Life-threatening ventricular arrhythmia	17 (17.3)
Arrhythmic syncope	38 (38.8)
Management	
Beta-blocker	84 (85.7)
Class I antiarrhythmics	5 (5.1)
Implantable cardioverter defibrillator	13 (13.3)
Pacemaker	4 (4.1)

Data are expressed as number (%) or mean ± standard deviation (minimum–maximum value).

2.4. Statistical analysis

Statistical analysis was performed using jamovi, version 2.3(The jamovi project) and JASP, version 0.18.3 (JASP Team). Continuous variables are expressed as mean ± standard deviation, whereas categorical variables are presented as frequencies and percentages (and minimum–maximum values). Agreement between devices and observers regarding ST-T wave patterns was assessed by calculating Cohen’s kappa coefficient (k), which was interpreted as follows: < 0.00 = poor agreement; 0.00–0.20 = slight agreement; 0.21–0.4 = fair agreement; 0.41–0.60 = moderate agreement; 0.61–0.80 = substantial agreement; 0.81–0.99 = near perfect agreement; and 1 = perfect agreement. For each measurement, the data obtained on the corresponding lead (II or V5) on the 12L-ECG was used as reference (differences were calculated as: 12 L-ECG – AW or 12L-ECG – K6L). The quantitative electrocardiogram measurements were compared between the devices using the paired Student’s t-test. The Shapiro-Wilk test was used to test the normality of the distribution of quantitative variables. The agreement between two observers for QTc duration measurement was assessed by the concordance correlation coefficient. The correlation of the quantitative measurement between the devices was estimated using Pearson correlation analysis for normally distributed variables and Spearman correlation analysis for non-parametric variables. The correlation coefficient r was interpreted as follows: 0.00–0.19 = very weak correlation; 0.20–0.39 = weak correlation; 0.40–0.69 = moderate correlation; 0.70–0.89 = strong correlation; and 0.9–1.00 = very strong correlation. The agreement for the measurement of QTc between the 12L-ECG and the two devices was evaluated using Bland-Altman analysis. For each test, a P value < 0.05 was considered statistically significant.⁴

3. Results

3.1. Clinical characteristics of the subjects

Among the 111 subjects screened, 98 patients with LQTS were included in the study (Fig. 2); 66.3% were female, the mean age was 35.3 ± 16.6 years and 12.2% were children (Table 1). A pathogenic or likely pathogenic genetic variant in an LQTS gene was present in 92.8% of the patients. The most represented genotypes were LQT1 (40.8%), LQT2 (36.7%), and LQT3 (7.1%), but rarer genotypes were also represented (Andersen-Tawil syndrome, 4.1%; LQT8 and Timothy syndrome, 3.1%; LQT5, 1%). Only 3.1% of the patients had a variant of uncertain significance, whereas 4.1% were of unknown genotype (Fig. 3A).

3.2. Electrocardiographic characteristics of the study population on the 12L-ECG

All patients were in sinus rhythm, with a mean heart rate of 60.9 ± 13.0 (37–124) beats/min. On the day of the recording, the mean QTc duration was 456.4 ± 35.5 (382–534) ms in II and 453.0 ± 35.5 (381–533) ms in V5. The mean maximum QTc between leads V5 and II was 460.6 ± 35.1 (382–534) ms; 49.0% of the patients had a maximum QTc ≥ 460 ms and 30.6% had a maximum QTc ≥ 480 ms (Fig. 3B). The maximum QTcs according to genotype are shown in Fig. 3C.

Among patients whose genotype was associated with well-described ST-T wave patterns (i.e. LQT1, LQT2, LQT3/8 and Andersen-Tawil syndrome, $n = 90$), 72 (80.0%) had an ST-T wave pattern typical of their genotype, 31 (34.4%) had a maximum QTc ≥ 460 ms and 14 (15.6%) had a maximum QTc ≥ 480 ms. The details of the ST-T wave patterns according to genotype are shown in Fig. A

3.3. Quality of the electrocardiograms from the two devices.

The quality of the electrocardiograms was sufficient for the determination of the QTc over three consecutive beats in most cases with both devices (AW: 96.7%; K6L: 95.9%). With the AW, the quality of the recording was insufficient to allow measurement of the QTc in three (3.1%) patients in lead II (T wave too flat, $n = 2$; artefacts, $n = 1$) and one (1.0%) patient in lead V5 (T wave too flat). With the K6L, the quality of the recording was insufficient to allow measurement of the QTc in four (4.1%) patients (T wave too flat, $n = 2$; artefacts, $n = 2$), and for one (1.0%) patient, the QTc could only be measured on a single cycle. The quality of the

electrocardiograms was sufficient to allow evaluation of the ST-T wave patterns in all the patients who had a recording via the AW, whereas artefacts prevented the evaluation of ST-T wave patterns in eight (8.2%) K6Lelectrocardiograms.

3.4. ST-T wave pattern classification with the two devices

The results of the ST-T wave pattern analysis by genotype and by device are detailed in Fig. 4. Regarding the categorization of ST-T wave patterns between the five previously mentioned pattern families (LQT1, LQT2, LQT3/8, Andersen-Tawil and non-specific pat-terns), the agreement was moderate between the 12L-ECG and the AW (73% of agreement, $k = 0.593$, 95% CI 0.462–0.724), substantial between the 12L-ECG and the K6L (78% of agreement, $k = 0.651$, 95% CI 0.524–0.778) and moderate between the two devices (68% of agreement, $k = 0.489$, 95% CI 0.341–0.637).

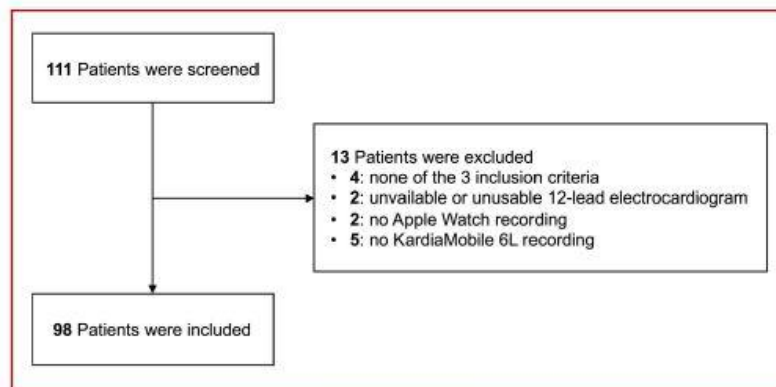


Fig. 2. Study flowchart.

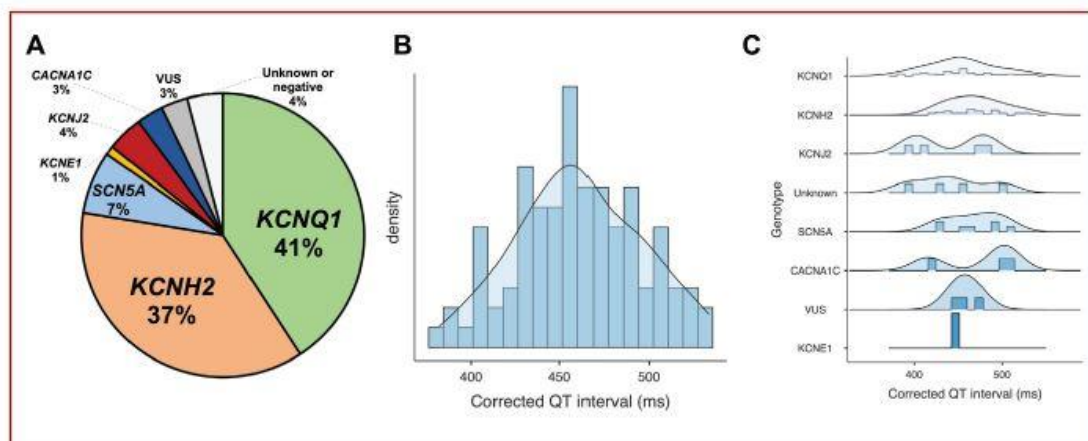


Fig. 3. Genetic and electrocardiographic characteristics of the study population. A. Genotypes of the patients; genes are reported when the variants are pathogenic or likely pathogenic (class 4 or 5 of the American College of Medical Genetics and Genomics / American Association of Molecular Pathology [ACMG/AMP] classification [11]). B. Corrected QT intervals (Bazett's formula) in the study population (maximum value between leads II & V5). C. Corrected QT intervals (Bazett's formula) according to genotype (maximum value between leads II & V5). VUS: variant of uncertain significance (class 3 of the ACMG/AMP classification [11]).

3.5. Measurement of QTc interval duration with the two devices

For all three devices, the QTc durations were normally distributed, whereas the heart rate had a non-parametric distribution. The heart rate was not significantly different between the 12L-ECG and the AW (mean difference -0.918 ± 0.716 beats/min; $P = 0.20$), and was slightly higher with the K6L (mean difference -3.96 ± 0.800 beats/min; $P < 0.001$). Regarding the QTc duration measurement, there was a strong correlation between the 12L-ECG and the AW ($r = 0.703$ in lead II and $r = 0.646$ in lead V5), a moderate correlation between the 12L-ECG and the K6L ($r = 0.593$ in lead II; Fig. 5) and a moderate correlation between the two devices ($r = 0.679$ in lead II). Compared with 12L-ECG, the QTc was slightly longer with the AW (bias of -14.2 ms in lead II [$P < 0.001$] and -17.1 ms in lead V5 [$P < 0.001$]) and slightly shorter with the K6L (bias of $+9.51$ ms; $P = 0.003$; Table 2).

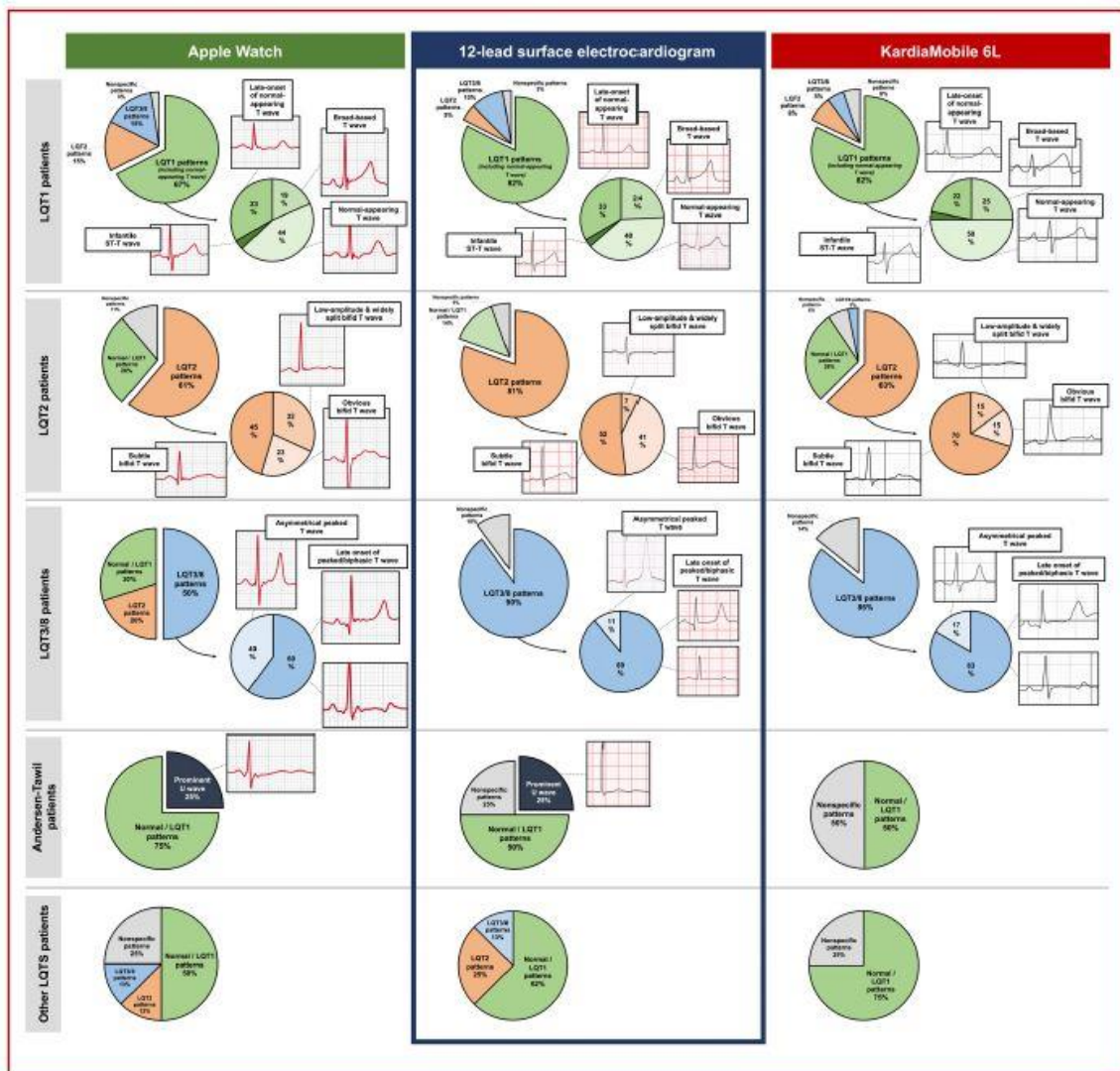


Fig. 4. ST-T wave patterns according to genotype and electrocardiogram device. LQT1: LQTS type 1; LQT2: LQTS type 2; LQT3/8: LQTS types 3/8; LQTS: long QT syndrome.

3.6. Performances of the two devices for QTc interval classification

The diagnostic accuracy for QTc interval classification (long ≥ 480 ms, normal < 480 ms) was 76.3% (95% CI 66.6–84.3%) for the AW and 77.7% (95% CI 67.9–85.6%) for the K6L. In detail, regarding the identification of a QTc ≥ 480 ms, the performances of the AW were as follows: sensitivity 96.7% (95% CI 82.8–99.9%), specificity 67.2% (95% CI 54.6–78.2%), positive predictive value 56.9% (95% CI 42.2–70.7%), negative predictive value 97.8% (95% CI 88.5–99.9%); and those of the K6L were as follows: sensitivity 29.6% (95% CI 13.8–50.2%), specificity 97.0% (95% CI 89.6–99.6%), positive predictive value 80.0% (95% CI 44.4–97.5%), negative predictive value 77.4% (95% CI 67.0–85.8%).

4. Discussion

The present study demonstrates that in patients with LQTS, both the AW and the K6L provide electrocardiograms of sufficient quality to allow assessment of the QTc duration and evaluation of the ST-T wave pattern in the vast majority of patients. When comparing the ST-T pattern families obtained with these devices with those obtained on the 12L-ECG, the level of agreement was moderate for the AW and substantial for the K6L. In terms of QTc duration assessment, the correlation between the 12L-ECG and the AW was strong, whereas that between the 12L-ECG and the K6L was moderate. In addition, both wearable electrocardiogram devices induced a systematic bias regarding the QTc duration: a slight overestimation for the AW and a subtle underestimation for the K6L. Consequently, for the identification of a prolonged QTc, the AW shows high sensitivity and low specificity, whereas the K6L shows low sensitivity and high specificity.

Both devices allow direct acquisition (not reconstructed) of lead II, in standard use according to the manufacturer's guidelines for the K6L, and following a simple manipulation for the AW (which is initially designed to record lead I) [7, 12]. As recommended by Postema and Wilde in their expert guide to measuring the QT interval [13], lead II should be favoured for measurement of the QTc.

However, it is not uncommon for T waves to be too flat in lead II to allow reliable QTc measurement, whereas this is rare in precordial leads [15]. This phenomenon constitutes a limit in the evaluation of the QTc based solely on the peripheral leads. In the present study, the QTc interval could not be measured because the T waves were too flat in two patients (2.0%) using the AW, in two patients (2.0%) using the K6L in lead II and in one patient (1.0%) using the AW in lead V5. The automatic computerized assessment of the QTc is often fooled when the T wave has an atypical morphology [16], and the QT should therefore always be measured manually in patients with LQTS. Both devices enable electrocardiograms to be recorded in digital format, which allows comfort in the manual measurement of the QT by taking advantage of the zoom and the digital calipers.

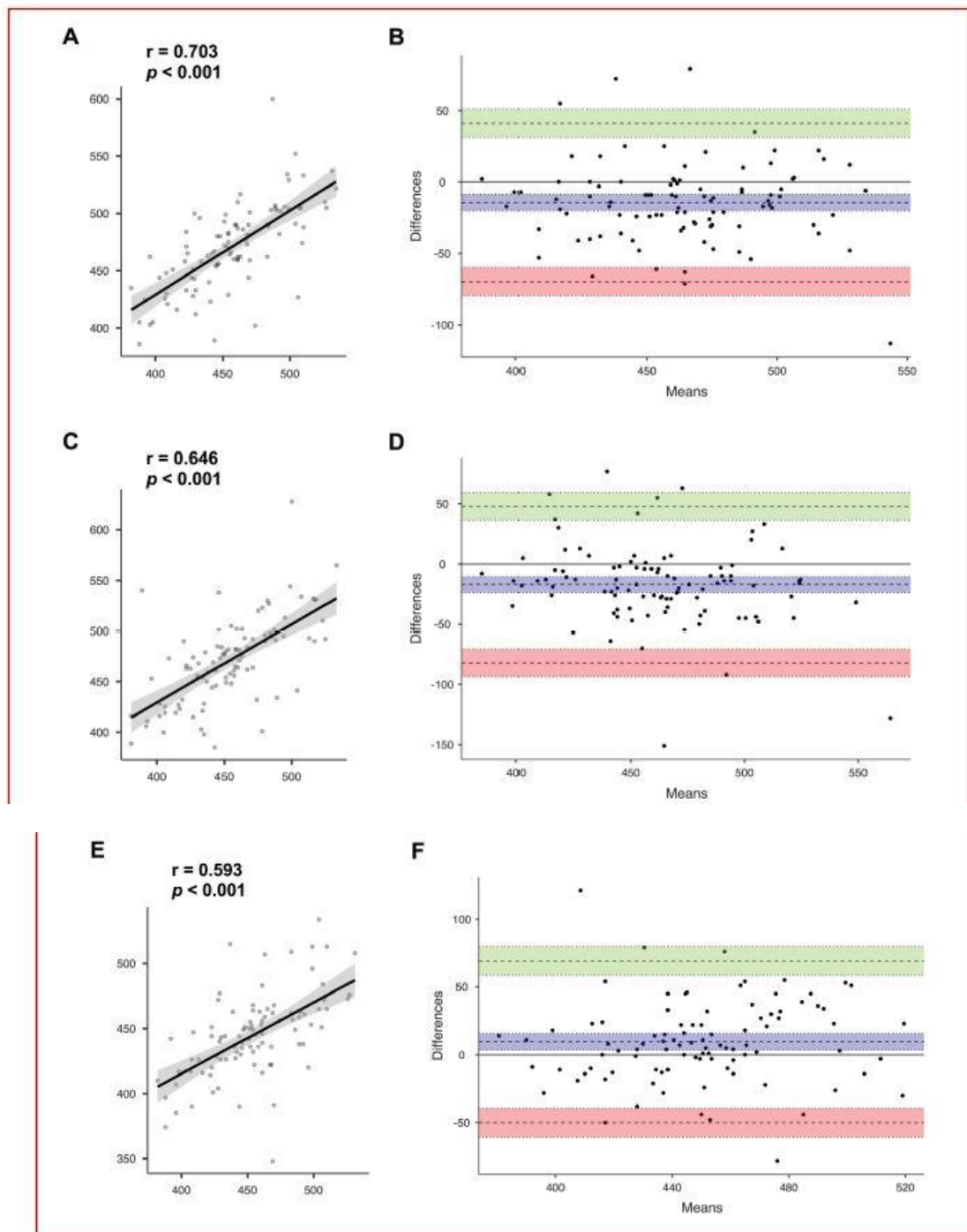


Fig. 5. Comparison of corrected QT interval measurement between the 12-lead surface electrocardiogram and the two wearable electrocardiogram devices. A. Correlation matrix for corrected QT (QTc; Bazett's formula) in lead II between the 12-lead surface electrocardiogram (12L-ECG) and the Apple Watch (AW) (Pearson's analysis). B. Bland-Altman plot for QTc in lead II between the 12L-ECG and the AW. C. Correlation matrix for QTc in lead V5 between the 12L-ECG and the AW (Pearson's analysis). D. Bland-Altman plot for QTc in lead V5 between the 12L-ECG and the AW. E. Correlation matrix for QTc in lead II between the 12L-ECG and the KardiaMobile 6L (K6L; Pearson's analysis). F. Bland-Altman plot for QTc in lead II between the 12L-ECG and the K6L.

Both devices allow relatively reliable measurement of the QTc, correlated with the reference values obtained on the 12L-ECG. The correlation of the 12L-ECG with the AW is slightly better than with the K6L. However, both devices resulted in a systematic bias, in opposite directions. In line with previous work, the AW leads to a slight overestimation (on average < 20 ms) of the QTc [7,9], whereas the K6L results in a subtle underestimation (on average < 10 ms) of the QTc [5,10]. Heart rate was significantly higher with the K6L than with the 12L-ECG, because recording with the K6L required patients to sit, whereas they were lying down

for the acquisitions using the 12L-ECG and the AW. In patients with LQTS, beta-blocker treatment results in a reduction of the QTc, which is proportional to the increase in heart rate [17]. In the present cohort, the rate of beta-blocker treatment was high (85.7%), and as the heart rate was higher with the K6L, this could possibly explain the shorter QTc obtained using this device. Taking these limitations into account, the use of these two devices may show potential for the remote monitoring of patients with LQTS, particularly in situations where patients present a transient risk of QTc prolongation (drugs, electrolyte disorders, fever in patients with LQT2, etc.), but only after having obtained a reference electrocardiogram with the wearable device in question, during a follow-up visit.

Table 2
Comparison between the 12-lead surface electrocardiogram and the two wearable electrocardiogram devices.

12-lead surface electrocardiogram	
QTc in lead II (n=98)	
Mean ± SD (ms)	456.4 ± 35.5
Minimum-maximum (ms)	382-534
QTc in lead V5 (n=98)	
Mean ± SD (ms)	453 ± 35.5
Minimum-maximum (ms)	381-533
Heart rate (n=98)	
Mean ± SD (beats/min)	60.9 ± 13
Minimum-maximum (beats/min)	37-124
Apple Watch	
QTc in lead II (n=95)	
Mean ± SD (ms)	470.5 ± 37.4
Minimum-maximum (ms)	386-600
Pearson correlation coefficient r	0.703 (P<0.001)
Bias (95% CI)	-14.2 (-20.0; -8.46)
Limits of agreement	-69.6 to +41.1
QTc in lead V5 (n=97)	
Mean ± SD (ms)	470.7 ± 42.2
Minimum-maximum (ms)	385-628
Pearson correlation coefficient r	0.646 (P<0.001)
Bias (95% CI)	-17.1 (-23.8; -10.4)
Limits of agreement	-82.1 to +47.9
Heart rate (n=97)	
Mean ± SD (beats/min)	61.9 ± 13.3
Minimum-maximum (beats/min)	35-124
Spearman correlation coefficient r	0.857 (P<0.001)
Bias (95% CI)	-0.918 (-2.34; +0.504)
Limits of agreement	-14.738 to +12.903
KardiaMobile 6L	
QTc in lead II (n=94)	
Mean ± SD (ms)	445.2 ± 32.3
Minimum-maximum (ms)	348-534
Pearson correlation coefficient r	0.593 (P<0.001)
Bias (95% CI)	+9.51 (+3.28; +15.7)
Limits of agreement	-50.08 to +69.10
Heart rate (n=94)	
Mean ± SD (beats/min)	64.7 ± 12.4
Minimum-maximum (beats/min)	40-124
Spearman correlation coefficient r	0.733 (P<0.001)
Bias (95% CI)	-3.96 (-5.55; -2.37)
Limits of agreement	-19.15 to +11.24

CI: confidence interval; QTc: corrected QT interval duration (Bazett's formula); SD: standard deviation.

Beyond the quantitative evaluation of the QTc, the present study proposes a qualitative evaluation of ST-T wave patterns in wear-able electrocardiogram devices, an important assessment method according to Peter J. Schwartz: “When I suspect the possible presence of LQTS, I not only measure the QT interval but, being aware that sometimes it may just be borderline, I also look at it. By this, I mean that I look carefully at the morphology of the T

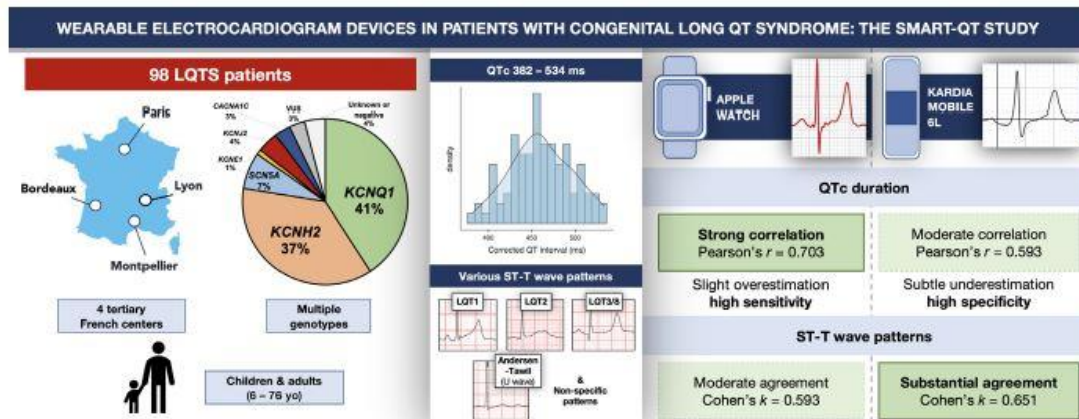
wave [. . .]” [18]. Because of the significant overlap between the QTc values in patients with LQTS and those observed in the general population [19], a meticulous assessment of the repolarization morphology in addition to the QTc allows better identification of patients with LQTS. Indeed, a significant proportion of patients with LQTS may have a non-prolonged QTc at the time of resting electrocardiogram acquisition, and LQTS screening based solely on the presence of a prolonged QTc (≥ 480 ms) has a sensitivity of only 19% [20]. Conversely, a large majority of patients with LQTS have an ST-T wave pattern typical of their genotype on the 12L-ECG, and LQTS screening based on the identification of specific ST-T patterns has better sensitivity (LQT1: 61%; LQT2: 62%; LQT3: 33%; and Andersen-Tawil:84%) [2,14]

.In the present cohort, among the patients with the most common genotypes (LQT1/2/3/8 and Andersen-Tawil), only 15.6% had a QTc ≥ 480 ms on the day of the evaluation, whereas 80% had an ST-T wave pattern typical of their genotype on the 12L-ECG. Regarding the classification of ST-T patterns, the level of agreement with the 12L-ECG was moderate with the AW ($k = 0.593$), and substantial with the K6L ($k = 0.651$). It should also be noted that the electro-cardiograms were too artefactual to allow evaluation of the ST-T wave patterns in 8.2% of the electrocardiograms obtained with the K6L, whereas the patterns could be evaluated on all electrocardiograms obtained with the AW. The present findings show that the ST-T wave patterns obtained with these two devices are of insufficient quality to replace the 12L-ECG for initial LQTS screening based on repolarization morphology analysis; they are, however, of sufficient quality to be used for the follow-up of patients with LQTS.

4.1. Study strengths and limitations

The present study is the first prospective multicentre study evaluating two wearable electrocardiogram devices in a large cohort of patients with LQTS, and is representative of the broad spectrum of patients with LQTS (in terms of genotypes, age and ST-T wave patterns). Several limitations should nevertheless be noted. There was no a priori sample size calculation, because the rarity of LQTS makes it difficult to recruit a large number of patients in a prospective study. The electrocardiogram recordings were made in the hospital, in a supervised manner, and it is therefore possible that the quality of the electrocardiograms is higher than that obtained when patients use their portable electrocardiogram devices in their daily life. In addition, the electrocardiogram recordings were made sequentially, which could artificially generate some differences between the recordings. Furthermore, no patient presented ST-T patterns indicative of a high short-term risk of torsade de pointes (i.e. giant T-U distortion, macroscopic T wave alternans, etc.), the ability of these devices to obtain such patterns is thus unknown. However, a major strength of the study lies in the fact that both quantitative (QTc duration) and qualitative (ST-T wave pattern) evaluations were carried out for both devices. Finally, it would be interesting to evaluate other wearable electrocardiogram

devices that are currently available on the market (Fitbit Sense, Samsung Galaxy Watch, Withings Scan Watch, etc.).



Central Illustration. Wearable electrocardiogram devices in patients with congenital long QT syndrome: The SMART-QT study. QTc: corrected QT interval; LQT1: LQTS type 1; LQT2: LQTS type 2; LQT3/8: LQTS types 3/8; LQTS: congenital long QT syndrome; VUS: variant of uncertain significance; yo: years old.

5. Conclusions

This prospective multicentre study of a large cohort of patients of all ages with LQTS shows the quantitative and qualitative abilities of two wearable electrocardiogram devices (AW and K6L) for the assessment of QTc in these patients. These devices cannot replace the 12L-ECG for the follow-up of patients with LQTS because of their limitations, but could be useful tools when a 12L-ECG device is not available (Central Illustration).

Sources of funding

This work received a grant from the French national network “Filière Nationale de Santé Cardiogen”. The work performed at Bordeaux University hospital received financial support from the French Government as part of the “Investments in the Future” programme, managed by the National Research Agency (ANR; grant reference ANR-10-IAHU-04).

Acknowledgements

The authors thanks Véréna Landel (Direction de la Recherche Clinique et de l’Innovation, **Hospices Civils de Lyon**) for language editing.

Disclosure of interest

The authors declare that they have no competing interest.

References

- [1] Schwartz PJ, Priori SG, Spazzolini C, Moss AJ, Vincent GM, Napolitano C, et al. Genotype-phenotype correlation in the long-QT syndrome: gene-specific triggers for life-threatening arrhythmias. *Circulation* 2001;103:89–95.
- [2] Zhang L, Timothy KW, Vincent GM, Lehmann MH, Fox J, Giuli LC, et al. Spectrum of ST-T-wave patterns and repolarization parameters in congenital long-QT syndrome: ECG findings identify genotypes. *Circulation* 2000;102:2849–55.
- [3] Mazzanti A, Maragna R, Vacanti G, Monteforte N, Bloise R, Marino M, et al. Inter-play between genetic substrate, QTc duration, and arrhythmia risk in patients with long QT syndrome. *J Am Coll Cardiol* 2018;71:1663–71.
- [4] Kirchhof P, Franz MR, Bardai A, Wilde AM. Giant T-U waves precede torsades de pointes in long QT syndrome: a systematic electrocardiographic analysis in patients with acquired and congenital QT prolongation. *J Am Coll Cardiol* 2009;54:143–9.
- [5] Bergeman AT, Pultoo SNJ, Winter MM, Somsen GA, Tulevski II, Wilde AAM, et al. Accuracy of mobile 6-lead electrocardiogram device for assessment of QT interval: a prospective validation study. *Neth Heart J* 2023;31:340–7.
- [6] Spaccarotella CAM, Migliarino S, Mongiardo A, Sabatino J, Santarpia G, DeRosa S, et al. Measurement of the QT interval using the Apple Watch. *Sci Rep* 2021;11:10817.
- [7] Strik M, Caillol T, Ramirez FD, Abu-Alrub S, Marchand H, Welte N, et al. Validating QT-interval measurement using the Apple Watch ECG to enable remote monitoring during the COVID-19 pandemic. *Circulation* 2020;142:416–8.
- [8] Viskin S, Rosovski U, Sands AJ, Chen E, Kistler PM, Kalman JM, et al. Inaccurate electrocardiographic interpretation of long QT: the majority of physicians cannot recognize a long QT when they see one. *Heart Rhythm* 2005;2:569–74.
- [9] Yee-Ming Li J, Kwok SY, Tsao S, Hoi-Yan Chung C, Hing-Sang Wong W, Cheung YF. Detection of QT interval prolongation using Apple Watch electrocardiogram in children and adolescents with congenital long QT syndrome. *Int J Cardiol Heart Vasc* 2023;47:101232.
- [10] Kleiman R, Darpo B, Brown R, Rudo T, Chamoun S, Albert DE, et al. Comparison of electrocardiograms (ECG) waveforms and centralized ECG measurements between a simple 6-lead mobile ECG device and a standard 12-lead ECG. *Ann Noninvasive Electrocardiol* 2021;26:e12872.
- [11] Richards S, Aziz N, Bale S, Bick D, Das S, Gastier-Foster J, et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. *Genet Med* 2015;17:405–24

- [12] Spaccarotella CAM, Polimeni A, Migliarino S, Principe E, Curcio A, Mongiardo A, et al. Multichannel electrocardiograms obtained by a smartwatch for the diagnosis of ST-segment changes. *JAMA Cardiol* 2020;5:1176–80.
- [13] Postema PG, Wilde AA. The measurement of the QT interval. *Curr Cardiol Rev* 2014;10:287–94.
- [14] Zhang L, Benson DW, Tristani-Firouzi M, Ptacek LJ, Tawil R, Schwartz PJ, et al. Electrocardiographic features in Andersen-Tawil syndrome patients with *KCNJ2* mutations: characteristic T-U-wave patterns predict the *KCNJ2* genotype. *Circulation* 2005;111:2720–6.
- [15] Krisai P, Vlachos K, Ramirez FD, Nakatani Y, Nakashima T, Takagi T, et al. Evaluation of the QT interval in patients with drug-induced QT prolongation and torsades de pointes. *J Cardiovasc Electrophysiol* 2020;31:2696–701.
- [16] Neumann B, Vink AS, Hermans BJM, Lieve KVV, Comert D, Beckmann BM, et al. Manual vs. automatic assessment of the QT-interval and corrected QT. *Europace* 2023;25:1–12.[
- [17] Bennett MT, Gula LJ, Klein GJ, Skanes AC, Yee R, Leong-Sit P, et al. Effect of beta-blockers on QT dynamics in the long QT syndrome: measuring the benefit. *Europace* 2014;16:1847–51.
- [18] Schwartz PJ. My approach to the long QT syndrome (LQTS). *Trends Cardiovasc Med* 2015;25:376–7.
- [19] Taggart NW, Haglund CM, Tester DJ, Ackerman MJ. Diagnostic miscues in congenital long-QT syndrome. *Circulation* 2007;115:2613–20.
- [20] Vink AS, Neumann B, Lieve KVV, Sinner MF, Hofman N, El Kadi S, et al. Determination and Interpretation of the QT Interval. *Circulation* 2018;138:2345–58.8