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Assessment of QT-measurement accuracy using the 12-lead electrocardiogram derived from EASI leads

Juan Pablo Martínez, PhD,[a,*] Pablo Laguna, PhD,[a] Salvador Olmos, PhD,[a] Olle Pahlm, MD, PhD,[b] Jonas Pettersson, MD, PhD,[c] Leif Sörnmo, PhD[d]

[a]*Aragon Institute of Engineering Research, Universidad de Zaragoza, Zaragoza, Aragon, Spain*
[b]*Department of Clinical Physiology, Lund University Hospital, Sweden*
[c]*Experimental Medicine, AstraZeneca R&D, Sweden*
[d]*Department of Electroscience, Lund Institute of Technology, Sweden*

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Abstract The purpose of the present study is to assess QT-interval measurements from the EASI 12-lead electrocardiogram (ECG) as compared with the standard 12-lead ECG. The QT interval was automatically determined in simultaneously recorded standard and EASI 12-lead ECGs, using a validated wavelet-based delineator. The agreement between the 2 sets of measurements was quantified both on a lead-by-lead basis and a multilead basis with global definitions of QRS onset and T-wave end.The results show that the agreement between QT-interval measurements from the 2 lead systems is acceptable, with negligible mean differences and with correlation coefficients ranging from 0.91 to 0.98 depending on the lead studied. Although the SD shows a clear dependence on the selected lead (ranging from 9.2 to 26.4 milliseconds), differences are within the accepted tolerances for automatic delineation. In a few patients, large differences were found, mainly because of changes in morphology present in both lead systems. QT intervals measured by the multilead approach were considerably more stable than single-lead measurements and resulted in a much better agreement between the 2 lead systems (correlation coefficient, 0.98; QT difference, 1.1 ± 9.8 milliseconds). Thus, the EASI 12-lead ECG may be used for reliable QT monitoring when the multilead delineation approach is adopted.

Introduction

It is well known that prolonged cardiac repolarization is associated with susceptibility to ventricular tachyarrhythmias, usually in the form of torsades de pointes, which can degenerate into life-threatening arrhythmias such as ventricular fibrillation. Causes for prolonged cardiac repolarization can be congenital, as for instance, in patients with long QT syndrome, or acquired, for example, drug induced. Delayed repolarization is manifested in the electrocardiogram (ECG) as a prolongation of the QT interval, representing the total duration of ventricular depolarization and subsequent repolarization. Despite the limitations suggested in some studies,[1] the QT interval remains the most widely used index for assessing the propensity to ventricular arrhythmias.

Certain drugs have the ability to delay myocardial repolarization; a list of drugs that can cause QT-interval prolongation and torsades de pointes is found in reference.[2] This fact has resulted in a substantial number of regulatory actions, including withdrawals of potential cardiotoxic drugs from the market. Therefore, rigorous monitoring of the QT interval is mandatory in early phases of clinical drug development. Drug regulatory agencies worldwide, including the US Food and Drug Administration, the European Medicines Agency, or Japan's National Institute of Health Services, have adopted the ICH E14 guidelines, which require the accomplishment of the so-called thorough QT/QTc studies.[3]

In phase 1 trials, standard 12-lead ECGs are usually recorded repeatedly at rest, sometimes with intervals between recordings as short as 5 to 10 minutes, to follow drug-induced changes in the QT interval as well as other

* Corresponding author. Departamento de Ingeniería Electrónica y Comunicaciones, Centro Politécnico Superior, Universidad de Zaragoza, 50018 Aragón, Spain. Tel.: +34 976762363; fax: +34 976762111.
E-mail address: jpmart@unizar.es

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alterations in the ECG. In addition, subjects are often continuously monitored during the drug study to detect possible transient arrhythmias, but this is done using only 1 or 2 ECG leads to minimize the number of electrodes and wires. However, if the 12-lead ECG could be monitored, repeated recordings of the resting ECG would be unnecessary, thus, simplifying the procedure.

In the last 2 decades, an alternative electrode placement system, the EASI lead system, has been introduced.[4] EASI lead monitoring is based on only 5 electrodes, 1 of which is a ground electrode. The 4 active electrodes are positioned as follows: 2 are placed on the sternum and 2 in the right and left midaxillary lines at the level of the lower sternal electrode (Fig. 1). Based on the signals from these positions, it is possible to mathematically construct an "EASI 12-lead ECG."

Several articles have described the agreement between the EASI and the standard 12-lead ECG. The studies by Drew et al,[5-7] Horacek et al,[8] and the recent one by Wehr et al[9] examined the diagnostic accuracy of the EASI 12-lead ECG for a number of cardiac abnormalities, concluding that it carries essentially the same diagnostic information as the standard ECG. Rautaharju et al[10] found no relevant differences between the lead systems with respect to the classification of acute myocardial ischemia and old myocardial infarction. Differences in waveform measurements between EASI and standard lead systems,[11] as well as to the Mason-Likar limb lead configuration,[12] have also been investigated. Recently, Chantad et al[13] concluded that ST-segment deviations can be accurately assessed using the EASI ECG. From the signal quality point of view, the susceptibility to baseline wander and myoelectric noise in both the Mason-Likar and the EASI lead placement schemes were studied by Welinder et al.[14]

The purpose of the present study is to assess QT-interval measurements from the EASI 12-lead ECG as compared with that from the standard 12-lead ECG. The main hypothesis is, therefore, that QT can be measured from EASI-derived 12-lead ECG with similar accuracy as from standard ECG. This is an issue that has not been addressed previously in the literature. The use of EASI leads is not only associated with faster electrode placement but also would considerably facilitate phase 1 clinical trials because continuous monitoring is more conveniently accomplished with fewer electrodes.

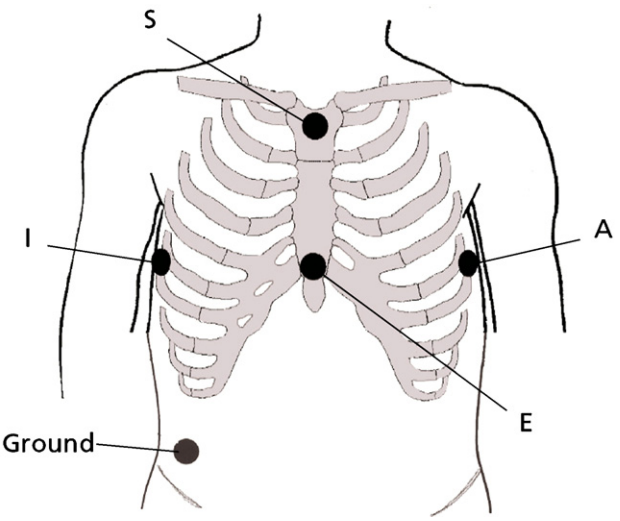

Fig. 1. Locations of the active electrodes (E, A, S, I). The ground electrode is placed anywhere in the torso.

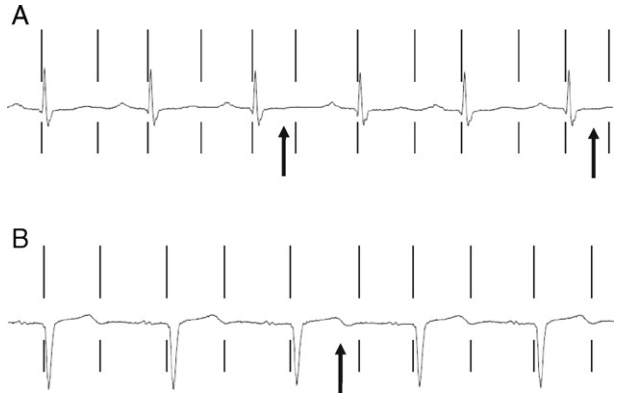

Fig. 2. Examples of leads discarded because of unstable delineation. A, EASI-derived lead II. The QT intervals of the third and last beats are considerably shorter than of the remaining beats, caused by very low T-wave amplitudes. B, Standard lead V_2. All T waves were considered to be positive except the third one whose morphology was biphasic, thus, causing unstable QT-interval measurements.

Materials and methods

Study population and acquisition

The initial study group consisted of 200 patients from the Rui Jin Hospital, Shanghai, China, having a wide range of ages and cardiac conditions. The hospital approved the study, and patient consent was obtained. For each patient, the standard 12-lead and EASI ECGs were recorded simultaneously during 11 seconds, using a Philips PageWriter XLi electrocardiograph (Philips Medical Inc, Thousand Oaks, Calif) (sampling rate, 500 Hz; amplitude resolution, 5 μV).

The exclusion criteria for ECG recordings were pacemaker, atrial fibrillation/flutter, right/left bundle branch block, Wolff-Parkinson-White syndrome, QRS duration

Table 1
QT interval, QRS onset, and T-wave end measurement differences between standard and EASI-derived leads

Lead	No. of patients P_l	$\Delta\overline{QT}_l$ (ms)	$\Delta\overline{Qon}_l$ (ms)	$\Delta\overline{Tend}_l$ (ms)
V_1	76	0.9 ± 25.5	−1.0 ± 8.6	0.0 ± 21.1
V_2	81	−1.0 ± 20.8	1.0 ± 7.5	0.0 ± 18.8
V_3	79	2.7 ± 17.9	−1.0 ± 4.8	1.7 ± 17.5
V_4	79	−0.8 ± 16.4	0.2 ± 4.2	−0.7 ± 16.5
V_5	88	−3.5 ± 13.6	−0.2 ± 4.6	−3.7 ± 12.8
V_6	87	−0.1 ± 12.5	−0.3 ± 6.3	−0.4 ± 9.4
aVL	67	−0.8 ± 20.1	2.3 ± 8.3	1.5 ± 18.6
I	74	−1.7 ± 9.2	2.8 ± 5.4	1.1 ± 7.7
−aVR	80	1.0 ± 12.8	0.8 ± 7.2	1.8 ± 10.1
II	84	−1.1 ± 19.1	−0.3 ± 8.5	−1.5 ± 14.7
aVF	82	−0.2 ± 21.8	−0.9 ± 10.5	−1.0 ± 20.9
III	76	−0.4 ± 26.4	−0.5 ± 9.9	−1.0 ± 24.8
Multilead	98	1.1 ± 9.8	0.5 ± 3.6	1.6 ± 9.4
Multilead (all patients)	104	0.8 ± 10.4	0.7 ± 3.6	1.4 ± 10.3

Note that the sampling interval is 2 milliseconds.

Table 2
Intralead SD of QT measurements in standard and EASI-derived leads

Lead	No. of patients	$\sigma_{QT_{l,p}^{STD}}$ (ms)	$\sigma_{QT_{l,p}^{EASI}}$ (ms)
V_1	76	9.3 ± 7.7	8.5 ± 7.8
V_2	81	5.0 ± 6.0	7.2 ± 6.5
V_3	79	3.8 ± 4.5	6.2 ± 6.2
V_4	79	5.2 ± 4.8	5.2 ± 4.8
V_5	88	5.2 ± 4.8	6.1 ± 5.5
V_6	87	6.1 ± 4.6	6.3 ± 5.5
aVL	67	10.4 ± 7.5	8.6 ± 6.4
I	74	8.9 ± 6.6	6.5 ± 5.7
−aVR	80	8.0 ± 5.7	5.7 ± 4.8
II	84	8.9 ± 7.0	6.0 ± 5.6
aVF	82	8.7 ± 6.6	7.1 ± 6.3
III	76	9.2 ± 5.2	8.9 ± 6.8
Multilead	98	6.1 ± 3.6	6.2 ± 4.2

greater than 120 milliseconds, acute ST-elevation myocardial infarction, resting heart rate greater than 100 or less than 50 beats/min, bad electrode location, or insufficient technical quality of the ECG recording. After exclusion, a total of 104 patients were used for further evaluation.

Single-lead waveform delineation

Automatic waveform delineation of the heartbeat is performed with a multiscale wavelet-based delineator previously described and validated.[15] A set of differentiated signals, smoothed at different scales, is obtained by means of the discrete wavelet transform, using a quadratic spline wavelet. First, detection and classification of waveforms are performed by searching for the maxima and minima at different scales. According to the number of significant slopes, the method classifies the T waves into 1 of 6 classes: positive, negative, biphasic (positive-negative or negative-positive), only upward, and only downward. Then, the waveform boundaries are located using a threshold approach across scales.[15] The rules for multiscale delineation are different for the QRS complex and the T wave, accounting for differences in spectral content.

Using an annotated QT database,[16] the performance of the wavelet-based delineator was assessed in terms of statistics for the differences between manual QT annotations

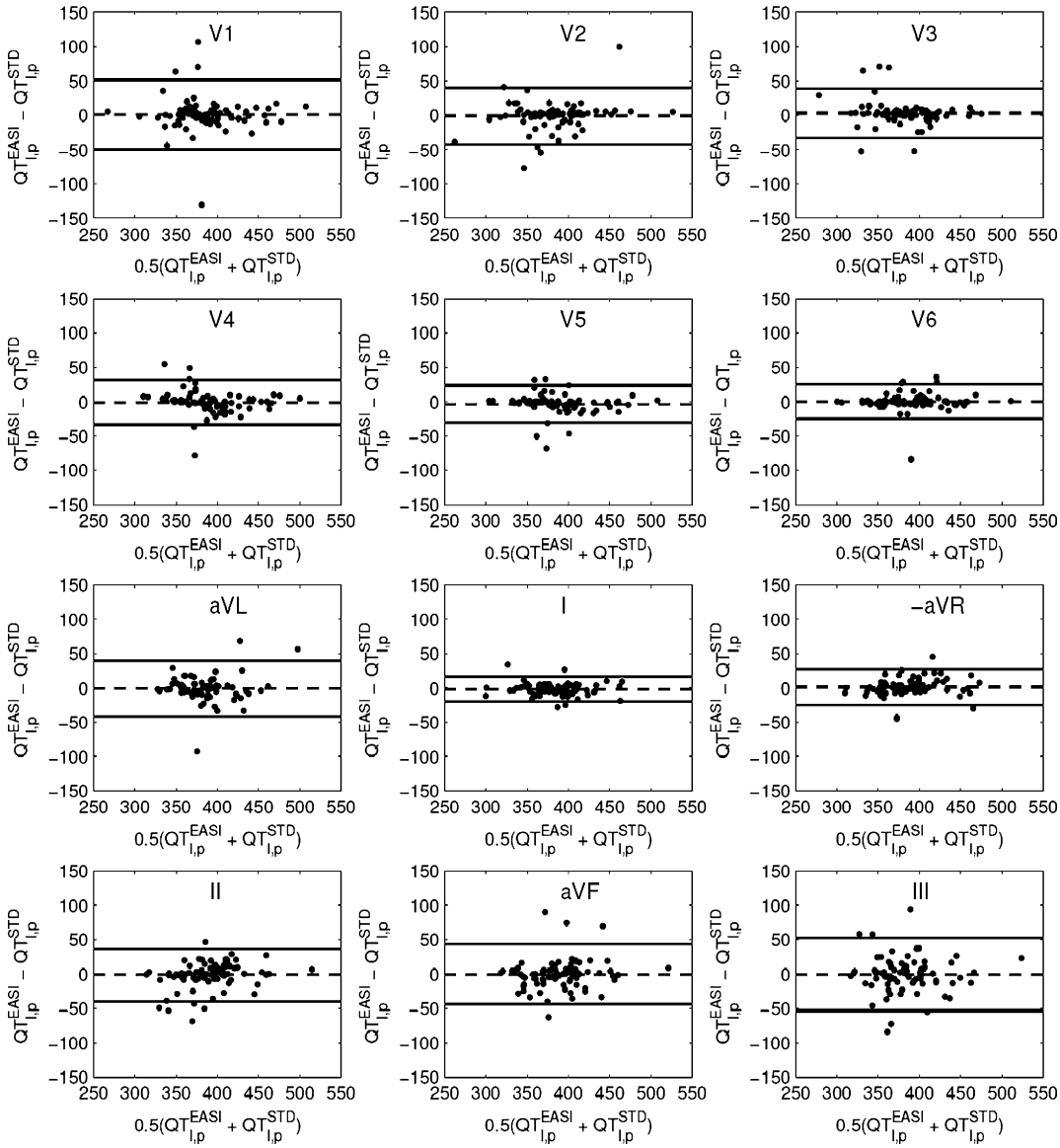

Fig. 3. Bland-Altman plots of QT measurements from EASI-derived and standard leads (ie, $QT_{l,p}^{EASI}$, $QT_{l,p}^{STD}$). Dashed line indicates mean difference; solid lines, mean ± 2 SDs.

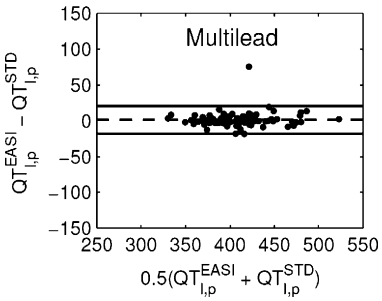

Fig. 4. Bland-Altman plot for the QT multilead measurements in EASI-derived and standard leads ($QT_{l,p}^{EASI}$ and $QT_{l,p}^{STD}$). Dashed line indicates mean difference; solid lines, mean ± 2 SDs.

and automatic measurements.[15] The disagreement between annotations and measurements was found to be comparable to interexpert differences in the same database.[15]

EASI vs standard lead QT comparison

The EASI 12-lead ECG was derived using the transformation matrix given by Feild et al[17] QT intervals were automatically measured in the 2 sets of simultaneously recorded ECGs. For a given patient, indexed by $P = \{1,\ldots, 104\}$, and beat, indexed by $n = \{1,\ldots, N_p\}$, the method supplied up to 24 measurements defining QRS onset, T-wave end, and related QT interval, denoted by $Qon_{l,p}^{s}(n)$, $Tend_{l,p}^{s}(n)$, and $QT_{l,p}^{s}(n)$, respectively. The leads are indexed by $\boldsymbol{l} = \{V_1, V_2, V_3, V_4, V_5, V_6, I, II, III, aVL, aVR, aVF\}$, and the lead system by $s = \{EASI, STD\}$. For each lead, differences between measurements of the derived and standard leads were computed and denoted $\Delta Qon_{l,p}(n) = Qon_{l,p}^{EASI}(n) - Qon_{l,p}^{STD}(n), \Delta Tend_{l,p}(n) = Tend_{l,p}^{EASI}(n) - Tend_{l,p}^{STD}(n)$, and $\Delta QT_{l,p}(n) = QT_{l,p}^{EASI}(n) - QT_{l,p}^{STD}(n)$, respectively.

After discarding the first and last detected beats, the mean QT interval was computed in every patient for each lead and lead system and denoted $QT_{l,p}^{EASI}$ and $QT_{l,p}^{STD}$. The mean differences in the measurements of QRS onset, T-wave end, and QT interval between the derived and standard leads for a given patient and lead are denoted by $\Delta Qon_{l,p}$, $\Delta Tend_{l,p}$, and $\Delta QT_{l,p}$.

To avoid unstable QT measurements, we discarded leads with less than 5 detected T waves or with large QT variability (the intralead SD exceeding 30 milliseconds) from further analysis; these criteria were applied to both lead configurations. The main reasons for instability were the presence of low-amplitude/flat T waves and "borderline morphologies," for example, switching between mono- and biphasic T-wave morphologies; 2 such examples are presented in Fig. 2.

Multilead waveform delineation

Lead-by-lead comparison between the EASI and standard ECG can be considerably influenced by the relative differences in axes' orientation of the resulting vectorcardiogram (VCG) in each of the lead systems. When these relative differences occur, the projections of the cardiac electrical vector into the leads are different for the 2 studied lead systems, resulting in differences in morphology and duration of the ECG waves. It is therefore desirable to consider a multilead approach in which all 12 leads are taken into account to produce a global QRS onset and T-wave end for each beat. Physiologically, if the QRS onsets and T-wave ends of all leads are correctly determined, the QT interval is ideally defined as the difference between the latest T-wave end and the earliest QRS onset among the 12 leads. However, this strategy is extremely sensitive to delineation errors due to, for example, noise and classification errors, which may cause large QT-measurement errors.[1,18]

To reduce the risk of such errors, we used a multilead rule for the determination of a global QRS onset and T-wave end.[18] First, the QRS onsets and T-wave ends of the different leads were sorted (a maximum of 12 for each of the 2). Then, the global QRS onset was defined as the earliest QRS onset followed by at least 3 other onsets in the next δ milliseconds. In the same way, the last T-wave end preceded by at least 3 other ends in the previous δ milliseconds was considered to be the global T-wave end. The value of δ was set to 12 milliseconds, previously applied in reference[16] for validation of the abovementioned wavelet-based delineator on the Common Standards for Quantitative Electrocardiography (CSE) multilead database.[19] This multilead rule, being robust to delineation errors, preserves the physiologic meaning of the QT interval as the period from the beginning of ventricular depolarization to the end of ventricular repolarization.

Statistics

Differences in QT measurements obtained from the EASI and standard 12-lead ECGs are described as mean ± SD across patients and in terms of their cumulative probability function. The Pearson correlation coefficient and the Bland-Altman plot were used to assess the agreement between the 2 sets of measurements.

Results

Standard vs EASI lead measurements

Table 1 presents the mean values of $\Delta QT_{l,p}$ across patients, that is, $\Delta\overline{QT}_l = \frac{1}{P_l}\sum_{p=1}^{P_l}\Delta QT_{l,p}$, and the similarly defined $\Delta\overline{Qon}_l$ and $\Delta\overline{Tend}_l$ (mean ± SD). For

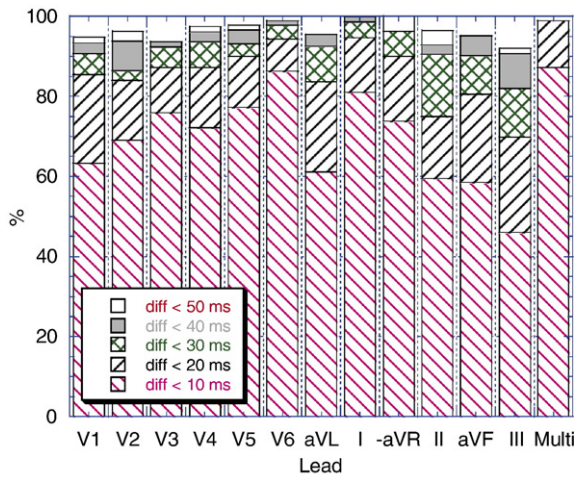

Fig. 5. Cumulative distribution of absolute QT differences.

each lead, the number of patients (P_l) with stable QT measurements is presented. In the case of multilead delineation, results are presented for records in which multilead QT accomplished the stability criterion previously defined, as well as for all patients (last row of Table 1).

The stability of the measurements in both lead systems was assessed by computing the beat-to-beat SD for each lead and patient, denoted as $\sigma_{\mathrm{QT}_{l,p}}^{\mathrm{STD}}$ and $\sigma_{\mathrm{QT}_{l,p}}^{\mathrm{EASI}}$, respectively. The mean values across patients are shown in Table 2. Note that all leads with SD greater than 30 milliseconds have been discarded, as explained in the "Materials and methods" section.

The Bland-Altman plots for each of the 12 leads and the multilead approach are shown in Figs. 3 and 4, respectively. Note that each point represents the agreement between both measurements $\{\mathrm{QT}_{l,p}{}^{\mathrm{EASI}}$ and $\mathrm{QT}_{l,p}{}^{\mathrm{STD}}\}$ of the pth patient.

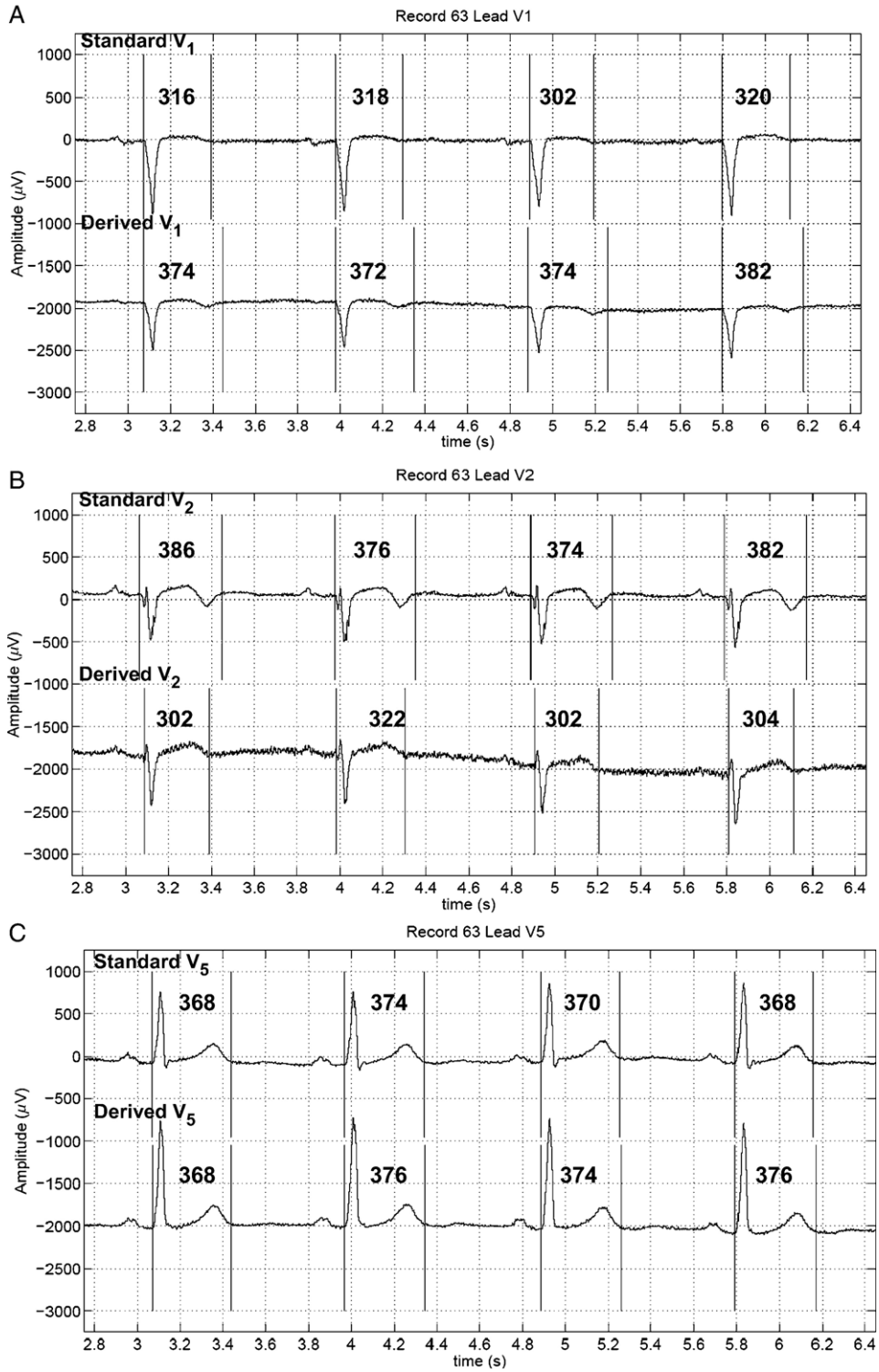

Fig. 6. Comparison of QT measurements in standard and derived V_1, V_2, and V_5 for a patient with large differences. Note that panels A and B (V_1 and V_2) show differences in T-wave morphology between the standard and derived lead, producing large QT-interval differences. On the other hand, lead V_5 exhibits similar T-wave morphology, and the QT differences are small.

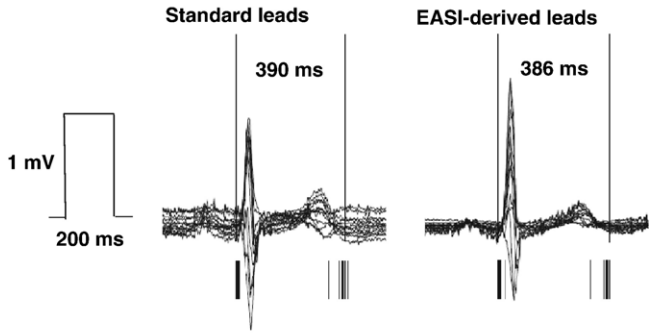

Fig. 7. Multilead delineation for the signal displayed in Fig. 6 but now displayed with a superimposed format. The global QRS onset and T-wave end are marked by long lines and single-lead delineations with short lines.

The Pearson correlation coefficients between QT measurements in EASI and standard leads ($QT_{l,p}^{EASI}$ and $QT_{l,p}^{STD}$) are V_1, 0.90; V_2, 0.94; V_3, 0.94; V_4, 0.96; V_5, 0.97; aVL, 0.91; −aVR, 0.97; II, 0.93; aVF, 0.91; and III, 0.88. The correlation coefficient is 0.98, using the multilead approach.

To gain insight into the error distribution, we computed the cumulative distributions of the absolute QT differences between STD and EASI leads $|\Delta QT_{l,p}|$ (Fig. 5).

An example with large QT-interval differences between the standard and derived ECG is shown in Figs. 6 and 7. It is obvious that the change in T-wave morphology of the derived leads V_1 and V_2 causes large difference in QT measurements. Fig. 7 illustrates the ability of the multilead approach to produce QT measurement robust to changes in the electrical axis, and consequently, the difference between the 2 lead systems is reduced.

Differences in T-wave morphology classification

Some of the largest QT-measurement differences were caused by the classification of T-wave morphology, which differed between the 2 lead systems. Table 3 shows the percentage of agreement for the dominant T-wave morphology as well as the percentages of selected disagreements.

T-wave detectability

Another source of differences in single-lead QT measurements is the situation when T waves are delineated in only 1 of the 2 lead systems. For example, T-wave amplitudes that are much lower in 1 of the lead systems are not accounted for in the above performance measures because only beats with T waves detected in both lead systems were considered. For that purpose, we computed the percentage of detected T waves in each of the 2 lead systems (including all the leads of the 104 patients) and the percentage of beats with T waves jointly detected in standard and derived leads. From these values, the sensitivity S and positive predictivity $P+$ of T-wave detection in EASI-derived leads were computed, assuming that the detection outcome in the standard ECG represents the criterion standard (Table 4).

Table 4
T-wave detection performance

Lead	Delineated T waves (standard leads) (%)	Delineated T waves (EASI leads) (%)	Delineated T waves (both lead systems) (%)	EASI $S/P+$
V_1	95.2	97.3	93.2	97.9/95.8
V_2	98.9	96.2	95.3	96.4/99.0
V_3	98.5	96.5	95.7	97.2/99.1
V_4	96.4	97.3	94.6	98.1/97.2
V_5	96.8	99.1	96.5	99.7/97.4
V_6	97.4	98.2	96.9	99.5/98.7
aVL	98.1	96.4	95.0	96.9/98.6
I	96.1	98.8	95.4	99.3/96.6
−aVR	98.6	98.9	97.8	99.2/98.9
II	96.7	97.6	95.6	98.7/97.8
aVF	96.5	97.5	94.5	98.0/97.0
III	98.2	96.9	95.8	97.6/98.8

The sensitivity (S) and positive predictivity ($P+$) of the delineator in the EASI-derived leads are computed, assuming the delineation of the standard leads as the criterion standard. A total of 1041 beats in 104 patients were analyzed.

Discussion

Tolerances and intraexpert variability in determination of waveform boundaries

Because both automatic and manual QT measurements are subject to errors, they exhibit an intrinsic variability. It is therefore useful to introduce reference values for the purpose of assessing measurement differences between the EASI and standard 12-lead ECG. In particular, it is highly desirable to determine whether the measurement differences are acceptable with respect to the accuracy of manual annotations. A good reference is provided by the

Table 3
Classification of T-wave morphology in standard and EASI-derived leads

Lead	Morphology agreement (%)	Negative STD, positive EASI (%)	Positive STD, negative EASI (%)	Monophasic STD, biphasic EASI (%)	Biphasic STD, monophasic EASI (%)
V_1	90.8	0	2.6	0	6.6
V_2	90.1	1.2	6.2	0	2.5
V_3	93.7	5.1	0	1.3	0
V_4	91.1	6.3	0	1.3	1.3
V_5	93.2	5.7	0	1.1	0
V_6	98.9	1.1	0	0	0
aVL	88.1	6.0	4.5	1.5	0
I	98.6	0	1.4	0	0
−aVR	100	0	0	0	0
II	91.7	1.2	2.4	4.8	0
aVF	85.4	1.2	9.8	2.4	1.2
III	81.6	5.3	10.5	1.3	1.3

interobserver and intraobserver variability of expert cardiologists. Such information has been established by the European project CSE with respect to the accuracy of ECG waveform boundary determination. According to the CSE working party recommendation, the SD of the differences between automatic measurements and reference values should not exceed a tolerance defined by twice the SD of the error of the median cardiologist in a panel of 5 experts. The tolerance limits for QRS onset and T-wave end were 6.5 and 30.6 milliseconds, respectively.[20] It should also be noted that there is a considerable intraobserver variability in determining the waveform boundaries from different readings of the same ECG. An intraobserver SD of 8 milliseconds in 3 different readings has been established for T-wave end.

Tolerance limits for automatic multilead QT measurements were determined by Zywietz and Celikag,[21] being equal to 7.0 milliseconds for the bias and 13.5 for the SD; these limits were set as those accomplished by 84% of the assessed programs.

Performance validations of the present wavelet-based delineator on other databases than the present one serve as a valuable reference. With the use of a QT database, the SD of the differences between automatic delineations and manual annotations of a cardiologist was 7.7 milliseconds for QRS onset and 18.1 milliseconds for T-wave end, whereas the SD between 2 cardiologists, in a subset of the same database, was 11.1 and 22.4 milliseconds, respectively.[15] With the use of the abovementioned multilead rule, the SD in the CSE database was 6.3 milliseconds for QRS onset and 21.8 milliseconds for T-wave end.

Single-lead QT measurements

Table 1 shows that QT intervals measured in EASI-derived leads differ less than 1 sampling interval (2 milliseconds) from QT intervals measured in the standard leads, except in V_3 and V_5 (with mean differences of 2.7 and −3.5 milliseconds, respectively). The SD of the differences is strongly dependent on the selected lead; the most stable measurements were found in V_5 (13.6 milliseconds), V_6 (12.5 milliseconds), I (9.2 milliseconds), and −aVR (12.8 milliseconds), all fulfilling the multilead tolerances proposed in reference.[21] Note that all these leads have an important component in the "right-to-left" direction, that is, the direction of the x-axis as defined in vectorcardiography. On the other hand, the largest SDs across patients occurred in III (26.4 milliseconds) and V_1 (25.5 milliseconds), most likely explained by the fact that these leads are more influenced by axis deviations.

The variability in QT-interval measurements is mainly due to a variability in the T-wave end delineation because the differences are much smaller for the QRS onset than for the T-wave end. The mean differences in the QRS-onset determination remained bounded by 1 millisecond, except for leads aVL and I (Table 1) in which a bias of more than 1 sample interval was found. The SD was lower than 10.5 milliseconds in all the leads. Differences were larger in the T-wave end delineation: The largest bias was found in leads V_5 (−3.7 milliseconds) and aVR (1.8 milliseconds), whereas the bias was lower than the 2-millisecond sampling interval in the other leads. The SD of the differences ranged from 7.7 (I) to 24.8 (III) milliseconds. The pattern of the lead-by-lead differences in T-wave end measure was similar to that of the QT interval.

The intralead QT SD ranges from 3.8 to 10.4 milliseconds in the standard leads (Table 2), whereas the QT SD ranges from 5.2 to 8.9 milliseconds in the EASI-derived leads. This variability can be attributed to the variability of the delineation algorithm, as well as to the natural heart-rate (HR)-driven QT variability. It should be noted that these figures fall, for most leads, within the accepted intraexpert variability (ie, 8 milliseconds for T-wave end).

The largest correlation between the 2 types of measurements was also found in leads V_5, V_6, I, and −aVR ($r > 0.97$ in all of them), whereas the lowest correlation was found in leads V_1 ($r = 0.9$) and III ($r = 0.88$). The Bland-Altman plots did not show any trend in the intermeasurement differences.

The distribution of the QT errors showed that there are some outlier cases with extreme lead-to-lead differences (Figs. 2-4). The distributions were very dependent on the selected lead. Although certain leads such as V_6 or I exhibited QT differences lower than 10 milliseconds in more than 80% of the records, more than half of the records exhibited errors larger than 10 milliseconds in other leads such as III (Fig. 5). As illustrated by the example in Figs. 6 and 7, the largest differences were mainly due to changes in T-wave morphology between the 2 lead systems. This hypothesis is also reinforced by the data presented in Table 3: the T-wave morphologies agreed between EASI-derived and standard leads in a percentage of beats ranging from 81.6% (III) to 100% (aVR). The leads with the largest morphologic disagreement were those with larger QT differences, and vice versa.

Regarding T-wave detection, T waves were delineated in more than 95% of the beats for either standard or EASI-derived leads. Assuming the standard lead as the criterion standard for T-wave existence, the best sensitivity in the corresponding EASI-leads was attained for V_5, V_6, I, and aVR, all leads with more than 99% of T waves being delineated (Table 4).

It can be concluded that differences in QT measurements from standard and EASI-derived leads are strongly dependent on the selected lead; leads with a large X component exhibited the lowest differences between the lead systems. Nonetheless, measurement differences were always within the standard tolerances given by the CSE working party (30.6 milliseconds for the T-wave end). However, the measurements were quite different between the lead systems in a significant percentage of the records. This is quite relevant because a small number of outlier measurements can bias the conclusion of a study on the QT prolongation. The largest differences were due to changes in T-wave morphology. Such morphologic changes can be attributed to differences in projection due to changes in the direction of the corresponding lead vectors. Under this hypothesis, a multilead approach is more appropriate for QT measurement in the EASI-derived leads.

Multilead QT measurements

The multilead approach used in this work reduces differences in QT intervals of the 2 lead systems, producing measurements with negligible bias (1.1 milliseconds for QT, 0.5 milliseconds for QRS onset, and 1.6 milliseconds for T-wave end) and SDs comparable to those of the best lead measurements (9.8 milliseconds for QT interval, 3.6 milliseconds for QRS onset, and 9.4 milliseconds for T-wave end). Moreover, stable beat-to-beat QT measurements are obtained in 99 of the 104 records. When considering all records for multilead QT measurements, the bias and SD of the differences are essentially the same (Table 1). These intersystem differences are negligible in view of the intrinsic variability of the multilead delineator observed in the CSE database.

The maximum correlation between the measurements in both lead sets was attained by the multilead measurement (r = 0.98, Table 3). Multilead QT differences were shorter than 10 milliseconds in almost 90% of the records and shorter than 20 milliseconds in all records except 1 (Figs. 4 and 5).

The adopted multilead approach offers a stable QT measurement with negligible differences between the 2 lead systems, despite the fact that it ultimately relies on single-lead measurements. A delineation approach based on the VCG loop, such as the one proposed in reference,[22] may offer measurements that are even less dependent on the selected lead system.

Limitations

In this work, the standard ECG was considered the criterion standard for automatic measurements. Because no manual annotations were available, uncertainty remains about how much of the intersystem variability should be attributed to delineator accuracy. However, because the same delineator has been validated on well-known test databases, it can be concluded that the intersystem variability, in most leads, was equal or lower than the SD of the differences with manual annotations obtained from other databases.

Conclusions

The results showed that QT measurements in EASI-derived 12-lead ECG essentially agree with measurements in standard 12-lead ECG. Although mean differences were negligible, large disagreements were found in several leads for some individual records because of differences in T-wave morphology. The agreement between both lead systems was improved, using a multilead approach for measuring QT. In conclusion, EASI-derived 12-lead ECG may be used for reliable QT measurements, adopting a multilead approach.

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