Prolonged QT Interval Diagnosis Suppression by a Widely Used Computerized ECG Analysis System

Running title: Garg et al.; “Prolonged QT” diagnosis suppression

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Abstract:

Background - Clinicians commonly rely on automated diagnostic interpretations for initial, point-of-care identification of electrocardiogram (ECG) abnormalities. Our study goal was to investigate how one widely used computerized ECG analysis system performs in labeling prolongation of heart rate (HR)-corrected QT interval (QTc), an arrhythmia risk marker.

Methods and Results - ECGs acquired in 2009-2010 from patients ≥18 years old within the University of Michigan Health System, analyzed by the Marquette™ 12SL™ ECG Analysis Program (GE Healthcare), and exhibiting sinus rhythms with HR <100 bpm and QRS duration <120 ms constituted our database. Of 97,046 study ECGs (48.2% from males), a prolonged 12SL™-calculated QTc value (i.e. ≥470 ms in females >60 years old, and ≥460 ms in other sex/age groups) was displayed in 16,235 (16.7%). Nonetheless, for only 7709 (47.5%) of these ECGs with prolonged QTc did the automated interpretation include an accompanying “Prolonged QT” diagnostic statement. Such “Prolonged QT” under-reporting was manifest across all patient environments and reflected algorithmic suppression of the diagnosis—due to ECG waveform-based criteria—in 8526 (52.5%) ECGs with prolonged QTc. Of the latter ECGs with “Prolonged QT” diagnosis suppression, the computer declared 3588 (42.1%) “Normal” despite QTc prolongation.

Conclusions - In evaluating an adult patient whose 12SL™-interpreted ECG lacks a “Prolonged QT” diagnostic statement (assuming sinus rhythm <100 bpm and QRS duration <120 ms), physicians should examine the actual QTc value displayed on the report before concluding that this parameter is normal. Assessment of the clinical impact of “Prolonged QT” diagnosis suppression by ECG waveform-based criteria is warranted.

Key words: computers; electrocardiography; long-QT syndrome; syncope; torsade de pointes
Introduction

Computerized electrocardiogram (ECG) analysis and interpretation is a staple of modern medical practice. Automated assistance particularly with regard to evaluation of the QT interval is of value to clinicians for two reasons. First, identification of a prolonged heart rate (HR)-corrected QT interval (QTc) may suggest an inherited propensity to sudden cardiac death (i.e., congenital long QT syndrome, a diagnosis of particular concern in patients presenting with syncope); or it may bring to light an increased susceptibility to development of life-threatening torsade de pointes ventricular tachycardia in patients being considered for treatment with a known QT-prolonging drug. Secondly, whereas manual measurement of QT intervals is a fairly challenging technical task for primary care providers, emergency department physicians, psychiatrists, and even cardiologists who are not arrhythmia specialists, computerized QT interval quantitation is highly reproducible and correlates very well with expert human measurements.

In addition to reporting QT interval measurements and corresponding QTc values, ECG analysis software can generate a diagnostic statement notifying the physician that a given QTc is prolonged. In a study of a single congenital long QT syndrome family, however, it was found that a widely utilized automated ECG interpretation system—the GE 12SL™ program—did not always output a “Prolonged QT” diagnostic statement when, in fact, the ECG report displayed a prolonged QTc value (with normal QRS duration). This discordance between QTc prolongation and diagnostic interpretation was shown to reflect deliberate application of certain algorithmic criteria within the 12SL™ software, resulting in suppression of the “Prolonged QT” diagnosis (as detailed below).

It would be important to determine the extent to which automated censoring of a
“Prolonged QT” diagnosis occurs in large scale clinical implementations of the 12SL™ program, given the potential for absence of a program-generated “Prolonged QT” diagnostic statement to divert physicians from recognizing a prolonged QTc value on the computer report, particularly at the point of care. Our health care system provided a suitable testing ground for such an investigation.

Methods

MUSE® ECG Database

Via portable carts, 12-lead ECGs were acquired and then processed by the Marquette™ 12SL™ ECG Analysis Program (GE Healthcare). A hard copy display of the resultant 12-lead ECG waveforms—accompanied by automated interval measurements, including QT/QTc, and computer-generated diagnostic interpretations—was printed out at the point of care and then uploaded, in digital form, to the MUSE® Cardiology Information System (GE Healthcare). This electronic database of 12-lead ECGs also stores patient demographics, clinical setting of ECG acquisition, and the original, computer-generated interval measurements and diagnostic interpretations as well as those revised by a cardiologist within 1-2 days after ECG acquisition.

Data Collection and Exclusion Criteria

We queried the MUSE® electronic database to extract data files containing the demographics, automated interval measurements and computer-generated diagnostic interpretations (but not original waveform data) corresponding to ECGs recorded from adult patients (≥18 years old) with sinus rhythms acquired within the University of Michigan Health System over calendar years 2009 and 2010. Data extraction from the MUSE® System was accomplished through a software interface kindly donated by GE Healthcare. For the purposes of our study we excluded
ECGs with QRS duration $\geq 120$ ms or computer diagnoses of atrial or ventricular pacing, non-sinus arrhythmias, $2^{\text{nd}}$ or $3^{\text{rd}}$ degree AV block, Wolff-Parkinson-White pattern or artifact. We further confined our study to ECGs with HR $<100$ bpm, in light of the well-known tendency of the Bazett formula\textsuperscript{13} to yield inflated QTc values at higher HRs.\textsuperscript{14,15} ECGs with computer interpretation using version 18, or earlier, of the 12SL™ ECG Analysis Program were also excluded, confining our study to more recent updates of the QT analysis algorithm (i.e., versions 19, 20, and 21).

This study was approved by the Institutional Review Board of the University of Michigan Health System, which determined that informed consent was not applicable to data collected from the MUSE® electronic database.

\textbf{12SL™ Algorithm\textsuperscript{12} for Diagnosing “Prolonged QT”}

QTc is calculated using the Bazett Formula.\textsuperscript{13} For all ECGs with QRS duration $<120$ ms (and HR $<100$ bpm, per our study protocol), the 12SL™ program defines QTc prolongation as: $\geq 460$ ms for males, $\geq 460$ ms for females $\leq 60$ years old, and $\geq 470$ ms for females $>60$ years old. (Except for females $\leq 60$ years old, these QTc cutoffs are higher than the 450 ms and 460 ms values in men and women, respectively, recommended in a 2009 Scientific Statement from three official cardiology organizations.\textsuperscript{16}) If QTc is prolonged, the 12SL™ software then applies ECG waveform-based criteria to the lowest and intermediate of three program-specified ranges of QTc prolongation, to determine whether a “Prolonged QT” diagnostic statement is actually reported or suppressed as part of the automated interpretation (Figure 1): For males of all ages and females $\leq 60$ years old, when QTc is between 460 and 479 ms (lowest range of prolongation), the algorithm requires satisfaction of program-defined criteria for non-specific T wave abnormality\textsuperscript{12} to report a diagnosis of “Prolonged QT”; when QTc is between 480 and 499 ms
(intermediate range of prolongation), the algorithm requires non-satisfaction of program-defined criteria for non-specific T wave abnormality and myocardial ischemia/infarction\textsuperscript{12} to report a diagnosis of “Prolonged QT.” (For females >60 years old, the above-listed cutpoints for ranges of QTc prolongation are shifted to values 10 ms longer.) However, when QTc is $\geq$500 ms (highest range of QTc prolongation; $\geq$510 ms for females >60 years old), “Prolonged QT” is reported independent of any ECG waveform characteristics (i.e., no diagnosis suppression occurs).

Data Analysis

Our analyses of data extracted from the MUSE® ECG database were performed using a customized computer program in Visual C++ written by one of us (AG).

Identifying “Prolonged QT” Diagnosis Suppression and Its Cause: The diagnostic statements of all study ECGs with a prolonged QTc value (defined above, per the 12SL™ program) were analyzed to determine if a “Prolonged QT” interpretation was lacking—in which case the “Prolonged QT” diagnosis was deemed to be suppressed by the 12SL™ algorithm. As dictated by the algorithm (Figure 1) and our study exclusion criteria, whenever “Prolonged QT” diagnosis suppression in our study occurred in the lowest QTc prolongation range, the reason was always attributable to lack of a 12SL™-defined nonspecific T wave abnormality; and whenever “Prolonged QT” diagnosis suppression in our study occurred in the intermediate range of QTc prolongation, the reason was always attributable to presence of either a program-identified nonspecific T wave abnormality or 12SL™-determined ECG stigmata of “ischemia” or “infarction.” This reasoning follows from the fact that our exclusion criteria, particularly by restricting study ECGs to those with HR <100 bpm and QRS duration less than 120 ms,
eliminated any other possible algorithmic basis for the 12SL program to ignore a prolonged QTc.\textsuperscript{12}

\textit{Main Analyses:} We analyzed reporting vs. suppression of the “Prolonged QT” diagnosis by the 12SL\textsuperscript{TM} software—for all ECGs; by sex/age groups; and by clinical setting of ECG acquisition. Clinical setting was classified into four categories: emergency department (ED), inpatient setting, outpatient setting, and unknown (missing data or procedural setting which defied simple inpatient/outpatient categorization).

\textit{Subanalysis Using Higher Threshold for QTc Prolongation:} An additional analysis was undertaken utilizing higher cutoffs for QTc prolongation (>470 ms for men and >480 ms for women, with QTc values >500 ms considered markedly prolonged), as specified in a 2010 American Heart Association/American College of Cardiology Foundation (AHA/ACCF) Scientific Statement.\textsuperscript{6} Although that report pertained exclusively to hospitalized patients, ECGs in this subanalysis were not limited to any one clinical setting. The diagnostic statements of all study ECGs with a prolonged QTc value, as now defined per the AHA/ACCF Scientific Statement, were analyzed to determine if a “Prolonged QT” interpretation was lacking—in which case the “Prolonged QT” diagnosis was deemed to be suppressed by the 12SL\textsuperscript{TM} algorithm. It should be noted that assessment of reporting vs. suppression of the “Prolonged QT” diagnosis by the 12SL\textsuperscript{TM} algorithm in this subanalysis utilized the already-extracted data files from the MUSE\textsuperscript{®} system, i.e., without any reapplication of the algorithm.

\textbf{Statistical Considerations}

We did not perform statistical testing of differences in proportions because the extremely large study sample size would yield very narrow 95% confidence intervals and, consequently, “statistically significant” differences in point estimates.
Results

Characteristics of Study ECGs

A total of 180,129 ECGs were acquired within the University of Michigan Health System from patients ≥18 years of age during the calendar years 2009 and 2010. After application of our inclusion and exclusion criteria (unrelated to HR), there remained 114,181 ECGs. We then excluded from these 114,181 the following additional ECGs: 13,422 (11.8%) due to HR ≥100 bpm, 764 (0.7%) due to missing data (unknown patient sex, or inaccessible original computer-generated diagnostic interpretations), and 2949 (2.7%) due to analysis by outdated versions of the 12SL™ ECG Analysis Program. The characteristics of the remaining 97,046 ECGs which comprised the basis of this study are presented in Table 1. The majority of ECGs were from females (51.8%), and most ECGs in each sex/age group were from Caucasian patients. There was an average of approximately 1.6–1.8 ECGs per patient amongst the three sex/age groups. About 44% of all study ECGs were acquired in the outpatient setting, with the remainder split mostly between the inpatient setting and the ED (Figure 2, left pie chart). Of the ECGs with 12SL™-defined prolonged QTc values and known location of acquisition, most were acquired in the inpatient setting and fewest in the outpatient setting (Figure 2, right pie chart).

Suppression of “Prolonged QT” Diagnostic Statement

Analysis for all ECGs and by sex/age groups: The 12SL™ software calculated and displayed a prolonged QTc value in 16,235 (16.7%) ECGs: 7236 (15.5%) of 46,811 ECGs in men, 6264 (20.3%) of 30,850 ECGs in women ≤60 years of age, and 2735 (14.1%) of 19,385 ECGs in women >60 years of age (Table 1). Yet, in only 47.5% of the total 16,235 ECGs with QTc prolongation did a “Prolonged QT” interpretation actually appear among the 12SL™ generated diagnostic statements. Of the remaining 8526 ECGs with QTc prolongation, the “Prolonged
QT” diagnosis was suppressed—a phenomenon occurring more often in the lowest vs. intermediate range of QTc prolongation (Table 2; examples shown in online-only Data Supplement, Figures I and II). Specifically, “Prolonged QT” diagnosis suppression was observed in 71-78% of ECGs within the lowest range of QTc prolongation for all three sex/age groups (Figure 3), dropping to 16-29% for ECGs within the intermediate range of QTc prolongation (highest for women > age 60, Figure 3). Consistent with the 12SL™ algorithm, there was essentially 100% reporting (i.e., virtually no suppression) of the “Prolonged QT” diagnosis for ECGs within the highest range of QTc prolongation (Table 2; Figure 3). Of the total 8526 ECGs with suppression of the “Prolonged QT” diagnosis, 3588 (42.1%) lacked other abnormalities and were labeled “Normal ECG” despite QTc prolongation.

Analysis by clinical setting of ECG acquisition: ECGs with unknown clinical setting of acquisition represented 6% of ECGs (Figure 2) and were excluded from this analysis to simplify data presentation. The 12SL™ software calculated and displayed a prolonged QTc value in 4760 (17.9%) of 26,600 ECGs acquired in the ED, 6507 (29.4%) of 22,147 ECGs acquired in the inpatient setting, and 3928 (9.1%) of 42,943 ECGs acquired in the outpatient setting. Among these ECGs with QTc prolongation, suppression of the “Prolonged QT” diagnosis was observed in more than 2/5 of inpatient tracings and more than 3/5 of outpatient tracings, with an intermediate fraction for ECGs from the ED (Table 3; left pie charts of Figure III in online-only Data Supplement). The proportion of ECGs labeled “Normal” despite QTc prolongation also varied by clinical setting (right-sided pie charts of Figure III in online-only Data Supplement).

Analysis based on AHA/ACCF Guidelines for QTc prolongation: A recent AHA/ACCF Scientific Statement6 recommends using 99th percentile QTc cutoffs of >470 ms for males and >480 ms for females to define QTc prolongation, with a QTc value >500 ms considered highly
abnormal for both sexes. Even with use of these higher QTc cutoffs, approximately 36% of
ECGs of male patients and 22% of ECGs of female patients with QTc prolongation had
“Prolonged QT” diagnosis suppression due to ECG waveform-based criteria (Table 4). Of note,
as a result of the 10 ms upward shift in 12SL™-based cutoffs for QTc prolongation in females
>60 years old, 63 of 1301 (4.8%) ECGs of all females with QTc >500 ms had “Prolonged QT”
diagnosis suppression. Furthermore, of the 1576 ECGs in male patients and 802 ECGs in female
patients with suppression of a “Prolonged QT” diagnosis, 410 (26.0%) and 144 (18.0%),
respectively, were labeled “Normal ECG” despite QTc prolongation per the AHA/ACCF cutoff
values.

Discussion
The 12SL™ automated ECG analysis program is a widely utilized and helpful clinical decision
support system,1, 17-21 but its performance in rendering a “Prolonged QT” diagnosis has not been
systematically evaluated. We observed that, of over 16,000 study ECGs for which the 12SL™
software calculated and displayed prolonged QTc values (≥470 ms in females >60 years old; or
≥460 ms in other sex/age groups), a “Prolonged QT” diagnostic statement actually appeared on
the computer-generated report in only 48% of these tracings—being algorithmically censored in
the remaining 52% on the basis of certain ECG waveform characteristics (proportionally a more
common occurrence in outpatient and ED settings; left pie charts of Figure III in online-only
Data Supplement). In turn, 42% of these ECGs with suppression of the “Prolonged QT”
diagnosis received a final automated interpretation of “Normal ECG” despite QTc prolongation.
A sub-analysis limited to ECGs with QTc exceeding higher cutoff values (470 ms in men and
480 ms in women, per AHA/ACCF recommendations6), showed that the ECG waveform-based
criteria still led to suppression of a “Prolonged QT” diagnosis in over 1/3 and 1/5 of ECGs,
respectively, from men and women with prolonged QTc values (according to the higher thresholds).

Our findings raise a concern that when clinical pathways rely on an automated ECG report to help guide further cardiologic assessment, such as recently recommended for the evaluation of syncope, a prolonged QTc value might not always be clinically recognized with use of the 12SL™ software. More generally, there is a realistic possibility that time-pressed physicians at the point of care viewing a 12SL™-generated ECG report which suppresses a “Prolonged QT” diagnosis could be influenced to conclude that the computer-calculated QTc is not prolonged—especially when the automated interpretation reads “Normal ECG.” A cognitive mechanism capable of contributing to such an oversight is automation bias, whereby questioning the veracity of computer output (in this case, 12SL™ diagnostic statements) is suspended, as documented in multiple settings of computer-aided decision-making including the ECG realm. When a “Prolonged QT” diagnosis is suppressed, non-recognition of the prolonged QTc value also could be fostered by physicians’ learned (negative) expectations from experience with computerized ECG analysis of PR and QRS intervals—namely, rarity of the need to review displayed values of these parameters when the automated interpretation does not include diagnostic statements (explicitly or implicitly) indicating their prolongation.

Algorithmic suppression of a “Prolonged QT” diagnosis by the 12SL™’s ECG waveform-based criteria—a feature of the software that has received relatively scant attention in the literature—is difficult to reconcile with current cardiologic knowledge and practice. For the lowest 12SL™-specified range of QTc prolongation, the criteria require concomitant presence of nonspecific T wave abnormalities to permit reporting of a “Prolonged QT” diagnosis (Figure 1). In contrast, the contemporary approach to defining QTc prolongation is simply in
reference to a certain cutoff value, i.e., independent of attendant T waveform features.\cite{4,6,16,28}

Exemplifying the soundness of this approach is the LQT1 genotypic variant of congenital long QT syndrome in which basically normal-appearing T wave morphology is nearly universally manifest (in affected individuals >5 years old) at all levels of QTc prolongation.\cite{29,30} For the intermediate 12SL™-specified range of QTc prolongation, suppression of a “Prolonged QT” diagnosis occurs if there are accompanying ECG waveform features of non-specific T wave abnormality, ischemia, or infarction (Figure 1). Yet, even in the setting of these cardiac pathologies, it is known that QTc prolongation may augur the occurrence of torsade de pointes.\cite{31-33}

Furthermore, when considering use of drugs with expected and potentially marked QT-prolonging effects, baseline QTc prolongation is a contraindication regardless of the presence or absence of prior myocardial infarction.\cite{34,36}

Particularly problematic is application of the waveform-based criteria to ECGs within the 12SL™-specified intermediate range of QTc prolongation for females ≥ age 60 (QTc between 490 and 509 ms), which led to suppression of a “Prolonged QT” diagnosis in nearly 5% of total study ECGs from women exhibiting QTc >500 ms. Such diagnostic censoring is at odds with the consensus warning of current clinical guidelines regarding the increased risk of torsade de pointes conferred by prolonged QTc values of this magnitude.\cite{2,6,37-39}

The ECG waveform-based criteria for “Prolonged QT” diagnosis suppression, utilized in versions of the 12SL™ software going back at least to 1996,\cite{11} presumably represent an attempt to reduce the number of false positive cases of 12SL™-identified QTc prolongation. Such false positives are likely to be, at least in part, sequelae of the 12SL™ program’s technique of measuring the absolute QT interval “globally” (i.e., over the 12 superimposed ECG leads)\cite{40} in contrast to the clinically utilized individual-lead QT measurement method (typically relying on
lead II or V5). The QT interval determined by the former technique exceeds that measured by the latter method by a mean difference of ~8 to 17 ms, yielding relatively inflated QTc values (false positives likely included among them). Devising an automated “Prolonged QT” diagnosis algorithm that takes into account such technical issues and balances the dual goals of minimizing overdiagnosis of QTc prolongation, while striving not to miss true positives, is certainly challenging and ultimately may require guidance from official cardiology organizations.

Limitations

By design, our study relied on 12SL™-determined (rather than manually measured) QT/QTc intervals because those are the ECG repolarization parameters—with associated automated diagnostic statements—most immediately available to point-of-care physicians using the computerized system. In ECGs with minimal noise contamination, global QT interval measurements by the current era 12SL™ program actually agree closely with manually measured global QT intervals. However, given that the globally-based values are somewhat inflated relative to individual-lead QT measurements (as explained above), the observed prevalences of 12SL™-defined QTc prolongation in our ECG database (e.g., 16.7% overall, and 9.1% among outpatient tracings) likely would have been lower had the QT intervals been measured manually in an individual lead. While, in turn, the prevalence of “Prolonged QT” diagnosis suppression would have been altered, and possibly reduced, we believe (based on the sizable magnitudes observed in our analysis) the extent of diagnostic censoring likely would have remained substantial.

It should be noted that the present study was not designed to analyze physician responses or clinical outcomes related to 12SL™-generated ECG interpretations. Thus, we were not able to assess either extent of physician under-recognition of prolonged QTc values or possible adverse
Clinical impact, if any, resulting from algorithmic suppression of a “Prolonged QT” diagnosis. Further investigations will be needed to address these relevant issues.

While our study was confined to versions 19, 20, and 21 of the 12SL™ ECG Analysis Program, a more recent software update (version 22), still being implemented, continues to rely on the previously-utilized ECG waveform-based criteria for “Prolonged QT” diagnosis reporting and suppression. However, the newer version additionally offers an option of automated notification of user-defined critical QTc values (generating a “*** Critical Test Result: Long QTc” statement when QTc ≥ a specified threshold). With a user-defined threshold set to 500 ms, this feature could be used to, in effect, override the occasional suppression of a “Prolonged QT” diagnosis that we documented in patients with QTc >500 ms; but diagnosis suppression for lesser degrees of QTc prolongation would not be affected.

We chose to confine our study to ECGs with HR <100 bpm due to the well-known tendency of the Bazett formula to inflate QTc values at elevated HRs, and, under the latter circumstances, one can make a case for considering all (or most) prolonged QTc values as false positives, depending on the magnitude of HR. The algorithmic approach of the 12SL™ ECG Analysis Program to prolonged QTc values at elevated HRs reflects this idea and remains in evolution: previous and recent program versions (as in our study) suppress a “Prolonged QT” diagnosis at HR ≥100 bpm while the latest update (version 22) utilizes HR ≥120 bpm. Further investigation is necessary to define the proper role of algorithmic suppression of a “Prolonged QT” diagnosis due to elevated HRs.

Conclusion

When adult patient evaluation includes use of the 12SL™ automated ECG interpretation system, absence of a “Prolonged QT” diagnostic statement (assuming sinus rhythm <100 bpm with QRS
duration <120 ms) must be corroborated by examination of the actual QTc value displayed on the computer report to determine whether or not this parameter is indeed normal. It is important to emphasize, however, that for patients in whom QTc quantitation is critical to clinical decision-making beyond point-of-care ECG screening (e.g., when considering a formal diagnosis of congenital long QT syndrome or seeking to ascertain drug-induced QT prolongation), the QTc value should be calculated from a manually measured QT interval—regardless of the particular computerized ECG software a health care facility utilizes.1,4,16,28,46

**Conflict of Interest Disclosures:** The authors have no conflicts of interest. The only relationship the authors have with industry is that GE Healthcare donated a software interface to facilitate extraction of ECG-related data from the MUSE® System at the University of Michigan, for analysis in the study (as noted in Methods section of the paper).

**References:**


Table 1. Characteristics of study ECGs by sex/age group

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Males</th>
<th>Females ≤ 60 y.o.</th>
<th>Females &gt; 60 y.o.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of ECGs</td>
<td>46811</td>
<td>30850</td>
<td>19385</td>
</tr>
<tr>
<td>Age, years</td>
<td>54.6 ± 14.5</td>
<td>45.1 ± 11.3</td>
<td>71.3 ± 8.0</td>
</tr>
<tr>
<td>HR, bpm</td>
<td>70.5 ± 13.4</td>
<td>73.2 ± 12.6</td>
<td>71.1 ± 12.4</td>
</tr>
<tr>
<td>QRS duration, ms</td>
<td>93.2 ± 10.2</td>
<td>85.7 ± 9.2</td>
<td>86.0 ± 10.5</td>
</tr>
<tr>
<td>QTc, ms</td>
<td>430.7 ± 30.8</td>
<td>439.0 ± 28.6</td>
<td>440.5 ± 30.0</td>
</tr>
<tr>
<td>QTc prolongation*</td>
<td>7236 (15.5%)</td>
<td>6264 (20.3%)</td>
<td>2735 (14.1%)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>25356 (54.2%)</td>
<td>15083 (48.9%)</td>
<td>11267 (58.1%)</td>
</tr>
<tr>
<td>Black</td>
<td>4543 (9.7%)</td>
<td>4990 (16.2%)</td>
<td>1826 (9.4%)</td>
</tr>
<tr>
<td>Other†</td>
<td>1635 (3.5%)</td>
<td>1286 (4.2%)</td>
<td>459 (2.4%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>15277 (32.6%)</td>
<td>9491 (30.8%)</td>
<td>5833 (30.1%)</td>
</tr>
<tr>
<td>Location ECG Acquired</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emergency Dept.</td>
<td>11489 (24.5%)</td>
<td>10384 (33.7%)</td>
<td>4727 (24.4%)</td>
</tr>
<tr>
<td>Inpatient</td>
<td>11345 (24.2%)</td>
<td>5928 (19.2%)</td>
<td>4874 (25.1%)</td>
</tr>
<tr>
<td>Outpatient</td>
<td>20908 (44.7%)</td>
<td>13331 (43.2%)</td>
<td>8704 (44.9%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>3069 (6.6%)</td>
<td>1207 (3.9%)</td>
<td>1080 (5.6%)</td>
</tr>
</tbody>
</table>

Age, HR (heart rate), QRS duration, and QTc are means ± standard deviation
* Defined here (and in Tables 2 and 3) as QTc ≥470 ms in females >60 years old, and ≥460 ms in other sex/age groups, per the 12SL™ program
† Defined as Asian, Hispanic, or Indian
Table 2. Suppression of “Prolonged QT” diagnosis by the 12SL™ software for ECGs with program-defined ranges of QTc prolongation

<table>
<thead>
<tr>
<th>“Prolonged QT” Diagnosis</th>
<th>460* ms ≤ QTc &lt; 480* ms</th>
<th>480* ms ≤ QTc &lt; 500* ms</th>
<th>QTc ≥ 500* ms</th>
<th>Total ECGs with QTc ↑</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suppressed</td>
<td>7692 (75.3%)</td>
<td>832 (21.8%)</td>
<td>2 (0.1%)</td>
<td>8526 (52.5%)</td>
</tr>
<tr>
<td>Reported</td>
<td>2520 (24.7%)</td>
<td>2982 (78.2%)</td>
<td>2207 (99.9%)</td>
<td>7709 (47.5%)</td>
</tr>
</tbody>
</table>

Each column includes aggregate total of ECGs from males, females ≤ 60 years old, and females > 60 years old.

* All QTc cutpoints shifted to values 10 ms longer in females > 60 years old, per 12SL™ program.

QTc ↑ = QTc prolongation.

Table 3. Suppression of “Prolonged QT” diagnosis by the 12SL™ software for ECGs with prolonged QTc by clinical setting of ECG acquisition

<table>
<thead>
<tr>
<th>“Prolonged QT” Diagnosis</th>
<th>Emergency Department</th>
<th>Inpatient Setting</th>
<th>Outpatient Setting</th>
<th>Total ECGs with QTc ↑</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suppressed</td>
<td>2668 (56.1%)</td>
<td>2896 (44.5%)</td>
<td>2397 (61.0%)</td>
<td>7961 (52.4%)</td>
</tr>
<tr>
<td>Reported</td>
<td>2092 (43.9%)</td>
<td>3611 (55.5%)</td>
<td>1531 (39.0%)</td>
<td>7234 (47.6%)</td>
</tr>
</tbody>
</table>

ECGs with unknown clinical setting of acquisition excluded from analysis for simplification of data presentation.

QTc ↑ = QTc prolongation.

Table 4. Suppression of “Prolonged QT” diagnosis by the 12SL™ software for ECGs with QTc prolongation defined by AHA/ACCF recommended cutoffs.

<table>
<thead>
<tr>
<th>“Prolonged QT” Diagnosis by Sex</th>
<th>(470 or 480)* ms ≤ QTc ≤ 500 ms</th>
<th>QTc &gt; 500 ms</th>
<th>Total ECGs with QTc ↑</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suppressed</td>
<td>1576 (46.8%)</td>
<td>0 (0.0%)</td>
<td>1576 (36.1%)</td>
</tr>
<tr>
<td>Reported</td>
<td>1794 (53.2%)</td>
<td>997 (100.0%)</td>
<td>2791 (63.9%)</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suppressed</td>
<td>739 (30.8%)</td>
<td>63 (4.8%)</td>
<td>802 (21.7%)</td>
</tr>
<tr>
<td>Reported</td>
<td>1659 (69.2%)</td>
<td>1238 (95.2%)</td>
<td>2897 (78.3%)</td>
</tr>
</tbody>
</table>

*470 ms for ECGs of male patients; 480 ms for ECGs of female patients.

QTc ↑ = QTc prolongation.
Figure Legends:

Figure 1. Algorithmic schema for automated diagnosis of “Prolonged QT” by 12SL™ Software.12 For ECGs displaying program-defined QTc prolongation (and QRS duration <120 ms), in the setting of heart rate (HR) <100 bpm, reporting versus suppression of a “Prolonged QT” diagnostic statement by the 12SL™ software is determined by application of ECG waveform-based criteria to the lower two of three program-defined ranges of QTc prolongation (termed “lowest,” “intermediate” and “highest,” respectively, in the text). NST = nonspecific T wave; Abn = abnormality.

Figure 2. Distribution of ECGs by clinical setting of acquisition. Left pie chart, for all ECGs; Right pie chart, for ECGs exhibiting QTc prolongation (percentages total 99% due to rounding).

Figure 3. Suppression of “Prolonged QT” diagnosis by the 12SL™ software for ECGs with prolonged QTc values by sex/age group. Extent of algorithmic suppression of the “Prolonged QT” diagnosis varied over the three program-defined ranges of QTc prolongation (with QTc values in ms). Per the 12SL™ program, all QTc cutoffs shifted to values 10 ms longer in females >60 years old.
[Given HR < 100 bpm]

\[ \text{QTc}^* \geq 460 \text{ ms} \]
AND
\[ \text{QRS} < 120 \text{ ms} \]

*QTc cutpoints shifted 10 ms longer in females > 60 y.o.

- **QTc**: 460 – 479 ms
  - Yes → NST Abn? No → Report "Prolonged QT"
  - Yes → Lack of NST Abn, ischemia, and infarction?
    - No → Report "Prolonged QT"
    - Yes → Suppress "Prolonged QT"

- **QTc**: 480 – 499 ms
  - Yes → NST Abn? No → Report "Prolonged QT"
  - Yes → Lack of NST Abn, ischemia, and infarction?
    - No → Report "Prolonged QT"
    - Yes → Suppress "Prolonged QT"

- **QTc**: ≥ 500 ms
  - Yes → NST Abn? No → Report "Prolonged QT"
  - Yes → Lack of NST Abn, ischemia, and infarction?
    - No → Report "Prolonged QT"
    - Yes → Suppress "Prolonged QT"
ECGs of Male Patients

ECGs of Female Patients ≤ 60 y.o.

ECGs of Female Patients > 60 y.o.

“Prolonged QT” Reported

“Prolonged QT” Suppressed
Prolonged QT Interval Diagnosis Suppression by a Widely Used Computerized ECG Analysis System
Anubhav Garg and Michael H. Lehmann

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Supplemental Material

(Figures I-III with legends)
Figure I. Reporting vs. suppression of “Prolonged QT” diagnostic statement, by the 12SL™ program, for lowest range of QTc prolongation. Computer-generated ECG parameters (QT/QTc values bolded) and interpretations are shown at the top of each panel, overlying the corresponding 12-lead ECG image (reduced size), with all patient identifiers and extraneous text omitted, except for age (y.o. = years old) and sex. The “Prolonged QT” diagnosis (shown in bold) is reported in Panel A, but suppressed—despite longer QTc values—in Panel B and Panel C (female, age > 60 years), due to ECG waveform-based criteria of the 12SL™ algorithm (see Methods).
<table>
<thead>
<tr>
<th>Panel</th>
<th>Patient Age</th>
<th>Gender</th>
<th>Vent. rate</th>
<th>PR interval</th>
<th>QRS duration</th>
<th>QT/QTc</th>
<th>P-R-T axes</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>75 y.o.</td>
<td>Male</td>
<td>72 BPM</td>
<td>152 ms</td>
<td>84 ms</td>
<td>440/481 ms</td>
<td>35 -3 119</td>
<td>Normal sinus rhythm, Prolonged QT, Abnormal ECG</td>
</tr>
<tr>
<td>B</td>
<td>46 y.o.</td>
<td>Male</td>
<td>64 BPM</td>
<td>154 ms</td>
<td>88 ms</td>
<td>484/499 ms</td>
<td>48 10 159</td>
<td>Normal sinus rhythm, Septal infarct, age undetermined, ST &amp; Marked T wave abnormality, consider anterolateral ischemia</td>
</tr>
<tr>
<td>C</td>
<td>74 y.o.</td>
<td>Female</td>
<td>62 BPM</td>
<td>158 ms</td>
<td>92 ms</td>
<td>502/509 ms</td>
<td>49 -40 -3</td>
<td>Normal sinus rhythm, Left axis deviation, Moderate voltage criteria for LVH, may be normal variant, Cannot rule out Septal infarct, age undetermined</td>
</tr>
</tbody>
</table>

Figure II. Reporting vs. suppression of “Prolonged QT” diagnostic statement, by the 12SL™ program, for intermediate range of QTc prolongation. Same format as Figure I. The “Prolonged QT” diagnosis (shown in bold) is reported in Panel A, but suppressed—despite longer QTc values—in Panel B and Panel C (female, age > 60 years), due to ECG waveform-based criteria of the 12SL™ algorithm (see Methods).
Figure III. Suppression of “Prolonged QT” diagnosis by the 12SL™ software for ECGs with prolonged QTc values by clinical environment. ECGs with unknown clinical setting of acquisition excluded from analysis. Fraction of tracings with algorithmic suppression of the “Prolonged QT” diagnosis in left-sided pie charts is broken down in right-sided pie charts into those labeled by the 12SL™ program as “Normal” vs. those labeled “Abnormal” (includes “Borderline”) ECG.