Impact of QTc formulae in the prevalence of short corrected QT interval and impact on probability of Short QT Syndrome.

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Short Title: QTc formula and SQTS

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Objective: To assess the prevalence of short corrected QT (QTc) intervals and its impact on short QT syndrome (SQTS) diagnosis using different QT correction formulae.

Methods: Observational study. The prevalence of short QTc intervals was estimated using 4 different QT correction formulae in 14,662 young adults from the "Sudden Cardiac Death Screening of Risk FactOrS" (SCD-SOS) cohort. Then, using data from this cohort and the pooled-cohort analysed by Gollob and colleagues, comprising 61 patients with SQTS, we assessed the impact of the different QTc correction formulae on SQTS-probability and diagnosis based on the Expert Consensus recommendations (QTc ≤330 ms or QTc 330-360ms + 1 additional risk feature).

Results: The prevalence of individuals with a QTc≤330ms and ≤320ms in the SCD-SOS cohort was extremely low (≤0.07% and ≤0.02%, respectively), and these were more frequently identified by the Framingham correction. The different QTc correction formulae led to a shift in SQTS-probability in 5-10% of individuals in both the SCD-SOS and Gollob cohort). Intermediate-probability Individuals were rare (<0.1%), and no high-SQTS probability individuals were identified in the SCD-SOS cohort. Based on Consensus criteria, instead of 12(0.08%) individuals being diagnosed with SQTS using the *Bazett* equation, a different number of individuals would meet diagnostic criteria with the other formulae: 11(0.08%) using *Fridericia*, 9(0.06%) with *Hodges*, and 16(0.11%) using the *Frammingham* equation.

Conclusion: Prevalence of SQTS in the apparently healthy adult population is low. Applying different QTc correction formulae leads to significant reclassification of SQTS-probability and their impact on predicting outcomes should be assessed.

Key-words: arrhythmia; channelopathies; sudden cardiac death; ion channel; prevention.

Key Messages

What is already known about this subject?

- Short QT syndrome (SQTS) is a recently described channelopathy with low prevalence. QT correction (QTc) for means of diagnosis is usually performed using the Bazett formula.

What does this study add?

- This study shows that the prevalence of individuals at risk of SQTS based on a set of criteria defined by *Gollob* and colleagues, and that the number of individuals meeting Expert Consensus Diagnosis Criteria for SQTS may be underestimated if we use Bazett correction.

How might this impact on clinical practice?

- This study may raise the awareness of physicians to this rare channelopathy, and its diagnosis and probability criteria, possibly increasing the number of diagnoses.
- This study suggests that different correction formulae, or an ECG performed while at 60bpm, may need to be considered if level of suspicion of SQTS is high and QTc interval is borderline and close to the diagnostic cut-off.

Abbreviations

SQTS – Short QT syndrome; QTc – corrected QT interval; SCD-SOS – Sudden Cardiac Death Screening Of risk factorS.

Background

Short QT syndrome (SQTS) is a recently described channelopathy presenting with a short corrected QT interval (QTc), and risk of atrial and ventricular fibrillation[1].

The prevalence of short QTc interval in the young adult population is low, and estimated to be 0.1 to 15.8%[2] depending on the utilized cut-offs[3-6].

Expert Consensus recommendations for diagnosis have been recently proposed[4]. *Gollob* and colleagues established criteria for SQTS probability based on ECG, clinical, and genetic data[7]. QTc obtained using *Bazett's* correction is the cornerstone of the Gollob's classification, and Expert Consensus recommendations. However, the *Bazett* correction formula is prone to inaccuracy[6, 8]. The American 2009 ECG interpretation recommendations[6] discourage its use, suggesting linear regression functions instead[9, 10].

We aimed to: (1) clarify the prevalence of short QT intervals, and individuals with and at risk of SQTS in a young adult cohort; (2) assess the impact of different QTc correction methods in the estimated probability of SQTS in low and high risk individuals.

Methods

Setting

From February 2012 to May 2013, 15,351 subjects had a 12-lead electrocardiogram performed as part of the *"Sudden Cardiac Death Screening of Risk FactOrS"* (SCD-SOS) survey (NCT01845909). In brief, SCD-SOS screened for potential channelopathies and cardiomyopathies in the young adult population (aged≤40 years) of the central region of Portugal. The survey included a 12-lead

electrocardiogram and, for patients willing to provide more information about their personal medical and family history, and symptoms, a digital-based questionnaire was completed.

Subjects were students, athletes, or young professionals, and were included in the study after providing informed consent.

12-lead ECG

A 12-lead ECG was performed in supine position using a *Mortara ELI 10 Portable Resting ECG* machine (*Mortara Instrument©, Milwaukee, WI*) with a paper speed of 25mm/s and amplification of 0.1mV/mm. The QT interval was measured using the recorder's automatic measurement software (VERITAS[TM] ECG algorithm, *Mortara Instrument ©, Milwaukee, WI*), and then, all subjects with a QTc ≤350ms (using Fridericia's correction, which was preset in the device) were manually revised and independently confirmed by 2 investigators (NK and NS), and in cases of discordance between this investigator and the algorithm, a third investigator (RP) intervened and settled any dispute. The QT interval with better definition in the precordial leads (measurement of biphasic, flat T waves or prominent QT-U complexes was avoided whenever possible) was manually measured by the tangent method[11]. For all ECGs with a QTc between 350 and 370ms, QT was measured by the VERITAS[TM] ECG algorithm. Cut-offs from different recommendations were used for defining short QTc intervals: ≤320ms[3], ≤330ms and <360ms[4].

QTc correction was performed using the 4 previously published formulae:

Bazett[12] $QTc=QT/RR^{1/2}$

Fridericia[13] QTc=QT/RR$^{1/3}$

Framingham[9] QTc=QT+0.154 (1−RR)

Hodges[10] QTc=QT+0.00175 ([60/RR]−60)

SCD-SOS Survey

Clinical information, including past medical and family history, was collected using the SCD-SOS V2.0 questionnaire (Supplementary Material) in digital format using laptops. This was a 7-question questionnaire filled mostly by ticking among different options, or providing written clarification in boxes, and was previously tested[14], with some changes having been introduced in order to refine its performance/provide clearer answers.

Gollob's Classification for SQTS(Table 1)

Using data from the pooled analysis published by *Gollob* and colleagues [7], we estimated the QTc interval using the four previously mentioned formulae, and the corresponding *Gollob* score (Table 1). The overall migration of patients between classes (low, intermediate, and high probability) with the different QTc formulae was assessed.

2013 Expert Consensus Recommendations

Based on the 2013 Expert Consensus, *"SQTS can be diagnosed in the presence of QTc ≤330 ms"*, or *"SQTS can be diagnosed in the presence of a QTc <360 ms and one*

more of the following: a pathogenic mutation, family history of SQTS, family history of sudden death at age ≤40, survival of a ventricular tachycardia/ventricular fibrillation episode in the absence of heart disease"[4]. We looked for individuals in the young adult population (SCD-SOS cohort) who could fulfil those criteria.

Gollob'cohort – Patients diagnosed with SQTS

Using data provided by *Gollob* and colleagues on 61 patients with SQTS [7] (namely QT measurements, and heart rate), we also assessed the impact of estimating QTc using the different formulae, and how it affects each patient's final *Gollob* score and Expert Consensus SQTS diagnosis criteria.

Statistical Analysis

SPSS 19.0 for descriptive and inferential statistical analysis. The Bland-Altman method for paired measurements, and paired samples T-test were used to examine interobserver agreement. Binary logistic regression (backward likelihood ratio method, probability for stepwise 0.05) was performed for assessing for independent predictors of higher probability of SQTS (defined as the 99th percentile of *Gollob* score, obtained using *Bazett's* correction). A two-tailed P value <0.05 was used for defining statistical significance in all comparisons.

Ethical and Protocol Approval

The SCD-SOS protocol was approved by the local Ethics Committee(355/Sec/10/03/2011), *Portuguese Central Health Region*, and by the

Portuguese Institute of Heart Rhythm. Handling of participant data was approved by the Portuguese Data Protection Commission.

Results

1. Baselines

From February 2012 to May 2013, 15,351 subjects had a 12-lead electrocardiogram performed as part of the SCD-SOS survey. Only 14,662 of patients who had an ECG were deemed eligible in the SCD-SOS survey (i.e. were aged≤40). Of these, 79.3% (n=11,623) agreed to provide more information and fill-in the SCD-SOS questionnaire.

Women accounted for the majority of participants (57.1%;n=8,375), and mean age was 20.5±5.9 years (IQR:17-23)(Table 2). Atrial fibrillation was not found in any of the performed ECGs. No patients reported family history of SQTS, or a previous episode of aborted sudden cardiac arrest.

2. Prevalence of short QTc

Strong interobserver agreement on QT measurements was observed (Annex A). Prevalence of short QTc intervals was low (<0.1% to <2.7%, depending on the cut-off), and is shown in Figure 1. The *Framingham* and *Bazett* corrections detected more individuals in the shorter QTc strata, with *Framingham* being able to identify a slightly higher number of individuals (2 and 3 ≤320ms, and 8 and 10 ≤330ms, with *Bazett* and *Framingham* correction, respectively, and only 3 individuals were identified with Fridericia and Hodges ≤330ms).

Figure 2 illustrates reclassification of QTc into points using the *Gollob* classification cut-offs and shows how the number of assigned points can change depending on the QTc correction formulae applied. The comparison of *Bazett with Framingham's* correction shows a 14,121 participants (96.31%) assigned with the same number or points, 373 (2.54%) more, and 168 (1.15%) less points.

Assessment of QTc/RR relationship with the different correction formulae in the SCD-SOS cohort shows that *Bazett* performs poorly (r=-0.60), as QTc obtained through this formula presents a moderate correlation with RR. On the other hand, *Framingham* has an acceptable performance (r=-0.19), and *Hodges* and *Fridericia* correction display the best results (both -0.07). More data on descriptive statistics of QTc using different formulae, and the performance of QTc correction formulae according to heart rate can be found in Annex B and C (Supplementary Material).

Annex D (Supplementary material) shows that for *Hodges* and *Fridericia* correction differences in QTc>10ms occur for >50% of individuals, and for *Framingham* formula differences >10ms occur in nearly half of the sample.

3. Probability of SQTS in participants from the SCD-SOS Survey

The percentage of participants at risk was higher if using *Fridericia's* correction (Figure 3). Almost three quarters of individuals in the low probability group (score 1-2), had a score of 1, which translates the presence of isolated short QTc (measuring ≥350 to 370ms), without any associated high risk clinical features. Individuals with a score of 2 account for 1.1 to 1.4% of the population, and were more frequently identified using *Fridericia* and *Framingham's* correction. Score≥2 identified the 99th SQTS-probability percentile in this population. Intermediate probability individuals

were rare and identified in ≈0.1% with all formulas, with *Bazett* and *Framingham* identifying a higher number of subjects. Irrespectively of the used formula, no high SQTS probability individuals (score≥4) were observed in the population.

Figure 4 illustrates the concordance of the different formulae when compared with *Bazett* with regard to risk of SQTS.

Distribution of baselines and different components of the score (using *Bazett's* correction), per each probability strata are shown on Table 3.

On multivariate analysis, male gender, non-Caucasian ethnicity and being involved in competitive sports were independent predictors of being in the highest percentile of SQTS-probability (score≥2)(Table 4).

Based on the Expert Consensus definition, according to QTc duration alone (QTc ≤330 ms), 9 individuals (0.06%) using the *Bazett* correction, 4 individuals (0.03%) with the *Fridericia* and 3 individuals (0.02%) with the *Hodges* correction, and 12 (0.08%) using the *Frammingham* equation, could potentially be diagnosed with SQTS. Combining QTc duration and additional risk factors (QTc <360 ms, and, in this cohort, family history of sudden death at age ≤40), 3 more individuals (0.02%) were identified using the *Bazett* correction, 7 (0.05%) using *Fridericia's* correction, 6 (0.04%) using *Hodges* correction, and 4 individuals (0.03%) were identified when using the *Frammingham* equation (Table S-1, Supplementary Material). In sum, 0.06-0.11% of individuals could potentially be diagnosed with a SQTS and were referred to the local Arrhythmia clinic for assessment and had 24-h Holter tapes with QTc monitoring, an exercise treadmill test, and echocardiogram. Genetic testing is being discussed and awaiting funding. All patients have been stable without major arrhythmic events.

4. Impact of different QTc formulae in *Gollob* and colleagues cohort

Among all 61 patients in *Gollob's'* cohort, 4 patients (6.56%) (Table S-2, Supplementary Material), all men, obtained a different score while using different formulae instead of *Bazett* to confer QT correction. Two patients (#31, #55), already classified as high risk (score=4) using *Bazett's* correction, were assigned one more point. However, the other two patients shifted in SQTS-probability level: patient #56 had a score of 3 (intermediate-probability), and was assigned 4 points when using *Fridericia's* correction, and 5 points both with *Framingham* and *Hodges* correction, causing him to move to the high SQTS-probability category. A more pronounced change was observed in patient #60 who had a QTc >370ms using *Bazett's* correction, and therefore was not assigned any points, but using *Fridericia's* correction was assigned 5 points (family history of SQTS, and known phenotype, besides ECG points), and 6 points with *Framingham* and *Hodges* correction, moving him directly from the "no probability" to the highest-probability category.

No patients were assigned with lower scores, or moved into a lower probability category.

Using the Expert Consensus criteria, nearly all patients in *Gollob's* cohort met criteria for a potential SQTS diagnosis. Exceptions were patient ♯60, where only using *Framingham* and *Hodges* correction would the patient be considered for a SQTS diagnosis. Patient ♯61 would not meet criteria with any QTc correction *formula*. Both patients, ♯60 and ♯61, had family history of SQTS and identified mutations, and criteria would not be met if using *Bazett* correction.

Discussion

In our sample of young adults from a voluntary large-scale screening for potential arrhythmic disorders, and patients with a diagnosis of SQTS in the original *Gollob* and colleagues publication we observed discrepancies in the prevalence of short QTc intervals and probability of SQTS, associated with the use of different QTc correction formulae. This shows that using different formulae may have an impact in the detection of individuals at risk, and thus can impact on risk stratification. This was clearly illustrated by the fact that in *Gollob's* cohort of patients diagnosed with SQTS[7], 6.56% patients were assigned more points, and 3.28% patients were positioned in a higher risk category. Similarly, using different formulae in the SCD-SOS cohort, between 1 and 5% of patients were classified into higher risk strata. Using *Bazett* formula we would miss some diagnoses of SQTS in the Gollob cohort. However, as this is a rare disease and the prevalence of short QT intervals is very low, this reclassification leads to small changes on a population level, but can be of importance to the affected individual in particular and his/her family.

Vanderbeck and colleagues have shown that *Fridericia* and *Framingham* correction provide the best rate correction for prolonged QT intervals and improved prediction of 30-day and 1-day mortality[15]. In the setting of short QTc intervals, the association of different formulae with a higher probability of arrhythmic events remains to be proven, and assessing which one of the linear regression functions (*Framingham*, *Hodges*, or others[8]) to use, should be the aim of future research. However, our findings call the use of *Bazett's* correction into question, as it may be underestimating the risk in a small group of individuals. *Bazett's* equation leaves a

strong positive residual correlation (*r*=0.32) with heart rate, and adjusted QTc values may be erroneous, especially for high heart rates [8, 16].

We do not believe there is as an ideal QT correction formula, and results should always be interpreted according to each subject's clinical history. From a population/epidemiological level, it may be important to understand which QT correction formula is associated with a lower number of false negatives, as this is a rare disease entity with severe implications and missing a diagnosis should be avoided. It is possible that such a formula may lead to a small increase in the number of false positives, which may be acceptable as long as the number of individuals is small. It is also important that ECGs are repeated in individuals judged to be at risk with a heart rate as close as possible to 60bpm to attenuate possible rate correction issues and confirm the initial suspicion of short QT syndrome.

Individuals with a short QTc≤320-330ms are rare in the pediatric population[17], young[2, 18, 19] and middle age adults[20, 21]. The SCD-SOS cohort differs from some of the abovementioned young adult cohorts as it was balanced with regard to gender (unlike other studies which included >90-99% men[18, 19]), approximately half was not involved in regular physical exercise (unlike *Kobza et al.* [18] in which all individuals were in the army), and was mostly composed of Caucasian individuals (nearly 98% were Caucasians; in *Dhutia's* cohort [2] non-Caucasians accounted for >10% of the sample). In the SCD-SOS cohort, QT≤330ms was observed in 0.02 to 0.07%, depending on the used formula for correction, and QT≤320 in 0% to 0.02% (no patients using *Fridericia* or *Hodges* formula, and more patients identified while using *Framingham's* correction). Non-Caucasian ethnicity and male gender were the two independent predictors for a short QTc interval identified by *Dhutia et al*[2]. In

our cohort, we identified the same two predictors, as well as involvement in competitive sports, possibly suggesting that high-intensity sports practice may lead to electrical repolarization remodelling with shortening of the QTc interval in a minority of individuals. Whether this can occur in all subjects, or only in those with a baseline ion channel defect, remains to be assessed.

Even though the prevalence of very short QTc intervals in the general population is small, we observed that nearly 10% of the population in the SCD-SOS survey classified as having at least some probability of having SQTS, based on the *Gollob* score. Using the Expert Consensus recommendations this figure is much lower (0.06-0.11%). Deciding the cut-off and formula/criteria to identify individuals at risk is of importance in the primary prevention setting, as we need to define each individuals and how much investigation (additional Holter monitoring, genetic testing, family screening, and search for additional clinical risk factors) each of these individuals should undergo, as it will clearly have economic implications. Cost-effectiveness analyses should be performed to determine the ideal cut-off point for screening these individuals: there may be a potential advantage of screening asymptomatic individuals with a score ≥3 as these are less prevalent in the overall population and may be at higher risk of events. Identifying more of these intermediate to high-risk individuals would be of importance to improve our knowledge of this channelopathy, and conduct research on primary prevention therapy with anti-arrhythmic QT prolonging drugs like quinidine or disopyramide[22, 23].

We did not identify a single high SQTS-probability individual in the SCD-SOS cohort. This could result from the fact that we did not yet perform genetic testing. However,

the indication for this test can be questioned as these individuals were asymptomatic/primary prevention and after examination of patient's clinical and family history and ECG, they were either low or intermediate risk. The 2011 Consensus for genetic testing in channelopathies states that the yield of identifying a mutation in these patients is <20%, and that comprehensive genetic screening may be considered if the cardiologist thinks there is a strong clinical index of suspicion[24].

Limitations

Some limitations should be highlighted. First, genetic testing was not performed in the SCD-SOS cohort, as explained above (low risk population), and some patients were not willing to provide clinical and family history data, reason why *Gollob* score may be underestimated. Second, only one ECG was performed per patient. As QT interval may also change overtime due to effects of autonomic tone, we cannot rule out that some patients with borderline QTc values may in fact have had pathologic short QTc if the ECGs had been repeated or performed at a different time. Third, we acknowledge that our population may not be representative of other young adult populations as it included nearly 98% Caucasian individuals and 25% of athletes involved in competitive sports. Fourth, based on the low rate of unexplained syncope and family history of sudden cardiac death <40, and the low prevalence of very short QTc intervals, we determined to undertake a best case scenario analysis and assign "0" to the missing answers. Finally, even though some individuals in the SCD-SOS cohort meet Expert Consensus criteria for SQTS, we cannot know for sure whether or not they are accurate or false positive diagnoses.

Conclusion

Prevalence of individuals with QT intervals ≤320ms and ≤330ms in the SCD-SOS cohort was extremely low. No high SQTS-probability individuals were identified in this young adult population, and intermediate-probability individuals accounted for approximately 0.1% of the sample. Based on the Expert Consensus, 0.07-0.11% of individuals may potentially have SQTS. Using different formulae for QTc correction was associated with significant reclassification of individuals within *Gollob's* score categories, and number of SQTS diagnoses, both in asymptomatic and symptomatic individuals, with Framingham formula identifying/diagnosing a slightly higher number of individuals.

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Author Contributions:

RP had the idea of developing the SCD-SOS survey protocol, and discussed it with MJF and LG, which later helped in developing it. Later, RP discussed the possibility of a short QT sub-analysis with PDL, and this was performed with the help of NK and NS. RP prepared the first draft of the manuscript which was revised by PDL, and later by all authors. The final version of the manuscript was prepared and revised by all authors before the final approval and submission of the manuscript.

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Table 1 – Short QT Syndrome Diagnostic Criteria by Gollob et al. [7].

	Points
QTc	
<370ms	1
<350ms	2
<330ms	3
J_{point}-T_{peak} interval < 120ms*	1
Clinical History**	
History of sudden cardiac arrest	2
Documented polymorphic VT or VF	2
Unexplained syncope	1
AF	1
Family History**	
1st or 2nd degree relative with high probability SQTS	2
1st or 2nd degree relative with autopsy negative SCD	1
Sudden Infant Death Syndrome	1
Genotype	
Genotype positive	2
Mutation of undetermined significance in a culprit gene	1

Based on the total number of points, subjects are classified as low probability (≤2 points), intermediate probability (3 points) and high probability (≥4 points) of SQTS.

Legend: QTc – corrected QT interval; VT – ventricular tachycardia; VF – ventricular fibrillation; AF – atrial fibrillation; SQTS – short QT syndrome; SCD – sudden cardiac death. Note: * Measured in the highest amplitude precordial lead; **Events must occur in the absence of identifiable etiology. Points can only be assigned once to each event;

Table 2 – Baselines in the SCD-SOS population and QT interval data.

Variable (n=14,662)	% or mean ±SD	QTc Correction Formulae	
Women	57.12% (8,375)	**Mean QTc Bazett (ms)**	402±23
Non-Caucasian	2.32% (340)	**P_1 ; P_{99} Bazzet (ms)**	351 ; 455
Age	20.5±5.9	**Mean QTc Fridericia (ms)**	392±18
BMI (Kg/m^2)	22.4±4.3	**P_1 ; P_{99} Fridericia (ms)**	353 ; 436
Sports Practice	50.58% (7,416)	**Mean QTc Framingham (ms)**	393±17
Competitive sports	28.86% (4,232)		
Hours per week	4.9±3.9	**P_1 ; P_{99} Framingham (ms)**	351 ; 435
QT (ms)	373±28	**Mean QTc Hodges (ms)**	393±17
P_1 ; P_{99} QT (ms)	310 ; 442	**P_1 ; P_{99} Hodges (ms)**	354 ; 435
RR (ms)	870±163		
P_1 ; P_{99} RR (ms)	545 ; 1,304		

Legend: SD – standard deviation; BMI – body mass index.

Table 3 – Distribution of baselines and other variables among the different *Gollob* score strata in the SCD-SOS cohort.

	Gollob score				P Overall
	0	1	2	3	
	(n= 13,559)	(n=906)	(n=180)	(n=17)	
QTc 1 point	0% (0)	100% (906)	54.8% (61)	0% (0)	<0.0001
QTc 2 points	0% (0)	0% (0)	45.2% (119)	52.9% (9)	
QTc 3 points	0% (0)	0% (0)	0% (0)	47.1% (8)	
JT 120	0.2% (31)	0% (0)	0% (0)	0% (0)	0.483
AF	0% (3)	0% (0)	0% (0)	0% (0)	0.970
Unexplained syncope	1.3% (173)	0% (0)	27.7% (48)	53.3% (8)	<0.0001
SCD 1st or 2nd degree relative	1.7% (187)	0% (0)	6.6% (13)	7.7% (1)	<0.0001
Women	59.2% (8,025)	32.6% (296)	27.8% (50)	17.6% (3)	<0.001
Non-Caucasian	2.3% (310)	3.0% (27)	5.0% (9)	0% (0)	0.053
Age	20.5±5.9	20.0±5.1	20.6±5.1	20.2±3.2	0.063
BMI	22.4±4.4	22.5±3.2	22.8±3.1	22.4±2.8	0.636
Regular sports practice	50.3% (6,823)	52.4% (475)	58.9% (106)	70.6% (12)	0.026
Competitive sports	28.5% (3,871)	30.9% (280)	41.1% (74)	41.2% (7)	0.001
n of hours (all)	1.9±3.4	2.1±3.5	2.0±3.2	2.9±2.7	0.061
n of hours (athletes)	3.5±4.2	3.9±4.1	3.5±4.0	5.6±1.7	0.341

Legend: QTc – corrected QT interval; JT – J to T peak interval; AF – atrial fibrillation; SCD – sudden cardiac death; BMI – body mass index.

Table 4 – Predictors* of higher probability of SQTS in the SCD-SOS cohort.

	Predictors of *Gollob* score *Bazett* ≥ 2				
	Univariate		Multivariate		
	OR ₉₅%CI	P	OR ₉₅%CI	P	
Men	3.60, 2.62-4.95	<0.001	3.41, 2.47-4.70	<0.0001	Constant:0.006
Age	1.00, 0.98-1.03	0.739	-	-	
BMI	1.01, 0.99-1.03	0.395	-	-	
Non-Caucasian	2.04, 1.04-4.02	0.035	1.94, 0.98-3.84	0.056	
Sports practice	1.43, 1.07-1.91	0.015	-	-	
Competitive Sports	1.67, 1.25-2.23	<0.001	1.33, 0.99-1.78	0.059	
Hours per week	1.02, 0.98-1.06	0.379	-	-	

Legend: OR – odds ratio; CI – confidence interval; BMI – body mass index.
*Note: Variables already part of *Gollob* score were tested as predictors.

Figure Legends

Figure 1. Prevalence of short QTc intervals in the SCD-SOS survey cohort using different QT interval correction (QTc) formulae.

Note: Bars represent Prevalence, and labels for each bar represent the number of individuals in each strata.

Figure 2. Corrected QT interval (QTc) migration within the interval cut-offs provided by *Gollob's* score while using different formulae.

Figure 3. Prevalence of Gollob score strata in the SCD-SOS survey cohort using different QT correction formulae.

Note: Bars represent Prevalence, and labels for each bar represent the number of individuals in each strata.

Figure 4. Changes in *Gollob* score observed while using different QT interval correction (QTc) formulae.