



## QT prolongation in non-telemetered hospitalized elderly patients<sup>☆</sup>

A. Bajrangee<sup>a,\*</sup>, S. Mahabir<sup>b</sup>, W. Khalifa<sup>c</sup>, A.O. Maree<sup>d</sup>, B. McAdam<sup>e</sup>

<sup>a</sup> New Cross Hospital, Wolverhampton, England, United Kingdom of Great Britain and Northern Ireland

<sup>b</sup> Leicester Royal Infirmary, Leicester, England, United Kingdom of Great Britain and Northern Ireland

<sup>c</sup> Sunderland Royal Hospital, Sunderland, England, United Kingdom of Great Britain and Northern Ireland

<sup>d</sup> St James Hospital, James's Street, Dublin 2, Ireland

<sup>e</sup> Beaumont Hospital, Beaumont Road, Dublin 8, Ireland

### Background

The QT interval is a measure of ventricular depolarization and repolarization. Prolonged QT and corrected QT (QTc) may result in a life threatening ventricular arrhythmia termed Torsade de Pointes (TdP) [1]. QT prolongation is often encountered in both general medical and surgical admissions attributable to underlying coronary heart disease (CHD), left ventricular hypertrophy (LVH), sepsis, polypharmacy and electrolyte disturbances.

The QT interval is known to demonstrate variability with aging due to prolonged cardiac repolarization and reduced RR variance [2]. Age dependence of the upper limits of normal QT is often overlooked with Rautaharju et al. reporting criteria for normal QT by age, with 430 ms in men and 440 ms in women <40 years old being normal increasing to 455 ms in men and 460 ms in women 70 years and older [3]. The elderly are more susceptible to QT prolongation with age >60 being reported as a risk factor in one study of hospitalized patients [4].

Mechanisms underlying an increased risk of QTc interval prolongation and TdP in older patients are unclear, but could include declining serum testosterone concentrations in older men and reduced serum progesterone concentrations in postmenopausal women [5–7]. Aging processes may affect the molecular determinants of the QTc interval or alter the myocardium with increased myocardial fibrosis [8]. Aging is also associated with alterations in the amount of sympathetic and parasympathetic tone that affects myocardial repolarization and the duration of the QTc [9].

Polypharmacy is a commonly encountered etiology for QT prolongations in elderly patients admitted to hospital. Drugs associated with QT prolongation include antiarrhythmics, antipsychotics, antibiotics and antidepressants, many of which the elderly are maintained on or prescribed in hospital. Additionally hospitalized patients are often in a physical condition that sometimes requires treatment with a number of these drugs. In combination with other known risk factors, such as female sex, bradycardia, electrolyte abnormalities, and renal dysfunction, fatal ventricular arrhythmia may occur.

Patients are screened for QT prolongation in hospital often on their baseline twelve lead electrocardiogram (ECG) at admission; this determines whether they admitted to a continuous telemetry bed. We know that the QT interval duration exhibits significant variability and a normal QT interval at admission does not portend a normal QT throughout an admission. In this study we sought to determine the incidence and etiology of undetected QTc prolongation in elderly patients admitted to medical and surgical wards in a tertiary referral hospital over a three-month period.

### Methods

In this prospective observational study we recruited consecutive patients who presented to the Accident and Emergency department of Beaumont Hospital, Ireland between February to May 2015. Beaumont Hospital is a tertiary referral center with 820 beds. The local ethics committee approved this study. Patients were included if they were able to give written informed consent and older than sixty years of age and had a QTc <470 ms for males and <480 ms for females on admission. All patients were acute admissions recruited both from the medical and surgical service. Patients were recruited Monday– Sunday between the hours of 9 am–5 pm. Patients with an acute myocardial infarction or angina pectoris, known long QT, bundle branch block on ECG, atrial fibrillation, delta waves, paced rhythm or any arrhythmia were excluded. Patients with known severe left ventricular (LV) dysfunction defined as an ejection fraction of <35% were excluded.

After consent was obtained baseline demographics, admission diagnosis, past medical history, baseline medication and biochemical data was recorded. Traditional cardiovascular risk factors (smoking, diabetes, hypertension, family history), alcohol intake or illicit drug use were noted. We measured weight and height and calculated body mass index (BMI).

The standard 12 lead ECG performed daily was used for the QT interval evaluation. Two physicians blinded to patients identity and characteristics performed all QT measurements utilizing calipers on hard copies of ECGs with lead V5 used to determine the QT. The QT was taken as the mean QT of three sequential ventricular complexes. The QT interval was measured utilizing the previously described tangent method [10]. The QT interval corrected for the previous cardiac cycle length (QTc) was calculated according to Bazett's formula (QTc =

<sup>☆</sup> The authors have no conflicts of interest to declare.

\* Corresponding author.

E-mail address: [amrit\\_bajrangee@hotmail.com](mailto:amrit_bajrangee@hotmail.com) (A. Bajrangee).

QT/√RR) [11]. Minor QTc prolongation was considered as a QTc above 470 ms in males and 480 ms in females with severe QTc prolongation considered as a QTc interval  $\geq 500$  ms [12].

Patients were followed for 30 days or up to discharge if sooner than 30 days. All patients had 12-lead ECGs performed daily over their admission for QTc determination. Factors that may influence the QT interval such as pharmacodynamic interactions due to changes in medication prescription, electrolyte disturbances, thyroid function and changes in clinical condition were recorded if available. Left ventricular function if measured within the previous year or on this admission was recorded. The primary outcomes were the incidence and etiology of QTc prolongation. If QTc prolongation was noted the primary clinician was informed by study investigators of the same and appropriate changes of treatment initiated.

### Statistical analysis

All statistical analysis was undertaken using *Graphpad Prism* version 6.0 and *IBM SPSS* version 22 (Chicago, IL, U.S.A.). Numerical data are presented as medians and interquartile ranges with comparisons performed by using the Student *t*-test for normally distributed continuous variables and the Mann-Whitney test for non-normally distributed continuous variables. Categorical data are presented as percentages and comparisons were made by using the Chi-squared  $\chi^2$  test or the Fisher exact test for contingency data with cell sizes  $< 5$ . Logistic regression with QTc as the dependent variable and a series of

independent variables including age, sex, left ventricular function, pharmacodynamic drug interactions between prescription of QTc prolonging medication in hospital and QTc prolonging medication at admission, interaction between electrolyte derangements and prescription of QTc prolonging medication were tested and presented if statistically significant.

### Results

In total seventy-four patients with a median age of 75 (67–82) were recruited, with 41 (53%) males and 33 (47%) females, 47 (64%) patients were admitted under the medical service and 27 (36%) under the surgical service (Fig. 1). There was no significant difference in the incidence of cardiovascular risk factors or ejection fraction in patients who developed QTc prolongation and those who did not. Left ventricular function was available in 16 (100%) of patients with QTc prolongation and 30 (53%) of patients with no QTc prolongation. The median length of stay for the entire cohort was 12 (8–24) days with no significant difference in length of stay between both cohorts as shown in Table 1.

The admission QTc of those patients who developed QTc prolongation was 443 ms (410–455), which was significantly longer than the admission QTc of 428 ms (410–441) in patients who did not develop QTc prolongation ( $p = 0.0019$ ). There were no significant differences in QRS width or mean heart rates for both cohorts (Tables 2).

Over the three-month study period a total of 16 patients (22%) had a prolongation in their QTc, 9 patients with severe QTc prolongation and 7

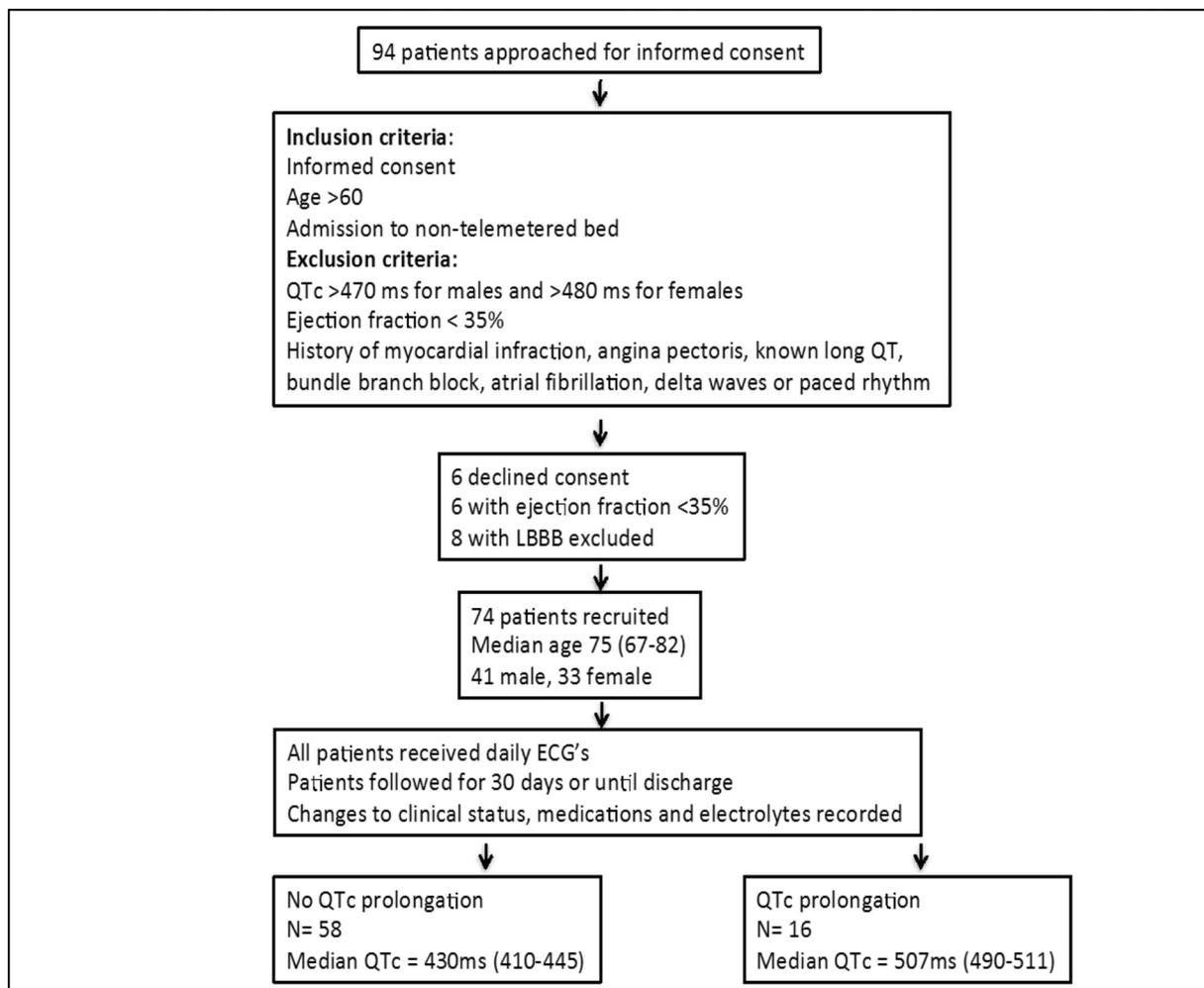


Fig. 1. Consort diagram for study. (LBBB-left bundle branch block).

**Table 1**

Baseline patient demographics at time of admission, presented as medians and interquartile ranges. (Admission meds- admission medication).

	No QTc prolongation (N = 58)	QTc prolongation (N = 16)	p value
Age	76 (67–84)	70 (66–77)	0.26
Female sex	25	8	0.1
Medical admission	33 (59%)	12 (78%)	0.06
Admission QTc	428 (410–441)	443 (410–455)	0.0018
Heart rate	76 (57–104)	83 (62–103)	0.3
QRS Duration (ms)	84 (80–91)	92 (79–97)	0.5
Cardiovascular risk factors			
Smoker	10 (18%)	4 (21%)	0.3
CKD	5 (9%)	1 (8%)	0.8
Hypertension	24 (42%)	8 (54%)	0.4
Diabetes	19 (34%)	5 (28%)	0.2
Admission Meds			
Antiarrhythmic			
Vaughan Williams Class			
I	2 (4%)	2 (11%)	0.3
II	7 (12.5%)	0%	0.001
III	1 (2%)	0%	–
IV	2 (4%)	0%	0.6
V	0%	0%	–
Antidepressants			
Tricyclic	3 (5%)	1 (6%)	0.8
SSRI	2 (3%)	1 (6%)	0.4
Benzodiazepines	5 (9%)	2 (11%)	0.7
Neuroleptics	4 (7%)	0%	0.04
Ejection Fraction	50 (45–50%)	50 (40–50%)	0.7
Admission electrolytes			
Calcium	2.1 (1.9–2.15)	2.1 (1.9–2.2)	0.9
Magnesium	0.8 (0.72–0.94)	0.7 (0.6–0.9)	0.7
Potassium	4.0 (3.5–4.7)	3.8 (3.4–4.6)	0.8

(Ejection Fraction calculated by Simpson's method, normal electrolyte ranges- Calcium 2.2–2.7 mmol/l, Magnesium 0.6–1 mmol/l, Potassium 3.5–5.5 mmol/l) (Specific medications which patients were on: antiarrhythmic- Class I- Phenytoin, Class II- Bisoprolol, Class III- Sotalol, Class IV- Diltiazem, Tricyclic- Amitriptyline, Selective serotonin reuptake inhibitors (SSRI)- Escitalopram, Citalopram, Neuroleptics-Olanzapine) (CKD- Chronic kidney disease).

**Table 2**

Results table comparing both cohorts.

	No QTc prolongation (N = 58)	QTc prolongation (N = 16)	p value
Longest QTc	430 (410–445)	507 (490–511)	<0.0001
Length of stay (days)	12 (8–24)	14 (7–24)	0.7
Medication prescription in hospital			
Antiarrhythmic	4 (8%)	1 (6%)	0.6
Anticholinergic	4 (7%)	1 (6%)	0.7
Antibiotics	45 (81%)	18 (100%)	0.01
Antidepressants	1 (2%)	0	0.9
Hypnotics	10 (17%)	2 (11%)	0.6
Electrolyte derangements			
Hypocalcaemia	5 (9%)	2 (11%)	0.6
Hypomagnesia	7 (13%)	9 (49%)	0.04
Hypokalemia	10 (18%)	4 (22%)	0.8
Hyperkalemia	4 (7%)	1 (5%)	0.9

(Specific medications prescribed during admission- Antiarrhythmic- Diltiazem, Bisoprolol; Anticholinergic- Tiotropium, Ipratropium, Oxybutynin; Antibiotics- Cefotaxime, Co-amoxiclav, Clarithromycin, Ciprofloxacin, Metronidazole, Piptazobactam, Trimethoprim; Antidepressants – Citalopram, Hypnotics- Chlordiazepoxide).

(Normal electrolyte ranges- Calcium 2.2–2.7 mmol/l, Magnesium 0.6–1 mmol/l, Potassium 3.5–5.5 mmol/l).

with minor QTc prolongation. The median QTc for those with severe prolongation was 507 ms (502–518) with the median for those with minor prolongation being 477 ms (475–480) ( $p < 0.0001$ ). The median

length of time after admission to development of QTc prolongation was 8 days (4–19). There were no significant sex differences between both groups ( $p = 0.8$ ).

**Table 3**

Odds ratios calculated by logistic regression with QTc prolongation as the dependent variable.

	Odds ratio	p value	95% CI
Interaction between electrolyte derangement and QTc prolonging hospital medication	1.3	0.05	1.1–1.6
QTc prolonging drug interactions	2.3	0.02	2.0–2.8

(QTc prolonging drug interactions -interactions between QTc prolonging medication at admission and QTc prolonging prescription in hospital; electrolyte derangement was a composite of hypokalemia, hypomagnesia and hypocalcaemia).

The odds ratio for pharmacodynamic drug interactions between prescription of QTc prolonging in hospital and antecedent QTc prolonging medication was 2.3 ( $p = 0.02$ ). Similarly the odds of QTc prolongation were 1.3 ( $p = 0.05$ ), if QTc prolonging medication was prescribed and there was significant electrolyte derangement. Age, sex, left ventricular function, electrolyte derangement and admission medication were not independent predictors of QTc prolongation in our cohort Table 3.

Pharmacodynamic drug interactions between medications prescribed in hospital or between admission medications and those prescribed in hospital were the cause of severe QTc prolongation in six of the nine cases. Specifically three patients on Simvastatin at admission were prescribed Clarithromycin and three patients were prescribed the combination of Metronidazole, Ciprofloxacin and Chlordiazepoxide. The remaining three patients developed severe QTc prolongation due to a combination of significant hypomagnesia and hypokalemia whilst being on hypnotics prescribed prior to admission (Table 4).

In the cohort with minor QTc prolongation pharmacodynamic drug interactions and electrolyte derangements were the primary cause. Three patients with abdominal infections were given Ciprofloxacin or Piptazobactam whilst on neuroleptics or antidepressant medication on admission and two patients with alcoholic liver disease were admitted with an acute decompensation with significant hypomagnesia and prescribed the combination of Cefotaxime and Chlordiazepoxide. With the final two patients developing QTc prolongation due to Ciprofloxacin prescribed for urinary infections (Table 5).

All patients who developed QTc prolongation during the study were commenced on twenty-four hour continuous cardiac monitoring with adjustments of offending drugs and correction of electrolyte disturbance where possible. There were no adverse outcomes related to QTc prolongation.

## Discussion

Our findings indicate that hospitalized older patients admitted to non-telemetry beds are at significant risk of QTc prolongation. Twenty two percent of patients in our cohort considered low risk on admission developed severe or minor QTc prolongation. Our findings corroborate those by Lubart et al. who reported that 27% of elderly patients in their cohort developed QTc prolongation, however they considered a QTc of  $>450$  ms for men and QTc  $>470$  ms for women as abnormal [13].

The main cause of QTc prolongation in our cohort was the pharmacodynamic interaction between prescribed medications during hospitalization and antecedent medications at admission. In some patients QTc prolongation was due to a combination of medication prescription and electrolyte disturbance attributed to the underlying disease process. Whilst with age there is a natural prolongation of the QTc interval there is also a susceptibility to significant abnormal prolongation [13,14]. Drugs that induce QTc prolongation may more readily reach hazardous levels in elderly patients compared to younger patients [15–17].

Our observation that 35% of our population was on a QTc prolonging medication at admission reflects the reality of patients in this age group. Patients with normal or mild QTc prolongation at admission are deemed lower risk and often admitted to non-telemetry beds. Patients admitted to critical care wards receive continuous cardiac monitoring and studies performed in this setting demonstrate a preponderance of QTc prolongation sometimes leading to adverse cardiac outcomes [18]. There is however no specific guidance on QTc monitoring in patients admitted to general wards. A consensus statement from the American Heart Association (AHA) recommends considering continuous QTc monitoring on the initiation QT prolonging agents in patients at risk of QT prolongation [19].

**Table 4**

Individual characteristics of patients who developed severe QTc prolongation in hospital. (F = female, M = male), (COAD = Chronic obstructive airway disease).

Severe QTc prolongation	Age	Sex	Diagnosis	Admission heart rate	Admission QTc (ms)	Ejection fraction	Median prolonged QTc (ms)	Medication at admission	Medication prescribed in hospital	Electrolyte derangement
1	74	F	Pancreatitis	105	437	50%	510	Aspirin Ramipril	Ciprofloxain Chlordiazepoxide Metronidazole	No
2	70	F	Pneumonia	112	442	50%	520	Aspirin Metformin Simvastatin Ramipril	Clarithromycin Co-amoxiclav Enoxaparin Ipratropium	No
3	68	F	Alcoholic liver disease	87	456	45%	530	Nil	Ciprofloxain Chlordiazepoxide Metronidazole	No
4	73	M	Pneumonia	84	440	55%	507	Aspirin Amlodipine Temazepam Escitalopram	Piptazobactam	Hypokalemia
5	81	M	Urinary infection	91	449	50%	503	Aspirin Alprazolam Omeprazole Perindopril	Co-Amoxiclav Enoxaparin	Hypokalemia
6	77	M	Pneumonia	70	412	55%	517	Aspirin Simvastatin Temazepam	Clarithromycin Co-amoxiclav Enoxaparin	No
7	81	F	Urinary infection	79	452	60%	501	Aspirin Amlodipine Valsartan	Trimethoprim	No
8	71	M	COAD	85	416	40%	500	Aspirin Memantine Simvastatin Salmeterol/fluticasone propionate	Clarithromycin Co-amoxiclav	No
9	76	M	Delirium tremens	101	439	55%	504	Thiamine	Ciprofloxain Chlordiazepoxide Metronidazole	Hypomagnesia Hypokalemia

**Table 5**

Individual characteristics of patients who developed minor QTc prolongation. (M = male, F = female), (COAD = Chronic obstructive airways disease).

Minor QTc prolongation	Age	Sex	Diagnosis	Admission heart rate	Admission QTc (ms)	Ejection fraction	Median prolonged QTc (ms)	Medication at admission	Medication prescribed in hospital	Electrolyte derangement
1	80	F	Urinary tract infection	87	410	45%	480	Aspirin Ramipril Phenytoin Felodipine Valsartan	Ciprofloxacin Enoxaparin	No
2	67	F	Alcoholic liver disease	72	418	55%	480	Nil	Cefotaxime Chlordiazepoxide Spironolactone Vitamin K	Hypomagnesia Hypokalemia
3	83	F	Sepsis -Acute abdominal	104	423	55%	480	Aspirin Citalopram Memantine Omeprazole Perindorpil	Ciprofloxacin Metronidazole	Hypokalemia Hypomagnesia
4	70	F	Alcoholic liver disease	79	437	50%	477	Aspirin Lercanidipine Atorvastatin Escitalopram	Cefotaxime Chlordiazepoxide	Hypokalemia
5	74	M	Sepsis- Gallstone pancreatitis	97	396	45%	477	Levetiracetam Phenytoin Omeprazole	Piptazobactam Enoxaparin	Hypomagnesia Hypocalcaemia
6	85	M	Cholecystitis	101	448	50%	475	Aspirin Atorvastatin Escitalopram	Piptazobactam Enoxaparin	No
7	77	M	Urinary tract infection	96	412	-	470	Nil	Ciprofloxacin Enoxaparin	No

An awareness and identification of risk factors associated with QT prolongation in patients admitted to general wards should be undertaken by admitting clinicians. Sarganas et al. showed that the majority of acquired QT prolongation is attributable to medication prescribed in hospital [20]. They along with other groups identified risk factors for QT prolongation as age, female sex, serum potassium and magnesium, admitting QTc interval, comorbid conditions such as acute myocardial infarction and heart failure, and specific concomitant drug therapy [20–22]. Yet hospitalized patients with QTc interval prolongation on admission often receive QT interval-prolonging drugs and are not routinely monitored.

What is an acceptable level of QTc prolongation and when should treatment be altered or an offending agent stopped? QT interval prolongation is shown to increase exponentially as the number of risk factors present increases, with each 10-ms increase in QTc interval contributing an approximately 5% to 7% increase in risk of TdP in these patients [23]. Trinkley et al. recommends that patients with a QTc of >500 ms or an absolute increase in QTc of 60 ms from baseline have their medication regime altered and electrolytes corrected [24]. Whilst both the AHA and European Society of Cardiology acknowledge that age >65 is a risk factor for in hospital QTc prolongation no specific recommendations for QT monitoring in this age group exist.

We must acknowledge the limitations of our study. Firstly this was an observational cohort in a single center and findings limit the generalizability of the results. Whilst not all patients in the study had an assessment of their left ventricular function performed patients who developed QTc prolongation had an echocardiogram performed. Finally the determination of QTc based on Bazett's has been critiqued for over correction at high heart rates but continues to be the most accessible and widely used method of QTc determination [25].

In conclusion our study identified that elderly patients admitted to general wards and not routinely monitored for QTc prolongation are at significant risk for QTc prolongation. Whilst this finding requires further confirmation in larger cohorts admitting clinicians should be aware of risk factors for QTc prolongation. At risk patients should have periodic QT assessments with a low threshold for continuous monitoring.

## References

- [1] Itoh H, et al. The genetics underlying acquired long QT syndrome: impact for genetic screening. *Eur Heart J* 2016;37(18):1456–64.
- [2] Piccirillo G, et al. Influence of age, the autonomic nervous system and anxiety on QT-interval variability. *Clin Sci (Lond)* 2001;101(4):429–38.
- [3] Rautaharju PM, Mason JW, Akiyama T. Corrigendum to "New age- and sex-specific criteria for QT prolongation based on rate correction formulas that minimize bias at the upper normal limits" (*Internat J Cardiol* 2014, IJCA 174/3 [535–540]). *Int J Cardiol* 2015;178:299.
- [4] Letsas KP, et al. Clinical characteristics of patients with drug-induced QT interval prolongation and torsade de pointes: identification of risk factors. *Clin Res Cardiol* 2009;98(4):208–12.
- [5] van Noord C, et al. The association of serum testosterone levels and ventricular repolarization. *Eur J Epidemiol* 2010;25(1):21–8.
- [6] Tisdale JE, et al. Influence of oral progesterone administration on drug-induced QT interval lengthening: a randomized, double-blind, placebo-controlled crossover study. *JACC Clin Electrophysiol* 2016;2(7):765–74.
- [7] Seth R, et al. Long QT syndrome and pregnancy. *J Am Coll Cardiol* 2007;49(10):1092–8.
- [8] Liu CY, et al. Evaluation of age-related interstitial myocardial fibrosis with cardiac magnetic resonance contrast-enhanced T1 mapping: MESA (Multi-Ethnic Study of Atherosclerosis). *J Am Coll Cardiol* 2013;62(14):1280–7.
- [9] Can I, et al. Physiological mechanisms influencing cardiac repolarization and QT interval. *Card Electrophysiol Rev* 2002;6(3):278–81.
- [10] Postema PG, et al. Accurate electrocardiographic assessment of the QT interval: teach the tangent. *Heart Rhythm* 2008;5(7):1015–8.
- [11] HC B. An analysis of time relations of electrocardiograms. *Hearts* 1920;7:353–70.
- [12] Drew BJ, et al. Prevention of torsade de pointes in hospital settings: a scientific statement from the American Heart Association and the American College of Cardiology Foundation. *Circulation* 2010;121(8):1047–60.
- [13] Lubart E, et al. QT interval disturbances in hospitalized elderly patients. *Isr Med Assoc J* 2009;11(3):147–50.
- [14] Rabkin SW, Cheng XJ, Thompson DJ. Detailed analysis of the impact of age on the QT interval. *J Geriatr Cardiol* 2016;13(9):740–8.
- [15] Piccirillo Gianfranco, M.C., Lionetti Marco, Nocco Marialuce, Di Giuseppe Vincenza, Moisea Antonio, et al. Influence of age, the autonomic nervous system and anxiety on QT-interval variability. *Clin Sci* 2001;101:429–38.
- [16] Keller GA, et al. Drug-induced QTc interval prolongation: a multicenter study to detect drugs and clinical factors involved in every day practice. *Curr Drug Saf* 2015;11(1):86–98.
- [17] Keller GA, et al. Drug-induced QTc interval prolongation: a multicenter study to detect drugs and clinical factors involved in every day practice. *Curr Drug Saf* 2016;11(1):86–98.
- [18] Pickham D, et al. High prevalence of corrected QT interval prolongation in acutely ill patients is associated with mortality: results of the QT in Practice (QTIP) Study. *Crit Care Med* 2012;40(2):394–9.

- [19] Drew BJ, et al. Prevention of torsade de pointes in hospital settings: a scientific statement from the American Heart Association and the American College of Cardiology Foundation. *J Am Coll Cardiol* 2010;55(9):934–47.
- [20] Sarganas G, et al. Epidemiology of symptomatic drug-induced long QT syndrome and Torsade de Pointes in Germany. *Europace* 2014;16(1):101–8.
- [21] Rabkin SW. Aging effects on QT interval: implications for cardiac safety of antipsychotic drugs. *J Geriatr Cardiol* 2014;11(1):20–5.
- [22] Astrom-Lilja C, et al. Drug-induced torsades de pointes: a review of the Swedish pharmacovigilance database. *Pharmacoepidemiol Drug Saf* 2008;17(6):587–92.
- [23] Zareba W, et al. Influence of the genotype on the clinical course of the long-QT syndrome. International Long-QT Syndrome Registry Research Group. *N Engl J Med* 1998;339(14):960–5.
- [24] Trinkley KE, et al. QT interval prolongation and the risk of torsades de pointes: essentials for clinicians. *Curr Med Res Opin* 2013;29(12):1719–26.
- [25] Rautaharju PM, Warren JW, Calhoun HP. Estimation of QT prolongation. A persistent, avoidable error in computer electrocardiography. *J Electrocardiol* 1990;23(Suppl): 111–7.