# Risk of QTc prolongation associated to drug therapy: incidence and prevention in a private hospital in Costa Rica

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## Purpose

This research aims to determine the incidence of drug induced QTc prolongation risk in hospitalized patients, to review the drug therapy of these patients related to this complication and evaluate which QTc interval measurement method (manual or automatic) and correction formulas is the most appropriate to use for electrocardiographic monitoring.

## Methods

A retrospective observational study of hospitalized patients from January to December 2018, who were admitted at Hospital Clinica Biblica was conducted.

| (n = 541) | (n =162) | (n = 141) |
|---|---|---|
| • Patients > 18 y/o., hospital stay > 48 hours, at leat one medication associated to QTc prolongation | • 378 patients excluded due to missing information in medical records | • 21more pacients excluded due to peacemakers and therapy issues |

The QTc interval values were measured using standard 12-lead resting electrocardiograms.

Electrocardiographic data (QRS, QT, RR) was determined both automatically and manually (with the tangent method) in lead II or 5, in order to compare and determine any difference between the two methods.

The manual QT intervals were corrected with the Fridericia formulas (if QRS <120 ms) and Rautaharju (if QRS> 120 ms), the automatic QT was corrected with the Bazett formula.

## Results

141 patients analyzed → 23 had an arrhythmia (clinical history) → 14 suffered a complication of their arrhytmia

| 141 patients analyzed | 70 EKG in admission |
|---|---|
| • 113 (80%) high value of RISQ PATH score<br>• 70 (113) had EKG in admission<br>• 62 (113) high risk even without drugs | • 22 QTc prolongation<br>• 5 (22) drug associated QTc prolongation<br>• Avg. 3 QTc risk drugs per patient |

**Table 1**
**Characteristics of the patients included in the study and clinical factors associated with QT prolongation**

| Characteristics | n (%) |
|---|---|
| **Age** | 66 ± 19 |
| **Male** | 59 (43) |
| **RISQ-PATH Score** | |
| High risk (≥ 10 pts) | 113 (80) |
| Low risk (< 10 pts) | 28 (20) |
| **Risk Factors** | |
| Age ≥ 65 years old | 79 (56) |
| Female | 76 (54) |
| Smoking | 15 (11) |
| IMC ≥ 30 | 30 (21) |
| Cardiomyopathy (Ischemic) | 12 (9) |
| Hypertension | 68 (48) |
| Arrhythmia | 23 (16) |
| Prolonged QTc [QTc ≥ 450 (♂) / 470(♀) ms] | 22 (16) |
| Thyroid disorders | 22 (16) |
| Liver failure | 1 (1) |
| Neurological disorders | 1 (1) |
| Diabetes | 29 (21) |
| Potassium levels ≤ 3,5 mmol/L | 14 (10) |
| Calcium levels < 2,15 mmol/L | 0 (0) |
| PCR > 5 mg/L | 95 (65) |
| Glomerular filtration rate ≤ 30mL/min | 14 (10) |

**Table 2**
**Drug prescribed associated with QTc prolongation**

| Drugs that prolong the QT interval and are clearly associated with TdP | |
|---|---|
| **Number of patients on (%)** | |
| Levosulpiride | 82 (58) |
| Ondansetron | 79 (56) |
| Amiodarone | 27 (19) |
| Ciprofloxacin | 23 (16) |
| Fluconazole | 20 (14) |
| Moxifloxacin | 18 (13) |
| Propofol | 17 (12) |
| Domperidone | 12 (9) |
| Levofloxacin | 10 (7) |
| Others | 29 (21) |
| **Drugs that can prolong the QT interval, but there is lack of evidence on their association with TdP** | |
| **Number of patients on (%)** | |
| Granisetron | 23 (16) |
| Tramadol | 9 (6) |
| Risperidone | 6 (4) |
| Dexmedetomidine | 3 (2) |
| Mirtazapine | 3 (2) |
| Others | 4 (3) |
| **Drugs associated with TdP, but only under certain specific uses** | |
| **Number of patients on (%)** | |
| Metronidazole | 16 (11) |
| Quetiapine | 12 (9) |
| Metoclopramide | 6 (4) |
| Esomeprazole | 3 (2) |
| Propafenone | 3 (2) |
| Others | 11 (8) |

**Table 3**
**Electrocardiographic data at admission**

| Patients with ECG during time of admission, n (%) | 70 (50) |
|---|---|
| Average QTc interval | 437 ± 73 |
| Non-prolonged Qtc at admission | 48 (69) |
| Patients with follow-up EKG | 17 (35) |
| Prolonged Qtc at admission* | 22 (31) |
| Patients with follow-up EKG* | 8 (36) |

**Table 4**
**Results of the comparison of QTc values using correction formulas**

| Comparison | Average difference (ms) | p Value |
|---|---|---|
| Bazett vs Fridericia | 24 ± 18 | ≤ 0,0001 |
| Fridericia vs Rautaharju | 47 ± 32 | ≤ 0,0001 |
| Bazett vs Rautaharju | 71 ± 50 | ≤ 0,0001 |

## Conclusions

The RISQ-PATH score showed to be a useful method to identify patients who are at risk of suffering QTc prolongation, even prior to drug therapy that may include medications that are related to this complication. It was shown this score and other risk factors were not considered while prescribing drug therapy.

A significant difference was found between measuring the electrocardiogram automatically and manually. The use of correction formulas showed significant differences based on collected data (Bazett vs Rautaharju and/or Fridericia). It is necessary to implement strategies to improve the monitoring of QTc interval and its risk to prevent related complications.

## Disclosures / Contact

The authors of this presentation have nothing to disclose. For more information please contact:: Dr. Esteban Zavaleta. ezavaleta@clinicabiblica.com

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