# DISTRIBUTION OF QT DURATION ACCORDING TO AMBULATORY ECG MONITORING DATA IN PATIENTS WITH HYPERTENSION DEPENDING ON CLINICAL MANIFESTATIONS

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The study was carried out to identify the distribution of QTc during ECG AM depending on clinical features of EH in 82 patients. As classified shortened was considered QTc < 320 ms, as normal > 320 ms and < 440 ms, as classified prolonged was considered QTc > 440 ms. Average, maximum and minimum QTc are registered in every patient during ECG AM. The results confirm low probability of short QTc and demonstrate presence of prolonged QTc in every patient during ECG AM. The largest duration of maximal QTc have adulthood male patients with obesity III st., with low and high circadian index, with II stage and mild EH, with for the first time diagnosed EH and with EH lasting more than 10 years, with mild cardiovascular risk, with diffuse cardiosclerosis, with I and II FC and I and IIA st of HF.

*KEY WORDS:* hypertension, duration of QTc interval, ambulatory ECG monitoring

## РОЗПОДІЛ ТРИВАЛОСТІ ІНТЕРВАЛУ QTc ЗА ДАННИМИ АМБУЛАТОРНОГО МОНІТОРУВАННЯ ЕКГ У ХВОРИХ З ГІПЕРТОНІЧНОЮ ХВОРОБОЮ В ЗАЛЕЖНОСТІ ВІД КЛІНІЧНИХ ПРОЯВІВ

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Проведено вивчення розподілу тривалості QTc при АМ ЕКГ в залежності від клінічних ознак ГХ у 82 пацієнтів. За класифікований укорочений приймали QTc < 320 мс, нормальний > 320 мс та < 440 мс, класифікований подовжений > 440 мс. У кожного пацієнта за даними АМ ЕКГ зареєстровані середній, максимальний та мінімальний QTc. Результати підтверджують рідку вірогідність укороченого QTc і показують існування подовженого QTc у кожного пацієнта при АМ ЕКГ. Тривалість максимального QTc найбільша у пацієнтів зрілого віку, чоловічої статі, з ожирінням III ст., із зниженим та високим циркадним індексом; II стадією та м'якою ступеню ГХ, з вперше зареєстрованою та більше 10 років ГХ, помірним кардіоваскулярним ризиком серцево-судинних ускладнень, дифузним кардіосклерозом, I і II ФК та I і IIA стадією ХСН.

*КЛЮЧОВІ СЛОВА:* гіпертонічна хвороба, тривалість інтервалу QTc, амбулаторне моніторування ЕКГ

## РАСПРЕДЕЛЕНИЕ ПРОДОЛЖИТЕЛЬНОСТИ ИНТЕРВАЛА QTc ПО ДАННЫМ АМБУЛАТОРНОГО МОНИТОРИРОВАНИЯ ЭКГ У ПАЦИЕНТОВ С ГІПЕРТОНИЧЕСКОЙ БОЛЕЗНЬЮ В ЗАВИСИМОСТИ ОТ КЛИНИЧЕСКИХ ПРОЯВЛЕНИЙ

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Проведено изучение распределения продолжительности интервала QTc при АМ ЭКГ в зависимости от клинических признаков ГБ у 82 пациентов. За классифицированный укороченный принимали QTc < 320 мс, нормальный > 320 мс и < 440 мс, классифицированный удлиненный > 440 мс. У каждого пациента по данным АМ ЭКГ зарегистрированы средний, максимальный и минимальный QTc. Результаты подтверждают редкую вероятность укороченного QTc и показывают существование удлиненного QTc у каждого пациента при АМ ЭКГ. Продолжительность максимального QTc наибольшая у пациентов зрелого возраста, мужского пола, с ожирением III ст., с пониженным и высоким циркадным индексом; II стадией и мягкой степенью ГБ, с впервые

зарегистрированной и более 10 лет ГБ, умеренным кардиоваскулярным риском сердечно-сосудистых осложнений, диффузным кардиосклерозом, I и II ФК и I и II А стадией ХСН.

*КЛЮЧЕВЫЕ СЛОВА:* гипертоническая болезнь, продолжительность интервала QTc, амбулаторное мониторирование ЭКГ

## INTRODUCTION

Hypertension (EH) – is one of the most common chronic diseases that significantly increase the risk of cardiovascular complications and sudden death [1–2].

Prolongation or shortening of QT interval is seen as the factor which increases risk of life-threatening arrhythmias [3–6]. Electro-physiological phenomenon of prolonged QT intervals considered to be independent predictor of fatal arrhythmias that leads to sudden cardiac death [7–9].

International guidance on the prevention of sudden cardiac death (SCD) [10] recommends evaluation of QT interval as class 1A indication for the ambulatory ECG monitoring (ECG AM) in risk groups of developing life-threatening arrhythmias.

Ambulatory ECG monitoring is one of the basic methods in identifying this class of arrhythmias [11–12]. We didn't find in the literature any information about the relationship between the distributions of QT duration in ECG AM and clinical signs of EH.

## OBJECTIVE

The aim of the work is to study the distribution of QTc duration in ECG AM depending on clinical manifestation of the EH.

The study was conducted as a part of research work «Development and research of automatic control system of heart rate variability», state registration 0109U000622.

## MATERIALS AND METHODS

82 patients were examined in the outpatient clinic № 24 in Kharkov (28 male and 54 female, age 33–76 years old, with duration of EH from first identified till 30yers lasting.

Among 82 patients with hypertension the mild hypertension took place in 51, 22 %, moderate – in 29, 27 %, severe – in19, 51 %. The largest proportion of patients with EH II stage was 71, 95 %, I stage – 14, 63 %, III stage – 13, 41 %. The Ischemic heart disease (IHD) was 73,17 % out of the total number of registered patients with EH, among them – 52,44 % diffuse cardiosclerosis (DC), 18,29 % – stable angina (SA), 2,44 % – post infarction cardiosclerosis (PIC). Patients with EH without IHD accounted 26, 83 %. Chronic heart failure (CHF) I stage – 42, 68 %, IIA stage – 30, 49 %. Chronic heart failure with functional class I (CHF FC) was registered in 40,24 %, II class – in 28,05 %, III class –in 4,88 %.

Patients with acute cardiovascular diseases, with stable exertion angina IV FC, HF IIB-III stages and with thyroid diseases were not included in the study.

Identifying of the duration of the medium, maximum and minimum QTc was conducted by results of ECG AM. For these goals we used combined Holter monitoring (ECG + BP). Calculation of QTc duration was carried out with the help of program «Cardio Sense». Corrected QT interval was used (QTc) taking into account the heart rate. Calculation was conducted by Bazzet formula [13–14]. As classified shortened was considered QTc < 320 ms, as normal > 320 ms and < 440 ms, as classified prolonged was considered QTc > 440 ms [6, 12, 15]. These indicators correspond to the resting ECG parameters.

We determined the dependence of average daily indicators of QTc duration in patients with essential hypertension according to gender, age, weight of patients, duration of EH, stage and degree of EH, cardiovascular risk, presence of diabetes, ischemic heart disease, FC HF, stage of HF and the type of circadian index.

Statistical data analysis was performed with applying of parametric criteria (average value – $x$ and standard deviation – $s$). For determining statistically significant difference in quantitative indicators of QTc in selected groups Student's t-test and multifactor test were used (MANOVA). Calculations were carried out on a personal computer using programs «Microsoft Office Excel 2010» and «STATISTICA 10».

## RESULTS AND DISCUSSION

Average, maximum and minimum QTc are registered in every patient during AM ECG. But only by one ECG episode of QTc duration it can't be assigned to the class of normal, prolonged or short QT as in majority of modern researches [6, 9]. That's why it is not

enough and required 24-hours ECG monitoring [6–7, 12].

QTc interval duration of patients with EH during AM ECG in general and depending on age, gender, BMI and circadian index are presented in table 1.

Table 1

**QTc interval duration QTc ($\bar{x}$, s) during AM ECG in patients with EH in general and depending on age, gender, BMI and circadian index**

| Clinical manifestation | Graduation of clinical features | N | P, % | Average QTc, ms | | Maximum QTc, ms | | Minimum QTc, ms | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | $\bar{x}$ | s | $\bar{x}$ | s | $\bar{x}$ | s |
| | | 82 | 100 | 421 | 18 | 486 | 31 | 382 | 27 |
| Age, years | Adulthood | 35 | 43 | 416* | 18 | 487* | 34 | 379 * | 26 |
| | Old age | 47 | 57 | 398* | 18 | 457* | 29 | 361* | 27 |
| Gender | Female | 54 | 66 | 426* | 18 | 490 | 31 | 385 | 27 |
| | Male | 28 | 34 | 411* | 19 | 497 | 32 | 377 | 27 |
| BMI, kg/m² | Normal weight | 9 | 11 | 420 | 20 | 479 | 40 | 391 | 16 |
| | Overweight | 27 | 33 | 418 | 18 | 480 | 33 | 384 | 22 |
| | Obesity I | 27 | 33 | 421 | 20 | 491 | 28 | 379 | 34 |
| | Obesity II | 14 | 17 | 422 | 15 | 491 | 31 | 380 | 28 |
| | Obesity III | 5 | 6 | 431 | 22 | 495 | 25 | 381 | 16 |
| Circadian index | Normal | 40 | 49 | 419 | 20 | 484 | 37 | 384 | 23 |
| | Low | 38 | 46 | 424 | 17 | 487 | 24 | 381 | 32 |
| | High | 4 | 5 | 419 | 11 | 488 | 17 | 378 | 11 |

_Note: N – number of surveys; P – specific gravity; $\bar{x}$ – arithmetic mean; s – standard deviation; QTc – corrected QT; * – p < 0,05 – between QTc values in clinical groups._

In all patients in group the only episode of shortened QTc was registered, the duration of average and minimum QTc are within normal range, while maximum QTc significantly exceeds the normal range. In adulthood patients maximum and minimum QTc were registered, but in aged patients – minimum QTc. Female patients had more prolonged average QTc, but male patients had more prolonged maximum and minimum QTc. In case of obesity of III degree average and maximum QTc intervals are more prolonged, while in case of obesity of I degree the least QTc was minimum. The longest duration of average QTc is in patients with low circadian index (CI), of maximum – in patients with low and high, and minimum duration of average QTc is in patients with high circadian index.

QTc interval duration QTc ($\bar{x}$, s) during ECG AM in patients with EH depending on stage and degree of EH, duration of the disease and cardiovascular risk are presented in tab. 2.

Table 2

**QTc interval duration QTc (x̄, s) during AM ECG in patients with EH depending on stage and degree of EH, duration of the disease and cardiovascular risk**

| Clinical manifestation | Graduation of clinical features | N | P, % | Average QTc, ms | | Maximum QTc, ms | | Minimum QTc, ms | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | x̄ | s | x̄ | s | x̄ | s |
| Stages of EH | I | 12 | 15 | 409 | 13 | 480 | 34 | 371* | 16 |
| | II | 59 | 72 | 423 | 18 | 492 | 30 | 383* | 29 |
| | III | 11 | 13 | 422 | 19 | 464 | 25 | 392* | 21 |
| Degrees of EH | Mild | 42 | 51 | 417* | 17 | 489 | 31 | 381 | 22 |
| | Moderate | 24 | 29 | 421* | 17 | 484 | 30 | 382 | 33 |
| | Severe | 16 | 20 | 430* | 22 | 484 | 35 | 386 | 29 |
| Duration, years | For the first time | 7 | 8 | 418 | 6 | 494 | 32 | 374 | 21 |
| | 0–5 | 31 | 38 | 418 | 18 | 489 | 31 | 381 | 27 |
| | 6–10 | 23 | 28 | 420 | 18 | 474 | 20 | 383 | 26 |
| | >10 | 21 | 26 | 426 | 21 | 494 | 39 | 386 | 30 |
| Cardiovascular risk | Low | 11 | 13 | 422 | 19 | 464 | 25 | 392 | 21 |
| | Moderate | 50 | 61 | 420 | 19 | 488 | 34 | 378 | 29 |
| | High | 13 | 16 | 424 | 18 | 484 | 29 | 386 | 29 |
| | Very high | 11 | 13 | 422 | 19 | 464 | 25 | 392 | 21 |

*Note: N – number of surveys; P – specific gravity; x̄ – arithmetic mean; s – standard deviation; QTc – corrected QT; * – $p < 0,05$ – between QTc values in clinical groups.*

The longest average daily and maximum QTc were recorded in group with EH II stage, minimum was in patients with EH I stage. An increase of average QTc duration was correlated with an increasing degree of hypertension. The longest duration of the maximum and minimum QTc was observed in patients with mild hypertension. Patients with course of the disease more than 10 years had the highest rates of average daily and maximum QTc, patients with EH diagnosed for the first time had maximum and minimum QTc. The duration of average daily QTc is longer in patients with high cardiovascular risk, while the duration of maximum and minimum QTc are longer in patients with mild cardiovascular risk.

QTc interval duration QTc (x̄, s) during AM ECG in patients with EH depending on IHD, HF stage and FK of HF, presence of diabetes mellitus are presented in Table 3.

Table 3

**QTc interval duration QTc ($\bar{x}$, s) during AM ECG in patients with EH depending on IHD, HF stage and FK of HF, presence of diabetes mellitus**

| Clinical manifestation | | Graduation of clinical features | N | P, % | Average QTc, ms | | Maximum QTc, ms | | Minimum QTc, ms | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | $\bar{x}$ | s | $\bar{x}$ | s | $\bar{x}$ | s |
| IHD | | In total | 60 | 73 | 416 | 19 | 478 | 30 | 376 | 28 |
| | | Stable angina | 15 | 18 | 417 | 20 | 475 | 37 | 377 | 29 |
| | | Diffuse cardiosclerosis | 43 | 53 | 424 | 18 | 491 | 26 | 384 | 28 |
| | | Focal cardiosclerosis | 2 | 2 | 425 | 12 | 478 | 20 | 396 | 13 |
| | | Absence of IHD | 22 | 27 | 416 | 17 | 487 | 37 | 382 | 25 |
| CHF | FC | I | 23 | 28 | 425 | 18 | 487 | 24 | 384 | 33 |
| | | II | 33 | 40 | 420 | 19 | 486 | 34 | 379 | 23 |
| | | III | 4 | 5 | 429 | 20 | 484 | 12 | 403 | 26 |
| | Stage | I | 35 | 43 | 425 | 19 | 483 | 31 | 382 | 30 |
| | | II A | 25 | 30 | 420 | 18 | 483 | 31 | 382 | 24 |
| Diabetes mellitus | | DM 2 type | 11 | 13 | 426 | 18 | 484 | 17 | 399 | 19 |
| | | Absence of DM | 71 | 87 | 420 | 18 | 487 | 33 | 381 | 27 |

*Note: N – number of surveys; P – specific gravity; $\bar{x}$ – arithmetic mean; s – standard deviation; QTc – corrected QT; * – p < 0,05 – between QTc values in clinical groups.*

In patients with focal cardiosclerosis the largest was average daily QTc, with diffuse cardiosclerosis (DC) – the maximum QTc and with stable angina – the minimum QTc. The longest duration of average daily QTc was observed in patients with HF FC III, and uniformly the same duration of QTc was observed in patients with FC I, I stage of HF and FC II, IIA stage of HF. The duration of the maximum interval QTc was the largest in patients with I and II FC of HF, and uniformly the same – in patients with FC III and I and IIA stages of HF; the duration of the minimum interval QTc was the least in patients with FC II of HF. The duration of average daily and maximal QTc more often was recorded in patients with DM, and minimal QTc interval – in patients without DM [16].

Student's t-test for independent groups showed that for grouping sign «stages of EH», accurately different at level p < 0,05 is minimal QTc, and for grouping sign «degrees of EH» – minimal QTc. Multifactorial test (MANOVA) confirms that researched effects are significant on level p < 0,05.

In all the above data accurate difference at level p < 0,05 between the average and the maximum QTc; between the average and minimum QTc; between the minimum and the maximum QTc is observed. That's why the corresponding marks are not put anywhere in the tables.

Therefore, obtained results not only confirm a rare probability of short QTc [4–5, 13], but also show presence of prolonged QTc in every patient during ECG AM. Based on the abovementioned it is necessary to use ECG AM in clinical practice to evaluate QTc duration in patients with EH. But such works have not been conducted before. Obviously, specific gravity of prolonged QTc during 24-hours must be the most important, but it requires further study.

**CONCLUSIONS**

1. Average, maximum and minimum QTc are registered in every patient during ECG AM. At the same time the average and minimum QTc are within normal ranges while maximum QTc far exceeds it.

2. The largest duration of maximal QTc have adulthood male patients with obesity III st., with low and high circadian index, with II stage and mild EH, with for the first time diagnosed EH and with EH lasting more than

10 years, with mild cardiovascular risk, with diffuse cardiosclerosis, with I and II FC and I and IIA stage of HF.

3. The presence of critical level of maximum indicators of the QTc duration in each patient with EH demonstrates the need to use ECG AM in its evaluation taking into account the specific gravity per day.

**PROSPECTS FOR FUTURE STUDIES**

The prospect of further research is studying of the relationship between specific gravity of maximum QT min ambulatory ECG monitoring and clinical manifestations in patients with essential hypertension.

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