

Dynamics of QT Interval and QT Dispersion as Predictors of Life-Threatening Arrhythmias in Patients with Oncological Diseases Receiving Cardiotoxic Treatment

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Abstract A clinical and diagnostic study of the frequency and structure of arrhythmias in patients with oncological diseases receiving cardiotoxic chemotherapy was conducted. Electrolyte imbalance, prolongation of the QTc interval, and an increase in QT variance were significantly associated with an increased risk of life-threatening arrhythmias. Active correction of potassium and magnesium levels reduced the frequency of rhythm disturbances, and combined prevention using cardioprotective therapy provided maximum protective effect and prevented the development of clinically significant arrhythmias. The obtained results confirm the feasibility of dynamic monitoring of electrolytes and QT/QTc indicators to improve the safety of antitumor treatment.

Keywords Heart arrhythmias, QT interval, QT dispersion, Chemotherapy, Cancer patients, Electrolyte balance, Hypokalemia, Hypomagnesemia

1. Introduction

Modern advancements in oncology related to the introduction of anthracyclines, tyrosine kinase inhibitors, anti-HER2-preparations, and immuno-oncological therapy have led to a significant increase in the survival rate of cancer patients. At the same time, the expansion of the range of anti-tumor drugs is accompanied by an increase in the frequency of cardiotoxic complications, among which heart rhythm disorders, including potentially life-threatening ventricular arrhythmias, occupy a special place [1,2].

One of the key electro-physiological markers of arrhythmogenic risk is the QT interval and its dispersion (QTd), reflecting the heterogeneity of myocardial repolarization processes. The prolongation of QTc and the increase in QT variance are considered independent predictors of the development of torsade de pointes, polymorphic ventricular tachycardia, and sudden cardiac death [3,4]. Under chemotherapy conditions, these changes can form both due to direct toxic effects on cardiomyocyte ion channels and against the background of electrolyte disturbances and inflammatory damage to the myocardium [5,6].

Dynamic monitoring of QT/QTc and QTd is of particular clinical importance in patients receiving targeted and immuno-oncological therapy, as these drugs are often

associated with subclinical changes in repolarization without a pronounced decrease in myocardial contractility [7,8]. It has been shown that an increase in QT variance can precede the clinical manifestation of arrhythmias and serve as an early diagnostic marker for an unfavorable prognosis [9].

The recommendations of the European Society of Cardiology for CardioOncology emphasize the need for regular monitoring of the QT/QTc interval in oncological patients receiving drugs with proarrhythmogenic potential, however, the issues of clinical interpretation of QT-dispersion dynamics, its prognostic significance, and threshold values remain debatable [10]. This determines the relevance of conducting research aimed at assessing the dynamics of the QT interval and its variance as predictors of life-threatening arrhythmias in patients with oncological diseases receiving cardiotoxic therapy.

The purpose of the study is to assess the dynamics of the QT interval and QT variance as predictors of life-threatening arrhythmias in patients with oncological diseases receiving cardiotoxic anti-tumor therapy, with the aim of early stratification of the arrhythmogenic risk and optimization of preventive measures.

2. Materials and Methods of Research

The study included patients ≥ 18 years old with confirmed oncopathology receiving cardiotoxic chemotherapy. Patients were divided into three groups: 1st group - standard management without preventive electrolyte correction; 2nd

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group - active monitoring and correction of K⁺ and Mg²⁺ levels before each cycle; 3rd group - combined prevention, including electrolyte correction and cardioprotective therapy (β -blockers, ACEI/ARB). All patients underwent a clinical examination, standard ECG registration with an assessment of the QT/QTc interval, and, if necessary, Holter ECG monitoring, echocardiography, as well as laboratory blood electrolyte levels.

The main endpoints of the study were the frequency of electrolyte imbalance disorders, the frequency of heart arrhythmias, and the dynamics of the QTc interval. Statistical processing of the data was carried out using standard methods of variation statistics; the differences were considered statistically significant at $p < 0.05$.

3. Research Results

To assess the prognostic significance of the QTc interval, a comparative analysis of its initial values and dynamics during chemotherapy was conducted in patients without clinically significant arrhythmias (subgroup A) and in patients with registered clinically significant or life-threatening arrhythmias (subgroup B). The QTc assessment was conducted before the start of antitumor treatment and after 2-3 cycles of chemotherapy (Table 1).

Table 1. Dynamics of the QTc interval in patients depending on the development of arrhythmias

QTc indicator, ms	Subgroup A (n=76)	Subgroup B (n=36)	p
Originally	421.6 \pm 18.4	423.9 \pm 19.1	0.48
After 2-3 cycles of CT	434.2 \pm 21.3	462.7 \pm 24.8	<0.001
Elongation QTc >470 ms	6.6%	41.7%	<0.001

The initial values of the QTc interval in both subgroups did not differ statistically significantly ($p=0.48$), which indicates comparable initial electrophysiological status of patients. During chemotherapy in subgroup A, moderate prolongation of QTc was noted, not reaching clinically significant threshold values in most patients.

In subgroup B, the dynamics of QTc was pronounced: after 2-3 cycles of chemotherapy, the average values of QTc significantly exceeded the indicators of subgroup A ($p < 0.001$), and a prolongation of QTc exceeding 470 ms was

registered in 41.7% of patients. The obtained data indicate the high prognostic significance of the dynamic prolongation of QTc as a marker of increased risk of developing life-threatening arrhythmias in oncological patients receiving cardiotoxic therapy.

To assess the prognostic significance of the heterogeneity of myocardial repolarization processes, an analysis of the QT (QTd) interval variance dynamics was conducted in patients without clinically significant arrhythmias (subgroup A) and in patients with registered clinically significant or life-threatening arrhythmias (subgroup B). QTd indicators were assessed initially and after 2-3 cycles of chemotherapy (Table 2).

Table 2. Change in QT (QTd) variance in the studied subgroups

QTd indicator, ms	Subgroup A	Subgroup B	p
Originally	34.8 \pm 6.9	36.2 \pm 7.4	0.32
After 2-3 cycles of CT	41.5 \pm 8.6	58.9 \pm 11.2	<0.001
QTd >60 ms	5.3%	47.2%	<0.001

The initial values of QT variance in the subgroups did not differ statistically significantly ($p=0.32$), indicating a comparable initial state of myocardial repolarization processes. During chemotherapy in patients of subgroup A, a moderate increase in QTd was noted, not exceeding the threshold values in most observed individuals.

In subgroup B, a pronounced and statistically significant increase in QT dispersion was revealed after 2-3 cycles of chemotherapy ($p < 0.001$), while QTd values greater than 60 ms were recorded in almost half of the patients (47.2%). The obtained data indicate the high prognostic significance of increasing QT variance as an early marker of arrhythmogenic risk and emphasize its leading role in predicting life-threatening arrhythmias in oncological patients receiving cardiotoxic therapy.

To assess the impact of various preventive approaches on the development of heart rhythm disturbances, a comparative analysis of the frequency of arrhythmias in patients receiving cardiotoxic chemotherapy was conducted. The frequency of supraventricular and ventricular arrhythmias, prolongation of the QTc interval, as well as clinically significant rhythm disturbances, was compared between the groups of standard management, active electrolyte correction, and combined prevention (Table 3).

Table 3. Frequency of heart rhythm disturbances in the studied groups

Type of arrhythmia	Group 1 - standard management (n=43)	Group 2 - active electrolyte correction (n=38)	Group 3 - Combined Prevention (n=37)	p
Supraventricular extrasystole	39.5%	23.7%	13.5%	0.02
Ventricular extrasystole (\geq Lown II)	25.5%	13.1%	5.4%	<0.01
Paroxysmal tachycardia	9.3%	5.2%	2.7%	0.24
QTc elongation (>470 ms)	18.6%	7.8%	2.7%	<0.01
Clinically significant arrhythmias	11.6%	5.2%	0%	0.03

The results of the analysis of the frequency of arrhythmias showed pronounced differences between the studied groups. In the standard management group, supraventricular extrasystole was detected in 39.5% of patients, and ventricular extrasystole \geq Lown II - in 25.5%, which was the highest indicator among all groups. Elongation of the QTc interval (>470 ms) was noted in 18.6% of patients, and clinically significant arrhythmias requiring changes in treatment tactics or enhanced monitoring were registered in 11.6% of patients.

In the group with active electrolyte correction, a significant decrease in the frequency of rhythm disturbances was observed: supraventricular extrasystole decreased to 23.7%, ventricular extrasystole to 13.1%, and prolongation of QTc was recorded in only 7.8% of patients. The frequency of clinically significant arrhythmias also decreased and amounted to 5.2%.

The most pronounced prophylactic effect was noted in the combined prophylaxis group, where supraventricular arrhythmias were detected in 13.5% of patients, ventricular arrhythmias - in 5.4%, and prolongation of QTc - only in 2.7%. Clinically significant arrhythmias were not registered in this group.

Statistical analysis confirmed significant differences between groups in the frequency of ventricular arrhythmias and the lengthening of the QTc interval ($p < 0.01$), which emphasizes the key role of active correction of electrolyte disorders and cardioprotective therapy in reducing the risk of therapy-induced heart rhythm disorders.

4. Conclusions

The conducted study showed that in patients with oncological diseases receiving cardiotoxic chemotherapy, electrolyte imbalance and changes in myocardial repolarization indicators (prolongation of QTc and increase in QT dispersion) are significant predictors of arrhythmia development. Standard management without preventive measures was associated with the highest frequency of supraventricular and ventricular rhythm disturbances, prolongation of the QTc interval, and clinically significant arrhythmias. Active control and correction of electrolytes significantly reduced the frequency of arrhythmias, while combined prevention

with the inclusion of cardioprotective therapy provided maximum protective effect and practically completely prevented the development of clinically significant rhythm disorders. The obtained data justify the need to implement comprehensive monitoring of electrolytes and QT/QTc parameters in clinical practice to improve the safety of antitumor treatment.

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