

# Electrophysiological Profile of Cardiovascular Disorders in Patients with Acute Leukemias

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**Abstract:** Cardiac rhythm disturbances in patients with oncological or oncohematological diseases may stem not only from the direct cardiotoxicity of anticancer drugs but also from anemia, infectious or inflammatory complications, electrolyte imbalances, neurohumoral activation, and pre-existing cardiovascular disease. Current guidelines classify arrhythmias as a distinct component of cancer therapy-related cardiovascular toxicity and emphasize the need for their proactive detection. [1–4].

To characterize the electrophysiological profile of patients with acute leukemias and to evaluate its role within the complex spectrum of cardiovascular involvement, taking into account clinical symptoms, anemia, echocardiographic parameters, and cardiospecific biomarkers.

**Keywords:** Acute leukemia, arrhythmia, sinus tachycardia, extrasystole, ECG, cardiotoxicity, anemia, troponin, NT-proBNP.

**Introduction:** Cardiovascular complications in patients with malignant diseases represent a heterogeneous group of conditions, including myocardial dysfunction, heart failure, arterial and venous vascular events, arterial hypertension, repolarization abnormalities, and various forms of arrhythmias. The 2022 ESC guidelines on cardio-oncology identify rhythm disturbances as an important component of the spectrum of cardiovascular toxicity associated with anticancer treatment. [1].

The IC-OS international consensus also highlights the need for a standardized approach to diagnosing electrophysiological complications in cancer patients. [2].

Arrhythmogenesis in the context of oncological

diseases is multifactorial in nature. Arrhythmias may be associated with the direct effects of an anticancer drug, structural myocardial damage, ischemia, inflammation, sympathetic activation, metabolic and electrolyte disturbances, infections, or drug-drug interactions [3,4]. Therefore, the detection of a rhythm disturbance in a patient with leukemia requires not only its electrocardiographic classification but also an analysis of the clinical context.

In patients with acute leukemias, this issue is particularly complex. Severe anemia can trigger compensatory tachycardia and increase cardiac output; fever and systemic inflammation enhance sympathetic activation; anti-infective and antiemetic drugs may affect the QT interval; and anthracyclines can exert

both structural and electrophysiological effects on the myocardium. [3–6].

In a meta-analysis of studies on anthracyclines, the use of agents in this class was associated with an increased risk of arrhythmias; an elevated risk of tachycardia and ST-segment/T-wave changes has also been reported [6]. In contemporary studies of patients with acute myeloid leukemia, cardiovascular events—including arrhythmias—remain clinically significant across various types of antileukemic therapy. [7–10].

Most research, however, focuses on heart failure and reduced left ventricular ejection fraction (LVEF). The electrophysiological profile of adult patients with acute leukemias has been studied to a significantly lesser extent. This shaped the focus of the present study, in which ECG changes are examined as a distinct phenotype rather than as a secondary component of overall cardiotoxicity.

#### RESEARCH OBJECTIVE

To characterize the pattern of electrocardiographic abnormalities in patients with acute leukemias and to evaluate their clinical significance in the context of anemia, echocardiographic changes, and elevated cardiac-specific biomarkers. Материалы и методы

The study was conducted at the Republican Specialized Scientific-Practical Medical Center of Hematology under the Ministry of Health of the Republic of Uzbekistan. The analysis included 102 adult patients with acute leukemia. The mean age was  $44.8 \pm 15.9$  years, with a range of 18–78 years. There were 43 men (42.2%) and 59 women (57.8%). Based on a comprehensive clinical and instrumental assessment,

cardiovascular complications were identified in 64 (62.7%) patients, while 38 (37.3%) patients showed no such complications.

All patients underwent a clinical assessment—including the collection of their medical history and a physical examination—as well as a standard 12-lead electrocardiogram and a transthoracic echocardiogram. Laboratory testing included a complete blood count and the measurement of cardiac-specific biomarkers. When interpreting arrhythmias, it was taken into account that in patients with hematologic malignancies, the underlying cause may be multifactorial and should not be automatically attributed to anticancer therapy. [1–4].

The mean hemoglobin level was 86.2 g/L, with a median of 88 g/L, indicating a significant anemic burden within the study cohort. The mean left ventricular ejection fraction (LVEF) was  $55.9 \pm 7.3\%$ ; an LVEF <50% was observed in 14 (13.7%) patients. The median troponin T level was 7.6 ng/L (maximum 276 ng/L), with levels >20 ng/L found in 29 (28.4%) patients. The median NT-proBNP level was 86.3 pg/mL (maximum 3967 pg/mL), with levels >300 pg/mL observed in 26 (25.5%) patients.

Quantitative variables are presented as mean  $\pm$  standard deviation or as a median, depending on their distribution; categorical variables are expressed as absolute numbers and percentages. This study utilizes validated aggregated metrics. Causal associations between specific arrhythmias, hemoglobin levels, biomarkers, and particular treatment regimens were not asserted without individual cross-analysis.

**Table 1. Clinical and cardiological characteristics of the patients examined**

| Indicator                            | Meaning          |
|--------------------------------------|------------------|
| The number of patients               | 102              |
| Age, year                            | $44,8 \pm 15,9$  |
| Age range                            | 18–78            |
| Male                                 | 43 (42,2%)       |
| Female                               | 59 (57,8%)       |
| Cardiovascular complications         | 64 (62,7%)       |
| Without cardiovascular complications | 38 (37,3%)       |
| Hemoglobin, mean                     | 86,2 г/л         |
| LVEF                                 | $55,9 \pm 7,3\%$ |
| LVEF <50%                            | 14 (13,7%)       |
| Troponin T >20 ng/L                  | 29 (28,4%)       |
| NT-proBNP >300 pg/mL                 | 26 (25,5%)       |

## RESULTS

### 1. Clinical manifestations

Palpitations were reported by 40 (39.2%) patients, chest pain or discomfort by 40 (39.2%), and dyspnea by 19 (18.6%). A comparison of these complaints with ECG data reveals that the subjective sensation of palpitations occurred somewhat more frequently than documented sinus tachycardia (39.2% vs. 32.4%). This is to be expected, as the sensation of palpitations is not

| EKG-sign                                  | n  | %    |
|-------------------------------------------|----|------|
| Sinus tachycardia                         | 33 | 32,4 |
| ECG signs of left ventricular hypertrophy | 28 | 27,5 |
| Ventricular extrasystole                  | 12 | 11,8 |
| Supraventricular extrasystole             | 8  | 7,8  |
| T-wave inversion                          | 4  | 3,9  |
| Ischemic changes                          | 2  | 2,0  |

The most frequent electrocardiographic phenomenon was sinus tachycardia, observed in 33 cases (32.4%). The second most common finding consisted of ECG signs of left ventricular (LV) hypertrophy, present in 28 cases (27.5%). Ventricular extrasystoles were identified in 12 patients (11.8%), while supraventricular extrasystoles were found in 8 patients (7.8%).

Thus, ventricular extrasystoles occurred approximately 1.5 times more frequently than supraventricular extrasystoles ( $11.8/7.8 \approx 1.51$ ). Repolarization abnormalities, specifically T-wave inversion, were noted in 4 patients (3.9%), and ischemic changes were observed in 2 patients (2.0%).

### 3. Sinus tachycardia as the dominant electrophysiological phenotype.

Sinus tachycardia was observed in nearly one in three patients. However, this finding requires a highly cautious interpretation. The mean hemoglobin level in the cohort was 86.2 g/L, indicating a significant anemic burden. In the context of anemia, an increased heart rate serves as a compensatory mechanism to maintain oxygen delivery to the tissues.

In addition to anemia, potential triggers for sinus tachycardia in this population include fever, infection, dehydration, pain, emotional stress, systemic inflammation, and the effects of medications. International guidelines recommend that when

synonymous with any specific rhythm disturbance.

Similarly, dyspnea cannot be considered a specific sign of heart failure; in patients with acute leukemia, it may be caused by anemia, infection, pulmonary involvement, or other factors. Therefore, clinical complaints in this patient population should be interpreted only in conjunction with ECG findings, echocardiography, and laboratory data.

### 2. Pattern of electrocardiographic changes

arrhythmias occur in cancer patients, clinicians should actively investigate reversible causes, such as electrolyte and metabolic disturbances, concomitant medications, and infectious conditions [3,4].

Therefore, in the present study, sinus tachycardia is viewed primarily as a marker of increased hemodynamic and neurohumoral stress, rather than as independent evidence of drug-induced cardiotoxicity.

### 4. Ventricular and supraventricular ectopic activity

Ventricular extrasystole was detected in 12 (11.8%), supraventricular - in 8 (7.8%) patients. Unlike sinus tachycardia, ectopic activity represents a more specific electrophysiological phenotype, but its clinical significance depends on the frequency, symptoms, complex morphology, duration of episodes and the presence of structural heart disease.

In cancer patients, arrhythmias can develop due to the direct effects of therapy, ischemia, myocardial damage, QT-prolonging drugs, electrolyte disturbances and systemic inflammation [3,4]. A meta-analysis of 26,891 patients showed a statistically significant increase in the overall risk of arrhythmias with anthracyclines, as well as an increased risk of tachycardia and conduction disorders [6]. Another systematic analysis also demonstrated an increased risk of arrhythmias and supraventricular disorders with anthracyclines [5].

### 5. ECG and the structural-functional state of the

## myocardium

The mean left ventricular ejection fraction (LVEF) was  $55.9 \pm 7.3\%$ , with an LVEF  $<50\%$  observed in 14 (13.7%) patients. The prevalence of sinus tachycardia (32.4%) was 2.36 times higher than the prevalence of an LVEF  $<50\%$ , while the frequency of ventricular extrasystoles (11.8%) was of a similar order of magnitude to the incidence of reduced LVEF.

These data do not prove that arrhythmias precede systolic dysfunction in any given patient; however, they do show that electrophysiological disturbances

constitute a distinct layer of cardiovascular pathology that is not captured by left ventricular ejection fraction (LVEF) alone.

## 6. ECG and cardiac-specific biomarkers

Troponin T  $>20$  ng/L was detected in 29 (28.4%) patients, and NT-proBNP  $>300$  pg/mL in 26 (25.5%). The frequency of elevated levels for both types of biomarkers was similar to the prevalence of sinus tachycardia (32.4%) but significantly higher than the prevalence of an LVEF  $<50\%$  (13.7%).

| Cardiac profile component                         | n  | %    |
|---------------------------------------------------|----|------|
| Sinus tachycardia                                 | 33 | 32,4 |
| Troponin T $>20$ ng/L                             | 29 | 28,4 |
| NT-proBNP $>300$ pg/mL                            | 26 | 25,5 |
| ECG signs of left ventricular hypertrophy (LVH)   | 28 | 27,5 |
| Left ventricular ejection fraction (LVEF) $<50\%$ | 14 | 13,7 |
| Ventricular extrasystoles                         | 12 | 11,8 |
| Supraventricular extrasystoles                    | 8  | 7,8  |

Taken together, these results justify the need for a simultaneous analysis of three independent domains: electrical (ECG), biochemical (troponin/NT-proBNP), and mechanical (echocardiography). This multimodal

approach aligns with the current cardio-oncology strategy, which focuses on the early detection of subclinical toxicity [1, 11].

## 7. Proposed electrophysiological stratification

| Level | Characteristic                                     | Clinical interpretation                                                   |
|-------|----------------------------------------------------|---------------------------------------------------------------------------|
| A     | No significant ECG changes                         | baseline electrophysiological profile                                     |
| B     | Isolated sinus tachycardia                         | screening for anemia, infection, dehydration, and other reversible causes |
| C     | Supraventricular/ventricular ectopy                | in-depth assessment of triggers and structural heart disease              |
| D     | ECG changes + $\uparrow$ TnT/ $\uparrow$ NT-proBNP | high index of suspicion for myocardial injury                             |
| E     | ECG changes + biomarkers + LVEF $<50\%$            | combined high-risk cardiac phenotype                                      |

The proposed classification is intended for research purposes and does not replace the ESC/IC-OS definitions. Its objective is to systematize the electrophysiological heterogeneity among patients with acute leukemias and to identify groups that require varying levels of monitoring intensity.

## DISCUSSION

This study demonstrates that electrophysiological disturbances represent a significant component of the cardiovascular alterations observed in patients with acute leukemias. The most common finding was sinus tachycardia (32.4%), while ventricular and

supraventricular extrasystoles were detected in 11.8% and 7.8% of cases, respectively.

The findings are consistent with the current understanding of arrhythmogenic risk in oncology. Gawlik et al. emphasize that both the tumor process itself and anticancer therapy can contribute to the development of atrial and ventricular arrhythmias, with traditional risk factors interacting with cancer-specific triggers [3]. A consensus document on acute cardiovascular complications in cancer patients identifies potential mechanisms including sympathetic activation, inflammation, metabolic and electrolyte disturbances, drug-drug interactions, and the direct effects of anticancer therapy [4].

Anthracycline therapy, traditionally used for acute myeloid leukemia, warrants particular attention. A systematic review and meta-analysis have shown that anthracyclines are associated with an increased risk of arrhythmias (RR 1.58; 95% CI 1.41–1.76), tachycardia, and conduction disturbances [6]. A broader meta-analysis also demonstrated an approximately 90% increase in the risk of arrhythmias, with the risk of supraventricular arrhythmias more than doubling [5]. These findings underscore the need for regular ECG monitoring in high-risk groups.

At the same time, electrophysiological changes in leukemia cannot be attributed solely to anthracyclines. Contemporary research on AML indicates that cardiovascular events also occur with other treatment strategies. In a study of patients receiving venetoclax in combination with hypomethylating agents, significant cardiac events were documented—a finding that underscores the need for monitoring, even outside the context of the classic anthracycline-related scenario [9, 10].

In a study of 571 patients with newly diagnosed AML, the cumulative incidence of non-fatal cardiac events was high, with complications including arrhythmias and QTc prolongation; severe cardiac events were associated with poorer survival [7]. A 2025 systematic review also highlights the broad spectrum of cardiovascular toxicity in AML and the need for early detection using biomarkers and multimodal imaging [8].

A novel aspect of this study is its focus on the relationship between electrophysiological changes and

the burden of anemia. A mean hemoglobin level of 86.2 g/L suggests that a significant proportion of the observed tachycardia may be compensatory in nature. Consequently, including all instances of sinus tachycardia in a composite endpoint of "cardiotoxicity"—without accounting for anemia, infection, or other reversible causes—could lead to overdiagnosis.

The relationship between the electrical, biochemical, and mechanical domains is also of practical importance. Sinus tachycardia was observed in 32.4% of cases, elevated troponin T in 28.4%, and elevated NT-proBNP in 25.5%, while a left ventricular ejection fraction (LVEF) <50% was found in 13.7%. This does not imply that these groups are identical, but it does demonstrate that a traditional assessment based solely on LVEF fails to capture the full spectrum of cardiovascular alterations.

Current ESC guidelines recommend personalized risk assessment and dynamic monitoring—incorporating clinical evaluation, ECG, biomarkers, and imaging—tailored to the type of therapy and baseline risk [1,11]. For patients with acute leukemias, this approach is particularly warranted due to the rapid evolution of their clinical status and the presence of multiple potential arrhythmogenic factors.

### Scientific Novelty

In contrast to previous studies focusing primarily on genetic predictors or structural and functional cardiotoxicity, the present study examines the electrophysiological component as a distinct clinical phenotype. It has been proposed to distinguish between isolated sinus tachycardia, ectopic activity and a combined ECG-biomarker phenotype.

The fundamental point is to reject the automatic interpretation of sinus tachycardia as cardiotoxicity. With an average hemoglobin of 86.2 g/L, tachycardia should be assessed taking into account anemia and other reversible causes. This increases the specificity of cardio-oncological diagnosis and reduces the risk of overdiagnosis of drug-induced heart damage.

### Practical Implications

For clinical practice, the following sequential approach is proposed. When tachycardia or ectopic activity is detected in a patient with acute leukemia, it is necessary to simultaneously evaluate hemoglobin

levels, signs of infection, electrolyte status, and concomitant medications, as well as to assess the QTc interval. If the abnormalities persist or are clinically significant, cardiac-specific biomarkers should be measured and an echocardiogram performed. This algorithm aligns with the principle of identifying reversible causes of arrhythmia and conducting a multimodal risk assessment [1,3,4].

Patients presenting with a combination of ECG changes, elevated troponin/NT-proBNP levels, and structural or functional abnormalities on echocardiography should be considered a high-risk group in the context of cardio-oncology and require more intensive longitudinal monitoring.

## CONCLUSIONS

1. Electrophysiological changes are a frequent component of the cardiovascular profile in patients with acute leukemia.
2. Sinus tachycardia was observed in 33 out of 102 (32.4%) patients, making it the most common ECG finding.
3. Ventricular extrasystoles were identified in 12 (11.8%) patients, supraventricular extrasystoles in 8 (7.8%), T-wave inversion in 4 (3.9%), and ischemic changes in 2 (2.0%).
4. Palpitations were reported by 40 (39.2%) patients; however, subjective symptoms should not be equated with documented arrhythmia.
5. Given a mean hemoglobin level of 86.2 g/L, sinus tachycardia should be interpreted in the context of significant anemia and other reversible causes, rather than automatically attributed to drug-induced cardiotoxicity.
6. The prevalence of sinus tachycardia (32.4%), elevated troponin T (28.4%), and elevated NT-proBNP (25.5%) was higher than that of a left ventricular ejection fraction (LVEF) <50% (13.7%), which confirms the multifactorial nature of cardiovascular involvement.
7. For risk stratification in patients with acute leukemia, an integrated assessment—incorporating ECG findings, hemoglobin levels, clinical triggers, troponin, NT-proBNP, and echocardiographic parameters—is advisable.
8. A promising avenue for future research involves the

individual correlation of arrhythmias with therapeutic regimens, biomarker dynamics, electrolyte imbalances, and molecular-genetic factors.

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