Kirichenko Yu. Yu., Varzieva V. G., Shestakova K. M., Chernichkina A. D., Palienko A. V., Budushcheva O. I., Khabarova N. V., Baskhanova S. N., Belenkov Yu. N., Ilgisonis I. S., Appolonova S. A.
Sechenov First Moscow State Medical University

Metabolomic profiling as a possible new method for predicting cardiovascular toxicity of chemotherapy: a pilot single-center study

Aim To determine the array of metabolomic profiles and structural and functional parameters of the vascular wall associated with the risk of cardiovascular toxicity of antitumor therapy (ATT) in oncohematological patients.

Material and methods This study included 59 patients, among them 34 patients with lymphomas (non-Hodgkin and Hodgkin lymphoma) and 25 with multiple myeloma. Before and after 3 courses of ATT (anthracyclines, proteasome inhibitors), finger photoplethysmography and transthoracic echocardiography were performed as well as metabolomic profiling (98 metabolites) by high-performance liquid chromatography in combination with tandem mass spectrometry. Statistical analysis of the results included parametric and nonparametric tests, logistic regression, and cross-validation.

Results The study showed that even before the initiation of ATT, cancer patients had signs of endothelial dysfunction and increased vascular wall stiffness (increased aSI, RI, and IO indices), which significantly worsened after the specific treatment. Metabolomic profiling identified a set of metabolites associated with the risk of cardiovascular toxicity, including increased concentrations of amino acids (asparagine, serine, glutamate, glutamine, taurine, citrulline), short-chain acylcarnitines (C18:1-OH-carnitine, C16:1-OH-carnitine, C14OH-carnitine, C2 carnitine), choline metabolism intermediates (TMAO, dimethylglycine, choline), tryptophan metabolites (hydroxyindoleacetic acid, kynurenic acid). Additionally, a logistic regression model was developed based on the analysis of the metabolomic profile, which showed a high prognostic power (AUC = 0.84) for predicting cardiovascular toxicity of ATT.

Conclusion The study identified key metabolites and structural and functional parameters of blood vessels that allow detection of an increased risk of cardiovascular complications of ATT in patients with lymphomas and multiple myeloma before the initiation of a specific treatment. Increased concentrations of amino acids, acylcarnitines, and choline metabolites may serve as an additional risk factor for the onset/progression of cardiovascular complications. The proposed integrative approach, including both metabolomic profiling and non-invasive assessment of the vascular wall condition, opens broad prospects for personalized cardioprotection of cancer patients and more accurate monitoring of the cardiovascular status during ATT.

Keywords Cardiotoxicity; vascular toxicity; oncohematology; metabolomic profiling; endothelial dysfunction; prevention of cardiovascular complications

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Corresponding author Kirichenko Yu. Yu. E-mail: kataraza@yandex.ru

Introduction

Over the past decades, cardiovascular (CV) pathology and oncological diseases have consistently dominated in the structure of mortality and morbidity among the world population [1, 2]. According to international and Russian epidemiological data, in the coming decades, the incidence of malignant neoplasms (MN) will grow. Thus, the need of the general population for antitumor therapy (ATT) in the coming years will increase by 53%. According to reports of 2023, the incidence of MN of lymphoid and hematopoietic tissue in the Russian Federation amounts about 5% of all oncological pa-

thology [3]. The most common tumors are non-Hodgkin's lymphoma (NHL), Hodgkin's lymphoma (HL), and multiple myeloma (MM) [3].

Current combinations of effective ATT significantly increase the time to disease progression and overall life expectancy [4]. Unfortunately, despite the proven effectiveness of chemotherapy, some predisposed individuals may develop severe, even life-threatening, complications, primarily CV ones (left ventricular (LV) systolic dysfunction, arterial hypertension (AH), arrhythmias and conduction disorders, thrombosis and embolism, ischemic events, etc.) [5, 6]. For example, in the USA in 2019, about 16.5 million patients faced various manifestations of CV toxicity (CVT) of ATT, and by 2040, their number is expected to increase to 26 million [7].

The term "vasculotoxicity" refers to vascular and metabolic disorders that develop as a result of either the oncological process itself or as side effects of ATT. The array of vasculotoxic manifestations is diverse: strokes, ischemic attacks, acute and chronic coronary syndromes, coronary and peripheral vasoreactivity, Raynaud's phenomenon, etc. [5, 6]. Vasculotoxicity is mediated primarily by severe endothelial dysfunction (ED) with subsequent vascular wall remodeling at all levels of the vasculature, including the microcirculation [8]. This initiates/aggravates the severity of myocardial damage [9]. ED has been demonstrated to be the first stage in the development of CV pathology and irreversible progression of heart diseases [10].

In recent years, numerous studies have been conducted to find additional risk factors for the progression of CV diseases (CVDs) [11, 12]. Much attention is paid to the group of "omics" sciences engaged in the systemic investigation of biological objects. One of the important omics components is metabolomics, a science that studies the end products of cell metabolism. Metabolomic profile is a set of endogenous metabolites that reflects the current phenotype of a person, with due regard for possible disorders and individual characteristics of the proteome, genome or transcriptome, and characterizes the individual index of biochemical processes.

There are few reports of the search for metabolomic predictors of CVDs associated with ATT. Thus, the search for early markers of future ATT vasculotoxicity is a relevant and important scientific problem in cardio-oncology in particular, and in cardiology in general. Solving this problem can lead to a deeper insight into the biology of blood vessels and myocardium, as well as the development of new individual therapeutic strategies to reduce the risk of CV complications (CVC) in cancer patients.

This pilot study is the initial part of a project for exploring the potential of using omics sciences to predict and identify early CV toxicity of ATT.

Aim

To determine the spectrum of metabolomic profiles and structural and functional parameters of the vascular wall related with the risk of ATT CVT in oncohematological patients.

Material and methods

A total of 59 people took part in the study, including 34 patients with newly diagnosed NHL and HL and 25 patients with MM.

The *inclusion criteria* for the study were the age of patients (men and women) of 18-75 years; newly diagnosed NHL, HL and MM; scheduled chemotherapy with drugs from the anthracycline antibiotic (AA) group and proteasome inhibitors (PI).

All patients signed a voluntary informed consent for participation in the study. Verification of the hematological diagnosis was performed in accordance with the 2023 Hodgkin's Lymphoma, 2022 Non-Hodgkin's Lymphomas, and 2022 Multiple Myeloma Clinical Guidelines of the Ministry of Health of Russia.

The *exclusion criteria* were the age under 18 and over 75 years, acute forms of ischemic heart disease (IHD), decompensated concomitant diseases of other organs and systems, autoimmune diseases, mental diseases, alcoholism, drug addiction, pregnancy, as well as refusal to further participate in the study.

Distribution by stages of the cancer disease was as follows: for lymphomas (according to Ann-Arbor): stage I, 4 (12%) patients, stage II, 8 (23%), stage III, 3 (9%), and stage IV, 19 (56%); for MM (according to ISS): stage II, 11 (44%) patients, and stage III, 14 (56%).

The study was conducted in accordance with the principles of the Declaration of Helsinki. The study was approved by the local ethics committee of the Sechenov University. All included patients signed the voluntary informed consent.

The clinical characteristics of the patients included in the study are presented in Table 1.

The choice of this particular cohort of patients was due to the fact that, according to modern data, drugs from the AA (doxorubicin, idarubicin, epirubicin) and PI groups have a greater cardio- and vasculotoxicity (80-90% of cases for AA, 2-25% for PI) manifested in the form of various acute CVCs (isch-

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Table 1. Clinical characteristics of study patients (n=59)

Parameter	Value
Age, years (mean±SD)	56.36±15.74
Females, n (%)	34 (56.7)
Cadiovascular diseases and their risk factors, n (%)	
Smoking	12 (20)
Dyslipidemia	30 (51)
Diabetes mellitus	8 (14)
AH	24 (41)
HF at baseline	9 (15)
IHD at baseline	6 (10)
Cardiac therapy at baseline, n (%)	
ACE inhibitor/ARB*	22 (37)
BB*	22 (37)
Statins*	19 (32)
Hypoglycemic drugs	6 (10)
Antiplatelet drugs	10 (17)
Anticoagulants	12 (20)
Calcium antagonists	12 (20)
Major laboratory and instrumental test results	
LV EF, % (Me [Q1; Q3])	62 [59; 64]
Positive NP, n (%) (NT-proBNP >125 pg/ml; BNP >35 pg/ml)	4 (7)
Positive troponin I, n (%) (>34.2 pg/ml)	2 (34)

*drug with documented cardioprotective effect. AH, arterial hypertension; HF, heart failure; IHD, ischemic heart disease; ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blockers; BB, beta-blockers; LV EF, left ventricular ejection fraction; NP, natriuretic peptide.

emia, acute myocardial infarction, acute cerebrovascular disease, AH, thrombosis in various locations), as well as the progression of long-term asymptomatic LV dysfunction [6, 9].

To assess the specific impact of ATT on the structural and functional state of the CV system (CVS) (myocardium, arterial wall at different levels of the vasculature), as well as the metabolomic profile, the following studies were performed in all patients: blood sampling for metabolomic analysis, electrocardiography (ECG), transthoracic echocardiography (EchoCG), 24-hour ECG monitoring, and laser finger photoplethysmography (PPG) (Angioscan-01, Angioscan, Russia) before and after three courses of specific therapy (3-4 months). All oncohematological patients received recommended treatment, including AA (doxorubicin, idarubicin, epirubicin) and PI (bortezomib).

During the PPG, a contour analysis of the pulse wave propagation velocity was performed. The following structural parameters were assessed: pulse rate, stiffness index of large conducting arteries (aSI), and reflection index (RI) of small muscular arteries. To determine the functional state of the endothelium, a reactive hyperemia test was performed. The test result was assessed by the increase in the amplitude of pulse waves on the brachial artery (occlusion index, OI) after its occlusion for 5 min with a sphygmomanometer, pulse wave delay time, or by the phase shift (PS) value.

The targeted analysis of blood plasma included the quantitative measurement of 98 endogenous compounds by high-performance liquid chromatography coupled with tandem mass spectrometry (HPLC-MS/MS).

Metabolomic profiling of the metabolite panel was performed by chromatography-mass spectrometric analysis using an Agilent 1200 high-performance liquid chromatograph coupled with an Agilent 6450C tandem mass spectrometer (Agilent Technologies, USA). Primary data were processed with a MassHunter software (Agilent Technologies, USA).

Statistical analysis was performed with a StatTech v.4.7.2 software (StatTech LLC, Russia). The data are presented as the median (Me) and [25th percentile; 75th percentile] for abnormal distribution, or as the arithmetic mean (M) and standard deviation (SD) for normal distribution. Statistically significant differences between the groups were determined by the nonparametric Wilcoxon test. Differences were considered statistically significant at $p<0.05$.

Correlation analysis was performed by the Spearman rank correlation method; the values of the correlation coefficient module greater than 0.3 were taken for the analysis.

The coefficients of the logistic regression model were calculated in the Python programming language using the Scikit-learn library. Due to the imbalance of the classes, the Random Oversampling method was used for the training sample. The quality of the model was assessed by the 20-fold cross-validation.

Results

Baseline cardio-oncological risk and cardiovascular toxic effects of antitumor treatment

Based on stratification scales for the assessment of the baseline cardio-oncological risk (2022 European Society of Cardiology Guidelines [6]), 24 patients were classified as a low-risk group, 17 as an intermediate risk group, 12 as a high-risk group, and 6 as a very high-risk group.

Signs of various types of CVT were found in 15 patients; 8 of them had LV myocardial dysfunction (symp-

tomatic in 3, asymptomatic in 5), four had AH, two had arrhythmia, and one had vasculotoxicity in the form of pulmonary embolism. All patients with documented CVT were prescribed optimal cardiac therapy in consistency with the CVT nosology.

Dynamics of the structural and functional state of the vascular wall, including microcirculation, in oncohematological patients

The study showed that even before ATT, oncological patients had structural and functional disorders at the level of large and small blood vessels: increased aSI and RI along with decreased OI and PS (Table 2). The correlation analysis determined significant direct strong associations between aSI and RI and the number of atrial extrasystoles (r=0.75; p<0.05 for both).

After the courses of specific therapy, all the studied parameters of vascular wall remodeling were significantly impaired as evidenced by a statistically significant increase in the aSI and RI by 13% and 9%, respectively (p<0.05 for both) and a decrease in the OI by 19% (p<0.002; see Table 2).

The correlation analysis determined moderate/strong associations between the parameters of structural and functional vascular disorders (aSI, RI, OI) and the age of patients (r=0.611; r=0.604; and r=–0.353 for age and aSI, RI, and OI, respectively; p<0.001 for all).

In order to find the most accurate structural and functional predictors of ATT CVT, patients were divided into two subgroups: with CVT and without signs of CVT (Table 3). According to the obtained results, no difference was found between the above parameters before the ATT courses in either subgroup.

Dynamics of intracardiac hemodynamic parameters in study patients

According to data of transthoracic EchoCG, no significant changes were found before and after the ATT courses in the major parameters, including the dimensions and volumes of the heart chambers, LV systolic and diastolic function, and myocardial wall thickness (p>0.05 for all comparisons). The absence of changes in intracardiac parameters can be apparently explained by the short observation period, as well as the use of cardioprotective drugs by some patients.

Results of metabolomic analysis in the study groups

Metabolomic analysis and determination of metabolomic predictors of CVD associated with ATT were also performed in two subgroups, with and without signs of CVT during the treatment. Targeted metabolomic profiling included quantitative determination of 98 endogenous metabolites.

Targeted metabolomic profiling revealed significant differences between the subgroups with and without CVT. Patients with signs of CVT associated with ATT showed statistically significant increases in amino acids, acylcarnitines, and choline derivatives that characterize chronic systemic inflammation, oxidative stress, and accelerated development of atherosclerosis and CVD (IHD, heart failure). Table 4 presents significantly different metabolites and indicates their chemical class and

Table 2. Parameters of structural and functional state of the vascular wall during the study

Parameter	Main group (n=59)		p*
	Before ATT courses	After ATT courses	
aSI, m/s (normal <8 m/s)	9.26 [8.55; 9.98]	10.44 [9.69; 11.18]	<0.001
RI, % (normal <30%)	34 [24.9; 38.8]	37 [31.3; 48.4]	0.032
PS, ms (normal >10 ms)	7.8 [6.2; 9.6]	7.2 [5.8; 9.8]	0.2
OI (normal >1.8)	1.6 [1.4; 1.8]	1.3 [1.2; 1.7]	0.002

Data are presented as Me [25th percentile; 75th percentile]. p*, significance of intragroup differences determined with the Wilcoxon test.
ATT, antitumor therapy; aSI, arterial stiffness index; RI, reflection index; PS, phase shift; OI, occlusion index by amplitude.

Table 3. Parameters of structural and functional state of the vascular wall before and after ATT depending on presence/absence of CVT

Parameter	Without CVT	With signs of CVT	p
aSI, m/s (normal <8 m/s)	9.2 [7.9; 10.3]	9.2 [8; 10.2]	>0.05
RI, % (normal <30%)	34.25 [25; 41]	35 [25; 41]	>0.05
PS, ms (normal >10 мс)	7.55 [5.9; 9.4]	7.5 [6; 9.5]	>0.05
OI (normal >1.8)	1.5 [1.3; 1.83]	1.3 [1.2; 1.8]	>0.05

Data are presented as Me [25th percentile; 75th percentile]. ATT, antitumor therapy; CVT, cardiovascular toxicity; aSI, arterial stiffness index; RI, reflection index; PS, phase shift; OI, occlusion index by amplitude.

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Table 4. Significantly different metabolites in groups with and without CVT

Parameter	Without CVT	With signs of CVT	Class	p	ROC AUC
Pantothenic acid	0.16±0.06	0.21±0.04	Water-soluble vitamins, nucleosides [systemic inflammation arterial hypertension]	<0.01	0.52
Cytidine	0.37±0.005	0.38±0.007		<0.001	0.58
Adenosine	0.22±0.01	0.23+0.01		<0.05	0.52
TMAO	2.63±2.9	4.48±2.7	Choline metabolism [atherosclerosis, progression of CVDs]	<0.05	0.67
DMG	0.38±0.07	0.47±0.12		<0.05	0.68
Choline	18.97±3.5	23.77±5.9		<0.05	0.72
Asparagine	23.75±5.0	27.95±5.1	Amino acid metabolism [oxidative stress, systemic inflammation, atherosclerosis]	<0.05	0.65
Serine	70.012±15.4	88.33±25.2		<0.05	0.60
Glutamate	102.53±41.8	145.14±57.1		<0.05	0.65
Glutamine	252.83±48.4	292.60±59.8		<0.05	0.63
Taurine	21.14±5.1	28.83±7.8		<0.01	0.69
Citrulline	19.80±5.6	24.40±7.5		<0.05	0.69
Kynurenic acid	0.044±0.01	0.056±0.02	Tryptophan metabolism [inflammation, progression of oncological disease]	<0.05	0.50
HIAA	0.069±0.05	0.094±0.03		<0.05	0.53
C18:1 OH-carnitine	0.0013±0.0007	0.0024±0.001	Acylcarnitines [oxidative stress, progression of CVD]	<0.05	0.51
C16:1 OH- carnitine	0.00079±0.0003	0.0015±0.001		<0.05	0.61
C14OH- carnitine	0.0022±0.0007	0.0036±0.002		<0.05	0.47
C2- carnitine	8.034±3.8	9.786±1.94		<0.05	0.58

Data are presented as mean ± standard deviation; CVT, cardiovascular toxicity; TMAO, trimethylamine oxide; DMG, dimethylglycine; CVD, cardiovascular disease; HIIA, hydroxyindoleacetic acid.

participation in the stages of the CV continuum, the directions of changes in the CVT group, the p value, and the area under the error curve.

According to the study results, the prognostic ability of the identified metabolites expressed as the area under the ROC curve is relatively low [0.50; 0.72]. At the same time, the logistic regression model, that takes into account the linear combination of metabolites, combines them into an equation (Formula 1) for calculating the probability of an unfavorable outcome (development of CVT). Despite the use of the linear combination of features, the application of sigmoid in the logistic regression method makes it possible to model nonlinear dependencies between features. The prognostic capacity of the trained logistic regression model, that takes into account the combination of absolute concentrations of fourteen metabolites (Supplementary Materials), was 0.84, which was higher than when using individual metabolomic markers (Fig. 1).

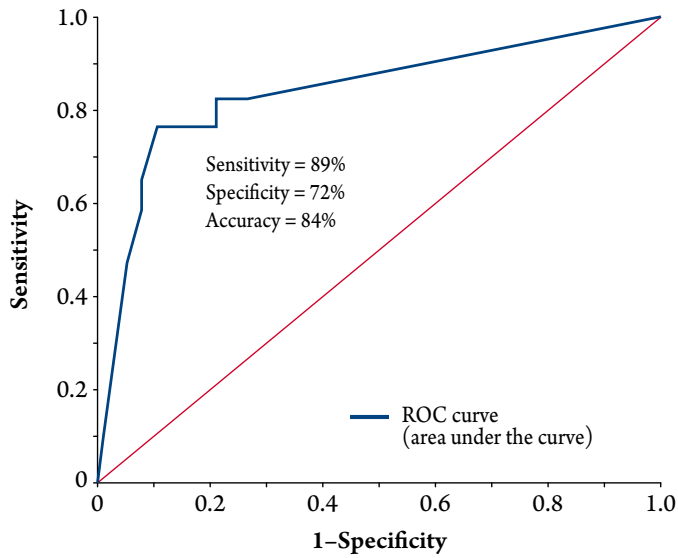
Based on this model, we calculated the coefficients of the logistic regression equation to compute the probability of CVT occurrence (Supplementary Materials). Thus, the probability of the presence of pathology is calculated Formula 1:

$$P(y=1 \mid X)=\frac{1}{1+e^{-z}} \qquad \text{(Formula 1)},$$

where: $P(y = 1 \mid X)$ is the probability that the target variable y is equal to 1 with the predetermined concentrations of metabolites X; e is the base of the natural logarithm (~2.71828); and z is a linear combination of metabolites calculated as:

$$z = \beta_0 + \beta_1 \times X_1 + \beta_2 \times X_2 + \ldots + \beta_{14} \times X_{14} \qquad \text{(Formula 2)},$$

Figure 1. ROC curve of the logistic regression model



The trained logistic regression model allows calculating the probability of cardiovascular toxicity of antitumor therapy with a high prognostic accuracy of 84%.

Table 5. Correlation analysis of the metabolomic profile and structural and functional parameters of the vascular wall in oncohematological patients after ATT

Metabolite	aSI	RI	OI	PS
5 Hydroxytryptophan	0.38	–	–	–
Anthranilic acid	–	–	–	0.39
Kynurenic acid	0.35	0.49	–	–
Indole-3 acetic acid	0.43	0.32	–	–
Indole-3 lactic acid	–	–	–	-0.34
Xanthurenic acid	0.39	–	–	–
Serotonin	–	–	–	0.59
Melatonin	-0.32	–	–	–
ADMA	0.46	–	–	–
SDMA	0.44	–	–	0.37
C16 OH-carnitine	0.38	–	–	–
C18:1 carnitine	–	–	–	-0.33
C5 carnitine	–	–	–	-0.31
C5 DC- carnitine	–	–	–	0.34
Betain	0.35	–	–	–
Riboflavin	0.33	–	–	-0.41
Cytidine	–	–	–0,32	–
Taurine	–	–	–	0.63
Uridine	0.38	–	–	–
Alanine	0.37	–	–	–
Glutamate	–	–	–	0.39
Glycine	–	–	–	0.40
Histidine	0.36	–	–	–
Tyrosine	0.37	–	–	–
Lysine	0.39	–	–	-0.32
Serine	–	–	–	0.37
Phenylalanine	–	0,43	–	–
NMMA	–	–	–	0.35

ATT, antitumor therapy; ADMA, asymmetric dimethylarginine; SDMA, symmetric dimethylarginine; NMMA, N-monomethylarginine.

where: β_0=0 is the free term (intercept); β_1, β_2,…, β_{14} are regression coefficients for the respective metabolites X_1, X_2,…, X_{14} presented in the Supplementary Materials.

The calculated cut-off value of the classification model was 0.91.

In addition, correlations were determined for the metabolomic profiles before the start of specific therapy and the vascular wall parameters after chemotherapy (Table 5).

The correlation analysis showed that the metabolomic profile is largely interconnected with aSI and PS (structural and functional changes in large vessels). Thus, a moderate positive correlation was found between aSI and symmetric/asymmetric dimethylarginine, several essential amino acids and tryptophan breakdown metabolites. At the same time, a close positive correlation was observed for serotonin and taurine with the PS, as well as a moderate negative correlation for the PS with acylcarnitines (C5- and C18-1 carnitine).

Discussion

This study for the first time comprehensively assessed the impact of chemotherapeutic drugs (treatments including AA or IP) on the structural and functional state of blood vessels of various diameters, including microcirculation, the status of the CV system, and the metabolic profile in oncohematological patients. Also, correlations were assessed between the quantitative characteristics of the metabolome and the severity of structural and functional disorders in the blood vessels. An "explainable" machine learning model was trained using the logistic regression algorithm, which allows predicting with a relatively high robustness the likelihood of developing CVT based on the patient's metabolic profile before the initiation of ATT.

Noteworthy, we did not find in modern literature any prototypes for such a comprehensive study of the significance of changes in the metabolic profile and subsequent structural and functional changes in the vascular wall at different levels. In the Russian Federation, the only center that works in this area is the Scientific and Practical Cardio-Oncology Center of the Sechenov University.

According to the study results, structural and functional disorders of the vascular wall are detected in oncohematological patients even before the ATT treatment, and significantly worsen after the treatment.

In the examination of pretreatment metabolomic profiles, the CVT subgroup showed significant increases in a number of amino acids, choline and carnitine metabolism intermediates. These endogenous metabolites are known to be responsible for systemic inflammation, ED, and oxidative stress [13-18].

A special role in the development of AAT CVT belongs to the disturbance of energy metabolism. The cardiomyocyte energy metabolism is known to largely determine the myocardial contractility by regulating glycolysis, beta-oxidation, mitochondrial oxidative phosphorylation, and ATP consumption by the creatine phosphate reaction [11]. Metabolic changes in these processes play an important role in the development of heart failure [11, 19, 20]. Thus, a decrease in the ratio of creatine phosphate and ATP indicates a critical energy deficiency and an impaired ATP-producing capability of the heart that supports its functions [21]. Changes in the tricarboxylic acid

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cycle activity after myocardial infarction correlate with a decrease in the ejection fraction. These changes also indicate an early response of the myocardium to damage [22].

Alpha-amino acids are important precursors of energy metabolism as they are closely related to the tricarboxylic acid cycle. Apparently, ATT-induced oxidative stress results in metabolic remodeling of α-amino acids to compensate for the energy demands of the myocardium [23]. Oxidative stress is characterized by an imbalance between the production of reactive oxygen species, reactive nitrogen species and intrinsic mechanisms of antioxidant defense, which makes oxidative stress the major toxicity factor [24]. Thus, excessive accumulation of choline metabolic intermediates may indicate atherosclerosis and vascular wall remodeling [25]. In this study, significant increases in plasma glutamate, trimethylamine N-oxide, choline, and dimethylglycine were observed in the group with vascular disorders associated with ATT. Considering that cardiomyocytes contain 35-40% more mitochondria than other tissues, the observed changes may serve as prognostically significant risk factors for the development of cardiotoxicity. At the same time, changes in the concentrations of acylcarnitines, especially long-chain ones, may reflect likely disturbances in beta-oxidation of fatty acids [26].

The revealed correlations between dimethylarginines (ADMA, SDMA) and vascular wall parameters after ATT, as well as the increase in citrulline, indicate a possible imbalance in the nitric oxide and urea cycle and, therefore, an increased risk of ED [27]. Nitric oxide, a vasodilator and inhibitor of vascular smooth muscle cell proliferation, is generally increased in patients with diagnosed CVDs [28]. Intensive production of nitric oxide results in the formation of peroxynitrite that promotes lipid peroxidation, mitochondrial oxidative stress, apoptosis, and necrosis [29].

Even though some patients took cardioprotective drugs at baseline, this study revealed a "metabolomic shift", which characterizes a high risk of CVCs. This fact highlights the need for more accurate and personalized approaches for timely identification of high-risk groups before administration of ATT. Implementing the screening for metabolomic profile in routine practice can become a basis for personalized assessment of the CVT risk during chemotherapy, and will also allow physicians to prescribe targeted cardioprotective therapy in a timely manner.

This article describes the first results of a large interdisciplinary project exploring the potential of using omics sciences and omics (transcriptomic or proteomic) risk factors to predict and detect early CVT in cancer patients.

Limitations of the study

Limitations of this pilot study included the small number of participants in the experiment, as well as the cross-sectional design of the study of metabolomic profile. Future studies will be designed for using larger patient samples and assessing time-related changes in the metabolomic profile after each course of chemotherapy.

Supplementary materials

Logistic regression coefficients for metabolites: creatinine, 0.30; serine, 0.29; tryptophan, -0.20; ornithine, 0.20; C0 carnitine, -0.16; glycine, –0.12; betaine, –0.12; threonine, 0.091; phenylalanine, 0.091; proline, 0.048; lysine, –0.021; glutamine, –0.021; valine, –0.012; glutamate, 0.0028.

Conclusion

The comprehensive assessment of the structural and functional state of the vascular wall and the metabolic profile in oncohematological patients receiving cardiotoxic therapy (anthracycline antibiotics, proteasome inhibitors) allowed us to reveal important changes preceding clinically evident cardiovascular toxicity. The determined spectrum of metabolomic markers and the developed logistic regression model along with regular instrumental monitoring (echocardiography, photoplethysmography) can timely identify patients at a high risk of cardiovascular toxicity and help adjust the prescribed complex therapy. In the future, the use of metabolomic profiling will facilitate the development of personalized therapeutic strategies aimed at reducing the risk of cardiovascular complications in patients with oncohematological diseases.

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