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4-Year Experience of the Cardio-Oncology Center of Sechenov University: Single-Center Epidemiological Study

Aim	To present the four-year experience and the accomplishments of the Scientific and Practical Cardio-Oncology Center of the Sechenov University.
Material and methods	The records of patients referred for cardio-oncology consultation from January 2020 through March 2024 were retrospectively analyzed. The patients' cardiovascular (CV) status was assessed at baseline and after optimizing the cardiac therapy during the antitumor treatment. The endpoints were the completion of all antitumor therapy courses and the level of overall and CV mortality.
Results	Among 233 enrolled patients (66% women), a considerable part belonged to the group of high/very high cardio-oncological risk (n=134, 57%). Various cardiovascular toxicities were observed in 22% of patients. At baseline, these patients significantly more frequently had heart failure and ischemic heart disease as well as previous radiation and chemotherapy. After the optimization of cardiac therapy, 88% of patients successfully completed all scheduled treatments. The overall mortality, including the CV mortality, was 14% (n=7).
Conclusion	Creation of cardio-oncological services allows considerably reducing the probability of adverse CV events during the antitumor therapy and successfully completing all scheduled treatments in most patients.

Keywords	Cardio-oncology; cardiotoxicity; vasculotoxicity; prognosis; overall mortality
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Introduction

Oncological and cardiovascular diseases (CVD) are consistently among the leading causes of mortality both on a global scale and in the Russian Federation [1, 2]. The widespread implementation of cancer prevention screening programs, coupled with the advent of modern, highly effective antitumor therapy (ATT), has resulted in a notable increase in the survival rates of cancer patients. Consequently, the duration of their follow-up has also increased [2]. As reported by Rosstat, approximately 8 million individuals are currently living with a diagnosis of cancer [3]. However, antitumor therapies, including chemotherapy, targeted and immune therapies, and radiation modalities, can also result in the emergence of diverse forms of cardiac and vascular toxicity [4]. Cardiovascular events represent a significant cause of non-cancer mortality and morbidity in cancer patients [4].

The field of cardio-oncology, an interdisciplinary medical specialty, has witnessed significant advancement in recent years. The objective of cardio-oncology is to assess the initial cardiac risk, facilitate timely detection, monitor, and treat any cardiovascular complications that may result from antitumor therapy. For several years, autonomous, highly specialized cardio-oncology clinics have existed in other countries, which are typically situated within larger, multidisciplinary hospitals. However, cardio-oncology is currently regarded as a subspecialty of cardiology, rather than as an autonomous specialty, in the Russian Federation. This necessitates the active engagement of professional associations to establish a robust regulatory, administrative, and financial foundation for the operations of specialized cardio-oncology departments.

In January of 2020, by the decree of the Rector of Sechenov University, the first Scientific and Practical Cardio-Oncology Center was established. This interstructural functional unit encompasses the clinical and diagnostic departments of the University Clinic.

Objective

The objective of this study is to present the four-year experience and results of the work of the Scientific

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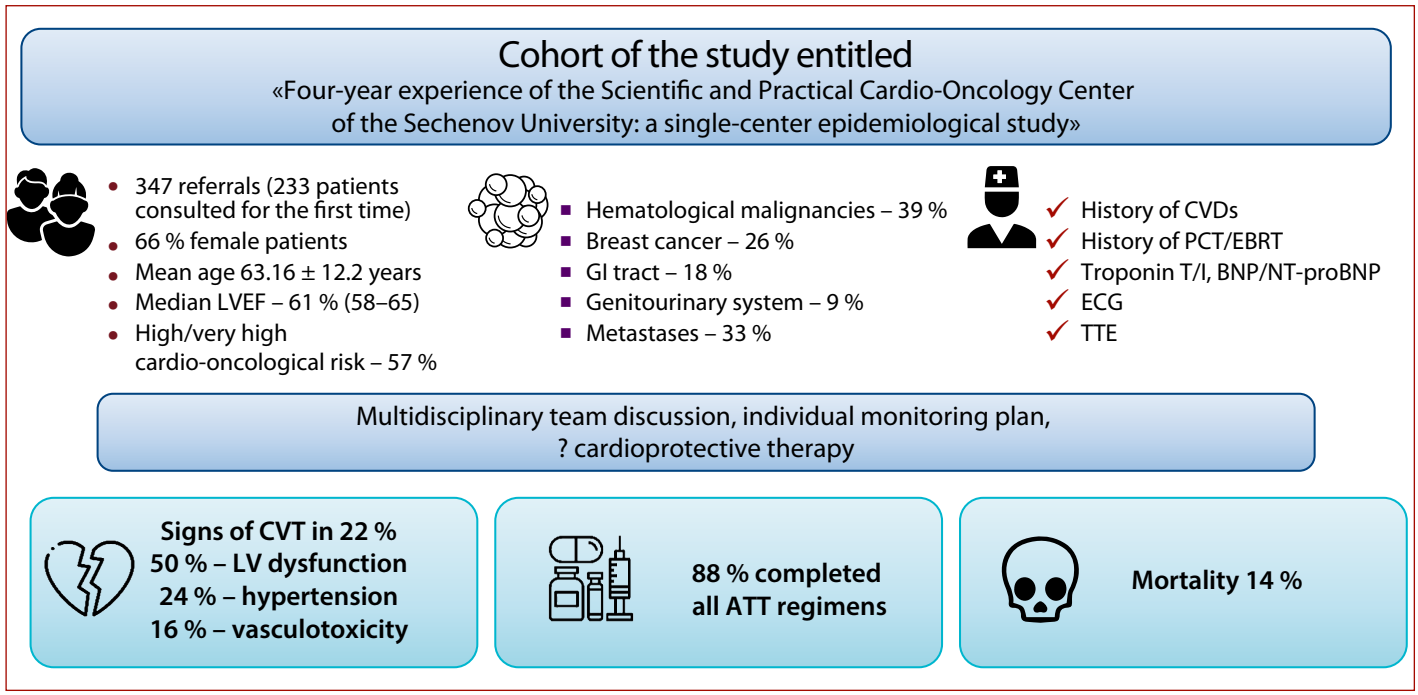
Central illustration. 4-Year Experience of the Cardio-Oncology Center of Sechenov University: Single-Center Epidemiological Study



and Practical Cardio-Oncology Center of the Sechenov University.

Material and Methods

A retrospective analysis was conducted on the electronic case records of 347 patients who were referred to the Scientific and Practical Cardio-Oncology Center of the Sechenov University. The main reasons for referring patients to a specialized consultation with a cardiologist or cardio-oncologist are outlined in Table 1. All primary patients underwent a standard cardiac examination, which included blood tests with mandatory determination of the lipid spectrum, a resting 12-channel electrocardiogram (ECG), and transthoracic echocardiography (TTE). If feasible, the levels of the recommended biomarkers of cardiotoxicity (troponin I/T, brain natriuretic peptide (BNP), and N-terminal pro-brain natriuretic peptide (NT-proBNP)) were also determined (Figure 1). In cases where indicated, individual patients underwent stress tests (assessment of signs of transient myocardial ischemia) and computed tomography (CT) angiography of the coronary arteries. The patients were divided into four groups according to their baseline cardio-oncological risk, as assessed by means of stratification scales in accordance with the 2022 ESC guidelines [5, 6] (Table 1).

Table 1. Reasons for Patient Referrals to the Scientific and Practical Cardio-Oncology Center of the Sechenov University and their baseline cardio-oncological risk

Reasons for appeals	Patients, n (%)
Assessment of baseline cardio-oncological risk prior to scheduled ATT	134 (57)
Repeated scheduled follow-up control during ATT	159 (68)
Assessment of the presence of CVT during treatment (first/subsequent appeal)	104 (44)
Baseline cardio-oncological risk	
Low	26 (12)
Moderate	72 (31)
High	52 (22)
Very high	82 (35)

ATT, antitumor therapy; CVT, cardiovascular toxicity.

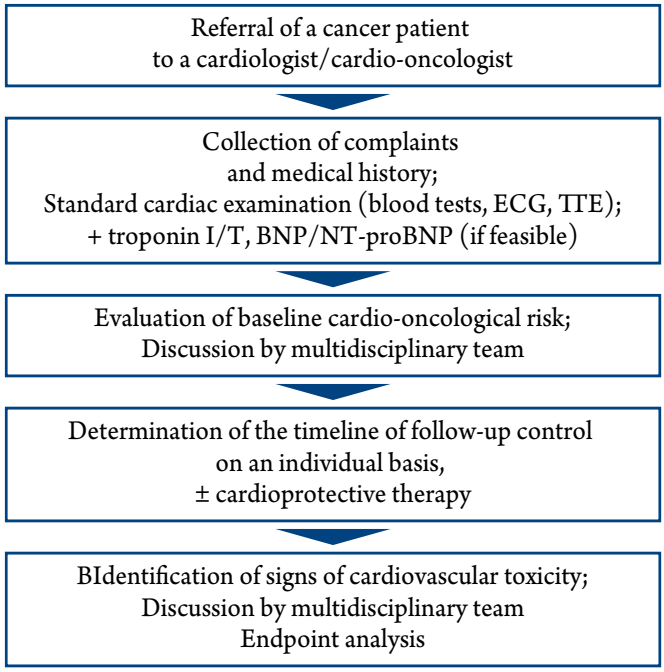
The verification of various variants of cardiovascular toxicity (CVT) of ATT was conducted in accordance with the 2022 ESC guidelines and classification for cardio-oncology [5, 6].

Following consultation and discussion by the multidisciplinary team, patients who required the initiation or continuation of ATT were classified as follows:

1) Patients eligible for treatment;
2) Patients at very high risk, requiring specific additional examination and treatment;
3) Patients requiring interruption or discontinuation of their current course of treatment in accordance with their clinical status (Figure 1).

The timing of repeated dynamic consultations with mandatory ECG, TTE with assessment of left ventricular (LV) systolic function, left ventricular ejection fraction (LVEF), and global longitudinal strain as indicated, as well as levels of cardiotoxicity biomarkers (if feasible) were determined on an individual basis for each patient, taking into account the baseline cardio-oncological status, current ATT regimen, CVT variant, cancer stage, and response to therapy.

Figure 1. Flow-chart of patients referred for consultation to a cardio-oncologist



ECG, electrocardiogram; TTE, transthoracic echocardiography; BNP, brain natriuretic peptide; NT-proBNP, N-terminal pro-brain natriuretic peptide.

In order to elucidate the distinctive characteristics of subgroups of patients, those exhibiting or lacking signs of different CVT variants were subjected to separate analysis.

The primary endpoint of the study was the rate of successful completion of all scheduled ATT regimens. The secondary endpoint was the incidence of all-cause mortality, including that resulting from cardiovascular causes.

A statistical analysis of data collected retrospectively based on the analysis of case records of patients was conducted using the StatTech 4.3.3 software (OOO Stattech, Russian Federation). The data were presented in accordance with the type of distribution, either as an arithmetic mean (M) and standard deviation (SD) or as a median with lower and upper quartiles (Me (Q1 – Q3)). For the purpose of comparison of normally distributed indicators, the Student's t-test was utilized. In the event of a non-normal distribution, the Mann-Whitney rank test was employed. Pearson's chi-squared test was employed for the purpose of comparing percentages in the analysis of multifactor contingency tables. The observed differences between the indicators being compared were statistically significant at the $p < 0.05$ level.

Results

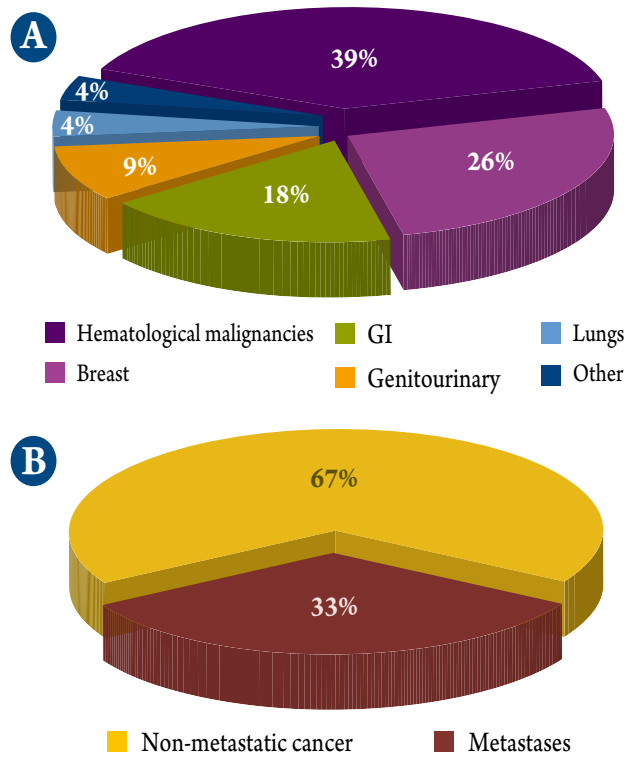
General characteristics of the patients

A total of 233 primary patients diagnosed with cancer (66% female) were seen for the first time between January 2020 and March 2024. The main characteristics of the subjects are presented in Table 2.

The most common reason for contacting a cardiologist or cardio-oncologist was the presence of baseline cardiovascular risk factors and baseline cardiovascular diseases (CVDs) in cancer patients (n = 134). The most prevalent forms of cancer were breast cancer and hematological malignancies. Of the patients, 77 (33%) exhibited distant metastases, and none demonstrated involvement of the heart in the tumor process (Figure 2 A, B). Approximately 60% of patients exhibited advanced stages of the oncological process (stages 3–4). A history of neoplastic disease was present in 10 (4.3%) patients. Of these patients, 3 (30%) had previously undergone polychemotherapy (PCT). The median duration of cancer at the time of the consultation was 12 months (ranging from 3 to 49 months).

The primary reasons for referring patients for consultation included the assessment of baseline cardio-oncological risk and the optimization of cardiovascular therapy prior to the initiation of PCT, the verification of the presence of CVT in the context of ATT, and the provision of repeated consultations over time (Table 1). Of the 233 patients, 42% were treated with any anti-tumor drug therapy options. Of the remaining patients, 79 (34%) underwent surgical treatment, while 34 (15%) received radiation therapy (RT)

Figure 2. Types of cancer in the population-based study



A – types of cancer among cardio-oncological patients;
B – the incidence of metastatic and non-metastatic lesions.
GI, gastrointestinal tract

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Table 2. Baseline characteristics of cancer patients with or without cardiovascular toxicity in antitumor therapy

Parameter	Total (n = 233)	No CVT (n = 183)	CVT (n = 50)	p
Age, years (M ± SD)	63.16 ± 12.2	63.1 ± 12.5	63.64 ± 11.1	0.924
Female, n (%)	154 (66)	118 (64)	35 (70)	0.495
Cardiovascular risk factors and cardiovascular diseases, n (%)				
Smoking	58 (25)	44 (24)	14 (28)	0.315
Hyperlipidemia	146 (63)	112 (61)	34 (68)	0.820
Diabetes mellitus	39 (17)	28 (15)	11 (22)	0.340
Hypertension	157 (67)	121 (66)	36 (72)	0.446
HF at baseline	69 (29)	46 (25)	23 (46)	0.005
CHD at baseline	43 (18)	28 (15)	15 (30)	0.019
Valvular heart disease at baseline	26 (11)	17 (9)	9 (18)	0.086
Baseline cardioprotective therapy among all recommended medicines, n (%)				
ACE inhibitors/ARBs	23 (10)	16 (9)	7 (14)	0.134
BBs	25 (11)	21 (12)	4 (8)	0.743
Statins	11 (5)	8 (4)	3 (6)	0.597
Antitumor therapy, n (%)				
Anthracyclines	66 (28)	52 (28)	14 (28)	0.851
Anti HER2 agents*	17 (7)	11 (6)	6 (12)	0.015
Drugs that induce vasospasm**	32 (14)	24 (13)	8 (16)	0.324
Immunotherapy	7 (3)	3 (2)	4 (8)	0.011
VEGF inhibitors	15 (6)	7 (4)	8 (16)	0.004
History of RT, n (%)	34 (15)	21 (12)	13 (26)	0.013
History of surgical intervention, n (%)	79 (34)	58 (32)	21 (42)	0.181
Laboratory and clinical examination findings				
LVEF, %, Me [Q1; Q3]	61 (58–65)	62 (59–66)	59 (55.5–64.5)	0.002
NP positive, n (%)	53 (23)	39 (21)	14 (28)	0.109
Troponin I/T positive, n (%)	9 (4)	7 (4)	2 (4)	0.605

* Trastuzumab, pertuzumab; ** 5 fluorouracil, capecitabine. CVT, cardiovascular toxicity; HF, heart failure; CHD, coronary heart disease; ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; BB, beta-blocker; ATT, antitumor therapy; VEGF, vascular endothelial growth factor; RT, radiation therapy; LVEF, left ventricular ejection fraction; NP, natriuretic peptide.

in the past. Among this latter group, 14 (6%) may have experienced cardiotoxicity due to irradiation of the left breast, left half of the chest, or the mediastinal area.

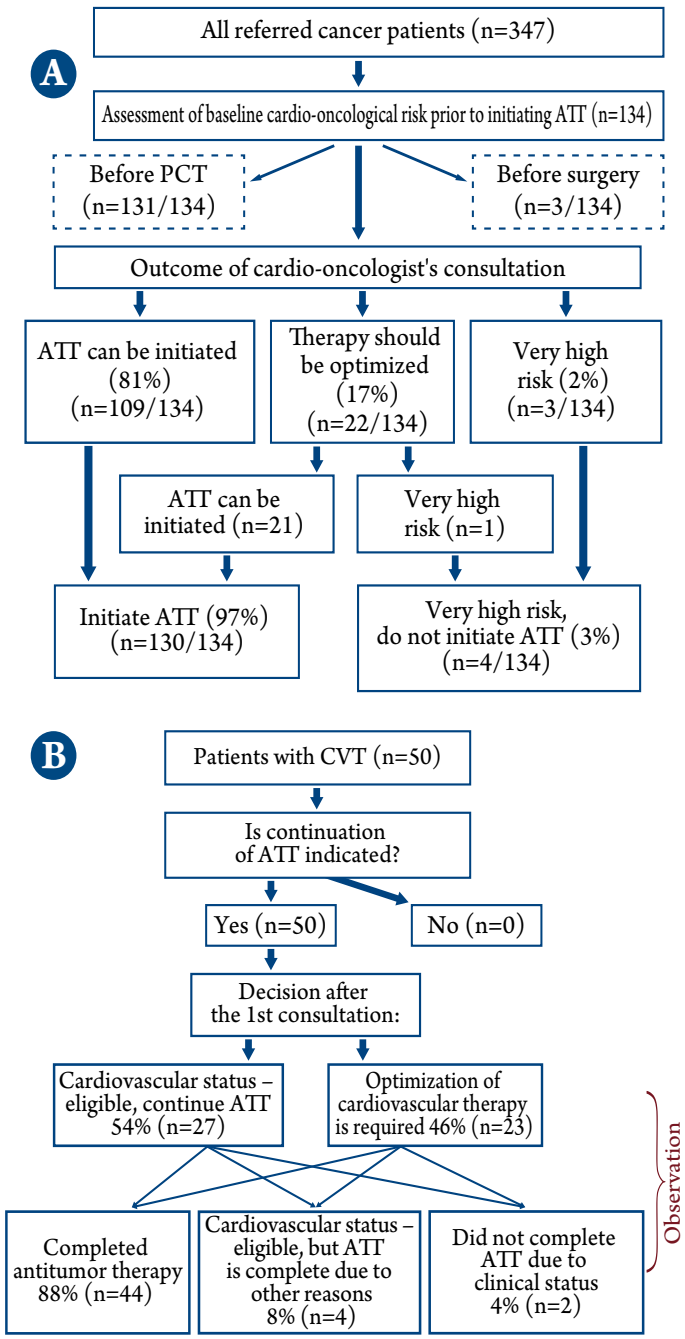
In accordance with the 2022 ESC guidelines [5, 6], stratification scales were employed to evaluate baseline cardio-oncological risk. The majority of patients were classified within the high-risk or very high-risk categories, representing 22% and 35%, respectively (Table 1).

The presence of various variants of CVT was identified in 50 patients, with LV myocardial dysfunction observed in 50% of the subjects (n = 25). In the remaining patients, other variants of complications were detected. Patients who developed cardiovascular complications during treatment were significantly more likely to have baseline heart failure (HF) and coronary heart disease (CHD), a history of radiation therapy and chemotherapy.

Patients at high/very high cardio-oncological risk

A total of 134 (57%) patients were classified as high or very high risk following a baseline consultation with a cardiologist or cardio-oncologist prior to the administration of potentially cardiovascular toxic chemotherapy (n = 131, 98%) or prior to surgery (n = 3, 2%). The median LVEF was 62% (58–65). However, the baseline incidence of significant cardiovascular risk factors and CVD was elevated in these patients: hypertension (81%), HF (48%), CHD (32%). To ascertain the condition of the coronary bed, 41 (30%) patients underwent CT angiography. Only three patients exhibited signs of hemodynamically significant lesions. Subsequently, the patients were referred for invasive coronary angiography and optimization of drug therapy, which resulted in a delay in the onset of ATT. Following the initial examination and consultation, all cancer patients were prescribed cardioprotective therapy (85%), or the baseline cardiovascular therapy was optimized (15%) with the mandatory inclusion of beta-blockers (n = 82, 61%), angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers (n = 79, 59%), and statins (n = 79, 59%). Following an initial consultation with a cardio-oncologist,

Figure 3. Flow-chart of referral of cardio-oncology patients



A – flow-charts of patients referred for consultation with a cardio-oncologist before initiating antitumor therapy; B – flow-charts of patients with signs of cardiovascular toxicity associated with antitumor therapy. ATT, antitumor therapy; PCT, polychemotherapy.

81% of cancer patients were admitted to commence ATT without delay, 2% were identified as very high-risk patients, and 17% were advised to optimize therapy prior to ATT regimens. Eventually, 97% of patients initiated specific therapeutic regimen (Figure 3).

Cardiovascular toxic effects of antitumor therapy

The signs of various variants of CVT were identified in 50 patients, with LV myocardial dysfunction in 25 cases. Of these, 12 were symptomatic and 13 were asymptomatic, with a median LVEF of 48% and 59%, respectively. Additionally, 8 patients experienced vasculotoxicity, 12 developed hypertension, and 5 had arrhythmias. The most commonly utilized cardiovascular toxic agents were anthracycline antibiotics, vascular endothelial growth factor (VEGF) inhibitors, and fluoropyrimidines. Various variants of myocardial dysfunction were more common in the context of anthracycline and VEGF inhibitor therapy, with incidences of 28% and 16%, respectively. Vasculotoxicity typically presented clinically as angina pectoris, with the progression to myocardial infarction in one patient and accelerated atherosclerosis, as evidenced by repeated Doppler ultrasound imaging of the carotid arteries, and cerebrovascular accident in two patients. These patients were more likely to receive anthracyclines and anti-HER2 medicines. Hypertension was prevalent among patients receiving VEGF inhibitors, fluoropyrimidines, and platinum-based drugs.

Management and outcomes of patients with signs of cardiovascular toxicity

A mere 14 out of the 50 patients exhibiting signs of CVT had received prior cardioprotective therapy (at least one medication), and only 7 had been initially consulted by a cardio-oncologist. All patients with confirmed CVT were administered comprehensive cardiac therapy in accordance with their specific nosological form. The majority of patients (n = 27, 54%) were able to continue the ATT regimens without modifications or delays in administration despite the observed cardiovascular side effects. A total of 23 patients required an interruption, change, or discontinuation of their current treatment regimen. Subsequently, following follow-up control, the PCT regimens were resumed for 17 patients. Consequently, 88% of all cancer patients referred to the Scientific and Practical Cardio-Oncology Center of the Sechenov University were able to successfully complete all the scheduled ATT regimens. The all-cause (including cardiovascular) mortality rate among the entire cancer cohort was relatively low, at 14% (n = 7).

Discussion

In the present publication, the actual four-year experience of the cardio-oncology service at Sechenov University is, for the first time in the context of domestic medical practice, subjected to analysis and description. The principal conclusion of this study is that the timely assessment of baseline cardio-oncological risk, along with the identification of early signs of CVT and mandatory subsequent consultation with a cardio-

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oncologist, has been shown to enhance the optimization of cardiac therapy and improve the survival of cancer patients, primarily due to the prolongation of ATT, which reduces the likelihood of its interruption.

The 2022 ESC Guidelines for cardio-oncology provide a detailed framework for a personalized approach to the management, prevention, and follow-up control of the condition of cancer patients with regard to the initial cardio-oncological risk and the scheduled ATT regimen, as well as the rules for the management and treatment of any cardiovascular complications that may arise during the specific therapy [5, 6]. In foreign countries, the field of cardio-oncology has undergone significant growth and development over the past decade. This included the establishment of specialized cardio-oncology clinics and the creation of certification and accreditation programs for cardio-oncologist [7]. Nevertheless, although the Russian Federation does not yet have a clearly formulated legal framework for cardio-oncology, which is a subspecialty of general cardiology, there are several cardio-oncology teams in different regions. Furthermore, a Russian consensus document on the cardiovascular toxicity of PCT has been published [8].

One of the principal objectives of cardio-oncology monitoring is to improve global contractility of the myocardium and the functional status of the patient, which will contribute to the patient's eligibility for the initiation or continuation of ATT. This is particularly important given the evidence that delays or interruptions in ATT regimens are associated with an increased risk of cancer progression [9]. A review of the Russian literature revealed no publications describing the experience of a cardio-oncology center. In the cohort of patients described herein, a considerable proportion exhibited high or very high baseline cardio-oncological risk (58%). This highlights a significant cardiovascular burden among cancer patients who require the initiation of potentially cardiotoxic therapy. The subsequent administration of cardioprotective therapy to all patients and optimization of cardiovascular status permit the majority of patients to commence specific ATT without delay. Furthermore, this approach has the potential to reduce the risk of developing CVT in the future.

The verification of various CVT variants was conducted in accordance with the ESC guidelines on cardio-oncology. The present study demonstrated an elevated incidence of cardiovascular complications, reaching a rate of 22%. Of these cases, LV myocardial dysfunction was identified in half of the patients. The analysis of this subgroup of patients determined that only one-third of them received at least one cardioprotective drug, and only seven out of the total of fifty patients were initially consulted by a cardio-oncologist. Following the administration of the necessary cardiac therapy and subsequent follow-up control, 88% of patients were able to complete all scheduled ATT regimens.

A review of the international literature revealed numerous publications describing the experience of cardio-oncology clinics. In their work, Pareek et al. report a higher level of cardiotoxicity associated with anthracyclines, anti-HER2 medicines, and tyrosine kinase inhibitors, with rates of 75.8%, 69.8%, and 62.1%, respectively [10]. Despite the active control and optimization of cardiac therapy, the number of patients who successfully completed ATT courses was low, amounting to only 65.3%. This was primarily due to oncological causes. The level of cardiovascular status and all-cause mortality was higher than that observed in our study, reaching 21%.

Conclusion

The article presents an epidemiological analysis of the four-year experience of the cardio-oncology service at the Sechenov University. A considerable number of patients present with an initially high or very high cardio-oncological risk, and a considerable prevalence of complications associated with cardiovascular toxicity has been demonstrated. A timely referral to a cardiologist/cardio-oncologist, followed by optimization of cardiac therapy, resulted in an improvement in the patient's left ventricular ejection fraction and functional status. Additionally, this approach increased the number of patients who successfully completed antitumor treatment.

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