

HEMODYNAMIC PARAMETERS IN RELATIONSHIP WITH MARKERS OF HEART FAILURE IN PATIENTS WITH BREAST CANCER AFTER CHEMIORADIOTHERAPY

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SUMMARY

Purpose: to study the relationship of hemodynamic parameters with the main markers of heart failure in patients with breast cancer and the incidence of side effects of chemotherapy according to the AC regimen in combination with doxorubicin. **Material and Methods:** 27 patients with breast cancer were examined after surgical treatment. All patients received both neoadjuvant and adjuvant chemotherapy (CT). The latter was carried out according to the AC scheme (doxorubicin 60-100 mg/m² + cyclophosphamide 600 mg/m² on the 1st day, every 21 days). All general clinical and laboratory studies were carried out. **Results:** women with breast cancer, as the number of courses of CT in combination with doxorubicin increased, despite a relatively young age, were characterized by a more pronounced tendency to tachycardia, the formation of arrhythmias and a decrease in exercise tolerance (ET), which, in turn, aggravated the phenomena of chronic HF in the form of a decrease in SV and LVEF. In addition, it was found that treatment with large doses of doxorubicin contributed to the formation of heart failure while maintaining central hemodynamic parameters. In 14.8% of cases, CT according to the AS regimen in combination with doxorubicin was accompanied by a high level of emetogenicity, which emphasizes the need for an integrated (oncological, cardiological, gastroenterological, etc.) approach in providing medical care to this group of patients. **Conclusion:** AC chemotherapy (doxorubicin + cyclophosphamide) remains the most commonly prescribed adjuvant regimen in the treatment of breast cancer. However, the toxicity of oncological drugs requires new approaches to solving this serious problem of modern health care. The range of application of doxorubicin in the treatment of malignant neoplasms is extensive, which allows it to be classified as a first-line drug, at the same time, its cardiotoxicity should alert specialists when prescribing it.

KEYWORDS: oncological, cardiological, gastroenterological, etc.**Relevance**

The clinical significance of the comorbidity of cardiovascular disease (CVD) and breast cancer cannot be overestimated. Epidemiological data indicate that 1 out of 3.3 deaths in patients with breast cancer is associated with CVD, and only 1 out of 31.5 deaths is directly related to breast cancer.^[1] The absolute risk of death from CVD in women with breast cancer ranges from 1.6% to 10.4%.^[2] The first population-based comparative study of cardiovascular outcomes in women with and without breast cancer showed that cancer survivors had a 1.8-fold and 1.3-fold increased risk of all-cause and CVD mortality, respectively, and this increased risk was most pronounced. about 7 years after the diagnosis of breast cancer.^[3]

Performing optimal complex treatment of early breast cancer is the most important task of oncologists. The complex therapy of these patients includes surgical

treatment, drug therapy and radiation therapy. The need for adjuvant drug therapy for breast cancer is now an axiom, and an oncologist chooses only the type of adjuvant therapy depending on the tumor subtype, based on clinical recommendations.^[4]

The first adjuvant anthracycline-containing treatment was the AS regimen (doxorubicin and cyclophosphamide). The AS scheme made it possible to reduce both the number of cytostatic injections and the duration of treatment.^[5] However, this type of therapy, like many other anti-cancer treatments, is very toxic, including from the side of cardiology.^[6]

At the same time, the modern literature presents an insufficient number of clinical studies studying the structural and functional changes in the myocardium of the left ventricle (LV) during doxorubicin therapy.

The aim of this work was to study the relationship between hemodynamic parameters and the main markers of heart failure in patients with breast cancer and the incidence of side effects of AS chemotherapy in combination with doxorubicin.

MATERIAL AND METHODS

27 patients with breast cancer were examined after surgical treatment. All patients received both neoadjuvant and adjuvant chemotherapy (CT). The latter was carried out according to the AC scheme (doxorubicin 60-100 mg/m² + cyclophosphamide 600 mg/m² on the 1st day, every 21 days).

General clinical examinations included: laboratory blood tests, physical examination with the calculation of body mass index (BMI, kg/m²) and the use of the clinical assessment scale (CAS) with the determination of the functional class (FC) of chronic heart failure (CHF) by measuring the length of the passed distance (LPD, m) according to the results of the 6-minute walk test (SWT).

Instrumental studies included the removal and interpretation of ECG in 12 standard leads, the analysis of heart rhythm disturbances (HRD) was carried out according to Holter monitoring (HMECG) and EchoCG with the determination of indicators - end-diastolic (EDV, ml), end-systolic (ESV, ml) left ventricular (LV) volumes, stroke volume (SV, ml) and left ventricular ejection fraction (LVEF).

The LV myocardial mass (LVMM) was calculated using the "area-length" method, the results obtained were indexed in relation to the body surface area (the indexed of LVMM – i-LVMM). The value for women of 104 g/cm², according to De Simone^[7], was used as the upper limit of i-LVMM.

The relative wall thickness index (RWT) in diastole was calculated by the formula:

$$RWT = (TIVS + TPW) / EDS,$$

where TIVS is the thickness of the interventricular septum, TPW is the thickness of the posterior wall of the LV, EDS is the end-diastolic size of the LV. All measurements were calculated in cm.

Based on the values of LVMM and RWI, the following geometric types of LV were distinguished^[7,8]:

- normal geometry (i-LVMM ≤ N, RWI < 0.45);
- concentric remodeling (i-LVMM ≤ N, RWI ≥ 0.45);
- concentric hypertrophy (i-LVMM > N, RWI ≥ 0.45);
- eccentric hypertrophy (i-LVMM > N, RWI < 0.45).

Statistical analysis. Data were described as mean ± standard deviation (M±SD) for interval and number (%) for categorical variables. We used the chi-square test and Fisher's test for categorical variables. For numerical variables, Student's t-test was used. To assess the presence of relationships between indicators, a correlation analysis was carried out with the calculation of the Pearson correlation coefficient. A p value ≤ 0.05 was considered a statistically significant result.

RESEARCH RESULTS

Depending on the number of CT courses, three groups were identified: 1g. – 10 patients with CT courses from 2 to 4 (median 2.9±1.0); 2g. – 9 patients with CT courses from 5 to 9 (median 7.6±1.2) and 3g. – 8 patients with CT courses from 10 to 20 (median 13.7±3.2).

The average age of the compared groups of women is presented in Table 1, from which it can be seen that the patients 3gr. turned out to be 2.5 and 4.2 years (both p>0.05) younger than women of the 1st and 2nd groups. In addition, women 3gr. according to the reference BMI values, they turned out to be "slenderer". Namely, the number of persons with BMI> 30 kg/m² in 3gr. was the smallest - 37.5%, which was 22.5% and 6.9% less than in the 1st and 2nd groups. In total, 13 (48.1%) women out of the entire surveyed sample were characterized by an increased level of BMI (Table 1).

Table 1: Comparative general clinical characteristics of patients depending on the number of chemotherapy courses.

Sign	1 group (n=10)	2 group (n=9)	p1	3 group (n=8)	p2
Average age, years	59,3±10,1	61,0±9,2	0,707	56,8±10,5	0,615
Average number of CT courses	2,9±1,0	7,6±1,2	0,000	13,7±3,2	0,000
dD, mg/m ²	78,0±19,9	70,0±18,5	0,378	80,0±21,4	0,840
Average number of RT courses	abs	21,2±7,5	-	24,0±4,1	-
Average BMI, kg/m ²	32,0±6,7	30,7±7,2	0,689	29,7±3,3	0,359
Number of persons with BMI > 30 kg/m ² , n (%)	6 (60,0%)	4 (44,4%)	p=0,827 χ ² =0,048	3 (37,5%)	p=0,625 χ ² =0,225
Mean SBP, mm Hg	144,0±23,7	127,8±15,6	0,100	121,3±14,6	0,031
Mean DBP, mm Hg	89,0±8,8	82,2±8,3	0,102	78,8±12,5	0,059 [#]
Number of persons with AH, n (%)	5 (50,0%)	2 (22,2%)	p=0,427 χ ² =0,604	1 (12,5%)	p=0,240 χ ² =1,378
Average heart rate, bpm	87,8±17,1	86,7±15,0	0,584	91,8±21,8	0,665
Heart rate > 90 bpm, n (%)	2 (20,0%)	4 (44,4%)	p=0,515 χ ² =0,422	3 (37,5%)	p=0,769 χ ² =0,087

Average QRS, ms	0,94±0,13	0,91±0,11	0,596	0,94±0,09	1,000
Average QT, ms	3,40±0,23	3,43±0,23	0,750	3,31±0,27	0,456
LPD for SWT, m	237,8±90,6	223,7±63,5	0,703	218,4±62,3	0,614
CAS, points	6,8±0,9	7,2±1,5	0,485	7,5±1,1	0,156
Average FC CHF according to NYHA	2,75±0,46	2,80±0,42	0,505	2,89±0,33	0,450
Arrhythmias according to HMECG, n (%)	abs	abs	-	2 (25,0%)	p=0,356 χ ² =0,851
VE, n (%)	abs	abs	-	1 (12,5%)	p=0,908 χ ² =0,012
SVE, n (%)	abs	abs	-	1 (12,5%)	p=0,908 χ ² =0,012

Notes: n is the number of patients; CT – chemotherapy; dD - the dose of doxorubicin; RT - radiation therapy; BMI - body mass index; SBP and DBP - systolic and diastolic blood pressure; AH - arterial hypertension; HR - heart rate; LPD - the length of the passed distance; SWT - 6-minute walk test; CAS – the clinical assessment scale; FC - functional class; CHF - chronic heart failure; HMECG - Holter ECG monitoring; VE and SVE - ventricular and supraventricular extrasystoles; p1 – significance of differences between the 1st and 2nd groups; p2 - significance of differences between the 1st and 3rd groups; # - tendency to significance of differences

Indices of blood pressure (BP) in the whole group were: SBP = 131.9±20.6 mm Hg. and DBP = 83.7±10.4 mm Hg. The presence of arterial hypertension (AH) of varying severity was observed in a total of 8 (29.6%) patients, of which 62.5% (of the total number of patients with AH, i.e. from 8) were from 1g., 25.0% - from 2g. and 12.5% - from 3g., i.e. women with fewer courses of CH were characterized by more pronounced AH (Table 1). Namely, in persons 1g. reference SBP values were 144.0±23.7 mm Hg, which is 16.2 and 22.7 mm Hg. exceeded the average SBP of the 2nd and 3rd groups, respectively, and DBP = 89.0±8.8 mm Hg, which is 6.8 and 10.2 mm Hg. was higher than in the 2nd and 3rd groups (Table 1).

The average heart rate values in the whole were 88.6±17.4 beats/min, while heart rate > 90 beats/min was observed in 9 (33.3%) patients, of which 22.2% (of the total number of patients with elevated heart rate, i.e. from 9) were from 1g, 44.4% - from 2g. and 33.4% - from 3g. Analysis of the mean values of heart rate in the compared groups revealed its highest indicators in patients 3g. Namely, mean heart rate in 3g. was 91.8±21.8, which was 4.0 and 5.1 beats/min higher than in the 1st and 2nd groups (Table 1).

It is noteworthy that (Table 2), namely, in patients from group 3, in addition to a tendency to tachycardia,

arrhythmias were detected (according to HMECG): 1 patient had ventricular extrasystole (total number of VE - 49 for 20 hours and 18 minutes of recording) and another patient had supraventricular extrasystoles (total number of SVE - 2400 for 21 hours and 27 minutes).

Assessment of the level of exercise tolerance (ET) in the compared groups found (Table 1) that women 3g. were characterized by a lower LPD (by 19.4 m - compared with the 1st group and by 5.3 m - compared with the 2nd group) and a higher number of points for CAS (by 0.7 and 0.3 points, respectively, from the 1st and 2nd groups).

Analysis of the parameters of cardiac hemodynamics established, that patients 3g. were characterized by the lowest values of SV (by 16.0 and 8.3 ml compared with those in 1g. and 2g.) and LVEF (by 10.6 and 4.5 % compared with groups 1 and 2), as well as LVMM (difference with 1g. - 46.4 g and with 2g. - 28.4g) and i-LVMM (difference 28.9 and 14.2 g/m², respectively, with the 1st and 2nd groups). Calculation of the RWT showed that the lowest values of this indicator were observed in women 3g., which amounted to 0.37 ± 0.06 units, i.e. was <0.45. This was due to the small number of persons with the level of RWT ≥ 0.45 units, which in this group occurred only in 12.5% of women (Table 2).

Table 2: Comparison of the main EchoCG parameters depending on the number of chemotherapy courses.

Sign	1 group (n=10)	2 group (n=9)	p1	3 group (n=8)	p2
EDV, ml	122,9±18,7	126,9±38,5	0,773	121,7±44,5	0,939
ESV, ml	50,6±12,9	62,3±34,6	0,332	65,5±39,4	0,275
SV, ml	72,2±12,1	64,5±14,8	0,229	56,2±19,3	0,047
LVEF, %	59,1±6,6	53,0±12,6	0,197	48,5±18,8	0,114
LVMM, g	246,2±59,3	228,2±55,4	0,505	199,8±81,8	0,152
i-LVMM g/m ²	210,8±38,6	196,1±43,9	0,448	181,9±44,1	0,155
RWT, units	0,42±0,04	0,40±0,07	0,449	0,37±0,06	0,050
OTS ≥ 0.45 units, n (%)	3 (30,0%)	2 (22,2%)	p=0,891 χ ² =0,019	1 (12,5%)	p=0,751 χ ² =0,100

Notes: *n* is the number of patients; EDV - end-diastolic volume; ESV - end-systolic volume; SV - stroke volume; LV - left ventricle; LVEF - ejection fraction of the LV; LVMM - mass of the myocardium of the LV; i-LVMM - indexed LV myocardial mass; RWT - relative LV wall thickness; *p*1 – significance of differences between the 1st and 2nd groups; *p*2 - significance of differences between the 1st and 3rd groups

Evaluation of i-LVMM and RWT indicators in order to clarify the geometric type of LV showed that most women had i-LVMM > N, RWT < 0.45 - which corresponds to eccentric LV hypertrophy, and only 6 patients (22.2% of the entire sample) had i-LVMM > N, RWT ≥ 0.45 - which corresponds to concentric LV hypertrophy.

Correlation analysis between the number of courses of CT and FC CHF established a direct relationship (*p*=0.741; *t*=0.332; *r*=0.066), on the contrary, between the number of courses of CT and LVEF - on the one hand (*p*=0.103; *t*= -1.694; *r*= -0.326) and CAS-scores, on the other hand, showed an inverse correlation (*p*=0.676; *t*= -0.421; *r*= -0.084). The revealed correlation dependences in women with breast cancer indicate that the more courses of CH they receive, the worse the picture of their clinical and functional state becomes.

Thus, women with breast cancer, with an increase in the number of CT courses taken, despite a relatively young age, were characterized by a more pronounced tendency to tachycardia, the formation of arrhythmias and a decrease in ET, which, in turn, aggravated the phenomena CHF in the form of a decrease of the SV and LVEF. However, here it is necessary to take into account the side effects of CH itself, its toxic effect on the body with all the ensuing consequences.

In view of the foregoing, we conducted an additional analysis to study the frequency and severity of manifestations of side effects of CT according to the AC regimen in combination with doxorubicin. The average dose of doxorubicin (dD) in the whole group was 86.7±23.1 mg/m². Of the side effects of doxorubicin, according to the literature^[9], the most common are:

- From the hemopoietic system: thrombocytopenia, leukopenia, anemia.
- From the cardiovascular system: cardiomyopathy, heart failure, arrhythmias.

- From the digestive system: stomatitis, esophagitis, abdominal pain, nausea, vomiting, diarrhea.
- From the reproductive system: amenorrhea.
- Allergic reactions: urticaria, fever, anaphylactoid reactions.
- Local reactions: when injected into veins of small diameter or when re-introduced into the same vein - sclerosis of the vessel; with extravasation - tissue necrosis.
- Others: alopecia, hyperuricemia, nephropathy, etc.

The patients were divided into 2 groups; A-g. – 15 patients with dD = 60 mg/m² and B-g. – 12 patients with dD > 60 mg/m². Comparative analysis of patients is presented in table 3, which shows that women B-g. turned out to be 8.3 years younger. Perhaps that is why they were characterized by relatively better hemodynamic parameters (Table 3). In particular, the level of BP, both systolic and diastolic, was relatively lower (difference in SBP - 23.7 mm Hg; in DBP - 11.2 mm Hg); there were fewer patients with AH (16.7% in the B-group versus 40.0% in the A-group); heart rate values were lower (by 5.1 beats/min), a smaller number of women with tachycardia was recorded (difference 15.0%). In addition, in B-g. recorded greater values of the duration of the QRS complex and the interval-QT, as well as arrhythmias were recorded in the form of VE (Table 3).

An analysis of intracardiac hemodynamic parameters established the opposite picture. Namely, women B-g. had clear signs of heart failure: large volumetric indices, low LVEF, higher values of LVMM and i-LVMM (Table 4). However, comparison of i-LVMM and RWT showed that out of 6 patients with concentric LV hypertrophy - to B-g. included only 2 women.

Table 3: Comparative general clinical characteristics of patients depending on the dose of doxorubicin in the chemotherapy complex.

Sign	A group (n=15)	B group (n=12)	p	χ ²
Average age, years	62,8±7,8	54,5±10,2	0,024	
Average number of CT courses	7,7±5,1	7,6±4,7	0,959	
dD, mg/m ²	60,0	98,2±6,0	0,000	
Average number of RT courses	21,3±7,5	24,0±4,1	0,274	
Average BMI, kg/m ²	32,3±6,2	29,1±5,3	0,165	
Number of persons with BMI > 30 kg/m ² , n (%)	8 (53,3%)	5 (41,7%)	0,820	0,046
Mean SBP, mm Hg	138,7±19,6	123,3±19,2	0,051 [#]	
Mean DBP, mm Hg	88,7±7,4	77,5±10,6	0,003	
Number of persons with AH, n (%)	6 (40,0%)	2 (16,7%)	0,371	0,802

Average heart rate, bpm	90,9±17,2	85,8±18,0	0,460	
Heart rate > 90 bpm, n (%)	6 (40,0%)	3 (25,0%)	0,681	0,169
Average QRS, ms	0,91±0,10	0,96±0,12	0,248	
Average QT, ms	3,33±0,23	3,45±0,24	0,185	
LPD for SWT, m	272,0±76,4	227,3±72,4	0,054 [#]	
CAS, points	6,8±1,2	7,3±1,2	0,292	
Average FC CHF according to NYHA	2,80±0,41	2,83±0,39	0,549	
Arrhythmias according to HMECG, n (%)	1 (6,7%)	1 (8,3%)	0,565	0,321
VE, n (%)	abs	1 (8,3%)	0,909	0,012
SVE, n (%)	1 (6,7%)	abs		

Notes: n is the number of patients; CT – chemotherapy; dD - the dose of doxorubicin; RT - radiation therapy; BMI - body mass index; SBP and DBP - systolic and diastolic blood pressure; AH - arterial hypertension; HR - heart rate; LPD - the length of the passed distance; SWT - 6-minute walk test; CAS – the clinical assessment scale; FC - functional class; CHF - chronic heart failure; HMECG - Holter ECG monitoring; VE and SVE - ventricular and supraventricular extrasystoles; p – significance of differences between the A- and B- groups

Table 4: Echocardiographic parameters of patients depending on the dose of doxorubicin.

Sign	A group (n=15)	B group (n=12)	p
EDV, ml	116,0±21,9	134,8±42,5	0,149
ESV, ml	46,2±13,0	75,8±36,8	0,005
SV, ml	69,8±13,9	59,0±17,1	0,052 [#]
LVEF, %	60,5±7,2	45,5±14,5	0,002
LVMM, g	225,1±67,9	230,7±63,1	0,825
i-LVMM, g/m ²	195,9±39,1	200,6±47,4	0,750
RWT, units	0,42±0,06	0,38±0,05	0,076 [#]
OTS ≥ 0.45 units, n (%)	4 (26,7%)	2 (16,7%)	p=0,877 χ ² =0,024

Notes: n is the number of patients; EDV - end-diastolic volume; ESV - end-systolic volume; SV - stroke volume; LV - left ventricle; LVEF - ejection fraction of the LV; LVMM - mass of the myocardium of the LV; i-LVMM - indexed LV myocardial mass; RWT - relative LV wall thickness; p – significance of differences between the A- and B- groups; # - tendency to significance of differences

When conducting a correlation analysis between dD and echocardiographic parameters, a negative relationship was found with the level of LVEF (p<0.001) and a positive relationship with the number of scores according

to CAS (Figs. 1A and 1B), i.e. the higher the dose of anthracycline, the worse the LVEF and the more pronounced the picture of CHF according to CAS.

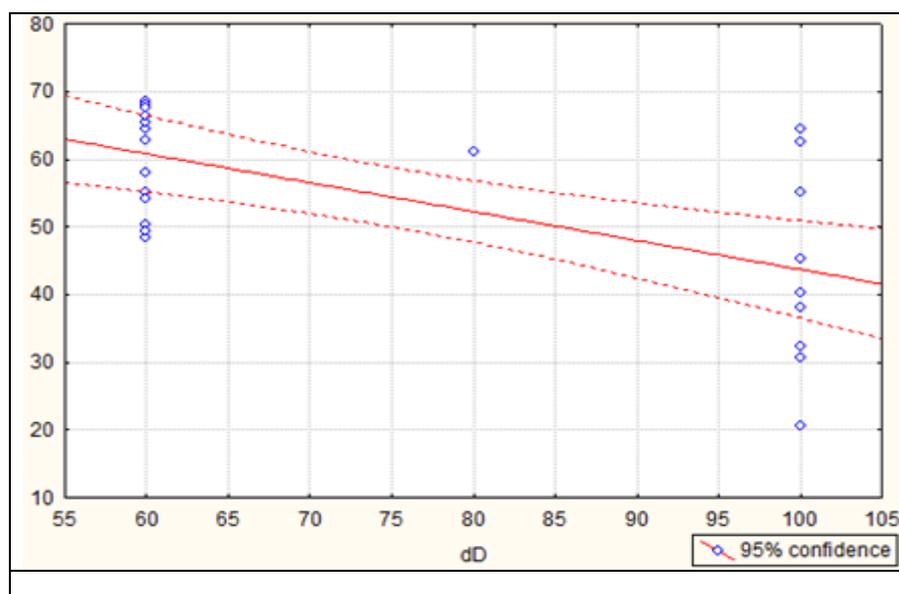


Figure 1A.
Correlation graph between the doxorubicin dose and the left ventricular ejection fraction.
p=0.0008; t= -3.813; r= -0.622
Notes: along the X-axis, doxorubicin dose values (mg/m²); along the Y-axis, the values of the LV ejection fraction (%).

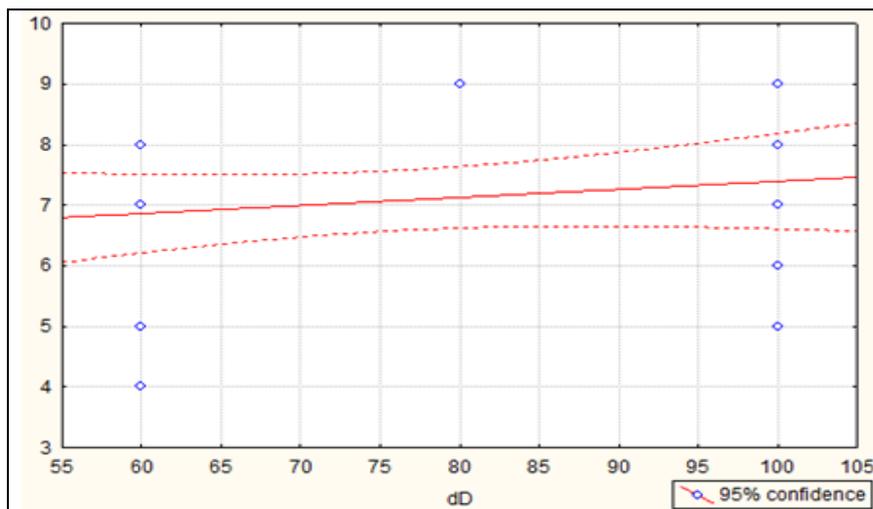


Figure 1B.

Correlation graph between the doxorubicin dose and points by the clinical assessment scale

$p=0.299$; $t=1.061$; $r=0.211$

Notes: along the X-axis – doxorubicin dose values (mg/m²); along the Y-axis – the total score for CAS.

Analysis of the data, in addition to the phenomena of HF and arrhythmias, also made it possible to assess the frequency of occurrence of other side effects of CT according to the AS regimen in combination with doxorubicin. During the study, it was found that 4 women (14.8% of the total) at the initial stages of CT noted painful emetogenicity, i.e. a high level of nausea and vomiting, while 3 patients had acute (in the first 24 hours after the administration of cytostatics) and 1 patient had delayed (after 24 hours) nausea and vomiting. It was noteworthy that all patients who noted emetogenicity were under 50 years old, two of them had a history of severe toxicosis during pregnancy, 1 woman – indicated that she had previously worked at a chemical plant.

Thus, the treatment of women with breast cancer with large doses of doxorubicin, as part of complex CT, contributes to the formation of HF while maintaining central hemodynamic parameters. In 14.8% of cases, CT according to the AC regimen in combination with doxorubicin was accompanied by a high level of emetogenicity.

DISCUSSION

Along with the increase in the prevalence of a number of oncological diseases, there is a general trend for many countries of the world towards an increase in the life expectancy of patients. For patients with breast cancer, the increase in survival was 8.1%.^[10] The increase in the survival rate and life expectancy of patients, of course, is primarily associated with the detection of the disease at an early stage, due to the widespread introduction of screening programs, as well as an increase in the effectiveness of complex therapy. In this regard, there is a reasonable increase in alertness regarding the increase in morbidity and mortality from cardiovascular causes among surviving patients, which may be a consequence of both side effects of therapy and accelerated development of CVD.^[11,12] In our study, 29.6% of patients had hypertension of varying severity and 7.4% had arrhythmias.

A recently published meta-analysis demonstrated that weight gain is associated with an 11% increase in breast cancer risk per 5 kg in postmenopausal women not taking hormone replacement therapy (RR 1.11, 95% CI 1.08–1.13).^[13] In our work, it was found that almost ½ of the surveyed (more precisely, 48.1%) had an increased level of BMI. Increased body weight, as shown by modern literature data, is not only a risk factor for the development of CVD, but also for breast cancer. This is explained by the fact that in postmenopause, the production of hormones in the ovaries decreases, the extragonadal synthesis of estrogens in adipose tissue and the liver is activated, which, with excess activity and the number of adipocytes, leads to hyperestrogenism.^[14,15]

Knowledge of the cardiotoxic effect of anthracyclines in the chemotherapy regimen has led to lower doses and less use of bolus injections of peak concentrations of the latter.^[16] But according to experts, the risk of HF associated with anthracyclines remains elevated even with the use of standard low doses of anthracyclines^[17], one of the brightest representatives of which is doxorubicin.

The combination of damage caused by anthracycline and its metabolites, their repair leads to the development of the so-called "anthracycline-induced cardiomyopathy". This is a dose-dependent, non-coronary, focal myocardial disease, manifested by structural and functional changes in the LV (remodeling), a progressive decrease in LV function with the development of congestive HF.^[6,18-20] The results of our work are consistent with the above. Namely, in the women examined by us, after the courses of CT, there was a decrease of the LVEF, a decrease of the SV, and an increase in LVMM. It is known that an increase in LVMM is an even stronger predictor of cardiovascular complications and mortality than the level of BP and other risk factors.^[21,22]

Other side effects of adjuvant therapy with doxorubicin included emetogenicity, which occurred in 14.8% of patients in our study. The level of emetogenicity

corresponds to the drug in mono-mode, for example, when prescribing moderately emetogenic cyclophosphamide without antiemetic drugs, the probability of vomiting is 30–90%.^[23] In a multicenter study, Bloechl-Daum B. et al., when comparing the tolerability of high- (cisplatin or dacarbazine) and moderately emetogenic CT (AS or carboplatin-based regimen), the incidence of acute nausea and vomiting was the same, amounting to 11.9% and 13.2%^[24], which is consistent with the results of our work. According to Koroleva I.A. et al. (2017), a group of increased risk of developing nausea and vomiting in CT are female patients under 50 years of age; women who experienced nausea during pregnancy; persons prone to motion sickness; as well as persons who do not drink alcohol.^[4] In our study, patients who reported emetogenicity had some of the listed risk factors.

According to Supronchuk N.V. et al. (2007), in patients with concomitant heart disease - hypertension, coronary artery disease, etc. - the processes that characterize remodeling during treatment with anthracycline drugs are more pronounced.^[6] Our results also support a similar conclusion regarding the use of doxorubicin in patients with breast cancer.

Thus, systemic adjuvant therapy with doxorubicin in women with breast cancer is associated with a risk of CVD, which should serve as a guide when deciding whether to prescribe this treatment.

CONCLUSION

AC chemotherapy (doxorubicin + cyclophosphamide) remains the most frequently prescribed adjuvant regimen in the treatment of breast cancer. However, the toxicity of oncological drugs requires new approaches to solving this serious problem of modern healthcare. The range of application of doxorubicin in the treatment of malignant neoplasms is extensive, which allows it to be classified as a first-line drug, at the same time, its cardiotoxicity should alert specialists when prescribing it.

The results of our study showed, that women with breast cancer, with an increase in the number of courses of CT in combination with doxorubicin, despite a relatively young age, were characterized by a more pronounced tendency to tachycardia, the formation of arrhythmias and a decrease the ET, which, in turn, aggravated CHF phenomena in the form of a decrease the SV and LVEF. In addition, it was found that treatment with large doses of doxorubicin contributed to the formation of HF while maintaining central hemodynamic parameters with doxorubicin was accompanied by a high level of emetogenicity, which emphasizes the need for an integrated (oncological, cardiological, gastroenterological, etc.) approach in providing medical care to this group of patients.

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