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HOLTER ECG MONITORING AND HEART RATE VARIABILITY IN BREAST CANCER PATIENTS

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When establishing indications for Holter ECG monitoring in 115 breast cancer patients, the criteria of the American Heart Association were used. The survey was carried out using the official versions of the EORTC QLQ-C30 questionnaires (a questionnaire approved by the European Organization for Research and Treatment of Cancer in 2005). The most common malignant neoplasms in the main group and in the control group were found in the upper quadrants of the mammary glands. Less often, the pathological process in both groups was diagnosed at the border of the inner quadrants. Compared with the control group, in the main group, the average 24 hours, average daily and average night heart rate was higher (p=0.001). Also in the control group, an increase in the maximum daily heart rate was revealed – here is the average dash. non-hyphenated 115.7±0.85 beats/min, versus 97.7±0.63 beats/min in the main group (p=0.001). When diagnosing metastatic lesions of lymph nodes, there is an increase in (corrected recovery time of sinus node function after AF paroxysm). Against the background of the lesion of regional lymph nodes, the minimum time interval of arousal by AV (P1-R1 min) increases by 152.6±1.08 ms, versus 138.4±1.18 ms, values recorded in the control group (p=0.001). The highest rates were recorded for two profiles "Pain" and "Fatigue" in the main group of patients burdened with metastases to regional lymph nodes (25.9±2.88 points and 44.2±1.78 points, p=0.001; 9.0±1.43 and 26.7±1.29, p=0.001, in the control and main groups, respectively). Thus, the best indicators in the control group are associated with the absence of serious complications of breast cancer, represented by metastatic lesions of the lymphatic system.

Keywords: quality of life, cancer, metastases, monitoring.

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ХОЛТЕРІВСЬКЕ МОНІТОРУВАННЯ ЕКГ І ПОКАЗНИКИ ВАРІАБЕЛЬНОСТІ РИТМУ СЕРЦЯ У ХВОРИХ НА РАК МОЛОЧНОЇ ЗАЛОЗИ

При встановленні показань для проведення холтерівського моніторування ЕКГ у 115 хворих на рак молочної залози користувалися критеріями Американської асоціації серця. Анкетування виконано за допомогою офіційних версій опитувальників EORTC QLQ-C30 (опитувач, затверджений Європейською організацією з дослідження та лікування раку 2005 р.). Найчастіше злоякісні новоутворення в основній групі та контрольній виявлялися у верхніх квадрантах молочних залоз. Рідше патологічний процес обох групах діагностувався межі внутрішніх квадрантів. Порівняно з групою контролю, в основній групі середня добова, середня денна та середня нічна ЧСС виявилася вищою (р=0,001). Також у контрольній групі виявлено збільшення максимальної денної ЧСС – 115,7±0,85 уд/хв, проти 97,7±0,63 уд/хв в основній групі (р=0,001). При діагностуванні метастатичних уражень лімфовузлів має місце збільшення коригованого часу відновлення функції синусового вузла після пароксизму ФП. На тлі ураження регіональних лімфовузлів відбувається наростання мінімального інтервалу часу проведення збудження за АВУ (P1-R1 min) 152,6±1,08 мс, проти 138,4±1,18 мс, значень, зафіксованих у групі контролю (р=0,001) . Найвищі показники зареєстровані за двома профілями «Біль» та «Втома» в основній групі хворих, обтяжених метастазами в регіональні лімфовузли, (25,9±2,88 бала та 44,2±1,78 бала, р=0,001; 9, 0±1,43 та 26,7±1,29, р=0,001, у контрольній та основній групах, відповідно). Таким чином, найкращі показники в контрольній групі пов'язані з відсутністю серйозних ускладнень перебігу раку молочної залози, які представлені метастатичними ураженнями лімфатичної системи.

Ключові слова: якість життя, рак, метастази, моніторинг.

The work is a fragment of a doctoral dissertation "The role of thoracic lymphatic dysfunction in the pathogenesis of arrhythmias and their regulation"

Breast cancer is a serious medical and social problem that has not yet been solved and is the leading oncological disease in women in all, including developed countries of the world [13].

The use of new modern regimens of standard chemotherapy to a certain extent has led to an increase in the survival of patients, but the use of certain chemotherapeutic drugs can very often cause a number of complications, including cardiotoxicity. At the same time, the main frequent causes of disability and mortality among cancer patients are cardiovascular diseases [7]. One of the markers of autonomic dysfunction, characterized by an increase in the concentration of vasoactive substances in the blood serum, is a violation of the regulation of vascular tone. This is manifested by pathological types of daily blood pressure profiles, which are detected even before the development of arterial hypertension with damage to target organs. Such patients have an increased risk of developing vascular complications in cancer and require timely correction of these disorders [2].

Currently, a highly sensitive predictor of cardiovascular complications is central aortic pressure, the assessment of which exceeds the measurement of peripheral blood pressure in prognostic significance. Based on the above, the main efforts of specialists should be aimed at early detection of side effects, their timely correction and preventive measures, which will also reduce the number of cardiovascular complications, for example, during antitumor therapy [10].

Due to the early diagnosis of these complications and new treatment methods, a decrease in mortality from malignant neoplasms was noted, which, in turn, led to the increased attention of specialists to the study of adverse cardiovascular disorders both in the pathology itself and at various stages of antitumor therapy [5]. It should be noted that there are few studies devoted to the study of the features of pathological changes in the cardiovascular system in breast cancer, especially complicated by metastatic lesions. In this regard, it seems relevant to study the pathogenetic mechanisms of the development of hemodynamic disorders in breast cancer patients, in particular against the background of the development of lymph node metastases, for the development of early laboratory and instrumental criteria for the diagnosis and prediction of cardiovascular disorders in this category of patients [11].

With long-term survival, in parallel with some criteria for the effectiveness of therapeutic and preventive measures, in particular with indicators of the survival rate and the duration of the relapse-free period, one of the main criteria determining the condition of patients with cancer and the effectiveness of their treatment, according to many experts, is the quality of life [12].

The purpose of the work was to develop diagnostic and prognostic criteria to identify the mechanisms of early cardiovascular disorders and quality of life in patients with breast cancer and metastatic lesions of regional lymph nodes.

Material and methods. The present study included 115 breast cancer patients undergoing basic therapy at the oncology clinic of the Azerbaijan Medical University, 45 of whom had signs of metastatic lesion of regional lymph nodes at the preoperative stage, according to clinical and instrumental examination methods. The mean age of the patients ranged from 30 to 60 years and older. A complex of atraumatic, minimally invasive, highly informative instrumental diagnostic methods were used: Holter ECG monitoring, which was carried out in two groups of breast cancer patients, in the main (45 people) and control (70 people) groups. Complex research methods also included: survey, anamnesis collection, physical examination, clinical and biochemical blood tests. Holter monitoring (HM) (24 hours) ECG is essentially a method of registering the electrical activity of the heart with the habitual activity of the patient.

When establishing indications for HM ECG, the criteria of the American Heart Association (Mond H.G., 2017) were used, according to which, the indication for HM ECG is the presence of complaints associated with cardiac arrhythmias in the patient [1]. The daily assessment of complaints was carried out in the form of diary entries.

During the monitoring process, a report was compiled that included the following blocks:

1. General part: a) passport data; b) the conditions under which the study is conducted (outpatient/inpatient); c) medications taken; d) the patient's daily routine, physical activity; e) the duration of the study, the ECG leads used and the quality of the signal received.

2. Assessment of the dynamics of heart rate (R-R intervals). The proportion of the main rhythm (in %), the average heart rate in 24 hours, the tendency to bradycardia, tachycardia in the daytime or at night were determined.

3. Revealed rhythm and conduction disturbances were: a) ventricular rhythm disturbances; b) supraventricular rhythm disturbances c) the presence of pauses, the duration of the PQ interval day and night, the presence of blockages; d) the duration of the Q-T interval.

The survey was carried out using the official versions of the EORTC QLQ-C30 questionnaires (a questionnaire approved by the European Organization for Research and Treatment of Cancer in 2005). The QLQ-C30 questionnaire, version 3.0, is common to all cancer patients and consists of 30 questions that characterize three scales.

Statistical processing of the results of the study was carried out on a personal computer, the STATISTICA for Windows 7.0 system, which is an integrated data processing environment, was used to analyze the clinical data obtained during the study. Comparison of the studied quantitative parameters (age, tumour localization, quality of life indicators of patients according to the questionnaire) in the study groups was carried out using the Wilcoxon-Mann-Whitney criteria.

Descriptive statistics of quantitative features included an estimate of the arithmetic mean, the mean square deviation, the error of the mean value, minimum and maximum. The criterion of the statistical reliability of the obtained conclusions was the generally accepted value of $p<0.05$ in medicine.

Results of the study and their discussion. In the course of the studies, a comparative analysis of the frequency of occurrence in patients of experimental groups of anatomical features of the development and location of the tumor process in the mammary gland was carried out, and when analyzing the results obtained by tumor localization, the following results were obtained: the most common malignant neoplasms in the main group and in the control were found in the upper quadrants of the mammary glands.

Less often, the pathological process in both groups was diagnosed at the border of the inner quadrants. Such localization of the tumor was recorded only in 1 (2.2 %) patients of the main group in the

absence of a tumor in this area in all patients of the control group without exception. At the border of the outer quadrants, neoplasm in the control group was detected in 1 patient (1.4 %), and in the main control group in 2, that is, in 4.4 % of cases (p>0.05).

The number and percentage of patients, depending on the localization of the tumor, is shown in table 1.

Table 1

The frequency of occurrence of various localizations of the tumor process

Tumor localization	Group of patients			
	Control group (n=70)		Main group (n=45)	
	abs. number	%	abs. number	%
Upper-outer	11	15.7	8	17.8
Lower-outer	4	5.7	5	11.1
Upper inner	24	34.3	12	26.7
Lower-inner	9	12.9	4	8.9
The border of the upper	16	22.9	8	17.8
The border of the lower	5	7.1	5	11.1
Internal boundary	0	0.0	1	2.2
The boundary of the outer	1	1.4	2	4.4

Notes: The difference in indicators between the groups is statistically unreliable (p>0.05)

The following clinical and morphological characteristics of the disease were studied in the patients included in the study: when studying the patterns of tumor localization in the left and right mammary glands, in most cases the tumor was localized in the upper inner quadrant, less often in the lower outer quadrant.

At the next stage, a comparative assessment of the cardiac conduction system was carried out in the presence and without metastatic lesions in patients burdened with breast cancer. Table 2 shows ECG and EF heart parameters in the main and control groups of patients, calculated using HM ECG.

Table 2

Electrocardiographic and electrophysiological parameters of the heart of patients with breast cancer according to HM ECG (M±m)

Indices	Atrial fibrillation		p
	Control (n=70)	Main (n=45)	
Maximum daily heart rate, beats/min	115.7±0.85	97.7±0.63	0.001
Maximum night heart rate, beats/min	75.5±0.48	64.4±0.66	0.001
Average daily heart rate, beats/min	73.2±0.37	61.8±0.35	0.001
Average daily heart rate, beats/min	82.9±0.56	69.8±0.50	0.001
Average night heart rate, beats/min	64.8±0.42	53.9±0.36	0.001
Minimum daily heart rate, beats/min	69.9±0.46	58.1±0.45	0.001
Minimum night heart rate, beats/min	64.5±0.61	52.9±0.43	0.001
Number of episodes of AF, pcs.	14.5±0.13	11.8±0.09	0.001
CRTSN, ms	287.8±2.28	355.1±2.93	0.001
ERP AVU, ms	371.4±2.09	370.4±2.75	0.762
ERP PR, ms	298.5±1.80	245.2±1.80	0.001
P1-R1 min, ms	138.4±1.18	152.6±1.08	0.001
P2-R2 max, ms	235.8±2.09	226.4±1.62	0.002
P2-R2 max/P1-R1 min	1.71±0.021	1.49±0.016	0.001
P2-R2 max/ERP AVU	0.64±0.007	0.61±0.007	0.018

Notes: p is the statistical significance of the difference between the groups (U is the Mann-Whitney criterion). Heart rate – heart rate; HM ECG – Holter ECG monitoring; AF – atrial fibrillation; EF – electrophysiological; – transesophageal electrocardiostimulation; CRTSN – corrected recovery time of sinus node function after paroxysm AF; ERP – effective refractory period; AV – atrioventricular node; PR – atria; P1-R1 min – minimum time interval of excitation according to the AV node; P2-R2 max – the maximum time interval for the excitation of the AV node; n – the number of patients; p is the probability of error and the statistical significance of the differences at $p < 0.05$.

As can be seen from the data obtained, compared with the control group, in the main group the average 24 hours, average daily and average night heart rate was higher (p=0.001). In addition, in the control group, an increase in the maximum daily heart rate was revealed – 115.7±0.85 beats/min, versus 97.7±0.63 beats/min in the main group (p=0.001).

A comparative statistical analysis of indicators of intervals and refractory periods of the heart revealed that, compared with the control group, in the diagnosis of metastatic lesions of the lymph nodes

is an increase in CRTSN (corrected recovery time of sinus node function after AF) to 355.1±2.93 MS, while 287.8±2.28 MS, compared to the group of cancer patients (p=0.001).

As a result of the analysis of the data obtained by us, it was revealed that despite the similar somatic status (breast cancer) and the mechanisms of occurrence of paroxysm of isolated AF against the background of the development of lymphastases, there were some distinctive features between the groups. Thus, in the presence of lymphastases, the ERP is slightly shorter (245.2±1.80ms) than in the normal course of the studied oncological disease (298.5±1.80ms) (p=0.001).

The analysis of the ECG and EF indicators of women of both groups showed that the complicated course of the background pathology under study is accompanied by a slight decrease in heart rate, an increase in CRTSN, a shortening of the ERP of the atrioventricular node and atria. In addition, a difference was revealed when comparing the experimental groups for the values of the minimum interval of the excitation time for the AVU (P1–R1 min) and the maximum interval of the excitation time for the AVU (P2–R2 max). So, in comparison with the control values, against the background of the lesion of the regional lymph nodes, the minimum interval of excitation time for the AVU (P1–R1 min) increases by 152.6±1.08 ms, against 138.4±1.18 ms, the values recorded in the control group (p=0.001). When comparing the intergroup indicators, some deviations were revealed in the values of the ratio of the indicators P2–R2 max/P1–R1 min and P2-R2 max/ERP AVU, on which the stability of the reciprocal tachycardia paroxysm depends.

At the same time, the ratio of the maximum to minimum time interval of excitation according to the AVU P2-R2 max/P1–R1 min in the control group was 1.71±0.021, versus 1.49±0.016 in the main group (p=0.001). Thus, in the course of observations, it was revealed that in the presence of metastatic lesions of lymph nodes, the trigger factor is an increase in CRTSN, the ratio of P1-R1 min AVU indicators at relatively low daily heart rate values. That is, in the main group, compared with the control group on the background of a relatively low heart rate, there is an opposite dynamics of CRTSN and P1-R1 min.

If we take into account that the frequency regulation of the heart rate is one of the manifestations of autonomic control of the heart rate, then we can assume a certain role of oncological pathology in the genesis of disorders in the cardiovascular system, which suggests expanding the list of necessary studies in the management of patients with breast cancer and its complications. The same can be said about the expediency, according to the recommendations of the World Health Organization (WHO), of studying the quality of life of the examined patients.

Self-assessment by the examined patients themselves of the quality of life and the state of their health, when surveyed by the EORTC QLQ-C30 questionnaire, is carried out according to the results of the "General Health" scale. In a comparative analysis of the statistical data obtained in the main group, the indicators for the domain of "Emotional functioning" characterizing the psycho-emotional state of the examined patients were also recorded in values much higher than those in the main group (84.8±0.59 and 74.6±0.75, p=0.007) (fig.).

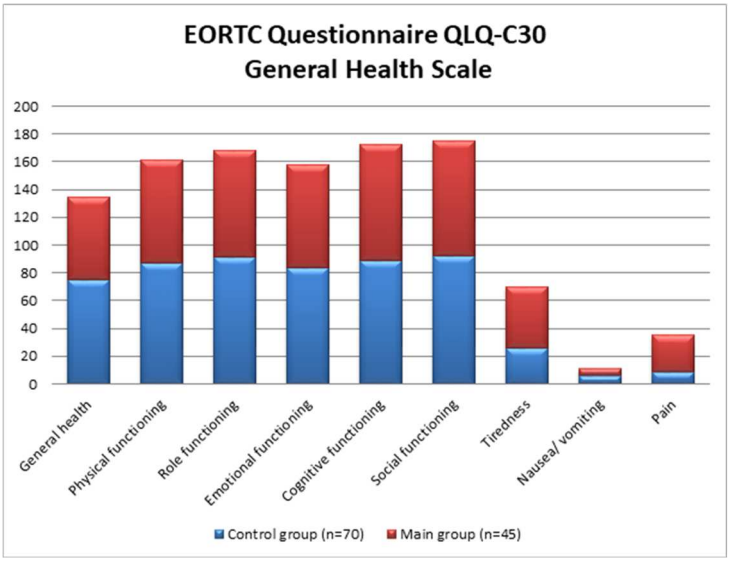

Fig. Results of the "General health status" scale of the EORTC QLQ-C30 questionnaire in the control and main groups.

A comparative analysis of the survey data obtained by the symptomatic scales of the questionnaire used revealed that the highest rates were recorded for two profiles "Pain" and "Fatigue" in the main group of patients burdened with metastases to regional lymph nodes (25.9±2.88 points and 44.2±1.78 points, p=0.001; 9.0±1.43 and 26.7±1.29, p=0.001, in the control and main groups, respectively).

There were no statistically significant differences in the comparative analysis of the data obtained and the indicators of the "Diarrhea" domains (p=0.728). Patients of the main group complained of "Decreased appetite" more than twice as often.

Currently, there is little data on the deterioration of the functional state of the cardiovascular system, which usually develop before and at certain times after the start of treatment of malignant neoplasms, mainly in patients with breast cancer and metastatic lesions of the lymphatic system. Cases of

both acute cardiotoxicity and late toxic effects of various antitumor drugs included in the treatment regimens of cancer patients on the heart muscle indicate a complex effect of side effects and serious systemic complications on the heart, possible before and after chemotherapy. Considering the insufficient information content of some electrocardiographic and ultrasound methods of heart examination, as well as hidden changes on the part of the cardiovascular system of cancer patients, which can lead to a significant deterioration in the quality of life of patients, a reduction in their life expectancy after, as well as fatal consequences at various stages of treatment, it is necessary to expand the list of studies to develop an optimal algorithm of therapeutic and diagnostic measures for the detection of coronary pathology in patients with various stages of breast cancer and metastatic lesions of the lymphatic system on its background. In our study, after continuous recording of heart dynamics using Holter ECG monitoring in breast cancer patients, a significant increase in heart rate was noted, which, according to other authors, may be due to tachycardia developed during the development of both the pathology itself and chemotherapy, and is a reflection of the toxicity of basic therapy [2]. The above requires urgent timely measures to maximize the correction of cardiovascular disorders, which could favorably affect the prognosis in people with cancer, including in the category of patients we examined [6, 14]. At the same time, it is important to study the possibility and effectiveness of using Holter monitoring before the start of complex antitumor treatment to detect disorders in the cardiovascular system among patients with breast cancer and metastatic lesions of the lymph nodes, who may subsequently additionally require supportive cardiotropic and antiarrhythmic therapy [8].

The best indicators of QOL in the control group are associated with the absence of serious complications of breast cancer, represented by metastatic lesions of the lymphatic system. In patients with breast cancer of the main group who underwent examination and damage to the signaling lymph nodes, the quality of life is lower in almost all scales and domains of the questionnaires used than in patients without complications [9].

Thus, our data, as well as the research results of some authors, show a pronounced negative effect of breast cancer on the psychoemotional and physical condition of the examined patients [3]. At the same time, it should be noted that as a result of the conducted studies, we came to the conclusion that the absence of metastases gives a relatively better quality of life, without a pronounced level of anxiety.

Questionnaires using questionnaires already tested in clinical practice, and thus assessing the quality of life can be used as diagnostic and prognostic criteria, as well as as a criterion for the effectiveness of ongoing therapeutic and preventive measures, to assess the prognosis of the course of the disease at various stages of the rehabilitation period, and statistically verified values for all domains and scales can serve to develop an optimal algorithm for the management of patients with cancer, This was reflected in the results of their own observations of foreign authors [12]. Thus, in the course of these studies, more positive dynamics in the picture of the well-being of patients and higher scores of questionnaires in the control group were revealed. Patients of the main group noted an increase in such indicators as deterioration of emotional status and a higher level of anxiety.

Conclusion

Against the background of the lesion of regional lymph nodes, the minimum time interval of arousal by AVU (P1-R1 min) increases – 152.6±1.08 ms, against 138.4±1.18 ms, the values recorded in the control group

In the main group, the indicators for the domain of “Emotional functioning” characterizing the psycho-emotional state of the examined patients were also recorded in values much higher than those in the main group (84.8±0.59 and 74.6±0.75).

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STATE OF DIFFERENT LINKS OF HORMONAL-METABOLIC CHANGES IN PATIENTS WITH METABOLIC SYNDROME AND OBESITY

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The article is devoted to the problem of surgical treatment of patients with metabolic syndrome and obesity. Research methods: general clinical, anthropometric, laboratory, morphological; mathematical and statistical. It has been established that in order to select the optimal surgical tactics and predict complications in the postoperative period, it is necessary to additionally determine the insulin level. It has been proven that metabolic syndrome and obesity negatively affect the state of carbohydrate metabolism, production of inflammatory cytokines and cortisol. Assessment of changes in the structure of comorbidities (hypertension, joint pain) had no significant differences and in all groups was positive. The analysis of complications in all groups showed the absence of significant problems during the postoperative period, and there are minor differences of no discussion interest.

Key words: obesity, insulin resistance, metabolic disorders, metabolic syndrome, surgical treatment, diabetes mellitus.

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СТАН РІЗНИХ ЗВ'ЯЗКІВ ГОРМОНАЛЬНО-МЕТАБОЛІЧНИХ ЗМІН У ПАЦІЄНТІВ З МЕТАБОЛІЧНИМ СИНДРОМОМ ТА ОЖИРІННЯМ

Стаття присвячена проблемі хірургічного лікування пацієнтів з метаболічним синдромом та ожирінням. Методи дослідження: загальноклінічні, антропометричні, лабораторні, морфологічні; математично-статистичні. Встановлено, що для вибору оптимальної хірумилицяргічної тактики та прогнозування ускладнень у післяопераційному періоді необхідно додатково визначати рівень інсуліну. Доведено, що метаболічний синдром та ожиріння негативно впливають на стан вуглеводного обміну, продукцію запальних цитокінів та кортизолу. Результати зміни показників супутніх захворювань (артеріальна гіпертензія, біль у суглобах) не мали різких відмінностей і в усіх респондентів мали позитивну динаміку. Аналіз ускладнень в усіх групах вказав на відсутність видимих проблем у післяопераційний період, відтак незначні відмінності не мають дискусійного підґрунтя.

Ключові слова: ожиріння, інсулінорезистентність, метаболічні порушення, метаболічний синдром, хірургічне лікування, цукровий діабет.

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As early as in the twentieth century, scientists concluded and later confirmed that obesity and insulin resistance create the pathophysiological foundation of further metabolic disorders with different clinical manifestations, first as single disorders (for example, coronary heart disease or hypertension), and then as metabolic expansion of almost all organs and tissues implemented in the form of numerous diseases that answer the description of Pickwick syndrome [4]. Therefore, the study of metabolic features of the