

PATHOMORPHOLOGICAL AND CLINICAL CHARACTERISTICS OF BREAST CANCER IN MEN IN THE REPUBLIC OF UZBEKISTAN.

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Article history:		Abstract:			
Received:		Oncological diseases remain a pressing problem in the world. In recent years,			
Accepted:	August 26 th 2023	according to official world medical statistics, the incidence of cancer has been			
Published:	September 28 th 2023	increasing worldwide. According to statistics from the World Health Organization (WHO), "by 2030, there will be 15 million people in the world with dangerous diseases, so the system for predicting early diagnosis, as well as surgical treatment and systemic treatment of oncological diseases has not yet been clarified." WHO notes an annual increase in breast cancer diagnosed in women, but detection of a similar cancer in men is very rare and accounts for 1% of the total number of detected cases, while this disease accounts for about 0.2. Scientific research on male breast cancer is being conducted all over the world, but there are few of them, in this regard, our research helps fill the gap in the assessment and scientific study of this oncological pathology in men, and there are also unique scientific studies devoted to the early diagnosis and prognosis of male breast cancer . Therefore, the pathomorphological and molecular genetic characteristics of breast cancer in men is one of the most important problems of fundamental medicine and oncology.			

Keywords: Breast cancer in men, pathogenetic mechanism, detection in the Republic of Uzbekistan.

PURPOSE OF THE STUDY: To improve modern methods of early diagnosis and prognosis of patients with breast cancer through the introduction of molecular genetic studies and the development of new screening algorithms.

MATERIALS AND METHODS:

As the object of the study, we took the medical records of 76 men who were undergoing treatment and follow-up for breast cancer at the Republican Specialized Oncological and Radiological Scientific and Practical Medical Center, the Tashkent City Oncology Clinic and regional oncology clinics of the Republic of Uzbekistan. The subject of the study was statistics on the incidence of breast cancer in men in the regions of the Republic of Uzbekistan, materials from clinical

laboratory, ultrasound, radiation, histological tumor necrosis, tumor differentiation, tumor infiltration with lymphocytes, lymphovascular invasion, the ratio of parenchyma to tumor stroma, localization, ratio affected vessels of tumor tissue, vascular density index, immunohistochemical study (RE, RP, Her2/neu, KI67). Research methods. When optimizing the pathomorphological and molecular genetic characteristics of breast cancer in men in the Republic Uzbekistan, clinical. immunohistochemical, of instrumental and statistical research methods were used.

RESULTS AND THEIR DISCUSSIONS:

The study included patients aged 44 to 95 years living in the Republic of Uzbekistan.

Patient age (by year)	Number of patients, (abs.,%)	Early life (average)	р
44-49 лет	6 (7,9%)	46,5	<0,001
50-59 лет	11 (14,5%)	54,5	<0,001
60-69 лет	21 (27,6%)	64,5	<0,001
70-79 лет	26 (34,2%)	74,5	<0,001

Table 1 Distribution of breast cancer patients by age groups.



80-95 лет	12 (15,8)	87,5	<0,001
44-95 лет	76	65,5	<0,001

The age of patients with breast cancer was 44-95 (average 65.5) years. In the study, breast cancer in men was most common in the category of patients aged 60 to 79 years - 47 (61.8%). All patients with a clinical diagnosis of breast cancer underwent a standard comprehensive examination, including general clinical and special research methods. In all patients, on the basis of postoperative pathological material, the degree of spread of the oncological process, the histological structure of the tumor and its

other important pathohistological indicators were determined. According to Table 2, in the studied category of men over 60 and under 80 years of age, more than half of the cases of breast cancer were detected in 47 patients (61.8%), respectively. This age range of the population is a risk group that should be taken into account in the diagnosis and prognosis of cancer, and age differences in the 5 groups examined are also statistically significant (p<0.001).

Table 2

Step-by-step division of breast cancer patients into age groups according to the FIGO-WHO anatomical classification

Disease stage	44-49 year,(%)	50-59 year, (%)	60-69 year(%)	70-79 year(%)	80-95 year,(%)
Ι	1(16,7)	2(18,2)	2(9,5)	3(11,5)	1(8,4)
II	1(16,7)	2(18,2)	3(14,3)	4(15,4)	2(16,8)
III	2(33,3)	3(27,3)	7(33,4)	9(34,6)	4(33,6)
IV	2(33,3)	4(36,3)	9(42,8)	10(38,5)	5(41,2)
Total (76)	6(7,9)	11(14,5)	21(27,6)	26(34,2)	12(15,8)

In the process of studying the history of breast cancer in men, after primary (clinical) diagnosis, after operations and treatment, as well as with the development of relapses and distant metastases, taking into account older age, the mortality rate of patients from this disease was determined to be much higher.

Table 3

Distribution of patients with breast cancer with initial diagnosis according to the TNM clinical classification.

Stage	Number of patients	(%)	
TXN2M0	2	2,63	
TisN0M0	1	1,32	
T1NxM0	1	1,32	
T1N0M0	3	3,95	
T1N1M0	4	5,26	
T2N0M1	11	14,48	
T2N1M0	5	6,58	
T2N1M1	5	6,58	
T2N2M1	6	7,89	
T3N0M1	6	7,89	
T3N1M1	4	5,26	
T3N2M1	4	5,26	
T4N0M0	2	2,63	
T4N0M1	9	11,85	
T4N1M0	2	2,63	
T4N1M1	3	3,95	
T4N2M1	5	6,58	
T4N3M1	3	3,95	
Total:	76	100	



According to the data presented in table. 3, in our study, the largest number of patients with breast cancer belonged to stage II (35.5%) and stage IV (31.5%). The reason for the observed situation is probably related to the late presentation of men and the lack of screening of this group of patients. Analysis of the table data shows that for all initial stage diagnoses (clinical diagnosis), metastases to regional organs were detected in 56 (73.7%) patients, and in 20 (26.3%) patients no metastases were observed.

Moreover, in most cases, at all stages of this cancer, in 43 of the total number of patients (56.6%), the spread of cancer cells to the lymph nodes was detected, affecting more than 1 lymph node. Based on the initial (clinical) diagnosis of breast cancer in men, subsequent surgical intervention and relapses after treatment, the development of regional metastases, the established pathological diagnosis, as well as the elderly age of patients, a fairly high mortality rate from this disease has been established. determined by studying the medical history.

The period from the onset of symptoms to hospitalization was 1-3 years in patients with breast cancer included in the study.

Compared with women, men exhibit clinical signs typical of advanced stages of the disease. However, the fact that men miss breast cancer requires the necessary oncological alertness from general practitioners. However, taking into account the age of the patients in our study, lymph node involvement is an important factor leading to a worse prognosis and reduced survival of patients. In the two groups, tumors were mostly of low quality, grades 3 and 4 in 54 patients, and grades 1 and 2 were detected only in 22 patients (table 4).

Table 4
Distribution of patients taking into account the involvement of regional lymph nodes according to the
FIGO classification

Qualitatively low degree.	Total (n=76)	Main group (n=48)		Control group (n=28)		χ2	P
		Completely white	%	Completely white	%		
I-degree	11	8	16,7	3	10,7	7,661	<0,01
(1-2 knots)	11	7	14,6	4	14,3	6,79	<0,01
II-degree (2-3 nodes)	25	16	33,3	9	32,2	0,425	>0,05
III-degree (3-4 nodes)	29	17	35,4	17	60,8	1,539	>0,05

When examining the presence of concomitant diseases, the following concomitant diseases were identified (table 5).

Table 5

Distribution of breast cancer patients into groups depending on concomitant diseases.

Name of comorbidity	Quantity, N	%
There is no concomitant pathology	24	31,6
Hypertonic disease	7	9,2
IHD	7	9,2
Cardiosclerosis	2	2,6
Cardiomegaly	2	2,6
Hydropericardium	2	2,6
Diabetes mellitus type 2	2	2,6
Chronic cholecystitis	6	7,9



Chronical bronchitis	9	11,9
BPH	4	5,3
Viral hepatitis B	2	2,6
Fatty hepatosis	4	5,3
Other	5	6,6

Most of the patients did not have somatic diseases, which amounted to 31.6% of the total number of patients, and among those who did, chronic bronchitis was observed to a greater extent, which may be associated with smoking of the patients (11.9%). %). The length of hospitalization of breast cancer patients included in the study ranged from 1 to 3 years from the onset of symptoms. Our studies set the stage in advance, since the origin and morphological features of the tumor vasculature are important both for disease prognosis and for assessing tumor sensitivity to treatment. Currently, there is no generally accepted classification that takes into account the various characteristics of tumor vessels, their clinical and morphological features in the pathological process, disease prognosis and sensitivity to treatment. In connection with the above, 48 patients with breast cancer took part in the study, who were examined and treated in the main group of the RSNPMTSROiR of Uzbekistan, the Tashkent City Oncology Dispensary and regional oncology hospitals. Group 2 included 28 patients with breast cancer. In our study, the groups were divided into: Group 1 - 48 patients with breast cancer, after radical treatment, relapses and metastases did not develop for 5 years; Group 2 - In 28 patients with breast cancer, after radical treatment, aggressive development of the oncological process was noted during dynamic observation. A study of the anamnesis of patients in groups shows that the main diagnosis of breast cancer in men in groups is palpation of the mammary gland, in addition, the presence of painless induration in the areola, pain in the chest or armpit, complaints of enlarged lymph nodes are auxiliary indicators for clarification diagnosis. Patients with breast cancer in the main and control groups underwent а comprehensive examination, including laboratory and instrumental studies, ultrasound, in rare cases, MSCT and MRI studies, as well as histological examination of postoperative material. In addition to MSCT, magnetic resonance imaging was used to assess local spread and invasion of nearby organs and anatomical structures. Even in a fully equipped clinic, there may be cases where malignant neoplasms are not detected during dynamic observation or preventive examination of men, which is confirmed by the patients' anamnesis; then all patients of both groups turn to doctors on

their own. This situation is mainly associated with the identification of non-palpable forms of the mammary alands, which are most difficult to diagnose in the pathology of the mammary glands in men; as mentioned above, the identification of early forms of cancer improves the prognosis of the disease. Despite the improvement in the diagnosis of breast cancer in women, in men, the identification of non-palpable formations with a dense structure of breast tissue remains a particular problem. Non-palpable forms do not cause pain, and men may not suspect the presence of pathology for a long time due to their small size and high density of breast tissue. The combination of sophisticated instrumental diagnostics and determination of the density of tumor vessels is important in the early diagnosis of the patient, which allows achieving an optimal result and reducing mortality from breast cancer in men. Tumor tissue with surrounding tissue was taken from the material for the study. The resulting samples were placed in a 10% solution of neutral formaldehyde, processed according to standard methods and embedded in paraffin. Sections 3-4 um thick were stained with Maer's hematoxylin and eosin. The preparations were studied using an Optika B-350 microscope (Optika, Italy) with a DCM500 digital video camera for the microscope. According to the anamnesis, family history (presence of mammary gland tumors in close relatives of the first and second generations) was not confirmed in patients of both groups.

CONCLUSIONS:

During the study period, an increase in incidence was noted mainly in Tashkent from 10 to 20 cases per year for 10 years, indicating an increase from 0.9 to 1.5 per 100,000 men. During this period, isolated cases were identified in other regions of the Republic of Uzbekistan, but their total number is more than half of the patients diagnosed in the city of Tashkent. During the examination, breast cancer was more common in men in the category of patients 60-79 years old - 44 (61.8%). Men over 60 years of age and under 80 years of age accounted for more than half of the cases of breast cancer; accordingly, men in this age range were at risk, and this situation must be taken into account in the early diagnosis and prognosis of cancer. If we take the disease according to the stages of the



disease, in our study the largest number of patients with breast cancer belong to stages II-IV, while breast cancer had no symptoms and in none of the cases were precancerous changes detected, which occur in the initial stages of the disease. The reason for this situation is probably due to the late conversion of men and the lack of sufficient control over this category of the population.

Comparison of clinical, morphological breast cancer in men, solving the problems of early diagnosis and prognosis of breast cancer makes it possible to reduce the incidence and identify the risk group, improve the prognosis of the treatment, resulting in a reduction in mortality, improved regional treatment results, improved quality of life and a reduction in disability.

REFERENCE:

- 1. Volchenko A.A., Pak D.D., Usov F.N., Fetisova E.Yu. Giant leaf-shaped tumor of the mammary gland: clinical observation // Tumors of the female reproductive system. 2017. N 2. P. 27-29.
- Dmitriev V.N. A comprehensive study of morbidity, mortality and disability due to malignant neoplasms of the female genital organs and PGTT for improving medical and social examination and rehabilitation: abstract of thesis. dis. ... doc. honey. Sci. Moscow, 2015. 337 p.
- 3. Zavyalova M.V. The relationship between the morphological phenotype of the tumor, lymphogenous and hematogenous metastasis in infiltrating ductal breast cancer: abstract. dis. ... doc. honey. Sci. Tomsk, 2019. 44 p.
- Malignant neoplasms in Russia in 2016 (morbidity and mortality) // ed. HELL. Kaprina, V.V. Starinsky, G.V. Petrova. M.: MNIOI im. P.A. Herzen - branch of the Federal State Budgetary Institution "National Medical Research Center of Radiology" of the Ministry of Health of Russia, 2018. 250 p.
- Imyanitov E.N. General ideas about targeted therapy // Practical Oncology. 2020. T. 11, N 3. P. 123-130.
- Kolyadina I.V., Poddubnaya I.V., Frank G.A. and others. Heterogeneity of stage I breast cancer: biological and prognostic significance // Malignant tumors. 2015. N 1. P. 35-45.
- Kuligina E.Sh. Epidemiological and molecular aspects of breast cancer // Practical Oncology. 2020. T. 11, N 4. P. 203216.
- 8. Mayborodin I.V., Krasilnikov S.E., Kozyakov A.E. and others. The feasibility of studying tumor angiogenesis as a prognostic factor for cancer

development // News of surgery. 2015. T. 23, N. 3. pp. 339 - 347.

- 9. Odintsova I.N. Epidemiology of breast cancer in the region of Siberia and the Far East: abstract. dis. ...doc. honey. Sci. Tomsk, 2021. 42 p.
- Semiglazov V.F., Semiglazov V.V., Manikhas A.G. and others. Individualization of adjuvant therapy for breast cancer // Farmateka 2021. N 7. P. 8-13.
- Snegovoi A.V., Manzyuk L.V. The importance of biomarkers for determining treatment tactics and prognosis // Practical Oncology. 2021. T. 12, N 4. pp. 166-170.
- The state of cancer care for the population of Russia in 2016 / Ed. HELL. Kaprina, V.V. Starinsky, G.V. Petrova. M.: MNIOI im. P.A. Herzen - branch of the Federal State Budgetary Institution "NMRRC" of the Ministry of Health of Russia, 2017. 236 p.
- 13. Tsoi L.K. Prognostic significance of clinical, morphological, immunohistochemical factors in patients with stage I and IIa breast cancer: abstract. dis. ...cand. honey. Sci. Moscow, 2021. 144 p.
- 14. Aalders K.C., Tryfonidis K., Senkus E. et al. Antiangiogenic treatment in breast cancer: facts, successes, failures and future perspectives // Cancer Treat Rev. 2017. Vol. 53. P. 98-110.
- 15. Acs G., Paragh G., Chuang S.T. et al. The presence of micropapillary features and retraction artifact in core needle biopsy material predicts lymph node metastasis in breast carcinoma // Am J Surg Pathol. 2019. Vol. 33, I. 2. P. 202 - 210.
- Acs G., Paragh G., Rakosy Z. et al. The extent of retraction clefts correlates with lymphatic vessel density and VEGF-C expression and predicts nodal metastasis and poor prognosis in early-stage breast carcinoma // Mod Pathol. 2012. Vol. 25, I. 2. P. 163-77.
- Adams S., Gray R., Demaria S. et al. Prognostic value of tumor-infiltrating lymphocytes (TILs) in two phases randomized adjuvant breast cancer trials: ECOG 2197 and ECOG 1199 // J Clin Oncol. 2014. Vol. 32, I. 27. P. 295966.
- Ahn K.J., Park J., Choi Y. Lymphovascular invasion as a negative prognostic factor for triple-negative breast cancer after surgery // Radiat Oncol J. 2017. Vol. 35, I. 4. P. 332-339.
- 19. Aird W.C. Endothelial cell heterogeneity // Cold Spring Harb Perspect Med. 2012. Vol. 2, I. 1.
- Aird W.C. Molecular heterogeneity of endothelium tumor // Cell Tissue Res. 2019. Vol. 335, I. 1. P. 271-81.