ORIGINAL ARTICLE

Women's Health

Morphological and Prognostic Characteristics of Breast Cancer in Women Living in the Sakha Republic (Yakutia)

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Abstract

Background: This article presents the results of the analysis of the clinical and morphological examination of breast cancer (BC) in women of the Republic of Sakha (Yakutia) (RS(Y)).

Methods and Results: The object of the study was fragments of breast tissue from 294 women who underwent surgical treatment and/or needle biopsy. By ethnicity, there were 118(40.1%) women of indigenous nationalities and 176(59.9%) women of non–indigenous nationalities. The greatest number of cases of BC was registered in the age group of 50-59 (32.6%). The age group of 40-49 was in second place (20.4%). Among the indigenous population, women in the age groups of 40-49 years (23.7%) and 50-59 years (26.3%) predominated. The age groups of 50-59 years (36.9%) and 60-69 years (22.2%) predominated among the non-indigenous women.

Tumors with a size of 2 cm to 5 cm prevailed; they were detected in 185(62.9%) women. Tumors with a spread to the chest wall and skin develop more often in women of non-indigenous nationalities (15.9% of cases), than in women of indigenous nationality (6.8% of cases). Regardless of ethnicity, the most common histological form of BC in women of the RS(Y) was infiltrative ductal cancer (65.3%). Cancer staging according to the TNM staging system showed that in the age group of women under 39 years, Stage IIIB+IIIC (43.2%) was most often registered (P=0.01), while in other age groups, Stage IIA (32.4%) was more often noted.

Conclusion: Our findings suggest that further investigation of the peculiarities of the course of BC in the female population of Yakutia would lead to much improved methods of diagnosis and treatment.**(International Journal of Biomedicine. 2021;11(2):201-205.)**

Key Words: breast cancer • ethnicity • TNM staging system • tumor grade

Introduction

Breast cancer (BC) is an urgent social and medical problem affecting a significant part of the female population. Tumors of this localization occur predominantly among women of active working age. The largest number of women with BC is found in the age group of 40-60 years. There is a period of the most intensive endocrine changes in women, and there is a progressive replacement of epithelial glandular tissue with connective and adipose tissue in the mammary gland.[1,2] Many researchers have found the age peak of the disease is 55-59 years during menopause, when the production of ovarian hormones decreases.[3] After 60 years, the risk for disease is quite high, but the process of tumor growth itself is slower than in young people.[4]

Today in assessing the features of the clinical course, the possible outcome of the disease, and the choice of the most appropriate treatment strategy, such clinical and morphological parameters as age, size of the primary lesion, histologic type of the tumor and the tumor stage, the presence of metastases in axillary lymph nodes, and several other indicators are taken

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into account.[5-7] There is no doubt that the detection of BC in the early stages contributes to the improvement of long-term treatment results. At the same time, an individual assessment of the prognosis of BC, even at an early process of tumor stage, is considered extremely relevant.

This article presents the results of the analysis of the clinical and morphological examination of BC in women of the Republic of Sakha (Yakutia) (RS(Y)).

Materials and Methods

The object of the study was fragments of breast tissue from 294 women who underwent surgical treatment and/or needle biopsy. Indigenous people were considered Yakuts, Evens, and Evenks and representatives of peoples of the North with low populations. Non-indigenous people were all other nationalities that arrived at various times from the regions of Russia and the CIS countries. By ethnicity, there were 118(40.1%) women of indigenous nationalities and 176(59.9%) women of non–indigenous nationalities.

Tumor grade (G) was determined by the Elston & Ellis grading system,[8] which took into account the preservation of the tubular structure in the tumor, polymorphism, and mitotic activity of cancer cells. This system divided BC into tumors with G1 (low-grade or well-differentiated tumor), G2 (intermediate grade or moderately differentiated tumor), and G3 (high-grade or poorly differentiated tumor).

Morphological method

A macroscopic study of breast tissue was performed with the measurement of tumor size, counting, and measuring of lymph nodes.

Microscopic study

The material was fixed in 10% neutral formalin for 24 hours, followed by pouring into paraffin in the Tissue-Tek 9589. Using the microtome Leica SM 2000R, sections with a thickness of 3–5 microns were made from paraffin blocks; the sections were straightened in a water-bath, and placed on glasses treated with protein. The glasses were left overnight in a dry-air sterilizer at a temperature of 38°C for better fixation and straightening of the sections. The sections were stained with H&E automatically on a Sacura DRS-60 device, according to the following step-by-step program: 1 – toluene 1(10 min); 2 – toluene 2(10 min); 3 – alcohol 1(10 min); 4 – alcohol 2(10 min); 5 – hematoxylin(1 min); 6 – flush in H_2O; 7 – HCL solution(1 min); 8 – H_2O(10 min); 9 – eosin (1 min); 10 – flush in H_2O; 11 – alcohol 3 (5 min); 12 - carbolic acid; 13-toluene. Sections were extracted from the last glass solution and enclosed in polystyrene under cover glasses.

*S*tatistical analysis was performed using statistical software package SPSS version 17.0 (SPSS Inc, Chicago, IL). The frequencies of categorical variables were compared using Pearson's chi-squared test or Fisher's exact test, when appropriate. A value of *P*<0.05 was considered significant.

Results and Discussion

The average age of patients was 54.2±12.1 years. The age groups were as follows: over 50-59 years - 96(32.6%);

60-69 years – 64(21.8%); 40-49 years – 60(20.4%); under 39 years – 37(12.6%); ≥70 years – 37(12.6%) (Table 1).

Table 1.
Distribution of women by age and ethnicity

Age group (yrs)	Indigenous women		Non-indigenous women		Total	
	n (%)	average age	n (%)	average age	n (%).	average age
<39	15 (12.7)	33.7±5.3	22 (12.5)	33.8±3.6	37 (12.6)	33.7±4.3
40–49	28 (23.7)	45.3±2.9	32 (18.2)	45.0±2.8	60 (20.4)	45.1±2.9
50–59	31 (26.3)	54.8±2.7	65 (36.9)	54.1±2.9	96 (32.6)	54.3±2.9
60–69	25 (21.2)	63.4±2.6	39 (22.2)	62.9±3.1	64 (21.8)	63.1±2.9
≥70	19(16.1)	74.2±2.9	18 (10.2)	73.3±3.3	37 (12.6)	73.8±3.2
Total	118 (100)	54.8±12.9	176 (100)	53.8±11.5	294 (100)	54.2±12.1

It should be noted that BC, which was traditionally considered a disease of women over 50 years old, is now noticeably "younger." Cases of 40-year-old, 30-year-old, and even 20-year-old women are not uncommon.[9] This trend can be found in our work. Thus, there were only 2 times more women over age 50 than women under age 50: 197(67%) versus 97(33%). In economically developed countries, postmenopausal women account for approximately 75% of BC cases.[10] The greatest number of cases of BC was registered in the age group of 50-59 (32.6%). The age group of 40-49 was in second place (20.4%). Women under age 39(12.6%) and women over age 70 (12.6%) were also diagnosed with BC.

In this study, there were fewer indigenous women (118 cases) than non-indigenous women (176 cases) (*P*=0.000). Among the indigenous population, women in the age groups of 40-49 years (23.7%) and 50-59 years (26.3%) predominated. This was followed by the age group of 60-69 years (21.2%). The lowest number of women were in the age groups under 39 years and over 70 years (12.7% and 16.1%, respectively). The age groups of 50-59 years (36.9%) and 60-69 years (22.2%) predominated among the non-indigenous women. This was followed by the age group of 40-49 years (18.2%). In the groups under age 39 and over age 70, the ratio of non-indigenous women was about the same (12. 5% and 10. 2%, respectively).

Thus, non-indigenous women aged 50-59 years provided the most surgical material for BC. There were no statistically significant differences between the groups.

A study of the clinical and morphological features of BC revealed that the majority of women (190/65.0%) were diagnosed with invasive ductal carcinoma. The second most common type of BC was mixed cancer (invasive ductal and lobular) (33/11.2%), and the third most common type was invasive lobular carcinoma (23/7.8%). Neuroendocrine cancer was diagnosed in 15(5.1%) cases, invasive cancer was diagnosed without specifying the form, due to the severity of therapeutic pleomorphism in 7(2.4%) cases, and Paget's cancer was diagnosed in 6(2.0%) cases. Other forms of cancer (medullary, tubular, papillary, etc.) accounted for 6.8% (20 cases).

When studying the occurrence of various forms of BC in age groups, statistically significant differences were found in neuroendocrine cancer between the age groups under 39 years and 50-59 years (P=0.005) , 50-59 years and 60-69 years (P=0.03). There are no statistically significant differences in other forms of BC, which does not contravene similar data from the WHO (2003).

Tumors with a size of 2 cm to 5 cm prevailed; they were detected in 185(62.9%) women; in 41(13.9%) women, there were tumors larger than 5 cm, in 32(10.9%) cases tumors of 1cm to 2cm and in 36(12.2%) cases – tumors with a spread to the chest and skin. Comparison of the data revealed that in women of non-indigenous nationality the tumor spread to the chest wall and skin was in 28(15.9%) cases, while in women of indigenous nationality it was in 8(6.8%) cases (χ2=5.479, df=1, P=0.019) (Table 2).

Table 2.

Distribution of BC patients (n/%) depending on the tumor size

Age group (yrs)	T categories for BC			
	T1 (<2 cm)	T2 (2-5 cm)	T3 (>5 cm)	T4 (Tumor of any size growing into the chest wall or skin)
<39 n=37	6 (16.2)	19 (51.3)	8 (21.6)	4(10.8)
40-49 n=60	7 (11.7)	32 (53.3)	9 (15)	12 (20)
50-59 n=96	7 (7.3)	67 (69.7)	12 (12.5)	10 (10.4)
60-69 n=64	5 (7.8)	43 (67.2)	8 (12.5)	8 (12.5)
≥70 n=37	7 (18.9)	24 (64.8)	4 (10.8)	2 (5.4)
total n=294	32 (10.9)	185 (62.9)	41 (13.9)	36 (12.2)
By ethnicity				
Indigenous n=118	13 (11.0)	80 (67.8)	17 (14.4)	8 (6.8)
Non-indigenous n=176	19 (10.8)	105 (59.7)	24 (13.6)	28 (15.9)

The relationship between the size of the tumor and the lesion of the lymph nodes was statistically significant (Fig.1). The frequency of lymph node damage showed a statistically significant increase with an increase in the tumor size (from 19% with a tumor size <2 cm to 94% with tumors spreading to the chest wall and skin; P=0.001)).

Cancer staging according to the TNM staging system (Table 3) showed that 26(8.8%) women had Stage I, 122 (41.5%) – Stage IIA, 50(17.0%) – Stage IIB, 20(6.8%) – Stage IIIA, 75(25.5%) – Stage IIIB+IIIC, and 1(0.3%) – Stage IV. In the age group of women under 39 years, Stage IIIB+IIIC

(43.2%) was most often registered (P=0.01), while in other age groups, Stage IIA (32.4%) was more often noted. Aggregate indicators in groups of indigenous and non-indigenous women with BC showed that Stage IIA of BC was most common in both ethnic groups. Thus, there was a high rate of detection in late stages (IIIB) in young women (<39 years). This can be explained by low clinical suspicion and the fact that this age group is not included in the breast disease screening program; the Republic of Sakha (Yakutia) screens women 40 years and older.
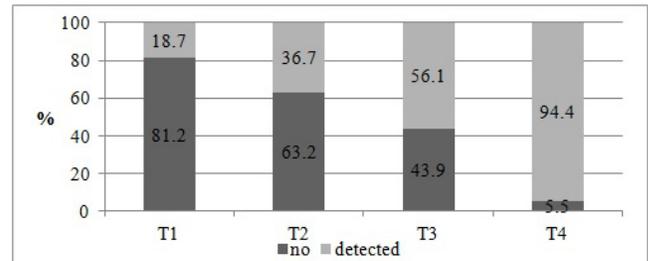

Fig. 1. The relation between the tumor size and the lesion of the lymph nodes.

Table 3.

Distribution of BC patients according to the TNM staging system

Age group (yrs)	I*	IIA**	IIB***	IIIA^	IIIB/IIIC^^	IV^^^
<39	4(10.8%)	12(32.4%)	2(5.4%)	2(5.4%)	16(43.2%)	1(2.7%)
40-49	5(8.3%)	19(31.6%)	15(25.0%)	5(8.3%)	16(26.6%)	-
50-59	7(7.3%)	44(45.8%)	19(19.8%)	6(6.2%)	20(20.8%)	-
60-69	5(7.8%)	25(39.1%)	13(20.3%)	5(7.8%)	16(25%)	-
≥70	5(13.5%)	22(59.5%)	1(2.7%)	2(5.4%)	7(19.0%)	-
Total	26(8.8%)	122(41.5%)	50(17.0%)	20(6.8%)	75(25.5%)	1 (0.3%)

*- (T1N0M0), **- (T2N0M0.T0N1M0), ***- (T3N0M0.T2N1M0), ^- (T3N1M0.T0-2N2M0), ^^- (T4N0-2M0.T0-4N3M0), ^^^- (T0-4N0-3M1)

G1 was found in 96 (32.6%), G2 in 146 (49.6%), and G3 in 52 (17.7%) cases (Table 4). When analyzing structural atypia with an assessment of the presence of tubular structures, it was found that 1 point (<75%) was 56(19%) cases, 2 points (10%-75%) – 88(29.9%), and 3 points (less than 10%) - in 150(51%) women.

The analysis of cellular atypia showed that small cells of the same size and shape with a dispersion distribution of chromatin, without nucleoli (1 point) were detected in 44(14.9%) women. A small polymorphism of the nuclei, some cell enlargement (2 points), was found in 168(57.1%) women. Large nuclei of various shapes with one or more nucleoli, coarse chromatin (3 points) were detected in 82(27.9%) cases. The calculation of mitoses showed that 1 point (0–9 mitoses in 10 visual fields) was present in 137 (46.6%) women, 2 points

in (10–19 mitoses) – 91(30.9%) women, and 3 points (20 or more mitoses) in 66 (22.4%) women. Statistically significant dependence of the malignancy degree on the age and ethnicity of the examined women was not found.

Table 4.

Distribution of BC patients depending on the degree of malignancy

	Total n=294	%
Degree of malignancy		
G1	96	32.6
G2	146	49.6
G3	52	17.7
Score (Points)	*Structural atypia*	
1	56	19.0
2	88	29.9
3	150	51.0
Score (Points)	*Cellular atypia*	
1	44	14.9
2	168	57.1
3	82	27.9
Score (Points)	*Mitoses*	
1	137	46.6
2	91	30.9
3	66	22.4

Eighty-six percent of women had an infiltrative form of cancer. Due to the small number of observations of other morphological forms of cancer, it was not possible to establish a relation between the degree of malignancy and the form of cancer.

A statistically significant relationship between the tumor size and the degree of malignancy was found (Figure 2). Thus, the T4 tumor has the degree of histological malignancy G3 (19.2%) significantly more often than G1 (6.2%).
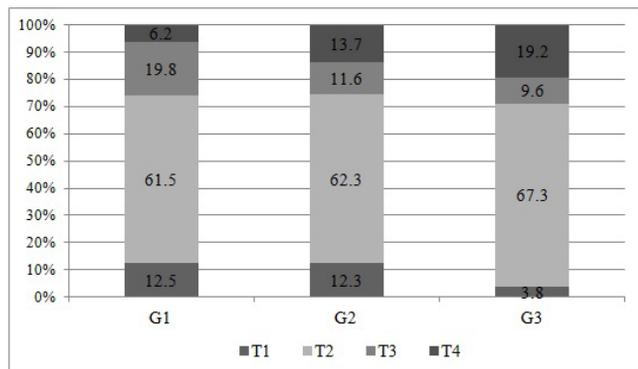
Fig.2. The degree of malignancy and the size of the tumor.

Statistically significant dependence by the degree of malignancy of the metastases presence in the lymph nodes was found (Fig.3). Thus, 61.5% of women with G3 had metastases to regional lymph nodes, while with G1- in 40.6% ($\chi2$= 5.1, df=1, P_{1-2}= 0.02), and with G2 – in 41.1% ($\chi2$= 5.6, df=1, P_{2-3}=0.01).
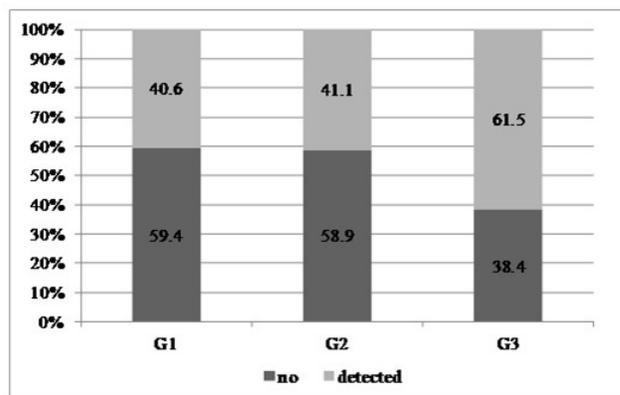
Fig. 3. The degree of malignancy and damage of the lymph nodes.

Conclusion

BC is most frequently reported in women of indigenous and non-indigenous nationalities in the age groups of 50-59 years (32.6%) and 60-69 years (21.8%). Tumors with a spread to the chest wall and skin develop more often in women of non-indigenous nationalities (15.9% of cases), than in women of indigenous nationality (6.8% of cases). Regardless of ethnicity, the most common histological form of BC in women of the RS(Y) is infiltrative ductal cancer (65.3%). The TNM staging system showed that the IIA and IIB stages were predominant (58.5% of cases) in the general age group of the examined patients, while in patients under age 39 – IIIB+IIIC stage (43.2%).

We also found a relationship between the size of the primary tumor and the number of lymph nodes affected by metastases (*P*=0.001), which can be considered as a criterion for the unfavorable clinical course of breast cancer.

Our findings suggest that further investigation of the peculiarities of the course of BC in the female population of Yakutia would lead to much improved methods of diagnosis and treatment.

Competing Interests

The authors declare that they have no competing interests.

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