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Male breast cancer: temporal trends and treatment in Lithuania

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Male breast cancer is a rare disease in Lithuania, comprising less than 0.2% of malignancies among men. During the last decade, there has been no change in the frequency of the disease, with 10–15 cases registered every year during 1988–2006, and only 16 of the more than 8000 new cases in 2006 presented male breast carcinoma. Data published in the *Cancer Incidence in Five Continents* during 1978–2002 show no changes in the variability of the rate of incidence of male breast carcinoma either.

Materials and methods. This investigation analyzed 100 male patients with breast carcinoma treated during the period 1988–2006 in two clinics: Institute of Oncology at Vilnius University and Hospital of Oncology at Kaunas University of Medicine. The average age of the patients was 67.5 years (range, 31–90 years). The patients were grouped according to the progression of the disease: 13 patients in stage I, 41 patients in stage II, 31 patients in stage III, and 15 patients in stage IV. The type of cancer was as follows: invasive ductal carcinoma was the most frequent (68 cases), lobular carcinoma in 9 cases, and adenocarcinoma in 6 cases. The most common method of treatment was modified mastectomy by Madden (75 cases). Furthermore, 53 patients received a combined treatment: 23 patients were treated with radiotherapy, 9 patients with chemotherapy, 14 patients received radiotherapy and chemotherapy, and 14 patients were treated with tamoxifen.

Results. The status of the patients was validated up to December 31, 2007 by checking the active follow-up examinations as well as utilizing the assistance and results of primary health care centers and the population registry. The overall survival rates were calculated using mortality issues as primary endpoints. The overall 5-year survival rate of all male patients with breast carcinoma was estimated to be 42.7%. The 5-year survival rate of the patients in stages I and IIA was 71.9% and 79.5%, respectively, and in stage IIB 53.5%. Lower survival rates (15.8% and 11.2%) were observed in stage IIIA and stage IIIB, respectively. None of the patients in stage IV survived beyond 5 years. A 2-year survival rate of 6.7% was the best estimate of this group.

Conclusion. The overall survival rate of male breast cancer patients treated at two major medical centers of Lithuania was estimated to be below 50%. The low survival rate can be explained by late detection of advanced cases and the lack of innovation during cancer treatment.

Key words: male breast cancer, treatment, survival

INTRODUCTION

Male breast cancer is a rare disease in Lithuania, comprising less than 0.2% of malignancies among men (1). During the last decade, there was no change in the frequency of the disease: usually 10–15 cases were registered every year, and only 16 of more than 8000 new cancer cases in 2006 were diagnosed as male breast carcinoma. Data published in the *Cancer Incidence in Five Continents* (1978–2002) show no variability in the incidence rate during the previous decades, either (Table 1). The worldwide variation in the rate of incidence of male breast cancer markedly lags behind that of breast cancer in women, with higher rates in North America and Europe and lower rates in Asia (2).

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Table 1. **The number of new cases, crude and age standardized rates (ASR), of male breast cancer in Lithuania 1978–2002**

Period	Number of new cases	Incidence rates	
		Crude rate	ASR, world
1978–1982	30	0.4	0.4
1983–1987	39	0.5	0.4
1988–1992	43	0.5	0.4
1993–1997	32	0.4	1.3
1998–2002	60	0.7	0.5

Breast irradiation, other environmental exposures, and genetic inheritance are among the main male breast cancer risk factors (3–7). The ageing of the male population cannot be excluded, as the majority of cases occur at age of 60–65 years – five years later than in female patients (8, 9). Based on the EUROCARE data, 5-year standardized relative survival rates vary in Europe from below 60% (Slovakia 40%, Estonia 52%, Austria 57%) to above 70% (Finland 70.4%, Sweden 72.1%). The survival rates in Europe for males (observed in 57% cases, relatively 72%) are lower as compared to those of females (observed in 65% cases, relatively 73%). According to the research literature as well as our own clinical experience, the interval between the onset of symptoms of the disease and the initiation of therapy was longer in males as compared to females. During the month after the onset of symptoms of the disease, only one third of male patients came for treatment (8).

Male breast cancer is a rare disease, although the incidence has increased slightly over the past 25 years. As many other rare diseases, male breast cancer has not been studied enough. In addition, a paucity of researchers and minimal funding has hindered work on breast cancer in men, and further work is clearly needed to better investigate this disease.

In this paper, we analyzed 100 male patients treated at two clinics: Institute of Oncology at Vilnius University and Hospital of Oncology at Kaunas University.

MATERIALS AND METHODS

During 1989–2006, 201 males were diagnosed with breast cancer in Lithuania. The average age of these patients was 64.6 years (range, 20–98 years). The present study analyzes 100 male patients treated in 1988–2006 at the Institute of Oncology Vilnius University and the Hospital of Oncology, Kaunas University of Medicine. The mean age of patients was 67.5 years (range, 31–90 years). The distribution of patients according to cancer stages in the population and in the present study is given in Table 2.

The distribution of patients according to TNM classification was the following: 13 patients had T1N0M0, 24 patients T2N0M0, 2 patients T1N1M0, 14 patients T2N1M0, 1 patient T1N2M0, 3 patients T2N2M0, 1 patient T3N0M0, 9 patients T3N1M0, 2 patients T3N2M0, 2 patients T4N0M0, 8 patients T4N1M0, 6 patients T4N2M0, and 15 patients had distant metastases (Table 3). The majority of patients (65 cases) had a tumour in the region of the nipple. In 19 of these patients, the tumour manifested as a large ulceration spread to the whole breast. Table 4 also includes a listing of the histological types of male breast cancer, with invasive ductal carcinoma as the most common type (68 patients), lobular carcinoma

Table 2. **Male breast cancer distribution during 1989–2006 in the population and the hospital samples***

Stage	Population		Study group	
	Cases	%	Cases	%
I	26	12.9	13	13.0
II	82	40.8	41	41.0
III	53	26.4	31	31.0
IV	26	12.9	15	15.0
unknown	14	7.0		0.0
Total	201	100.0	100	100.0

Note. * $P > 0.05$ (Kruskal–Wallis equality of populations rank test).

Table 3. **The distribution of patients according to pTNM and the histological type of tumour**

pTNM	Adenocarcinoma	Solidum	Ductal	Lobular	Carcinoma NOS	Ductal & lobular	Total
$T_1N_0M_0$		1	11		1		13
$T_2N_0M_0$	1		20	2	1		24
$T_1N_1M_0$			2				2
$T_2N_1M_0$	2	1	9	2			14
$T_1N_2M_0$			1				1
$T_2N_2M_0$			2	1			3
$T_3N_0M_0$			1				1
$T_3N_1M_0$			6	1	2		9
$T_3N_2M_0$					2		2
$T_4N_0M_0$			1	1			2
$T_4N_1M_0$	1		5	1	1		8
$T_4N_2M_0$	1		4			1	6
$T_2N_{1,2}M_1$			4				4
$T_3N_{1,2}M_1$				1	1		2
$T_4N_1M_1$					4		4
$T_4N_2M_1$	1	1	2		1		5
Total	6	3	68	9	13	1	100

Table 4. **The distribution of patients according to disease stage and method of treatment**

Method of treatment	Stage						Total
	I	IIA	IIB	IIIA	IIIB	IV	
Mastectomy simplex	1	1					2
Mastectomy simplex + rad*		4	1				5
Quadrantectomy	1						1
Mastectomy	7	5	3		3	1	19
Mastectomy + tam**	1	2	1		3		7
Mastectomy + rad	2	9	3	5	2	2	23
Mastectomy + che***		1	4	1	1	2	9
Mastectomy + rad + che		2	5	5	2		14
Radiotherapy	1			2	2	1	6
Chemotherapy						3	3
Radiotherapy + che					1	1	2
Palliative treatment				2	2	5	9
Total	13	24	17	15	16	15	100

Note. Rad – radiotherapy, tam – tamoxifen, che – chemotherapy.

(9 patients), adenocarcinoma (6 patients), and other rarer histological types (17 patients). Hormone receptors were recorded in as many as 78% of male breast carcinomas. Five patients worked under unfavourable environmental conditions, three were electricians, and 24 were agricultural workers. Ten patients had a strong family history of breast cancer.

Modified mastectomy by Madden was the most common method of treatment; it was applied in 75 cases. Simple mastectomy (mastectomy simplex) was performed in 7 cases, one patient was treated with quadrantectomy, 6 patients received radiotherapy, while 3 patients received only chemotherapy. Due to the late stage of the disease, 2 patients were treated conservatively – with chemotherapy and radiotherapy. Palliative treatment was undertaken only in 9 cases because of the poor health of the patients. In addition, 53 patients received a combined treatment: after mastectomy 23 patients were treated with radiotherapy, 9 patients with chemotherapy, 14 patients with radiotherapy and chemotherapy, and 7 patients with tamoxifen. Another 7 patients received tamoxifen after adjuvant therapy: 4 patients after chemotherapy, 2 after radiotherapy and chemotherapy, and 1 patient after radiotherapy. The treatment options and disease stages are shown in Table 4.

Follow-up results

The last follow-up treatment was carried out in December 31, 2007. Out of the 100 patients, 34 patients survived and 66 died (Table 5). Data on the 5-year survival rates of patients with male breast carcinoma are presented according to disease stage in Table 6. The 5-year survival rate of patients in stages I and IIA was 71.9% (95%, CI 34.2–90.4) and 79.5% (95%, CI 57.3–90.9), respectively. In stage IIB it was 53.5% (95%, CI 57.3–90.9), and for patients in stages IIIA and IIIB it was only 15.8% (95%, CI 2.7–39.1) and 11.2% (95%, CI 0.9–41.1), respectively. None of the patients in stage IV survived a 5-year period. Only 6.7% (95%, CI 0.4–26.0) of patients in stage IV survived for 2 years. Those surviving for 5 years and more were 42.7% (95%, CI 31.9 – 52.9) of the entire group. The 10-year survival rate was 22.58% (95%, CI 13.2–33.6), while the 15-year survival rate was 14.1% (95%, CI 6.0–25.6).

The majority of patients were 65 years old and older (67.2%). The age of a patient was inversely related to the rate of survival. For example, patients younger than 60 years in stages I–II lived longer than older patients (Figure). The results of the follow-up of patients in stage III indicate that the cancer treatment regimen was not satisfactory. Many of these patients presented large tumours with ulceration and were of older age; these factors had a negative influence on the survival of patients in stage III. The latest results of treatment produced favourable outcomes only in the early stages of the disease. Statistical analysis of the survival rate of patients surgically treated for breast carcinoma showed that the stage of the disease had a significant positive effect on the survival.

Table 5. **Patient follow-up status (through December 31, 2007)**

Stage of disease	Number of patients on follow-up	Alive	Dead
I	13	9	4
II	41	21	20
III	31	4	27
IV	15	0	15
Total	100	34	66

Table 6. **The disease stage and 5-year survival rate**

Stage of disease	5-year survival of patients (%)	95% confidence interval
I	71.9	34.2–90.4
IIA	79.5	57.29–90.9
IIB	53.5	57.3–90.9
IIIA	15.8	2.7–39.1
IIIB	11.2	0.9–41.1
IV	–	–

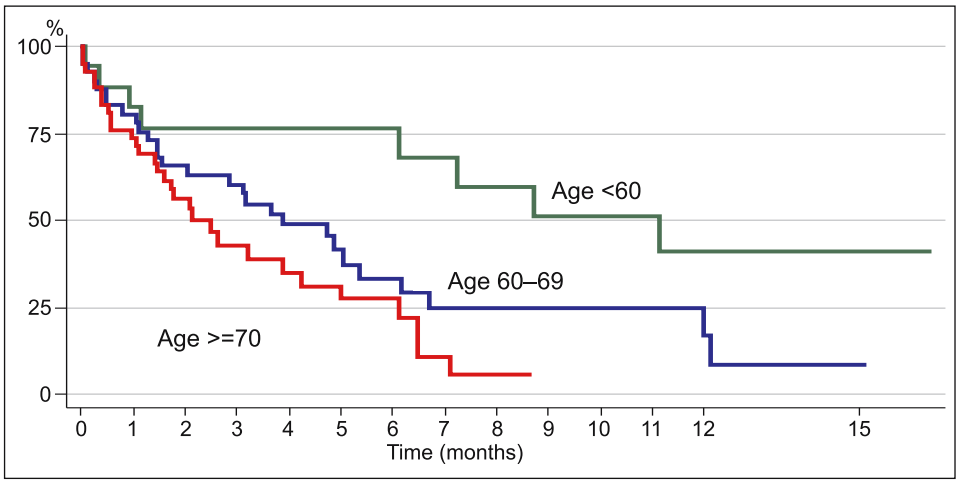

Figure. Survival of patients in stages I–III according to age

The overall survival of patients not included in the study group (101 of 200) was approximately the same as that of the cancer patients, i. e. 46.3% (95%, CI 38.1–54.0), with the log rank test showing no significant difference (log rank test, p = 0.253).

DISCUSSION

Compared to Nordic countries, studies of patient survival in the Baltic countries still lack power. A joint Nordic study encompassing 1429 patients diagnosed over a 25-year period and reported to the Nordic cancer registries indicated a 5-year survival below 50%, where the factors of age at diagnosis and late stage of detection were the most likely explanations for the unfavourable prognosis (10). Similar findings were observed in our study.

According to the anamnesis of the disease, our patients had no risk factors such as radiation exposure, hepatic schistosomiasis, or Klinefelter's syndrome (11–14). Many of our patients were agricultural workers who employed many chemical agents in their work. Also, 10% of our patients had female relatives with breast cancer. We agree with Canadian authors (15) that obesity and family history increase the risk of breast cancer. Similar factors were observed among our patients. Among the medical conditions examined, a new finding emerged regarding an increased male breast cancer risk associated with a history of bone fracture (16). Gonadal insufficiency and low testosterone levels also contribute to bone density and osteoporosis (17).

Some authors note that c-erbB-2, p-53, bcl-2 are significant in the prognosis of male breast cancer (18); however, data regarding the oncogenes and their prognostic significance in male breast cancer are limited (19).

While the lack of physical activity is suggested as an important risk factor for developing male breast cancers, most of our retired patients had been blue-collar workers and so our observations do not support this suggestion (15).

Male breast carcinoma is a rare oncological disease. There are no randomized trials for the treatment of male breast carcinoma. According to published sources, the clinical management of male breast cancer is similar to that of women with breast cancer. Because of the central location and small size of the male breast, modified mastectomy with axillary dissection sparing pectoralis muscles is the treatment of choice for male breast carcinoma. We agree with Schuchardt and coauthors (20) that patients with central lesions and positive axilla should receive irradiation of homolateral lymphatic nodes including the parasternal and homolateral infra- and supraclavicular region. It is necessary to optimize the treatment of male patients with positive lymph nodes: systemic chemotherapy must often be used together with radiotherapy. We agree with the recommendations of Czene et al. and other authors to increase the public awareness of male breast cancer, which ought to result in an earlier diagnosis of cancers. The more negative outcome for men compared with that for females may also be due to men's receiving less optimal therapies (21–23).

CONCLUSIONS

1. The incidence of male breast cancer in Lithuania shows an insignificant increase over the last decades.

2. The majority of male breast cancer patients are diagnosed at an advanced stage of the disease, and early detection is still lacking power.

3. The overall 5-year survival rate was estimated at 42.7%. The stage of the disease was the major determinant of the patients' survival. Patients treated at major hospitals had no advantage in survival as compared to the patients treated elsewhere.

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VYRŲ KRŪTIES VĖŽYS – IŠPLITIMO TENDENCIJOS IR GYDYMAS LIETUVOJE

Santrauka

Vyrų krūties vėžys yra reta onkologinė liga Lietuvoje, sudaranti tik 0,2% visų vyrų piktybinių navikų. Pastaruoju dešimtmečiu nepastebėta didesnių šios onkologinės ligos dažnio pokyčių, kiekvienais metais užregistruota po 10–15 naujų šios ligos atvejų. 2006 m. nustatyta 16 vyrų krūties vėžio atvejų iš 8000 naujai užregistruotų piktybinių navikų. Rinkinyje „Cancer incidence in Five Continents (1978–2002)" paskelbti duomenys nerodo didesnių šio naviko paplitimo pokyčių per kelis dešimtmečius.

Medžiaga ir metodai. Pateikta 100 vyrų, gydytų 1988–2006 m. Vilniaus universiteto Onkologijos institute ir Kauno medicinos universiteto Onkologinėje ligoninėje, krūties vėžio atvejų analizė. Vidutinis pacientų amžius buvo 67,5 metai (nuo 31–90 metų). Pagal ligos stadiją ligoniai pasiskirstė: 13 sirgo I stadijos, 41 – II stadijos, 31 – III stadijos ir 15 ligonių – IV stadijos vėžiu. Nustatyti 68 invazyvios duktalinės karcinomos atvejai, lobulinės karcinomos – 9 atvejai, adenokarcinomos – 6 atvejai. Dažniausiai buvo atliekama modifikuota mastektomija pagal Madden – 75 ligoniams. Kombinuotas gydymas taikytas 53 pacientams: 23 pacientai gydyti spinduline terapija, 9 pacientai – priešnavikiniais preparatais, 14 – spinduline terapija ir chemoterapija, 14 – tamoksifenu.

Rezultatai. Panaudojus gydymo įstaigų ir gyventojų registro duomenis, vėlyvieji pacientų gydymo rezultatai stebėti iki 2007 m. gruodžio 31 dienos. Penkerius metus gyveno 42,7 % visų vyrų, sirgusių krūties vėžiu, iš jų 71,9 % pacientų, sirgusių I stadijos liga, 79,5 % – IIA stadija, 53,5 % – IIB stadija sirgusių pacientų. Trumpiau gyveno pacientai, sirgę IIIA ligos stadija (15,8 %) ir IIIB ligos stadija (11,2 %). Nė vienas pacientų, sirgusių IV ligos stadija, nepragyveno penkerių metų. Iš šios grupės dvejus metus gyveno 6,7 % pacientų.

Išvada. Krūties vėžiu sergančių vyrų, gydytų pagrindinėse Lietuvos onkologinėse klinikose, išgyvenamumas buvo mažesnis nei 50 %. Priežastis, kodėl krūties vėžiu sirgę vyrai gyveno neilgai, buvo jų pavėluotas kreipimasis į gydymo įstaigas, dėl to nustatytas jau išplitęs krūties vėžys, kai nebegalimas optimalus gydymas.

Raktažodžiai: vyrų krūties vėžys, gydymas, gyvenimo trukmė