

PROGNOSTIC VALUE OF AGE FOR PATIENTS WITH EARLY BREAST CANCER

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The aim of the investigation is the study of prognostic significance of age in early breast cancer (T₁N₀M₀-stage) on the basis of large clinical data.

Materials and methods. In multi-centre study included archival data of patients with early breast cancer (T₁N₀M₀-stage) who had been treated from 1985 to 2009 in Russia (N.N. Blokhin Russian Cancer Research Center of Russian Academy of Medical Science and Clinic of Russian Medical Academy for Postgraduate Education — 1036 female) and in the Netherlands (Leiden University Medical Center, LUMC — 560 patients). For comparison there were studied the data of Dutch Cancer Database (22 196 patients included into National Archive from 1989 to 2009).

Results. Age of patients is an important prognostic factor for early breast cancer: the rate of recurrences is higher in patients <40 years and free-relapse survival is better for patients >50 years. In analyses was found predominance of patients >50 years in the Netherlands for comparing with Russia and also was shown the growth of age of patients with early breast cancer during the twenty years in both countries.

Key words: early breast cancer T₁N₀M₀-stage, prognostic significance of patients age.

The age of patients is of great concern both for risk of breast cancer, and for the course and prognosis of the disease [1]. Many studies show the onset of cancer in young women to be associated with unfavourable clinicopathological characteristics (large masses, the

involvement of regional lymph nodes, high grade of malignancy, negative status of steroid receptors, the presence of HER2 hyperexpression, etc), as well as the worse course of the disease (high recurrence rate and low survival rate) [2, 3]. All the above determines the choice of

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various therapy algorithms taking into account the age of patients [4, 5].

The aim of the investigation is to study the prognostic significance of age in early breast cancer (T₁N₀M₀-stage) on the basis of large clinical data. The tasks of the investigations was the comparison of age characteristics of patients with early breast cancer in Russian and Dutch clinics, as well as the study of the dynamics of age characteristic of patients with the course of time in different countries.

Materials and Methods. In multi-centre study there were included archival data of female patients with early breast cancer (T₁N₀M₀-stage) who had been treated from 1985 to 2009 in Russia (N.N. Blokhin Russian Cancer Research Center of RAMS and Clinic of Russian Medical Academy for Postgraduate Education — 1036 patients) and in the Netherlands (Leiden University Medical Center, LUMC — 560 patients). For comparison there were studied the data of Dutch Cancer Database (22196 patients included into National Archive from 1989 to 2009). All women underwent radical surgery (radical mastectomy or organ saving surgeries with axillary lymph dissection or biopsy of sentinel gland), a part of the female patients received adjuvant medical and/or radiation therapy. There have been analyzed the age characteristics of Russian and Dutch female patients, the dynamics of age history in early breast cancer within 20 years, estimated prognostic value of age according to the findings of Russian studies. The results were statistically analyzed using international statistical program SPSS 16.0, the differences were considered significant in p<0.05.

Results and Discussion. The age of Russian patients included into the study was 21–88 years (mean age — 52 years, median — 51 years), the patients of the age group of 40–50 years predominated (36.2%), and the number of patients aged under 50 years and over 50 years was the same (49.7 and 50.3%) (Fig. 1). The analysis of LUMC archival data showed the mean age of patients to be older — 57 years, patients over 60 years (39.9%) predominating, while the part of the patients aged over 50 years was twice as large than the part of the patients under 50 years (69.9 and 30.1%, p<0.05). Even greater differences were found when analyzing Dutch Cancer Database: the mean age of female patients with T₁N₀M₀-

stage who had undergone the treatment in the Netherlands was 63 years (+11 years compared to Russian female patients, p<0.05), more than the half of the patients (55.6%) were over 60 years, and the part of the patients under 40 years was 3 times as less than in Russia (5.1% and 13.5%, p<0.05) (See Fig. 1).

The study of the changes in age the female patients with early breast cancer in the course of 20 years showed “growth” of patients’ age in both Russian and Dutch clinics: the number of Russian female patients over 60 years has increased from 19.2 (before 1995) to 29.8% (after 2005), the growth being +10%, p<0.05; in the Netherlands — from 53.1 to 63.8%, p<0.05. Moreover, according to LUMC a part of female patients over 60 years has not practically changed (Fig. 2).

Such a significant age difference between Russian and Dutch patients can be explained by demographic and diagnostic variations of these countries. The analysis of demographic characteristics (www.gks.ru) showed life expectancy of women in Russia for the last two decades has slightly increased — c 74.6 (1985) to 76.1 года (2011), while from 1988 to 1994 there was the decrease of mean lifetime of women in Russia up to 71.2 years. By contrast to this, life expectancy of women in the Netherlands within the last two decades is on stable high level (80.4 years — in 1996, and 82 years — in 2011). The diagnostics of early breast cancer is based on screening mammography: in Russia it is performed in women aged 40–60 years, while according to national program in the Netherlands screening mammography is performed in women aged 50–75 years once in 2 years that enables early diagnosis of breast cancer in women over 60 years.

Prognostic value of age in early breast cancer for the risk of further progression of the disease was estimated based on the analysis of Russian data (1036 patients). The follow-up median being 82 months (7–312 months), 241 female patients (23.3%) had the recurrences, and the time of disease progression ranged from 6 to 228 months (median — 36 months).

Univariate analysis revealed the age of female patients to be statistically significant factor correlating with further progression of the disease: the number of female patients with further advance of the disease aged under 40 years

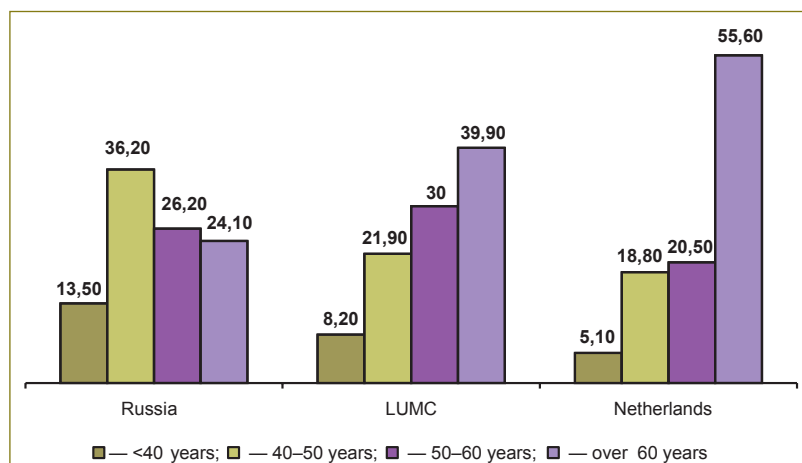


Fig. 1. The distribution of patients with breast cancer, T₁N₀M₀ stage, (in %) depending on the age in Russia (N.N. Blokhin Russian Cancer Research Center of RAMS and Clinic of Russian Medical Academy for Postgraduate Education) and in the Netherlands (LUMC and all clinics) in 1985–2009

Fig. 2. Time dynamics of the number of female patients >60 years in Russia, LUMC and Netherlands, in %

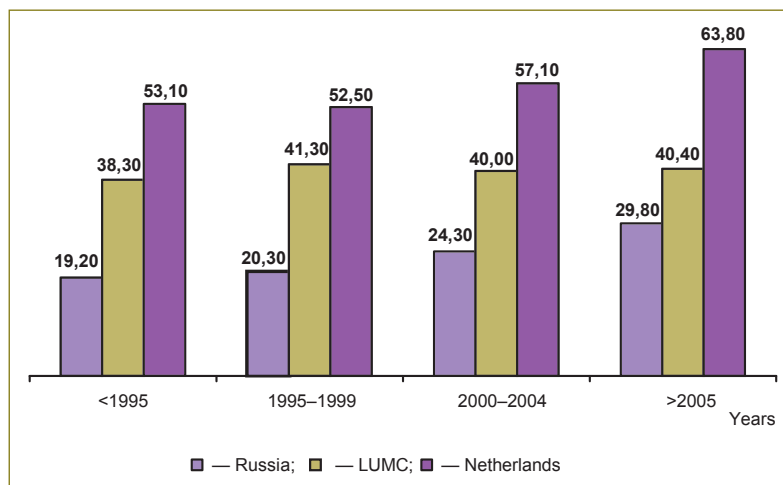


Table 1
The part of recurrences in different age groups (according to Russian data)

Patients' age	Recurrences, absolute number/%		Patients, total
	with no recurrences	with recurrences	
Age, years	24-88	21-81	
mean	52.7	49.8	
median	51.0	48.0	
Under 40 years	98/70.0	42/30.0	140
40-50 years	275/73.5	99/26.5	374
50-60 years	220/80.9	52/19.1	272
Over 60 years	202/80.8	48/19.2	250
Total	795/76.7	241/23.3	1036

Table 2
Indices of total and recurrence-free survival rate in age groups, %

Survival	Age groups of patients				p
	<40 years	40-50 years	50-60 years	over 60 years	
Total survival rate:					
5-year	85.8	90.4	90.2	85.3	
10-year	77.3	77.8	80.6	77.6	
15-year	71.6	67.5	64.0	62.0	0.09
Recurrence-free:					
5-year	76.3	76.8	85.3	82.6	
10-year	66.4	69.4	77.7	73.3	
15-year	56.3	47.8	50.7	62.8	0.05

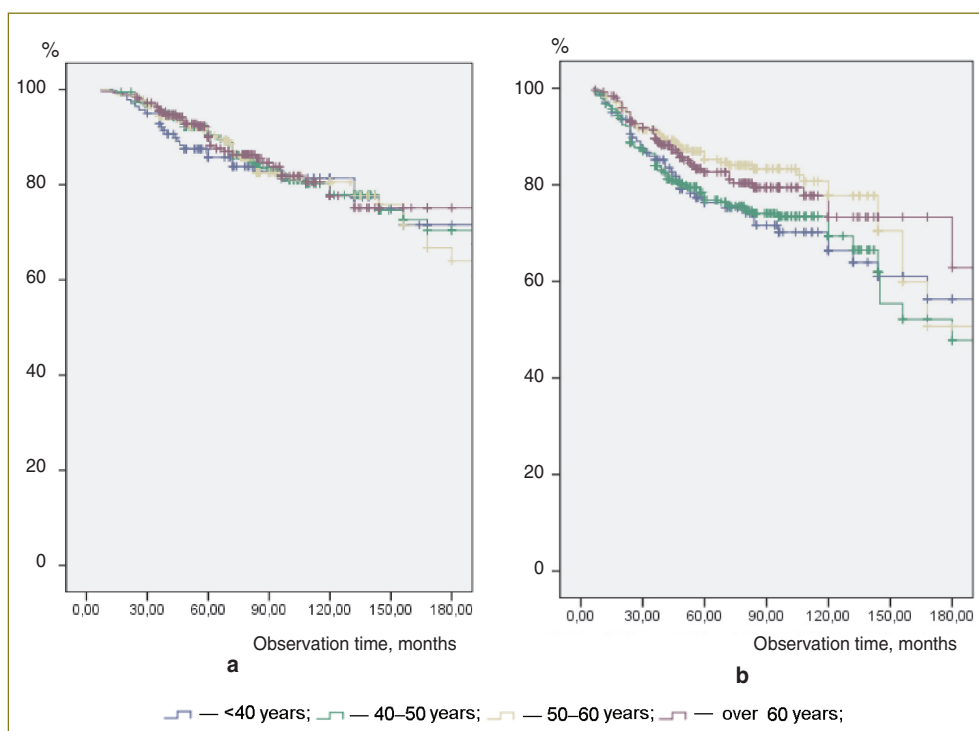


Fig. 3. Total (a) and recurrence-free (b) survival rate in different age groups

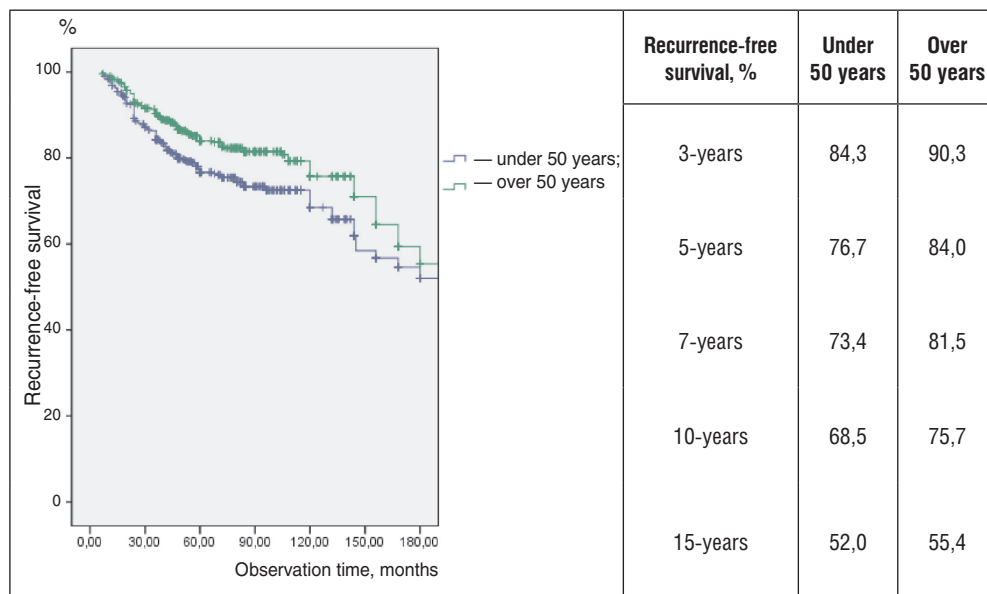


Fig. 4. The indices of recurrence-free survival rate in female patients under and over 50 years ($p=0.007$)

is notably higher than that of female patients with disease progression aged over 50 years — 30 vs. 19%, $p<0.05$ (Table 1).

The analysis of survival rate in these age groups stated the indices of total 5-, 10- and 15-year survival are identical in all groups ($p=0.09$), and recurrence-free survival rate is significantly higher ($p=0.05$) in female patients over 50 years (Table 2).

Fig. 3 demonstrates the total and recurrence-free survival rate of female patients.

The age of 50 years appeared to be “critical” to divide the patients with breast cancer ($T_1N_0M_0$ -stage) into prognostic groups: recurrence-free survival is statistically significantly higher in the female patients over 50 years compared to those under 50 years ($p=0.007$) (Fig. 4). Moreover, when comparing the values of recurrence-free survival rates, statistically significant difference was noted in 3-, 5-, 7-, and 10-year periods, and it is evened by the 15-year period (Fig. 4).

Conclusion. Age of patients is an important prognostic factor for early breast cancer: the rate of recurrences is statistically more significant among female patients under 40 years, and free-relapse survival is better in female patients over 50 years. Female patients over 50 years predominated in the Netherlands compared to the data of Russian clinics. The growth of age of patients with early

breast cancer during the twenty years was found in both countries.

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