Survival of Women With Breast Cancer in Kaunas Region, Lithuania

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Key words: *breast cancer; observed survival rate; prognostic factors.*

Summary. *Objective. The assessment of breast cancer survival rates and comparison with those of other countries may help to deepen knowledge among decision makers in the health care system and to improve the inequalities in accessibility to early detection and effective treatment.*

The aim of this study was to evaluate breast cancer survival rates in Kaunas region, Lithuania, and to compare them with those in the selected European countries.

Material and Methods. A retrospective study was carried out using medical records and data gathered from the Lithuanian Cancer Registry. A group of 240 patients with primary breast cancer diagnosed in 2008 in Kaunas region was analyzed. All causes of death were included in the analysis. The closing date of follow-up was September 30, 2010. Survival was determined using the life-table method and the Kaplan-Meier method. Cox proportional hazard models were used to estimate the effects of prognostic risk factors on survival.

Results. The median age of the patients was 63 years (range, 28–95). The 1-year and 2-year cumulative survival for breast cancer patients in Kaunas region, Lithuania, was 94.2% and 90.1%, respectively. As expected, the survival of patients with diagnosed advanced disease (stage III and IV) was significantly worse than that of patients with stage I ($P<0.001$) and II ($P=0.003$) disease. The screening group (aged 50–69 years) showed better survival in comparison with the group older than 69 years. Age, T4 tumor, and distant metastasis were the prognostic factors significantly associated with an increased relative mortality risk of breast cancer.

Conclusions. Compared to the European survival rates, the 1-year and 2-year survival of patients with breast cancer in Lithuania was found to be similar to most European countries.

Introduction

The World Health Organization has developed 3 main principles for cancer control in developing countries: prevention strategies, screening, and a comprehensive treatment strategy (1).

Breast cancer is the most common oncologic disease among women in Lithuania. The growing incidence of breast cancer is associated with estrogens, reproductive factors, nutrition, and life style (2, 3). Around the world, breast cancer ranks as the fifth cause of death from cancer overall and the most frequent cause of death from cancer in women in both developing and developed regions (4). The data of the European cancer register EUROCARE-4 showed that the average 5-year survival rate of breast cancer patients in Europe in 1995–1999 was 79%. Despite the fact that survival in Eastern Europe is below the European average, it has increased from 60% to 73.9% during the last decade. Increasing survival is associated with implemented screening programs and, consequently, early diagnosis of cancer in most EU countries. Since 1990, because of early detection and improved treatment, breast cancer mortality has been declining by 1%–2% per year in many European countries. However, it has been reported that there are still wide differences in treatment modalities offered for patients with breast cancer. It has also been shown that the specialized multidisciplinary breast cancer care is associated with a significant reduction in mortality (5).

Survival is one of the most important clinical outcomes, defining the quality and effectiveness of health care system (6, 7). The assessment of breast cancer survival rates and comparison of results with other countries in the region may help the decision-makers to deepen knowledge in the health care system and to improve the inequalities in accessibility to early detection and effective treatment. To our knowledge, there are only few studies on breast can-

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cer survival from Eastern Europe, involving populations diagnosed with cancer recently. The aim of this study was to evaluate survival rates in patients with breast cancer in Kaunas region, Lithuania, and to compare with the results of other studies carried out in neighboring countries.

Material and Methods

A total of 240 patients with a diagnosis of primary breast cancer were examined in Kaunas region, Lithuania, in 2008. The data were gathered from the Lithuanian Cancer Registry, Institute of Oncology, Vilnius University. Breast cancer was defined by the pTNM staging system for patients who underwent primary surgical treatment or the cTNM criteria for others as confirmed in patients' medical records. All the patients were followed up; their status (alive or dead) was checked from medical documents and migration services. Deaths in the study cohort were identified by matching cases to their death certificates. All causes of deaths were included into analysis. The closing date of follow-up was September 30, 2010. The women who did not visit their physicians or emigrated during the study period were excluded.

Statistical data analysis was conducted using the statistical package SPSS for Windows 16.0. Survival was determined using the life-table method and the Kaplan-Meier method. Cox proportional hazard models were used to estimate the effects of prognostic risk factors on survival. A stepwise selection procedure for the evaluation of prognostic risk factors was applied. The risk factors selected included age, tumor size, number of lymph nodes affected by the disease, and metastatic spread of breast cancer. Not only overall survival rates, but also specific rates by age categories, breast cancer stage, and observation period were examined. Quantitative variables were described by arithmetic mean and standard error of the mean. Differences in survival by disease stage were estimated by employing the Kaplan-Meier method. Censored data displayed by the Kaplan-Meier curve show the number of individuals enrolled in the study since the date of diagnosis, who are lost to follow-up, but not confirmed as dead. The significance of any difference between the survival curves was determined using the log-rank (Mantel-Cox) test, and any difference was considered significant at the 5% level.

The study was approved by the State Data Protection Inspectorate of the Republic of Lithuania.

Results

The median age at diagnosis of study patients was 63 years (range, 28–95 years). More than half (52.9%) of patients were 50 to 69 years old (Table 1).

Table 1. Patients' Characteristics by Age, Cancer Stage at Diagnosis, and Status at the End of Follow-Up (n=240)

Characteristic	No. of Patients (%)
Age groups	
⩽49 years*	42 (17.5)
50–69 years	127 (52.9)
⩾70 years	71 (29.6)
Disease stage at diagnosis	
I	84 (35.0)
II	111 (46.3)
III	32 (13.3)
IV	13 (5.4)
Status on September 30, 2010	
Alive	216 (90.0)
Dead	24 (10.0)

*Only 4 patients were younger than 35 years.

It should be noted that since 2005 the national mammography screening program in Lithuania has been implemented, and women aged 50 to 69 years are invited to undergo mammography every 2 years.

Early diagnosed tumors (stage I and II) accounted for 81.3% of all the cases analyzed. The distribution of patients with stage I and II breast cancer by age groups was similar. The mean follow-up was 2.84 years.

A total of 24 deaths occurred during the follow-up period. Our analysis revealed that the greatest proportion (n=14) of all deaths occurred during the first follow-up year: there were 6 death cases among patients with stage IV cancer, 5 among patients with stage III cancer, 1 case among patients with stage II cancer, and 2 cases among patients with stage I cancer. During the second study year, 9 deaths occurred. In the last year of follow-up, only 1 woman with stage II breast cancer died. It should be noted that during the first year of the study, the cause of death in 2 patients with early breast cancer was not related to breast cancer.

The overall survival rate of breast cancer patients at the end of the study was 89.85%±0.02%. The 1-year and 2-year cumulative survival rates were 94.17%±0.01% and 89.07%±0.02%. The highest survival rates were observed for patients with stage I and II cancer; the number of deaths by different cancer stages is given in Table 2.

Differences in survival among patients with different diseases stages revealed that the observed cu-

Table 2. Estimated Cumulative Survival Rates by Disease Stage

Disease Stage	No. of Patients at the Beginning of the Study	No. of Deaths During the Study	Cumulative Survival Rate at the End of the Study, % (SE)
I	84	2	97.62 (1.2)
II	111	6	94.30 (2.3)
III	32	7	77.49 (7.3)
IV	13	9	30.77 (12.8)

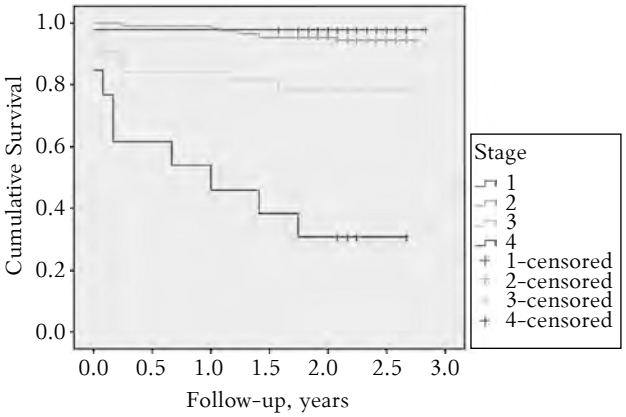

Fig. Kaplan-Meier analysis: survival by disease stage

Table 3. Prognostic Factors Associated With Relative Mortality Risk

Prognostic Factor	Hazard Ratio (95% CI)	*P* value
Age	1.04 (1.01–1.07)	0.049
Regional lymph nodes affected (N)		
N1	1	
N2	1.03 (0.06–16.25)	0.986
N3	0.96 (0.18–6.45)	0.972
Tumor size (T)		
T1	1	
T2	0.23 (0.03–2.15)	0.198
T3	4.45 (0.68–29.15)	0.119
T4	8.58 (1.67–44.06)	0.01
Metastasis (M)		
M0	1	
M1	42.92 (9.45–194.47)	<0.001

mulative survival rate among patients with stage I disease remained stable during the overall follow-up. Among the patients with metastatic breast cancer, a significant decrease in survival was observed every year: from 53.85% in the first year to 30.77% in the last year of the study.

According to the results of survival analysis by the Kaplan-Meier method, disease stage was proved to be a significant factor, determining the differences in survival. Statistically significant differences in the subgroups of local, locally advanced, and metastatic disease were determined. Our study showed that the overall survival of patients with stage I cancer at the end of follow-up was 97.62%±1.20%; the survival rates of patients with the disease of other stages decreased gradually (94.30% in stage II, 77.49% in stage III, and 30.77% in stage IV). The survival of patients with stage III and IV cancer was significantly worse than that of patients with stage I cancer (log-rank test, χ^2=12.26, P<0.001, and χ^2=60.37, P<0.001, respectively). Moreover, the survival of patients with stage III and IV cancer was worse than that of patients with stage II (log-rank test, χ^2=8.92, P=0.003, and χ^2=67.45, P<0.001, respectively) (Fig.).

There were statistically significant differences in the cumulative survival rates between two age groups: the patients aged 50–69 years had better survival as compared with the patients older than 69 years (92.65% vs. 80.51% at the end of follow-up; χ^2=4.76, P=0.030).

All women younger than 35 years survived the whole observation period, but it should be noted that there were only 4 patients in this age group. The estimated survival rates among the age groups (0–49, 50–69, and more than 70 years) were compared. A significant difference in the survival rate was found comparing 50–69- and ⩾70-year age groups.

According to the results of relative mortality risk (RMR) analysis, carried out by means of Cox proportional hazards regression model, age was significantly predictive of shorter survival in women with breast cancer (HR=1.04; 95% CI, 1.01–1.07; P=0.049) (Table 3). Our analysis showed that there was no association between metastasis to regional lymph nodes and survival: prognosis for women with cancer metastasized to regional lymph nodes was not worse than that for women without metastasis to regional lymph nodes (Table 3). Women with tumor directly infiltrating the chest wall or skin (T4) had nearly a 9-fold higher relative mortality risk than those diagnosed with tumor of 2 cm or less (T1) (HR, 8.58; 95% CI, 1.67–44.06; P<0.05). As expected, distant metastasis was the strongest prognostic factor: patients with distant metastasis were 43 times more likely to have a poor prognosis than those without distant metastasis (HR, 42.49; 95% CI, 9.45–194.47; P<0.001).

Table 4. Survival Rates of Breast Cancer Patients and Total Expenditure on Health in Lithuania and Neighboring European Countries

Country	1-Year Cumulative Survival, %	2-Year Cumulative Survival, %	Total Expenditure on Health as % of GDP[1]
Kaunas Region, Lithuania[2]	94.17	89.07	6.5
Lithuania[2]	90.30	–	6.5
Poland[3]	94.83	85.23	5.5
Czech Republic[3]	90.65	83.07	6.5
Finland[3]	95.23	90.64	6.6
Norway[3]	94.00	88.32	8.4
Sweden[3]	95.01	89.89	8.2

[1]According to the World Health Organization, Statistical Information System, in 2000.
[2]Survival of breast cancer patients diagnosed in 2008.
[3]Survival of breast cancer patients diagnosed in 1995–1999 (15).
GDP, gross domestic product.

Comparison of our results with those of different countries showed that the 1-year and 2-year cumulative survival rates for breast cancer patients in Kaunas region, Lithuania, were similar to the neighboring European countries. Table 4 shows the estimated survival rates for breast cancer patients and the resources of national health care expressed as a percentage of gross domestic product in Lithuanian and its neighboring countries. However, we should acknowledge that there is a large gap in the study periods compared. During the decade, many factors, such as diagnostic and treatment strategies, might have changed.

Discussion

The analysis of 1-year survival in the EUROCARE-4 study showed a good discriminatory power and identified a group of countries with consistently high survival estimates (Switzerland, France, Sweden, Belgium, and Italy) and another group of countries with lower survival estimates (Poland, Czech Republic, Ireland, Denmark, and the United Kingdom) (8). In countries with generally high cancer survival estimates, the 1-year survival of breast cancer patients was more than 95%. These differences can be explained most likely by a shortage of infrastructure and the lack of financial resources for cancer care in these countries. Comparison of the data of the international registry EUROCARE-4 with our study data has revealed that the 1-year survival of breast cancer patients in Kaunas region is comparable to the European average, i.e., 93.8%.

The data of the Lithuanian Cancer Registry showed that the distribution of patients by breast cancer stage in Kaunas region and overall Lithuanian population was similar: the majority of cases had stage II breast cancer (46.3% and 37.7%, respectively), and stage IV breast cancer was diagnosed just in 5.4% and 7.6% of patients, respectively (9). The similar proportions of cases were reported comparing the populations of Kaunas region and overall Lithuania by age at diagnosis: the majority of patients were in the 50–69-year age group (52.9% and 47.7%, respectively), and patients younger than 50 years accounted for 17.5% and 21.6% of all patients, respectively. The 1-year overall survival of breast cancer patients was 94.2% and 90.3% in Kaunas region and general Lithuanian population, respectively (9).

Screening, early detection, and progress in effective therapy might change the patterns of survival in countries, included in the EUROCARE study, but we did not find any data of later studies that could be compared to our results. Different study periods may have an impact on differences in the examined observed cumulative survival. Improved breast cancer survival, accompanied by declining mortality rates, suggests a real improvement in care (10). Currently, new assessment and treatment methods are emerging in clinical practice, and accessibility to optimal treatment has been improved. The initial survival rates in the EUROCARE-4 study were estimated for patients, which were diagnosed with breast cancer in 1995–1999. The studies in breast cancer patients in later periods confirmed a significant improvement in survival in many countries worldwide (11–13).

A study examining the associations between socioeconomic variables and all-cancer survival in EUROCARE-3 patients from 19 European countries diagnosed during 1990–1994 and followed up to 1999 showed that gross domestic product and total national expenditure on health correlated highly with all cancer survival. Wealthy northern and western European countries reported high survival; eastern European countries had low all-cancer survival (14).

Conclusions

Our study showed the overall survival rate of breast cancer patients to be 89.85%. The 1-year and 2-year cumulative survival rates were 94.17% and 89.07%, respectively. Compared to the European survival rates, the 1-year and 2-year survival of patients with breast cancer in Lithuania was found to be similar to most European countries.

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Statement of Conflict of Interest

The authors state no conflict of interest.

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