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Original Paper

Survival of Breast Cancer Patients in Lithuania and Norway, 1988–1992

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In Norway, the incidence of breast cancer is almost twice that in Lithuania, whereas the mortality rates of the disease are approximately the same in both countries. The aim of the present study was to compare the survival of breast cancer patients in the two countries according to stage. The material from both countries included cases diagnosed between 1988 and 1992 with complete follow-up of date of death to the end of 1995. The Norwegian data consisted of all 9403 new cases recorded by the Norwegian Cancer Registry. The Lithuanian data included all 1649 new cases treated at the Oncology Centre in Vilnius, which represents 40% of breast cancer cases in Lithuania—these cases had the same distribution of the disease by age and stage as for the whole country. The overall 5-year relative survival was lower in Lithuania (57.3%) than in Norway (78.4%). Lower survival was observed in Lithuania compared with Norway for all stages. In stage I, the difference was 7.8% in absolute terms which could be explained by a higher proportion of small tumours among the Norwegian cancer cases (63.7% of tumours were 2 cm or less, while in Lithuania the proportion of small stage I tumours was only 27.9%). Therefore, early diagnosis within the stage I category seems relevant. The difference in survival was, however, most pronounced in stage II (20%) and III (29%). In Norway, the better overall survival is partly explained by a more favourable stage distribution. The lower survival of Lithuanian cases within stage categories could be explained by more advanced metastases to regional lymph nodes and by higher proportions of large tumours within stage. © 1998 Elsevier Science Ltd. All rights reserved.

Key words: breast cancer, survival, stage, lymph node status, tumour size

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INTRODUCTION

IN WOMEN, breast cancer is the most frequent malignancy, with increases seen in most populations [1]. Age distributions differ throughout the world [2]. In most Western European countries 40% of breast cancers are diagnosed at the age of 65 years or more [3], whereas in most Eastern European countries a relatively lower incidence is reported in the elderly [4]. The disease accounts for 16 and 11% of all cancer deaths in developed and developing countries, respectively [5]. A stable or decreasing trend in breast cancer mortality has been reported in many Western European countries whilst some Eastern European countries continue to experience increases in mortality rates [6].

Variations in survival from breast cancer have been reported from several population-based studies [7–9], including some from Baltic countries [10, 11]. One study has shown a poor survival for young patients aged less than 40 years [12], although this finding is contradicted in other studies [13, 14]. In a Norwegian study, the poorest survival was reported in very young (34 years and younger) and elderly patients (75 years and over) [15]. The impact of stage on survival has also been investigated and better survival for patients in the early stage at diagnosis has been shown consistently [16, 17]. Other prognostic indicators of survival are tumour size, nodal status, oestrogen receptor status, tumour growth rate, histological type, oncogenes and growth factors [18].

Incidence rates of breast cancer are higher in Nordic countries compared with Baltic countries [4]. Based on data from the cancer registries in Lithuania and Norway, the incidence rate was almost 50% higher in Norway than in

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Lithuania between 1988–1992, but the mortality rates in women aged 30–79 years were approximately the same in both countries. The aim of the present study was to compare survival in Lithuania and Norway, which represent low and high incidence European countries, and to investigate factors related to survival.

MATERIALS AND METHODS

Cancer registration in both Lithuania and Norway is based on compulsory reporting [19, 20]. The incidence data in the present study were based on the first recognised female breast cancer in an individual and included all cases diagnosed between 1988 and 1992 in Lithuania (3976 cases) and Norway (9403). These data were obtained from the respective cancer registries.

The Lithuanian survival data used in the study were from the Oncology Centre in Vilnius and included all 1649 new cases of breast cancer treated in that institution between 1988 and 1992. The survival analysis was restricted to these data because of complete follow-up of dates of death and complete information on tumour, lymph nodes and distant metastases which are classified according to the TNM system [21]. When we compared these with the data from the cancer registry for the whole country, the distribution of the disease did not differ by age and stage.

The Norwegian data were based on 9403 new breast cancer cases reported to the Cancer Registry of Norway between 1988 and 1992. Cases diagnosed at autopsy or based on death certificates alone were excluded (0.5%).

In the present data from both countries TNM classification was used for definition of tumour size (T), lymph node status (N) and distant metastases (M). As only 47% of the Norwegian records included information on tumour size and, in order to have comparable material, we used the following definition of stages in both the Lithuanian and the Norwegian material: stage I, localised tumour without involvement of lymph nodes; stage II, localised tumour with regional lymph node metastases; stage III, tumour spread into skin or surrounding tissues with or without regional lymph node metastases; and stage IV, cases with distant metastases (Table 1).

The follow-up for deaths or emigration in Norway was based entirely on the national 11-digit personal identification number. The registry records were matched against the Register of Deaths at the Central Bureau of Statistics [20], with complete follow-up to the end of 1995.

The follow-up procedure in Lithuania was conducted in three steps: first, by matching the patient records by name

and date of birth with a database of death records at the Lithuanian Cancer Registry; second, by linkage with outcome data from the out-patient clinic of the Oncology Centre and finally, linkage with records from the Lithuanian Address Bureau, which accumulates information on all inhabitants of Lithuania, including places of residence, dates of death and date of emigration. 62 patients were excluded from the analysis due to foreign citizenship or incomplete information on vital status. Finally, 1587 breast cancer cases with complete follow-up to the end of 1995 were included in the survival analysis.

The data were analysed by stage (I–IV), lymph node status (N0–N3), tumour size (T1–T4) and age at diagnosis (younger than 35, 35–54, 55–69 and 70 years and older). The four age groups were intended to represent very young women, 'premenopausal', 'postmenopausal' and elderly women, respectively.

Relative survival was calculated as the ratio between observed and expected survival where the observed survival is the estimated probability of survival of the breast cancer patients at a specified time after diagnosis, calculated using the life table method [22]. The expected survival was calculated as age and period specific for the total population [22]. In Norway, data on the mortality rate for each year of age and for each calendar year were available [23] while, for the Lithuanian population, mortality by 5-year age groups for the year 1994 was used [24]. The Lithuanian mortality data were

Table 2. Distribution of breast cancer by stage and age in Lithuania and Norway 1988–1992

Age group (years)	Stage	Lithuania		Norway	
		No. of cases	%	No. of cases	%
0–34	I	26	41.9	80	45.7
	II	29	46.8	74	42.3
	III	3	4.8	6	3.4
	IV	4	6.5	13	7.4
	Unknown	0	0.0	2	1.2
	Total	62	100.0	175	100.0
35–54	I	262	36.2	1397	54.2
	II	372	51.4	969	37.6
	III	28	3.9	81	3.2
	IV	57	7.9	113	4.4
	Unknown	4	0.6	16	0.6
	Total	723	100.0	2576	100.0
55–69	I	199	31.8	1416	54.2
	II	309	49.3	891	34.1
	III	43	6.9	104	4.0
	IV	72	11.5	179	6.9
	Unknown	3	0.5	20	0.8
	Total	626	100.0	2610	100.0
70+	I	63	35.8	2568	63.5
	II	68	38.6	847	20.9
	III	15	8.5	241	6.0
	IV	28	15.9	286	7.1
	Unknown	2	1.2	100	2.5
	Total	176	100.0	4042	100.0
All ages	I	550	34.7	5461	58.1
	II	778	49.0	2781	29.6
	III	89	5.6	432	4.6
	IV	161	10.1	591	6.3
	Unknown	9	0.6	138	1.4
	Total	1587	100.0	9403	100.0

Table 1. Stage definition of breast cancer in the study of survival in Lithuania and Norway

Stage	Tumour (T)*	Regional lymph nodes (N)*	Distant metastases (M)*
I	1,2,3,X	0	0
II	0,1,2,3,X	1,2	0
III	0,1,2,3,X	3	0
	4	0,1,2,3	0
IV	0,1,2,3,4,X	0,1,2,3	1
Unknown	0,1,2,3,4,X	X	0
	0,1,2,3,4,X	0,1,2,3	X
	0,1,2,3,4,X	X	X

*Defined according to TNM classification. X, unknown.

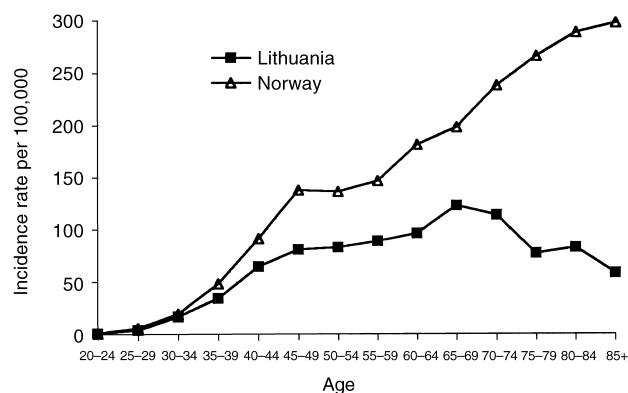


Figure 1. Age-specific incidence of breast cancer in Lithuania and Norway between 1988 and 1992.

made 1-year specific using proportional death rates between Lithuania and Norway within each 5-year age group. The standard error of the relative survival rate was computed according to Greenwood's formula [25].

RESULTS

Breast cancer patients in Lithuania had a mean age of 55 years (range 21–88) at diagnosis and were on average 9 years younger than the Norwegian patients. The incidence increased with age in both countries with a higher incidence in Norway up to the age of 69 years. At the age of 70 years and older there was a further increase in Norway, while a decrease was observed in Lithuania (Figure 1).

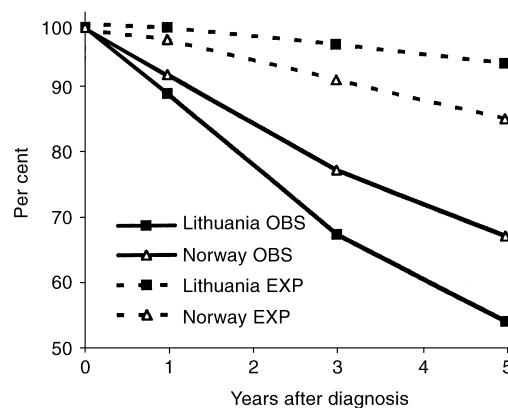


Figure 2. Observed (OBS) and expected (EXP) survival rates (%) of breast cancer patients in Lithuania and Norway between 1988 and 1992.

Table 2 shows the more favourable stage distribution in Norway, with 58.1% of cases diagnosed in stage I for all ages combined, while in Lithuania the corresponding figure was 34.7%. The difference between the two countries was most pronounced in the oldest age group, where the highest percentage of stage I was observed in Norway. The percentage of patients with stages III and IV was higher in Lithuania in the age groups 35 years or older. The expected 5-year survival rate for all ages combined was 84.6% in Norway and 93.3% in Lithuania (Figure 2). This difference is due to the higher proportion of young patients in the Lithuanian dataset. The figure also shows a better observed survival at 5 years after

Table 3. Relative survival rate (%) of breast cancer patients in Lithuania and Norway between 1988 and 1992 by age, stage and duration of follow-up

Age group (years)	Stage	Lithuania				Norway			
		1-year	3-year	5-year	SEM	1-year	3-year	5-year	SEM
0–34	I	96.3	92.7	88.7	6.4	100.1	95.2	92.0	3.2
	II	86.3	58.8	41.6	9.5	97.3	63.6	42.2	6.1
	III	–	–	–	–	83.4	50.1	50.1	20.5
	IV	25.0	25.1	–	–	61.6	–	–	–
	All*	84.0	68.0	58.3	6.4	95.5	72.7	61.6	3.8
35–54	I	99.3	93.3	85.0	2.4	99.3	94.9	91.1	0.8
	II	94.2	68.2	53.1	2.7	98.4	84.2	72.4	1.5
	III	82.5	21.7	14.7	6.8	91.5	62.2	45.7	5.8
	IV	56.4	19.6	6.1	3.9	58.5	26.7	12.0	3.3
	All*	92.7	71.5	59.5	1.9	96.9	86.7	79.0	0.8
55–69	I	97.7	90.5	79.8	3.4	99.0	95.2	92.5	1.0
	II	90.8	68.1	55.5	3.1	97.1	82.3	69.5	1.7
	III	70.7	43.7	21.1	6.9	92.2	62.6	41.5	5.4
	IV	49.2	18.8	7.5	3.4	58.7	24.8	13.6	2.8
	All*	86.7	67.8	55.5	2.2	95.2	84.4	76.7	1.0
70+	I	100.9	90.9	88.1	7.6	96.1	92.3	90.8	1.5
	II	85.0	53.7	35.4	7.5	97.9	85.1	80.5	2.4
	III	106.3	89.8	54.2	18.6	92.2	69.3	61.2	4.9
	IV	71.2	37.7	13.3	7.5	43.1	22.3	18.5	3.0
	All*	90.6	67.8	52.7	5.0	91.5	83.2	80.4	1.2
All ages	I	98.7	92.0	83.6	1.9	97.8	93.9	91.4	0.7
	II	91.8	66.7	52.4	2.0	97.8	83.3	72.5	1.0
	III	78.9	41.7	22.6	4.9	92.0	65.7	51.6	3.1
	IV	54.9	22.2	8.1	2.4	51.4	23.5	14.9	1.7
	All*	89.7	69.6	57.3	1.4	94.1	84.4	78.4	0.6

*All stages combined (I–IV and unknown). SEM, standard error of 5-year relative survival rate. –, no results given due to small number of cases (less than 5).

diagnosis for patients in Norway (66.3% compared with 53.4% in Lithuania). The overall 5-year percentage relative survival was significantly lower in Lithuania (57.3%) compared with Norway (78.4%) and the difference varied by stage and age (Table 3). The difference in 5-year relative survival rate between the two countries was 7.8% in absolute terms in stage I patients, 20.1% in stage II, 29% in stage III and 6.8% in stage IV. The difference in the relative 5-year survival between Lithuania and Norway increased with age. It was 3.3% in the group of youngest women and 27.7% in the elderly group. The table also shows a substantial decrease in the relative 5-year survival by stage in both countries: in Lithuania this was from 83.6% in stage I to 8.1% in stage IV, whilst in Norway the corresponding figures were 91.4% to 14.9%.

The percentage distribution of cases by tumour size within stage categories (based on 47% of the Norwegian material and 99% of the Lithuanian data) showed an advantage in Norway with 63.7% of stage I tumours being 2 cm or less (T1) and 40.7% in stage II, while in Lithuania the proportion of T1 in stage I was 27.9% and in stage II only 8.9% (Table 4). Relative survival was also calculated by tumour size, showing a decrease in survival with increasing tumour size in both countries (Table 5). In Norway, the 5-year relative survival in stage I decreased from 96.4% for tumours less than 2 cm (T1) to 88.9% for tumours of 2–5 cm (T2).

Table 4 shows a more favourable distribution by lymph node status among the Norwegian cases for stages II–IV. A

substantial decrease in the 5-year relative survival with involvement of regional lymph nodes was observed in both countries (Table 5). For cases without regional lymph nodes metastases (N0) in stage I this was 91.4% in Norway and 83.6% in Lithuania, while for cases with metastases to movable metastatic axillary lymph nodes (N1) in stage II the relative survival in Norway was 72.7% and 60.3% in Lithuania.

DISCUSSION

The present study shows substantial differences in the overall survival of breast cancer patients in Lithuania and Norway. The relatively lower 5-year relative survival in Lithuania corresponds to similar findings from Estonia and Poland [9]. In contrast, survival in Norway corresponds to reported results from most other Western countries [9]. The Norwegian patients had more favourable stage, tumour size and lymph node status distributions. The absolute differences in survival in the present study were most pronounced in stages II and III.

The age distribution of the incidence of breast cancer in Lithuania was similar to the other Baltic countries [4]. The observed difference in the incidence between Lithuania and Norway in the elderly and the low proportion of stage I tumours in the Lithuanian dataset in the group of 70 years and older could suggest an underestimation of the disease in the oldest age group in this Baltic country. However, a decrease in the incidence in the elderly population has also been reported from other countries [26].

Table 4. Percentage distribution of tumour size (T1–4) and lymph node status (N1–3) by stage in Lithuania and Norway 1988–1992, all ages combined

Stage	Lithuania					Norway				
	No. of cases*	T1	T2	T3	T4	No. of cases*	T1	T2	T3	T4
I	549	27.9	65.0	7.1	0.0	2413	63.7	33.5	2.8	0.0
II	772	8.9	62.3	28.8	0.0	1286	40.7	51.4	7.9	0.0
III	87	0.0	0.0	1.1	98.9	403	1.0	4.7	1.7	92.6
IV	156	1.9	20.5	35.9	41.7	275	18.2	18.6	8.7	54.5
Stage	Lithuania					Norway				
	No. of cases†	N0	N1	N2	N3	No. of cases†	N0	N1	N2	N3
I	550	100.0	0.0	0.0	0.0	5461	100.0	0.0	0.0	0.0
II	733	0.0	71.5	28.5	0.0	2781	0.0	99.5	0.5	0.0
III	85	10.6	21.2	55.3	12.9	431	40.1	39.0	5.3	15.6
IV	148	0.7	25.0	41.9	32.4	545	48.4	36.1	6.1	9.4

*Only cases with known tumour size were included. †Only cases with known lymph node status were included.

Table 5. Five-year relative survival rate (%) of breast cancer patients by tumour size (T1–4) and lymph node status (N1–3) in Lithuania and Norway 1988–1992, all ages combined

Stage	Lithuania				Norway			
	T1 (SEM)	T2 (SEM)	T3 (SEM)	T4 (SEM)	T1 (SEM)	T2 (SEM)	T3 (SEM)	T4 (SEM)
I	91.2 (3.0)	83.8 (2.4)	53.9 (8.9)		96.4 (1.1)	88.9 (2.1)	86.1 (7.0)	
II	81.7 (5.5)	61.0 (2.5)	22.2 (3.1)		81.8 (2.2)	69.6 (2.2)	56.2 (6.1)	
III			–	22.0 (4.9)	27.0 (23.4)	40.2 (12.3)	14.7 (13.6)	55.7 (3.4)
IV	–	12.7 (7.1)	13.0 (4.9)	2.3 (2.2)	23.7 (6.8)	13.6 (5.6)	13.2 (7.1)	9.4 (2.7)
Stage	Lithuania				Norway			
	N0 (SEM)	N1 (SEM)	N2 (SEM)	N3 (SEM)	N0 (SEM)	N1 (SEM)	N2 (SEM)	N3 (SEM)
I	83.6 (1.9)		0.0	0.0	91.4 (0.7)			
II		60.3 (2.4)	40.0 (3.8)			72.7 (1.0)	47.3 (14.0)	
III	38.6 (20.0)	30.5 (11.7)	17.4 (6.0)	6.5 (7.7)	64.6 (5.6)	55.5 (4.8)	19.0 (9.2)	28.8 (6.3)
IV	–	13.2 (6.3)	6.5 (3.5)	8.9 (4.5)	19.8 (2.9)	14.5 (3.0)	3.3 (3.2)	3.0 (2.8)

SEM, standard error of 5-year relative survival rate. –, results are not given due to small number of cases (less than 5).

The present study includes data from 1988 to 1992 since 1988 is the first year with complete follow-up of all deaths in Lithuania. For cases diagnosed in 1992 we had only 3.5 years of follow-up. However, since results of survival 3 years after diagnosis showed the same tendency in differences as after 5 years, such a limitation most likely had little influence on the results.

The study also contains some other limitations. Eighty per cent of the patients in the Lithuanian dataset were from the two geographical regions where the Oncology Centre in Vilnius was the only institution responsible for treatment of breast cancer patients and 20% of the patients were from the other regions of the country. This might suggest a selection bias but the present analysis showed the same age and stage distribution for study subjects as for the whole country. Furthermore, the relative 5-year survival did not differ for the group of patients from the two geographical regions and for the group of patients from other parts of Lithuania included in the present study.

The differences in the overall relative survival between the two countries can be partly explained by a more favourable stage distribution in Norway. The early diagnosis of breast cancer certainly plays an important role in this context [9, 14]. In the study period, no organised screening activity took place in either country. However, in Norway there were some opportunistic screening activities induced by information campaigns on breast self-examination, especially in big cities. An impact of women's breast self-examination on mortality from breast cancer has been investigated and positive effects in reducing breast cancer mortality have been reported [27].

Age as a prognostic factor of survival from breast cancer has been investigated in a number of studies [28–31]. The results in our study showed a better survival in the elderly group in Norway compared with Lithuania, which could mostly be explained by differences in stage distribution. The low survival in young women observed in both countries could suggest an existence of other factors responsible for poor prognosis in this age group or an existence of a different type of malignancy in very young women.

In the present analysis there were differences observed in the relative survival within stage categories. The distribution of the cases according to lymph node involvement showed a disadvantage in the Lithuanian patients. This corresponds with other studies reporting lymph node involvement as a major prognostic factor for breast cancer patients [32–34].

Tumour size is also reported to be an important prognostic factor [33–35] and since a better survival for cases with smaller tumours was shown in the present study, the distribution of tumour size within each stage was analysed. The proportions of T1, T2 and T3 in the Norwegian data were more favourable both in stage I and stage II (the proportion of cases in stages III and IV was low in both countries). The observed differences in the distributions of tumour size within stage could, therefore, explain most of the differences in survival by stage between the two countries. We also suggest that about 5% lower relative survival in absolute terms observed in Lithuania compared to Norway in stage I for cases with T1 and T2 could probably partly be related to a possible difference in distribution of the cases by tumour size within the range of T1 and T2 cases. Thus, lead-time bias could be suggested as an effect of early diagnosis which lengthens the duration of survival by bringing forward the date of diagnosis.

Treatment is an independent prognostic factor for breast cancer [9], and specific survival is likely to have been influenced by differences in treatment in the two countries. However, types of surgery performed in Lithuania and Norway are very similar, using the same procedure—predominantly modified radical mastectomy with axillary lymph node dissection and breast conservative surgery. Cobalt was the main source for radiotherapy in Lithuania, whilst in Norway radiotherapy was performed using a linear accelerator. Tamoxifen was most often used as hormonotherapy in both countries. A combination of cyclophosphamide methotrexate and 5-fluorouracil was applied most often as chemotherapy both in Lithuania and Norway [36, 37]. Thus, differences in treatment could be observed in types of radiotherapy, doses of medicines and combinations of a few specific types of treatment by stage. Investigation of these differences in treatment with regard to influence on survival could be of importance. Alternatively, a possible advantage in treatment of patients with smaller tumours in the same stage could also explain some of the differences in survival.

Other possible prognostic factors, such as fertility [8, 38], social class [39], dietary habits [40] and use of hormonal therapy, which differ in Lithuania and Norway, could also influence survival in the two countries.

In conclusion, a large overall difference in survival was observed, which can be explained partially by differences in the stage distributions, although variations in tumour size were observed within stage categories. We were not able to assess treatment variables analytically, even though these may also be relevant. Efforts to diagnose breast cancer in Lithuania at an early stage should have priority in measures to improve survival in the country.

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