Place of residence predicts breast cancer stage at diagnosis in Estonia

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Background: Stage at diagnosis is one of the most important predictors of breast cancer survival. The objective of this population-based study was to examine the impact of age, period of diagnosis and place of residence on breast cancer stage at diagnosis in Estonia. Methods: Female breast cancer cases reported to the Estonian Cancer Registry in 1995–2006 with a known extent of disease were included. Logistic regression was used to estimate the risk of advanced stage (non-localized) disease. Results: Overall, 56% of the 6936 women included in the analysis were diagnosed at advanced stage. The risk of advanced disease at diagnosis decreased over the study period in all age groups, but the change was much larger among women aged 50–69 years than among women in younger and older age groups. Multivariate analysis indicated that the strongest predictor of advanced stage disease was the place of residence. Compared with Tallinn (the capital of Estonia), living in Tartu (a small town with a university hospital) was associated with a significant 36% reduction in risk while the odds ratio associated with living in a marginal industrial county (Ida-Viru) was 1.52 (95% confidence interval 1.29–1.79). Conclusions: The observed regional variations are most likely due to differences in education, unemployment and health care access. Younger and elderly women, those living in remote areas and of lower socio-economic status should be addressed with specific measures to promote earlier detection of breast cancer, particularly in view of current economic difficulties and a sharply rising unemployment rate.

Keywords: breast cancer, early detection, Estonia, health care access, stage at diagnosis, screening mammography

Introduction

Breast cancer in women is a major health burden worldwide. As in other European countries, it is the most common cancer among women in Estonia, one of the ten new member states of the European Union. While breast cancer mortality has shown a levelling off and subsequent decline in many European countries starting from the early 1990s, both the incidence and mortality of breast cancer have continued to increase in Estonia. A recent analysis identified breast cancer as a third-ranking cause of years of life lost among women in Estonia. Survival from breast cancer, although improving, is still much lower in Estonia than in most other European countries: the estimated 5-year relative survival rate of women diagnosed with breast cancer in Estonia in 2000 was 58% and in 2004 was 72%. One of the most important predictors of breast cancer survival is stage at diagnosis. Stage was shown to be largely responsible for the notable differences observed in breast cancer survival across Europe. Information on the stage distribution of breast cancer at diagnosis in Estonia and related factors is scarce. This study was undertaken to examine whether there have been any changes in the stage distribution of breast cancer at diagnosis over a 10-year period and what are the major predictors of advanced stage diagnosis.

Methods

The study used data collected by the Estonian Cancer Registry (ECR), a population-based registry that has had complete nationwide coverage since 1968. All cases of breast cancer (ICD-O-2 topography codes C500–C509), except death certificate only cases (n = 15) and cases diagnosed at autopsy (n = 14), diagnosed in women in Estonia between 1995 and 2006 were included, regardless of cancer sequence. Information on the extent of disease at the time of diagnosis is available from the ECR as reported on the notification form: (i) in situ, (ii) localized, (iii) metastases only in regional lymph nodes, (iv) direct extension into surrounding tissues, (v) distant metastases, (vi) advanced cancer, not otherwise specified, (vii) unspecified. After the exclusion of cases with unspecified extent of disease, the diagnoses were grouped into two categories for the purposes of this study: (i) early stage was defined as in situ or localized disease at the time of diagnosis; (ii) advanced stage diagnosis included all non-localized cases.

Other variables used in the analysis, in addition to age and year of diagnosis, were place of residence at the time of diagnosis (available for all cases) and self-reported nationality. The latter is notified rather poorly to the ECR and was available for 62% of cases. The place of residence was collapsed into four categories based on a priori interest and
preliminary analyses (data not shown). Regions included in the analysis are shown on the map of Estonia (figure 1). The two specialist cancer centres in Estonia are located in Tallinn, the capital of Estonia, and in Tartu, a small university town in the southern part of the country. Another region of interest was the North-Easternmost county of Estonia, Ida-Viru, which borders Russia, has a specific population profile, and has been identified previously as a problematic region from a public health perspective, particularly drug abuse and HIV infection.7 All remaining regions that include smaller towns and rural areas were collapsed into one category. Selected census-derived socio-economic indicators for these regions are presented in table 1.

To evaluate the effect of age at diagnosis, period of diagnosis and place of residence on the likelihood of advanced stage breast cancer diagnosis, univariate and multivariate logistic regression models were used to estimate odds ratios (ORs) with 95% confidence intervals (CIs). All analyses were done with STATA 10.0 (Stata, College Station, TX, USA).

Results

A total of 6936 breast cancer cases were available for the analysis. Overall, 2971 cases (42.8%) were diagnosed at early stage and 3866 cases (55.7%) at advanced stage. The extent of disease was unspecified for 99 cases (1.4%) and these were excluded from subsequent analyses.

Figure 2 presents the changes in the proportion of advanced stage diagnosis over the study period within four age groups. The steepest decline was seen among women 60–69 years of age (13%, from 61 to 49%) and 50–59 years of age (12%, from 60 to 49%). The changes were more moderate in the youngest (7%, from 57 to 50%) and oldest age groups (4%, from 61 to 57%). The proportion of patients diagnosed with advanced stage disease varied considerably across regions of residence (table 2). Multivariate analysis confirmed that the risk of advanced stage disease increased with age and decreased over time. Compared with women living in Tallinn, the risk associated with living in Tartu was significantly lower and with living in Ida-Viru County was significantly elevated. The analysis within age groups showed a significant decline in risk from the first to the last period only among women between 50 and 69 years of age; very little improvement was seen in the youngest and oldest age groups. The risk elevation associated with living in Ida-Viru County was largest among women in age group 60–69 and those younger than 50 years.
Self-reported nationality was known for 62% of the cases and was therefore not included in the final model. However, in order to assess whether the observed risk associated with the place of residence was due to differences in the ethnic profile of the population, we performed a stratified analysis among women with known self-reported nationality. After adjusting for age and period of diagnosis, the OR associated with living in Ida-Viru County was 1.66 (95% CI 1.05–2.61) among Estonians (n = 2966) and 1.55 (1.19–2.03) among non-Estonians (n = 1293). In both subgroups, the magnitude of the protective effect of living in Tartu compared with Tallinn was similar to that seen in the total cohort.

**Discussion**

In this study, cancer registry data were analysed to find associations between breast cancer stage at diagnosis and some temporal and patient characteristics in Estonia. The scope of the investigation was limited due to the lack of individual data on education, socio-economic status, health and behaviour, which have been shown to influence stage at diagnosis of breast cancer.8–12 Another limitation of the study was the rather crude staging (localized versus non-localized) as the TNM classification is not routinely available from the registry database. Third, the quality of the data used may have been compromised by legislative issues that have prevented the ECR to use death certificate data for case ascertainment and quality control purposes since 2001.13 Overall, an estimated 5% of incidence cancer cases have been lost for registration each year.13 Fortunately, the effect of these inadequate quality control procedures on capturing breast cancer cases is rather small, since the vast majority of patients are diagnosed and treated in two cancer centres where notification procedures are of high quality. Also, cases of breast cancer first diagnosed at death are very rare.

In 1995–2006, over 6900 women in Estonia were diagnosed with breast cancer, and 3866 of them (56%) were diagnosed when the disease had spread beyond the initial site. Women aged 50–59 are the only age group where the percent of advanced stage disease has fallen consistently below 50% during recent years. Stage at diagnosis is one of the most important determinants of long-term prognosis of breast cancer patients.14 The experience of many countries indicates that regular screening contributes to earlier detection of the disease and can thereby substantially reduce breast cancer mortality.15 In Estonia, opportunistic mammography became gradually accessible during the 1990s, particularly in Tallinn and Tartu. As a preparation phase for organized mass screening, a breast cancer early detection programme was launched in 2002 and during the first years, a free mammogram was offered to all self-referred women of the target age group (45–59 years) who were covered by national health insurance, although personal invitations were also sent to four birth cohorts 50–59 years of age. From 2004 onwards, screening is offered to women only in selected birth cohorts who have been personally invited. Accurate screening statistics are not available due to the lack of a screening registry and very limited data have been published. The number of annual screening mammograms increased gradually from 15 000 in 2002 to over 22 000 in 2006; the total number of mammograms taken during the 5-year period was over 94 000.16

To reach its goals in reducing mortality, a screening programme requires high attendance rates. The targeted attendance rate of the Estonian programme is 70% but only 37% and 51% of women who were invited had a screening mammogram taken in 2003 and 2006, respectively.16 Given that invitations are sent only to women with current health insurance, the actual screening coverage of the respective population group is even lower. In 2006, for example, according to population statistics,17 the number of women in respective birth cohorts in Estonia was over 49 000, but the number of women invited to screening was about 45 000 (91%).16 While a variety of factors, including socio-economic deprivation, immigrant and employment status, distance between the residence and screening facility and attitudes towards screening have been suggested to be associated with non-attendance, these are largely country-specific.18–20 Predictors of attendance have not been comprehensively investigated in Estonia and remain unclear. In addition to screening, free mammography is available for women who have been referred by a primary care provider, given the woman is covered by national health insurance. In all other cases, the cost of a mammogram, which is rather substantial for a woman is covered by national health insurance. In all other cases, the cost of a mammogram, which is rather substantial compared with the mean income level, must be covered by the patient. In 2002 and 2006, the percent of women not covered by national health insurance was 8.8 and 6.2, respectively.21

Consistent with previous studies,9,11 the risk of advanced stage diagnosis increased with age. This association has not been well explained, but possible causes include the masking of symptoms by co-morbid conditions, lower knowledge level and several age-related access barriers.9,11,22 Overall, there was an improvement over time that was most obvious in women 50–69 years old. However, the change was very small in the youngest and oldest age groups. Place of residence appeared to be the strongest predictor of advanced stage diagnosis in all age groups. Compared with women from Tallinn, those living in

<table>
<thead>
<tr>
<th>Advanced stage</th>
<th>OR (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (%)</td>
<td>diagnosis (%)</td>
</tr>
<tr>
<td>Age at diagnosis, years</td>
<td></td>
</tr>
<tr>
<td>&lt;50</td>
<td>1582 (23.1)</td>
</tr>
<tr>
<td>50–59</td>
<td>1719 (25.1)</td>
</tr>
<tr>
<td>60–69</td>
<td>1703 (24.9)</td>
</tr>
<tr>
<td>≥70</td>
<td>1833 (26.8)</td>
</tr>
<tr>
<td>Period of diagnosis</td>
<td></td>
</tr>
<tr>
<td>1995–98</td>
<td>2119 (31.0)</td>
</tr>
<tr>
<td>1999–2002</td>
<td>2283 (33.4)</td>
</tr>
<tr>
<td>2003–06</td>
<td>2435 (35.6)</td>
</tr>
<tr>
<td>Place of residence</td>
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<tr>
<td>Tallinn</td>
<td>2453 (35.9)</td>
</tr>
<tr>
<td>Tartu</td>
<td>541 (7.9)</td>
</tr>
<tr>
<td>Other</td>
<td>3001 (43.9)</td>
</tr>
<tr>
<td>Ida-Viru County</td>
<td>842 (12.3)</td>
</tr>
</tbody>
</table>

a: Simultaneously adjusted for age at diagnosis, period of diagnosis and place of residence.
Tartu had the most favourable outcome while women from Ida-Viru County were more than 50% more likely to be diagnosed with advanced cancer. There was no difference between Tallinn and the remaining regions of the country.

One possible explanation for the observed risk difference is the ethnic profile of the population in the respective regions. The balance between ethnic Estonians and non-Estonians in the population has largely evolved as a consequence of the Soviet industrialization programme that was accompanied by massive immigration from other parts of the Soviet Union. The Ida-Viru industrial region and Tallinn were mainly affected and the consequences are still evident in the ethnic profile of the population of different regions (Table 1). Breast cancer incidence has been found to be slightly higher among Estonian than among Russian women. A recent study observed 20% higher breast cancer mortality in Russian women compared with that in Estonian women. Although we were not able to include self-reported nationality into the final model due to a large amount of missing data, we attempted to assess the effect of nationality, performing a stratified analysis within subgroups with known nationality. These analyses indicated that regional differences were similar in both ethnic groups.

Educational level is considered as an important determinant of breast cancer incidence and mortality. While the incidence of breast cancer follows a positive relationship with education and higher incidence rates are seen among higher educated women, the opposite is usually seen for breast cancer mortality. A recent study of four Eastern European countries, including Estonia, showed that from 1990 to 2000, breast cancer mortality decreased among higher educated women and increased among lower educated women, resulting in an inverse educational gradient, similar to other developed countries. In several studies, poorly educated women have been shown to be more likely to have a delayed diagnosis than their better educated counterparts. As shown in Table 1, the percent of women with higher education was nearly twice as high in the two largest cities compared with other regions. It is likely that education and health-related knowledge and attitudes explain some, but not all of the observed regional differences in stage distribution.

Ida-Viru County has been a predominantly industrial region for the past 50 years with oil-shale mines, heavy, chemical and textile industries as the main employers. With the transition towards a liberal market economy and technological advances, the employment opportunities in these industries have decreased considerably. The unemployment rate in Ida-Viru County has consistently been among the highest in the country (see Table 1), similar to the unemployment rate in some mostly agricultural marginal counties of Southern Estonia. However, these southern marginal areas did not differ from the rest of the country with regard to breast cancer stage distribution and were therefore not included separately in the analysis. For the working-age population, unemployment has a direct effect on health care access since unemployed persons maintain their insurance coverage only for a limited period of time, whereas health care access should be ensured for women of retirement age as the national insurance plan fully covers retired persons receiving state pension.

Our finding that living in Ida-Viru County was less pronounced as a risk determinant of advanced stage disease among women 50–59 years of age, who to a certain extent had access to free mammography through the early detection programme supports the suggestion of overall poor access to health care in this region. Primary care in Estonia is provided by family physicians practising across the country. Specialized diagnostic and treatment facilities for cancer patients are located in Tallinn and Tartu; county hospitals offer limited diagnostic and consulting opportunities. Until 2007, the mammography equipment used in the Ida-Viru County Hospital did not meet modern standards. Most patients with suspected cancer diagnosis are referred to Tallinn or Tartu, which are geographically remote and may have long waiting lists. Cost and transportation issues may prevent some patients from seeking timely diagnostic management even if they have been referred by their primary care providers. In 2004, the proportion of adult population who reported not receiving primary and specialized care when they needed it was higher in the North-Eastern region than in other parts of the country. There are no studies available assessing the referral practices of primary care providers. It is also unknown to what extent family physicians inform their patients about available preventive services and encourage them to take part in screening programmes.

In conclusion, this study revealed striking regional differences in stage distribution of breast cancer at diagnosis in Estonia. Due to the scarcity of available data, underlying causal pathways could not be addressed directly. It is unlikely that the observed effect of residence could be explained by a single mediating mechanism; it is rather a complex issue involving several, partly interrelating factors. Further studies are needed to identify specific patient-related and health-care-related factors causing delay of diagnosis in different regions. Nevertheless, it is clear that not only is there a need for health education for the whole population but there are groups of especially disadvantaged women who should be addressed with specific measures, particularly younger and elderly women, those living in remote areas and of lower socio-economic status. In view of current economic difficulties and a sharply rising unemployment rate, ensuring equal access to health care becomes even more challenging.

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Conflicts of interest: None declared.

Key points

- This population-based study identified place of residence as a major determinant for breast cancer stage at diagnosis in Estonia. The most likely factors behind these regional variations are education, unemployment and health care access. Ethnicity does not appear to play a major role in the timely detection of breast cancer.
- The risk of advanced stage disease decreased significantly over the study period among women 50–69 years of age, but very little improvement was seen in women younger than 50 years and those 70 years and older.
- There are groups of especially disadvantaged women in Estonia who should be addressed with specific early detection measures, particularly those living in remote areas and of lower socio-economic status. Efforts are needed to ensure equal access to health care to women across the whole country.
References


