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Comparison of survival time of women with breast cancer depending on whether they participated in the mammography screening program

Porównanie czasu przeżycia kobiet z rakiem piersi w zależności od tego, czy brały udział w programie przesiewowych badań mammograficznych

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Abstract

Key words: *Breast cancer, mammography, average survival time*

Introduction and objective: Preventive screening mammography is a very important test that allows early detection of the disease and introduction of effective treatment. The aim of the study was to compare the survival time of women with breast cancer participating in the screening program in relations to women who do not undergo these tests.

Material and methods: The material for analysis was obtained from the NHF. There were two groups of patients between 50-69 years of age who were diagnosed with breast cancer in 2010, a total of 12,093 women. The observation period was terminated either at the time of patient's death or at the end of the observation, that is on December 31st, 2016. In the study group, 5,071 women did not undergo mammographic screening tests, and 7,022 women had preventive examinations. The average survival times were compared in both groups using the Kaplan-Meier estimation method.

Results: The statistical tests performed showed a statistically significant difference between the studied groups ($p<0.001$). The percentage of five-year survival was 61.4% for a group of women without preventive screening before the diagnosis in comparison to 85.8% in those performing the tests. The average survival times were 58.7 months for the group without preventive screening and 75 months for those who had mammography tests.

Conclusions: Performing mammographic screening in women at risk of developing breast cancer, i.e. between 50 and 69 years of age, statistically increases the average survival time and gives a much greater chance of 5-year survival compared to women who do not undergo breast cancer screening.

Streszczenie

Słowa kluczowe: *Rak piersi, mammografia, średni czas przeżycia*

Wprowadzenie i cel: Rak piersi jest najczęstszym nowotworem złośliwym kobiet w Polsce. Ważnym badaniem pozwalającym na wczesne wykrycie choroby i wprowadzenie skutecznego leczenia jest profilaktyczna mammografia przesiewowa. Celem pracy było porównanie czasu przeżycia kobiet z rakiem piersi biorących udział w programie badań przesiewowych w stosunku do kobiet, które nie poddały się tym badaniom.

Materiał i metody: Materiał do analizy uzyskano z baz danych NFZ. Były dwie grupy pacjentów w wieku 50-69 lat, u których w 2010 roku zdiagnozowano raka piersi, łącznie 12093 kobiet. Okres obserwacji kończył się albo w momencie zgonu pacjentki, albo z końcem obserwacji, tj. 31 grudnia 2016 r. W badanej grupie 5071 kobiet nie zostało poddanych badaniom mammograficznym, a 7022 kobiety przeszły badania profilaktyczne. Średnie czasy przeżycia porównano w obu grupach metodą estymacji Kaplana-Meiera, wiarygodność oceniono testami statystycznymi: log-rank, Wilcoxona, -2Log (LR) z istotnością statystyczną $p < 0,05$.

Wyniki: Wykazano istotną statystycznie różnicę pomiędzy badanymi grupami ($p<0,001$). Odsetek 5-letnich przeżyć wyniósł 61,4% w grupie kobiet bez profilaktycznego badania przesiewowego przed diagnozą w porównaniu z 85,8% w grupie wykonujących badania wyniósł 58,7 miesięcy w grupie bez profilaktycznych badań przesiewowych i 75 miesięcy w grupie, która miała profilaktyczne badania mammograficzne

Wnioski: Przeprowadzenie mammograficznych badań przesiewowych u kobiet zagrożonych zachorowaniem na raka piersi, tj. między 50 a 69 rokiem życia, statystycznie zwiększa średni czas przeżycia i daje znacznie większą szansę na 5-letnie przeżycie w porównaniu do kobiet, które nie poddają się badaniom przesiewowym piersi rak. Programy badań przesiewowych mogą mieć istotny pozytywny wpływ na długość i jakość życia kobiet z rakiem piersi w Polsce.

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Introduction

The aim of screening tests is to detect asymptomatic patients in an early stage of the disease that allows intervention, which will result in reduced mortality. Although data is conflicting breast mammography screening may reduce the risk of death from breast cancer. This finding established the recognized role of this screening and has been the basis for formation of population screening programs in many countries, including Poland. In Poland, screening mammography examination covers women aged 50-69 years and is performed every 2 years (in women with factors significantly increasing the risk of breast cancer, the screening is performed every year). An participation rate in the screening program should be over 70%, however thisgoal is not met with an estimated coverage of about 43% of the target population [1]. The aim of this study was comparison of survival in women suffering from breast cancer depending on whether they participated in the screening program or not.

Material and methods

Individual patient IDs (in order to protect the patient's personal data, this number has been anonymized) were collected from the National Health Fund (NFZ) databases and combined with ICD-10 diagnostic codes group C50 i.e. malignant neoplasm of breast. Population aged 50-69 was selected from the entire collection for the analysis (the population in which the screening was carried out). This collection was then combined with database about the mammography tests performed, indicating those patients who had undergone at least one mammography examination over the analyzed period. In order to eliminate from the analysis the patients with suspected disease only (before detailed cancer diagnostics), the database was narrowed down to the level (type) of "hospital treatment" benefits. The next step was to select from such database patients who appeared in 2010 but did not appear in the database in the years 2008-2009 (new patients in 2010). Patients were followed until the end of 2016. The starting date in the survival analysis using the Kaplan-Meier method was determined as the date of the first application of active, targeted therapy of the diagnosed malignant breast cancer. The following were taken into account: administration of chemotherapy, administration of a chemotherapeutic agent as part of a drug program, radiotherapy or performing surgical procedures (JGP treatment group). The termination date for the observation of survival was set for December 31st, 2016. Analysis was performed using SAS E.G. software, v 7.1. The difference in survival time was assessed by two-way log-rank tests, Wilcoxon, -2Log (LR), assuming statistical significance, when $p<0.05$.

Results

In the analyzed period, 364 915 patients diagnosed with C50% were selected from the National Health Fund database. From that number 18.8% of cases received in-patient therapy. The number of patients who were diagnosed with malignant breast cancer and did not appear in 2008-2009 (new patients in 2010) amounted to 18 951, compared to 17 152 (90.5%) and were treated with active anticancer treatment. The analyzed group of new patients in 2010 therefore consisted of 17 152 people, including 12 093 people aged 50-69. Out of this group 5,071 patients had not undergone mammography (layer 1), whereas other 7,022 patients were screened with a mammogram (layer 2). Based on the time that elapsed from the first application of active targeted therapy in both sets of patients until their death (or December 31st, 2016), Kaplan-Meier curves were generated (Figure 1).

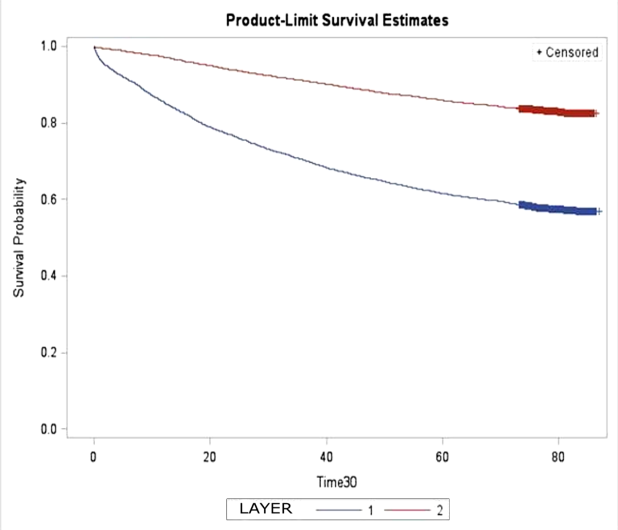

Figure 1 *Estimation of total survival (OS) with malignant breast cancer for patients not participating in the mammography screening (layer 1) and those participating (layer 2).*

In the cohort (layer) 1 there were 5 071 observations, among which there were 2 917 (57.5%) censored observations. In the cohort (layer) 2 there were 7 022 observations, among which 5 826 (82.9%) observations were marked as censored. The median value of the observation period was 79.3 months; for the cohort (layer) 1 it was: 79.6 months (95% CI: 79.3-79.7), and for the cohort (layer) 2: 79.3 (95% CL: 79.2-79.4). In both sets, the median survival time was not attained. The performed statistical tests: log-rank, Wilcoxon, -2Log (LR) showed statistical significance between both cohorts ($p<0.0001$). The percentage of five-year survival rate for the cohort (layer) 1 was 61.4%; for the cohort (layer) 2: 85.8%. Average survival times were: for cohort (layer) 1 - 58.7 months, and for cohort (layer) 2 - 75 months.

Discussion

The reduction in the relative risk of death due to breast cancer attributed to mammography screening varies from about 15% to 25% for women aged 50-69 in early randomized clinical trials, as well as from 13% to 17% in more recent meta-analysis of observational studies, sometimes not reaching statistical significance [2,3,4]. In Poland, within the population of patients aged 50-69, to whom screening is dedicated, a reduction in mortality from about 55/105 in the early 1990s to 39/105 in 2013 was observed [5]. However, after many years of widespread approval of mammography, the Cochrane meta-analysis published in 2000 [6] has brought an ongoing lively discussion on the importance of mammography and the benefits and harms associated with its use [2,4,7]. The review of the methodological quality of mammographic tests carried out at that time, along with their results, showed that there were baseline imbalances in 6 of 8 clinical trials and inconsistencies in the number of women randomized were found in 4, whereas the other two did not indicate the impact of mammography on mortality from breast cancer and total mortality [6]. The results of studies on the population of Polish patients are comparable [8,9]. Additionally, apart from the problem of false positive results (in Europe the risk is estimated at about 20%) and the related risk of biopsy, which is about 3% [2,10], one of the primary allegations raised recently is overdiagnosis, which increases with the prevalence of digital mammography [2,4,11]. It is defined as the detection of changes (e.g. Carcinoma in situ (CIS)) which, without the screening tests, would not appear to be clinically relevant or life-threatening, and which, following the performed diagnosis, undergo treatment, resulting in the exposure of women to side effects of treatment without a real benefit. Since the exact assessment of overdiagnosis is difficult, there are very significant discrepancies in the frequency of its occurrence from less than 5% to even up to 54% [2,4,11]. It cannot be excluded that excessive treatment results in increased mortality from non-cancerous causes, which may be the reason for the observed lack of benefits in relation to mortality from the general. Furthermore, the highest reduction in mortality from breast cancer (median 37%), observed in European countries since 1998, among women under 50 (not covered by screening tests) compared to 21% in the population aged 50-69 promotes the interpretation that improved prognosis is the result of greater awareness of the disease and progress in treatment than the mammography itself [2,4,12]. The progressive improvement in treatment results leads to a gradual reduction in the absolute advantage given by the screening. Based on data from 1980, the Euroscreen working group estimated that between 111 and 143 women in the age group of 50-69 should be screened in order to prevent one death caused by breast cancer, while based on Norwegian data from 2009 on mortality from breast cancer, similar figure was already estimated at 368 women [13]. However, conducting mammography screening tests seem particularly justified in countries where the disease awareness is lower and breast cancer is detected at higher stages of advancements. In Norwegian observations, screening tests led to the diagnosis of 58% more stage I and 22% more stage II tumours, without any reduction in the frequency of the advanced stage diseases (stage III and IV) [2,11]. It is known that the earlier diagnosis of the disease is associated with better results of treatment and a longer survival time. Considering worse results of breast cancer treatment in Poland compared to Western European countries (5-year survival rate - 73% vs. 83% in Europe), it seems reasonable to say that in Poland the percentage of late diagnoses is still too high [14]. The results obtained indicate a much better prognosis of women participating in the screening program, with the difference in the 5-year survival rate of about 25%. The patients participating in the screening program reached a 5-year survival rate similar to that observed in all patients in Northern or Western European countries. The most obvious reason seems to be that they were diagnosed with an earlier stage of cancer. In addition, women applying for mammography test have undoubtedly greater health awareness. This means that not only screening, but also greater awareness of the risk of disease in women voluntarily participating in screening program and, consequently, faster medical consultation may contribute to earlier diagnosis of cancer. The greatest value of this study is the analysis and long-term observation of the entire population of breast cancer patients in Poland. The accuracy of the adopted methodology is confirmed by the fact that, according to the National Cancer Registry in Poland, in 2010 almost 16 thousand women suffered from breast cancer [15]. Considering the possible insufficient registration of diseases, the extracted number of approximately 17,000 women from the national payer's database who have been treated for breast cancer is very likely. Undoubtedly, our work also has weaknesses. The population-based nature of the analysis made it impossible to collect the number of important data, such as the stage of breast cancer, the exact type of treatment used, and the calculation of the disease free survival. What's more, we do not have any information about the mammography results. It should be kept in mind that improved survival may in part represent lead time bias and does not prove efficacy of the screening programme itself, and may be only hypothesis generating.

Conclusion

Hospitalized women with the ICD10 diagnosis of malignant neoplasm of breast who underwent mammography screening had significantly better outcomes. It remains to be determined to what extend screening contributed to this survival benefit.

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