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Follow-up after breast cancer treatment

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ABSTRACT

Background: Breast cancer (BC) is the most common malignancy in women. Due to improved detectability and modern methods of treatment, the number of breast cancer survivors is estimated at 6 million women globally and is still increasing. The follow-up (FU) visits carried out at the Greater Poland Cancer Centre were assessed for compliance with Polish Society of Clinical Oncology (PTOK) and European Society for Medical Oncology (ESMO) guidelines.

Materials and Methods: The database covered 484 women who were treated for breast cancer in the Greater Poland Cancer Centre in 2013. Of these, 233 attended FU visits for 5 years after completion of radical treatment and had no cancer relapse. The number of FU visits and the number and type of additional tests performed were analyzed.

Results: The median number of FU visits over 5 years was 14, which is in line with the guidelines. 51.6% women had a mandatory annual mammography. A significant number of women had additional tests that are not recommended in the guidelines.

Conclusions: There is a need to educate both physicians and patients on the principles of FU check-ups.

Key words: breast cancer; follow-up; scientific societies guidelines

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Introduction

Breast cancer is the most common cancer in women worldwide. Thanks to improved detection and modern methods of treatment, the number of breast cancer survivors is still increasing and is estimated at 6 million women globally [1]. Such a large number of survivors, who need to be followed-up for many years, places a heavy burden on healthcare systems in many countries. Follow-ups are primarily aimed at detecting early local or regional recurrence of breast cancer. Screening for distant metastasis in asymptomatic patients is not recommended. The guidelines of oncological societies, both Polish (PTOK) [2] and European (ESMO) [3], recommend mammography as the only imaging examination, since the detection of a local/regional recurrence and/or a carcinoma of the contralateral breast owing to mammography in asymptomatic patients increases the overall survival. The aim of this study was to assess the FU visits conducted at the Greater Poland Cancer Centre and their compliance with PTOK and ESMO guidelines.

Material and methods

This was a retrospective study. The database covered a group of 484 women treated for breast cancer in the Greater Poland Cancer Centre in 2013. The final analysis comprised 291 patients who attended follow-up examinations for 5 years after completion of radical treatment. Of these,

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233 had no cancer relapse. An analysis was made of the number of the visits and the number and type of additional tests performed.

Statistical methods

The structure and correlation analysis were done. The significance level was adopted as 0.05. Programming language used was Python, version 3.7.

Results

233 women without cancer relapse attended FU visits for 5 years. The median number of visits over 5 years was 14, which is compatible with the guidelines. Usually, however, the number of visits was too high (34% > 15 visits) or too low (26% < 13 visits) and only 43% of the women had the recommended number of visits. 53% of the patients had an annual mammography done, and 31% had 4 mammograms during 5 years. The percentage of the patients that had annual mammography done increased from 75% in the first year to 99.6% in the fifth year of the follow-up. The majority of patients had additional tests despite the absence of any symptoms or abnormal physical examination. 193 patients (75%) had the level of CA 15.3. checked at least once. The complete blood count was performed at least once in 165 (71%) patients, the blood chemistry tests in 139 (60%) patients. 226 women (88.2%) had an ultrasonography of the abdomen and 218 (85.1%) had a chest X-ray carried out at least once. Many of them had these tests done regularly, once a year.

The estimated costs of additional tests were calculated, assuming that abdominal ultrasonography costs EUR 12.75; chest X-ray examination EUR,8.50; complete blood count, EUR 1.71; blood chemistry, EUR 6.40 and CA 15.3 level, EUR 8.10 [18]. In total, all tests performed in the course of a 5-year FU period of patients without cancer relapse, cost EUR 23,377, which is EUR 100 per patient. The total cost of all imaging tests for 5 years was EUR 14,174 and laboratory tests EUR 9,203.

Discussion

Breast cancer is the most common malignancy in women. Improved treatment methods and cancer detection at ever lower stages mean that the number of women who have recovered and remain under long-term control is constantly growing. This is obviously a reason for satisfaction for doctors and patients, but it also causes numerous logistic problems in oncology centers and outpatient clinics related to the constantly growing number of patients who need to be admitted for a medical appointment and undergo additional tests.

The aim of this study was to assess the course of medical check-ups performed at the Greater Poland Cancer Centre and their compliance with PTOK and ESMO guidelines. We analysed the number of the visits and also the number and type of additional tests performed.

Over a period of 5 years, the average number of visits by a patient in this study was 14, which is consistent with Polish as well as European recommendations. A Dutch study investigated the pattern of follow-up visits and the manner of diagnosing cancer relapse within 5 years after the completion of radical treatment [4]. The average number of visits per patient was 13, although, according to the Dutch guidelines, there should be 9 visits over 5 years. Thus, as in the present study, the number of follow-up visits was higher than recommended. Most often, the date of the next follow-up visit is set by the doctor, so it is the doctors who should adjust the frequency of visits to the current guidelines.

This study assessed whether the number of follow-up visits depended on the stage of the disease, the biological subtype of breast cancer, and the patients' menopausal status. A statistically significant relationship was found only in the last group: pre- and perimenopausal patients had significantly more follow-up visits than postmenopausal women (the ratio of surplus visits was 61% *vs.* 36%). This may be due to the fact that younger women are more aware of their disease, more often pay attention to disturbing symptoms and, therefore, attend appointments more often, have many questions about treatment or additional tests, and are also more concerned about keeping appointments. If the number of visits could be reduced to the number recommended in the guidelines, time could be saved for both patients and healthcare professionals. Physicians could spend this time treating patients with ongoing treatment, and they would also have more time to see patients suspected for relapses who manifest disturbing symptoms.

Table 1. Patients characteristic

Feature	Number of patients without cancer relapse (%) (n = 233)
Age [years]	
< 40	18 (8)
41–50	56 (24)
51–60	75 (32)
> 61	84 (36)
Menopausal status	
Before menopause	53 (23)
Perimenopausal	51 (22)
Postmenopausal	129 (55)
Histological differentiation degree	
NHG1	16 (7)
NHG2	90 (39)
NHG3	127 (55)
Tumor size[1]	
T1	117 (50)
T2	96 (41)
T3	16 (7)
T4	4 (2)
Regional lymph node involvement[2]	
N0	118 (51)
N1	73 (31)
N2	26 (11)
N3	16 (7)
Clinical stage	
I	73 (31)
II	121 (52)
III	39 (17)
Breast cancer subtype	
Luminal	138 (59)
HER2-positive	59 (25)
Triple negative	36 (15)

[1]T1 — tumor ≤ 20 mm in the greatest dimension, T2 — tumor > 20 mm but ≤ 50 mm in the greatest dimension, T3 — tumor > 50 mm in the greatest dimension, T4 — tumor of any size with direct extension to the chest wall and/or to the skin (ulceration or macroscopic nodules); [2]N0 — regional lymph node metastasis identified or ITCs only, N1 — micrometastases or metastases in 1–3 axillary lymph nodes, N2 — metastases in 4–9 axillary lymph nodes, N3 — metastases in 10 or more axillary lymph nodes

Performing additional imaging and laboratory tests (apart from those recommended in the guidelines) in asymptomatic women after breast cancer treatment is a big problem in everyday cancer practice. In this study, only 12% of such patients did not have an abdominal ultrasound within 5 years of follow-up, and 17% did not have an X-ray of the chest. 29% had no complete blood count, 40% had no blood chemistry tests and the level of CA 15-3 was not determined in 27% of patients. This means that the vast majority of patients underwent extra examinations that did not comply with the guidelines. And those examinations burden the hospital both financially and logistically. Moreover, they may cause anxiety for a patient as well as the doctor when the results turn out to be abnormal, although, especially in the case of elevated CA 15-3 levels, may be false-positive. More intensive follow-up tests are associated with 10–50% of false positives results [5]. Frequently, in everyday clinical practice, abnormal abdominal ultrasound or chest X-ray results require additional tests, e.g. computed tomography, which is associated with the risk of renal failure (or damage), anaphylactic shock and lead to the exposure to harmful ionizing radiation [6].

Intensive follow-up appointments began to be abandoned first in 1999 and 2005, following clinical trials that showed no effect of intensive follow-up on overall survival [7, 8]. Many studies have proven that in terms of time to detect distant recurrence, overall survival and the quality of life, intensive follow-up visits with laboratory and imaging tests are as effective as physical examination and annual mammography. The Cochrane analysis included 5 large studies (GIVIO, Grunfeld 1996 and 2006, Gulliford 1997 and Roselli Del Turco 1994) involving a total of 4100 patients [9]. No significant gains were found for overall survival and relapse-free survival in the intensively controlled groups, both for the overall study population and for age, tumor size, or nodal status subgroups.

Trying to understand the reasons why doctors do not follow the guidelines, this study assessed the dependence of the number of additional tests on the stage of the disease, the immunophenotype of the breast cancer and the menopausal status of the patients. It could be assumed that doctors more often tend to send for additional tests patients with a higher risk of recurrence of the disease. Several of these correlations were statistically significant — abdominal ultrasound was performed more often in stage I and III and in patients with HER2 overexpression, chest X-ray was also ordered more often in HER2-positive and pre- and perimenopausal patients, while laboratory tests were more commonly administered to patients with luminal subtype A or B. In turn, CA 15-3 was most often assessed in triple negative cancers. There is no obvious regularity in the above results, which, unfortunately, may

Table 2. Additional tests performed during follow-up (FU) visits

Type of tests	Number of tests done				
	Year 1	Year 2	Year 3	Year 4	Year 5
Laboratory tests[1]	473	405	299	256	188
Imaging tests[2]	315	311	260	247	173

[1]complete blood count, blood chemistry tests, level of CA 15.3.; [2]ultrasonography of the abdomen, chest X-ray

prove that additional tests were ordered randomly. The question is whether new recommendations should be made based on the biological subtype of breast cancer or the clinical stage of the disease. In this study, during the collection of data, it was observed that many patients had been monitored in more than one outpatient clinic, or after some time they changed clinics, e.g. from surgery to chemotherapy. Perhaps this is also one of the reasons for the incorrect number of additional tests: when a patient is under the care of several physicians of different specialties whose recommendations sometimes differ.

Mammography is the only imaging test that is recommended in follow-up examinations in patients after radical treatment for breast cancer. According to Polish, European and American guidelines, it should be performed once a year. Additionally, PTOK recommends performing the first follow-up mammography 6 months after the surgery in the case of breast-conserving therapy. Research confirms, that early detection of asymptomatic local recurrence by mammography prolongs overall survival and improves the quality of patients' life [10]. Early detection of a second breast cancer reduces mortality from this disease by 17–28% — if the recurrence is detected by mammography, not by physical examination[11].

Most guidelines are silent on how long mammogram screening should be conducted. With the ever-increasing number of women after radical treatment for breast cancer, this poses an increasing logistical problem for healthcare systems in many countries. Polish recommendations of cancer societies do not specify how long to conduct check-ups or perform mammography. Hence, the logistic problem of oncology centers, which will grow over the years, is how to manage the increasing number of women after breast cancer requiring a FU mammography every year, while the number of new breast cancer patients increases. Moreover, in Poland a family doctor is not allowed to refer a woman for mammography and this examination cannot be performed without a referral (if financed from the National Health Fund); therefore, it is practically performed only in oncology centers or regional oncology outpatient clinics. Importantly, in Poland, unlike for example Great Britain, women who have previously been diagnosed with breast cancer can no longer obtain mammography under the Breast Cancer Prevention Program. As a result, FU visits and mammography are performed in oncological centers also for women who had breast cancer more than a decade or even several decades ago.

The prognostic value of CA 15-3 has been confirmed in some studies [12, 13] and negated in others [14, 15]. In a meta-analysis of almost 13,000 patients from 36 clinical trials, elevated CA 15-3 levels were associated with significantly worse disease-free time and shorter overall survival [16]. Among the subjects of this study, only 27% had no CA 15-3 test, and 72.9% had at least one test done during the 5 year FU. On average, one patient had this test done 2.99 times. The number of tests performed decreased each year — from 229 in the first year of observation to 69 in the fifth year. This downward trend in the number of performed tests was in line with the number of visits and imaging tests. Many patients who come for check-ups want to have a marker level test done. However, the author's own practice shows that if the patient is informed about the current recommendations, sensitivity and specificity of CA 15-3 determinations, she often accepts FU visits without determining the level of CA 15-3 or other markers. Unfortunately, patients' knowledge is strongly influenced by their family and friends or by online forums and social media which often contain views that have nothing to do with scientific knowledge. If patients were better informed by their physicians about the exact rules of FU, unnecessary additional tests (laboratory and imaging) could be avoided.

Many problems of women who have been cured of breast cancer remain unresolved, and many problems are not discussed by the physicians during visits. Access to "on-demand" visits, i.e. when a patient experiences disturbing ailments, may be difficult in many centers. Also psychosocial services and support are very important for the well-being of patients with breast cancer and long-term outcomes of breast cancer [17] and often there is not enough time to take care of it. Perhaps the situation could be improved by the recently introduced telephonic visits, especially if it was possible to provide advice by qualified cancer nurses who would pre-qualify patients for urgent visits. Having received appropriate training nurses could also carry out some of the counseling visits. Possibly some of the FU visits could be performed in primary health care clinics. This would certainly require improved communication between oncologists and GPs. It would be useful to copy the tradition from many countries of sending a letter to the family doctor after the end of the treatment, informing him/her about the treatment received and further necessary checks. Continuity of control is important for patients, i.e. the same doctor, the same clinic. Ideally, FU visits should be carried out by the physician who has treated the patient previously. This condition is often difficult to meet in large cancer centers, which is why the role of the primary care physician in caring for a convalescent is so important. Patients should also be educated about breast self-examination, paying attention to disturbing symptoms, reporting for planned follow-up visits, as well as regular use of medications, especially hormone therapy. Another point worth discussing regarding the follow-up of patients after breast cancer treatment is the fact that the current recommendations were developed at a time when there was no current division of breast cancer into immunohistochemical subtypes (luminal A, luminal B, HER2 positive, triple negative). We know that each of these subtypes can cause a relapse at different times and to other organs. Therefore, it might be appropriate to divide the recommendations depending on the diagnosed cancer subtype [19].

At the time when most recommendations presented in this study were made, treatment for breast cancer was at a different level. The recent years have seen significant advances. The life span of patients with disseminated disease has increased significantly. Therefore, extensive new clinical trials are needed to establish new guidelines for FU of patients after radical treatment of BC.

Conclusions

There is a need to educate oncologists, family doctors and patients, on how to carry out and better adhere to FU in breast cancer. Physicians need to follow the scientific societies' guidelines. However, the existing recommendations were made many years ago. It seems advisable to conduct new studies on possible modifications to these guidelines, bearing in mind the tremendous advances in breast cancer treatment and the fact that BC today is divided into several biological subtypes. Family doctors and oncological nurses should be trained and be given more competences to perform FU visits, whereby the logistical burden on oncological centers could be reduced.

Conflict of interest

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