

Breast-conserving surgeries in HER-positive breast cancer patients are performed too rarely in Poland

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Breast cancer is the most common cancer among women in Poland and worldwide; after lung cancer it is the second highest cause of death among females with malignancies. HER2 positive breast cancer occurs in ca.15–20% of all cases. More often than other subtypes, it affects younger patients and more often spreads metastasises to internal organs. The new drugs against the HER2 receptor significantly improve patients' prognoses, regardless of the initial stage. The authors of the study involved 1503 patients with HER2 positive breast cancer from all stages (I–IV); 482 patients received preoperative systemic therapy (chemotherapy or hormonal therapy), 385 trastuzumab. Among the 1219 females qualified to surgery, 734 (60%) underwent a mastectomy, 485 (40%) had breast conserving therapy with adjuvant radiotherapy, some of them had preoperative systemic treatment.

Key words: breast cancer, HER2 positive breast cancer, surgery, mastectomy, breast conserving therapy

Introduction

Breast cancer is the most commonly diagnosed cancer in women in Poland and worldwide. It is the second (after lung cancer) most common cause of cancer mortality. The prognosis depends, among other things, on the stage of the disease at the time of diagnosis, the biological subtype of cancer,

the general clinical status of the patient, as well as access to different types of therapy [1].

Approximately 15–20% of all cases are HER2-positive cancers, overexpressing the HER2 receptor or amplifying the gene coding for this receptor protein. Compared to other subtypes, this biological subtype is diagnosed more commonly in young

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patients. The average age of diagnosis is approx. 50 years, so it is clearly lower than in the general breast cancer population. The predominant location of distant metastases in HER2-positive breast cancer is the liver and central nervous system [2]. Over the past few years, new HER2 inhibitors have significantly improved the efficacy of treatment of both early and advanced forms of the disease. The therapy now considered most active is the dual blockade of pertuzumab and trastuzumab, anti-HER2 monoclonal antibodies, combined with chemotherapy. This is the standard in preoperative care for HER2-positive breast cancer patients with a primary tumour diameter exceeding 2 cm or with metastases to axillary lymph nodes. The prognosis of patients is improved when a complete pathological response (i.e. the absence of invasive cancer cells in the post-operative specimen) is achieved as a result of preoperative treatment [3]. Effective neoadjuvant therapy increases the likelihood of breast-conserving therapy.

A question arises as to whether the increasing effectiveness of preoperative treatment, leading to downsizing of the primary tumour and downstaging of the tumour status, entails a real change in the proportion of breast cancer patients treated with conserving therapy in Poland. Therefore, this article presents data on the type of breast surgeries performed in HER2-positive breast cancer patients treated in selected national cancer centres between January 2014 and July 2017.

Material and methods

The study analysed retrospectively collected clinical data from 1503 HER2-positive breast cancer patients treated across 7 Polish cancer centres (Wielkopolskie Centrum Onkologii [Greater Poland Cancer Centre], Centrum Onkologii w Warszawie [Maria Skłodowska-Curie National Research Institute of Oncology in Warsaw], Białostockie Centrum Onkologii [Białystok Oncology Centre], Mazowiecki Szpital Onkologiczny Wieliszew [Masovian Oncological Hospital in Wieliszew], Opolskie Centrum Onkologii [Opole Oncology Centre], Oddział Onkologiczny z Pododdziałem Hematologicznym Wojewódzkiego Szpitala Zespołowego w Koninie [Department of Oncology with the Hematology Section at the Regional Polyclinical Hospital in Konin], Szpital Uniwersytecki w Krakowie [Krakow University Hospital]) between January 2014 and July 2017. The doctors from the centres completed a questionnaire prepared and distributed by Roche, which included age as a categorised value (<40 years of age, 41–50, 51–65, 66–75, >75 years of age), patients' body weight, stage of the disease at the time of cancer diagnosis, and course of treatment including type of systemic treatment, surgery and adjunctive radiation therapy. All patient data was anonymous and gathered collectively, i.e. the responders stated how many patients in each centre meet the criteria of each question in the questionnaire. This method of data collection prevents tracking of the individual patients' survival status.

The questionnaire also asked the participating doctors for their opinion about potential qualification for therapies not reimbursed in Poland at the time concerned, provided that such therapies were feasible in specific patients. These therapies were meant to include the combination of trastuzumab and pertuzumab in preoperative treatment and in treatment of generalised disease, as well as the combination of trastuzumab and emtansine in the treatment of advanced breast cancer. This paper selectively presents the results of an analysis of data concerning the surgical treatment method.

All patients enrolled in the study were more than 18 years old and they were of good performance status (i.e. ECOG 0–2, Eastern Cooperative Oncology Group).

Results

More than ¾ of the study group were over 65 years of age, which is typical of the HER2-positive breast cancer population. The age structure of the study group is presented in figures 1 and 2.

The majority of the study group were patients with early breast cancer, accounting for 68% of the total group (331 patients with TNM stage I and 688 patients with TNM stage II, representing 22% and 46% of the total group, respectively). 327 patients (22%) had been diagnosed with stage III cancer, and 157 patients (10%) had been diagnosed with stage IV cancer. (tab. I). In the group of women with distant metastases at study entry, the majority (62%, n = 98) were patients with primarily generalised disease, while 38% of them (n = 59) had a relapse

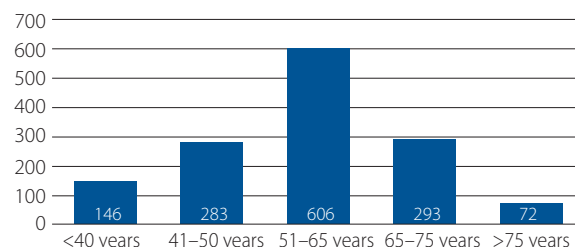


Figure 1. Classification of patients by the presented age categories, data for 1400 patients

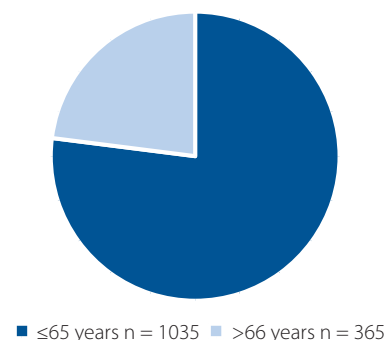


Figure 2. Classification of patients by two age categories, data for 1400 patients

of the disease after radical treatment. For the last mentioned subgroup of patients, the baseline advancement stage was unknown; therefore, the analysis classified them as stage IV.

Part of the patients (n = 482) received preoperative systemic treatment: chemotherapy, hormone therapy and trastuzumab therapy. Chemotherapy was used in more than half of the patients, and the proportion of patients treated in this way was higher in the stage III group than in the stage II group (68% and 50%, respectively). Trastuzumab was used in approximately 60% of patients, and its use was equally common in stage II and III patients.

Of all patients qualified for primary surgery or for systemic treatment followed by surgery (1219 patients in total), 734 (60%) underwent a mastectomy and 485 (40%) received conserving therapy (fig. 3).

Table I. Patient classification by breast cancer advancement stage (TNM), n = 1503 (100%)

Clinical advancement stage	Number of patients	%
I		22%
T1N0	331	
IIA	397	26.4%
T0N1	2	
T1N1	113	
T2N0	282	
IIB	291	19.4%
T2N1	248	
T3N0	43	
IIIA		6.9%
T3N1	103	
IIIB	170	11.3%
T1N2	30	
T2N2	37	
T3N2	31	
T4N2	72	
IIIC	54	3.6%
T1N3	14	
T2N3	19	
T3N3	8	
T4N3	13	
IV	157	10.4%
primary generalisation	98	
relapse	59	

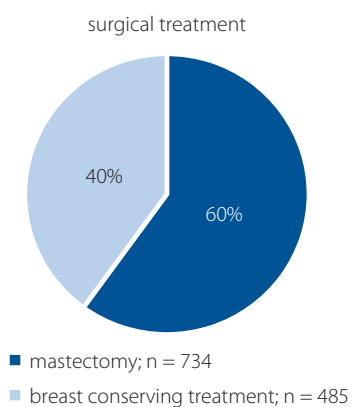


Figure 3. Breast surgery treatment methods, n = 1219

In the group of patients who underwent preoperative systemic treatment (n = 413), mastectomy was significantly more common in patients with a higher stage of disease at baseline. In stage II patients (n = 174), mastectomy was performed in 59% of the cases (n = 102) and conserving therapy was used in 41% of the cases (n = 72); whereas in stage III patients (n = 239), these methods of treatment were used in 83% (n = 199) and 17% (n = 40) of the cases, respectively (fig. 4). More than half of the patients (54%, n = 806) underwent primary surgical treatment. These were exclusively patients diagnosed with stage I and II of the disease. Also in this group, mastectomies was performed more frequently than breast-conserving therapy (54%, n = 433 and 46%, n = 373, respectively).

Discussion

Having analysed the data presented above, it should first be noted that the proportion of advanced cases of the disease is not as high as mentioned before in the report from the Polish Society for Research on Breast Cancer, where it was claimed to exceed 50% [4]. In contrast, the analysed material, involving a total of >1500 patients, showed that 2/3 of patients were diagnosed with stage I and II disease (1019 patients in total). Therefore, it could be expected that the proportion of patients receiving conserving therapy would be high in this group. That said, conserving therapy was performed in only 40% of patients out of 1219 patients qualified for surgery. It is worth highlighting, however, that conserving therapy was more common in patients with lower stages of the disease. Because the data was gathered collectively and analysed as a whole, individual patients' survival status could not be tracked. Since the questionnaire did not provide details about surgical qualification, it was not possible to determine the reasons for the relatively low proportion of patients who had conserving therapy administered. This proportion differs significantly from the level of 60–80% which is recommended by international scientific societies [5, 6].

However, the proportion of patients treated with a breast-conserving approach should not be indiscriminately accepted as an independent indicator of the quality of treatment of

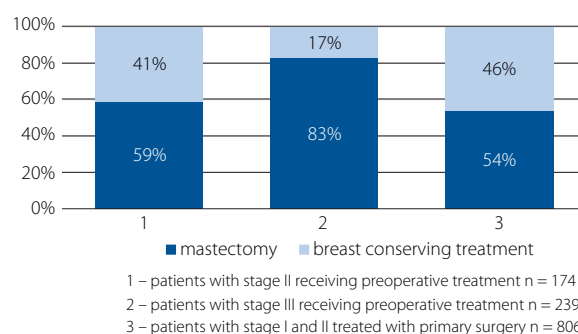


Figure 4. Surgical treatment methods according to advancement stage at baseline and preoperative systemic treatment, n = 1219

breast cancer patients in Poland. Current analysis from Australia and New Zealand indicates that in these countries also, where a modern and efficient healthcare system is implemented, the recommended values of the indicator mentioned above or other similar quality measures are not universally met and are often below the desired levels [7]. However, notwithstanding this observation, reference should be made to last year's ESMO recommendations, which clearly state that 'breast-conserving surgery is the primary surgical choice for breast cancer' [6]. In Poland, as indicated by the presented results, the proportion of breast-conserving procedures is still relatively low, despite the fact that in 2/3 of patients, the disease was diagnosed early.

Nonetheless, the observed proportion of conserving procedures, although not satisfactory, is twice as high as that observed in previous years. Data from 2005 to 2007 indicates that breast-conserving therapy was used in Poland at that time in approx. 21% of cases (with geographical variation ranging from 10% to 30%) [8]. From this perspective, significant progress can be observed.

It should also be noted that in the study period, the pre-operative targeted therapy was not used in HER2-positive breast cancer patients in Poland. On 1 January 2017, this type of therapy started to be reimbursed from public funds under the drug programme of the National Health Fund. Since that time, trastuzumab combined with chemotherapy could be used in HER2-positive breast cancer patients if the size of the primary tumour was at least 2 cm or there were metastases to axillary lymph nodes. Since only a few months ago, the combination of trastuzumab and pertuzumab plus chemotherapy has been reimbursed, which is the combination recommended for neoadjuvant treatment of HER2-positive breast cancer by both the European and American oncology societies [6]. Before that time in Poland, patients received HER2 antibodies only after surgery, and if initial systemic treatment was required due to high stage at baseline, only chemotherapy was administered. It is possible that these limitations might have played a part in the reduced efficacy of preoperative treatment and might have resulted in higher incidences of mastectomy, although this is merely a hypothesis. Meta-analysis of 5 randomised clinical trials showed that the addition of trastuzumab to preoperative chemotherapy increased the likelihood of achieving a complete pathological response without increasing treatment toxicity; however this did not translate into reduced incidence of mastectomy [9].

The efficacy of treatment in breast cancer patients depends on, among other things, a well-organised and properly functioning breast cancer unit (BCU), and a structure which unites specialists across multiple diagnostic, treatment and broad patient care (psychological support, rehabilitation) fields. In Poland, the first accredited BCU was established in Szczecin in 2013, the second – in Kielce in 2015, and since 2017, the Senologic International Society has accredited 5 further units: Bydgoszcz (2017), Krakow (2017), Gdynia (2018),

Warsaw (2018) and Opole (2019). The improved quality and efficacy of diagnostics and treatment within a BCU is linked to the close cooperation between specialists in different fields, who make collaborative decisions about different stages of patient management. Year-on-year, there is a growing number of accredited units that declare to perform at least 70% of breast-conserving surgeries in cancer patients. In recent years, BCUs in Poland have seen significant improvement in the availability and quality of oncoplastic procedures. Active units are subject to regular evaluation and, once specific criteria are met, reaccreditation.

In recent years, many European countries have seen a desired trend towards an increased number of conserving surgeries at the expense of mastectomies. Between 2005 and 2010, the number of mastectomies was observed to decrease by approximately 4% a year, whereas the average proportion of conserving surgeries accounted for 73% of the observed total surgeries. A different trend is observed in the USA, where the number of bilateral mastectomies increases – especially among younger patients, and the number of breast-conserving surgeries decreases, whereas the proportion of unilateral mastectomies remains stable. This phenomenon can be explained by, among other things, the increased popularity and availability of genetic tests and bilateral mastectomies being performed in breast cancer patients who are known carriers of *BRCA1/2* germinal mutations. It is also often mentioned that patients' preference to undergo a bilateral mastectomy is attributed to a sense of increased safety after both breasts are removed. Such a perception is quite common, as is the perception of greater efficacy of unilateral mastectomy compared to surgery that conserves the breast. It should be noted, however, that prognosis after conserving surgeries and mastectomy is comparable due to the increasing efficacy of adjuvant treatment [10]. In this context, it is extremely important that patients must be thoroughly informed about the benefits and possible complications of different procedures. The misconception among women that mastectomy is a less risky procedure compared to conserving therapy is alarming; it indicates the need to properly educate and inform the patient during the informed consent process.

In everyday practice, validated questionnaires, completed by patients before and after surgery (e.g. BREAST Q), may be helpful and provide a valuable source of information on the patient's motivation when selecting the type of surgery, as well as their level of satisfaction after surgery. Conclusions from the analysis of such data should be discussed by the entire team involved in the treatment and rehabilitation of breast cancer patients.

An increase in the number of breast-conserving surgeries depends, among others, on the stage of the disease, systemic treatment, and the availability of oncoplastic procedures carried out by highly qualified surgeons. In HER2-positive breast cancer patients, the addition of pertuzumab to chemotherapy

and trastuzumab has increased the proportion of complete pathological responses, making neoadjuvant treatment more effective [3]. The dual HER2 blockade has been reimbursed in Poland since 2019, and, consequently, it would be desirable to conduct studies into investigating the types of surgeries selected by patients and surgeons.

Conclusions

The presented data shows that the proportion of breast cancer patients treated with breast-conserving therapy is still relatively low in Poland. Breast-conserving procedures are performed in approx. 40% of patients and the data is mainly derived from referencing oncology centres. However, this proportion is twice as high as it was in the last decade.

The introduction of preoperative systemic therapy targeted at the HER receptor may significantly increase the incidence of breast-conserving procedures. Key importance is attached to interdisciplinary collaboration between BCUs and taking the utmost care when informing patients about their planned treatment.

Conflict of interest: none declared

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