

# Triple-negative breast cancer patients treated with subcutaneous mastectomy with immediate reconstruction: single institution experience

Artur Bocian<sup>1</sup>, Paweł Macek<sup>2,3</sup>, Piotr Kędzierawski<sup>3,4</sup>

<sup>1</sup>Oncological Surgery Clinic, The Holycross Cancer Centre, Kielce, Poland

<sup>2</sup>Scientific Research, Epidemiology and R&D Centre, The Holycross Cancer Centre, Kielce, Poland

<sup>3</sup>Jan Kochanowski University *Collegium Medicum*, Kielce, Poland

<sup>4</sup>Radiotherapy Clinic, The Holycross Cancer Centre, Kielce, Poland

Artur Bocian, Paweł Macek and Piotr Kędzierawski contributed equally to the preparation of this article.

## Abstract

**Introduction:** Triple-negative breast cancer (TNBC) accounts for approximately 15–20% of all breast carcinomas. In the last two decades, both nipple-sparing mastectomy (NSM) and skin-sparing mastectomy (SSM) with immediate reconstruction have been used in the surgical management. The aim of our study was to analyze the outcomes of the combined treatment of patients with TNBC treated with NSM or SSM.

**Material and methods:** A total of 114 women with TNBC were enrolled in this study. All diagnostic, therapeutic and follow-up procedures were conducted in one center of the Holycross Cancer Centre in Kielce. In all patients, subcutaneous mastectomy was performed. Overall survival was estimated by the Kaplan-Meier method. The influence of selected prognostic factors on the risk of death was analyzed using the Cox proportional hazards models.

**Results:** The probability of survival at 1, 3, and 5 years was 0.982, 0.894, 0.850, respectively. Based on the 5-factor Cox model, all included features had a significant relationship with the risk of death. In conclusion, the presence of a genetic mutation, adjuvant chemotherapy, complete pathological regression, and the absence of radiotherapy significantly reduced the risk of death.

**Conclusions:** The results of the treatment with subcutaneous mastectomy are good. The early stage of the cancer is associated with a better prognosis. Complete pathological regression after systemic treatment, particularly in patients with BRCA1 mutation, is a good prognostic factor and can help diminish the range of surgery in the axilla region.

**Key words:** combined treatment, triple-negative breast cancer, subcutaneous mastectomy.

## Introduction

Breast cancer (BC) remains the most frequently diagnosed cancer in females [1]. Triple-negative breast cancer (TNBC) accounts for approximately 15–20% of all breast carcinomas and is immunohistochemically characterized by the absence of three receptors: estrogen receptor (ER), progesterone receptor (PR) and human growth factor receptor (HER2) [2]. The prognosis for TNBC is worse than that for luminal subtypes. Recurrences and cases of death are observed within 3–5 years after a diagnosis [3, 4]. Chemotherapy has become the main approach for the treatment of TNBC because, as studies in clinical practice have shown, TNBC is more responsive to chemotherapy than any of the other molecular subtypes [5, 6]. Neoadjuvant chemotherapy (NAC) allows for the reduction of the tumor volume and regional lymph nodes, which can facilitate more options for surgical treatment. Complete patho-

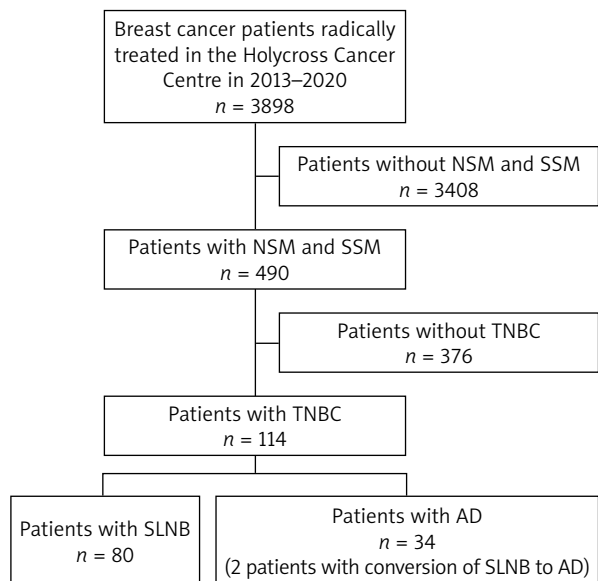
logic regression allows one to conduct breast-conserving treatment (BCS). However, TNBC commonly harbors BRCA mutations, so mastectomy is the preferred surgical treatment for patients with mutations [7]. In the last two decades, both nipple-sparing mastectomy (NSM) and skin-sparing mastectomy (SSM) with immediate reconstruction with a prosthesis or an expander have been used in the surgical management of nonmetastatic breast cancer patients. According to the literature, outcomes of treatment with NSM, SSM, and modified radical mastectomy (MRM) are similar, but, significantly, subcutaneous mastectomies preserve the patient's body shape and can increase the quality of life [8, 9]. The introduction of sentinel lymph node biopsy (SLNB) into the surgical treatment has replaced the routinely utilized axillary dissection and made it possible to avoid the complications of axillary lymphadenectomy. NSM or SSM can be connected with sentinel lymph node biopsy in patients with clinically negative lymph

Corresponding author:

Piotr Kędzierawski, PhD, Radiotherapy Clinic, The Holycross Cancer Centre, Artwińskiego 3, 25-734 Kielce, Poland, e-mail: [piotrkedzierawski@wp.pl](mailto:piotrkedzierawski@wp.pl)

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**Fig. 1.** Flowchart for breast cancer data collection and verification process

nodes. The aim of our retrospective study was to analyze the outcomes of combined treatment of patients with TNBC treated with subcutaneous mastectomy.

### Material and methods

Detailed information on data verification is presented in Figure 1.

A total of 114 women with TNBC were enrolled in this study. All diagnostic, therapeutic, and follow-up procedures were conducted in one center, the Holycross Cancer Centre in Kielce, Poland, in the years 2013–2020. The mean age of women was 45.7 years (ranging from 27 to 75), the most common type of cancer was non-specific type, and in all patients, subcutaneous mastectomy was performed. The sentinel lymph node biopsy procedure was applied in 82 patients, in 61 cases after the neoadjuvant chemotherapy (NAC), and in 21 patients before the adjuvant chemotherapy (AC).

The mean number of sentinel lymph nodes was 3.13 (ranging from 1 to 9). The most common regimen of chemotherapy was 4 cycles of doxorubicin and cyclophosphamide followed by 12 cycles of paclitaxel – applied in 91 (80%) patients. Adjuvant chemotherapy was received by 23 patients, and in 30 patients it was applied as an adjuvant with capecitabine after neoadjuvant chemotherapy due to the lack of complete regression of cancer. Radiotherapy was applied in 43 out of 114 patients. In 38% of patients, a genetic mutation was established. We did not ask for the approval of the Ethics Committee due to the retrospective nature of the analysis. Upon admission to hospital, the written consent of the patients to be included in the study was obtained. Detailed patient characteristics and the types of treatment are depicted in Table 1.

**Table 1.** Basic characteristics of 114 triple-negative breast cancer patients

Characteristic	n (%)
<b>Age [years]</b>	
Mean (SD)	45.7 (10.1)
Median (Q1–Q3)	44 (39–53)
Range	27.0–75.0
<b>Cancer side</b>	
Left	62 (54.4)
Right	52 (45.6)
<b>Cancer type</b>	
NST	112 (98.2)
Carcinoma medullare	1 (0.9)
Carcinoma metaplasticum	1 (0.9)
<b>Clinical stage (CS)</b>	
I	13 (11.4)
II	87 (76.3)
III	14 (12.3)
<b>Grading (G)</b>	
G1	3 (2.6)
G2	39 (34.2)
G3	72 (63.2)
<b>Gene mutation</b>	
No mutation	72 (63.2)
BRCA1	39 (34.2)
BRCA2	2 (1.8)
CHEK2	1 (0.9)
<b>Neoadjuvant chemotherapy</b>	
No	23 (20.2)
Yes	91 (79.8)
<b>Adjuvant chemotherapy</b>	
No	61 (53.5)
Yes	53 (46.5)
<b>Type of surgery</b>	
NSM	112 (98.3)
SSM	2 (1.8)
<b>Lymph-node dissection</b>	
SLNB	80 (70.2)
Lymphadenectomy	32 (28.1)
SLNB and lymphadenectomy	2 (1.8)
<b>Radiotherapy</b>	
No	71 (62.3)
Yes	43 (37.7)
<b>Complete pathological regression</b>	
No	62 (54.4)
Yes	52 (45.6)
<b>Cancer progression</b>	
No	98 (86)
Yes	16 (14)
<b>Death</b>	
No	102 (89.5)
Yes	12 (10.5)
<b>Follow-up [months]</b>	
Mean (SD)	38.6 (22.9)
Median (Q1–Q3)	33.5 (20–57)
Range	4–109

Data are presented as number (percentage), unless stated otherwise. SD – standard deviations, Q1–Q3 – interquartile range, NST – no special type, NSM – nipple-sparing mastectomy, SSM – skin-sparing mastectomy, SLNB – sentinel lymph node biopsy

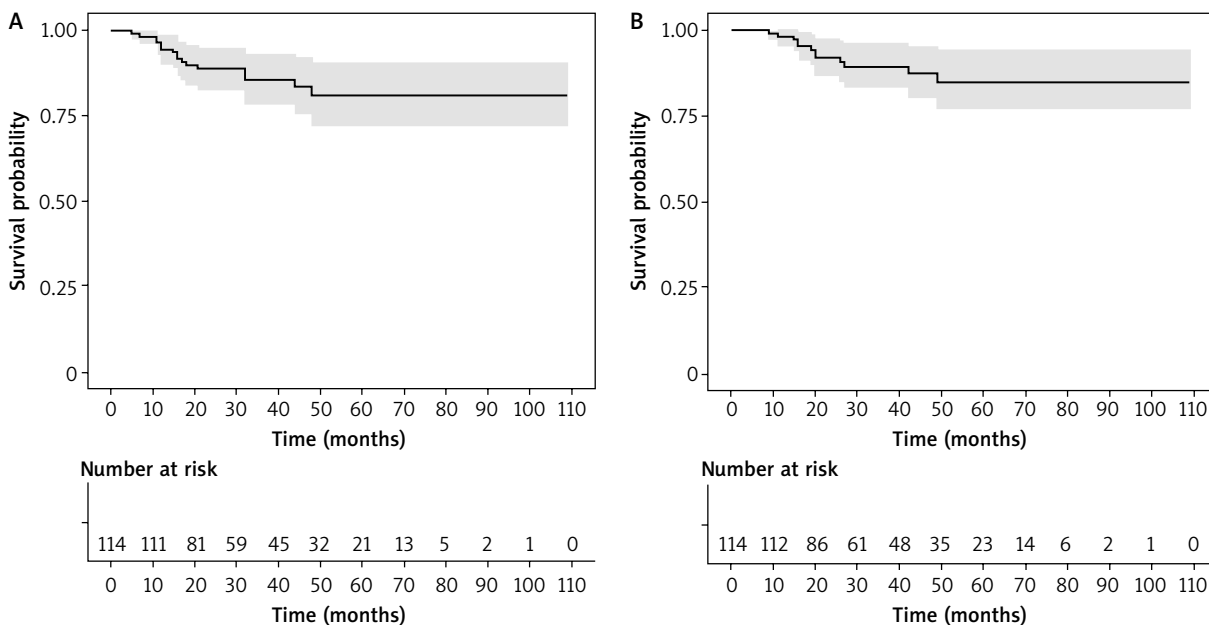


Fig. 2. Disease-free survival (A) and overall survival (B) in the study group

**Statistical analysis**

Basic statistics are presented as the mean ± standard deviation, median (Q1–Q3), the range or number and proportion, depending on the type of variables studied. Disease-free survival and overall survival were estimated by the Kaplan-Meier method. Survival time in months was calculated from the date of the treatment initiation to the date of the last follow-up, cancer relapse and/or death from any cause. The results of the analysis are presented as 1-, 3-, and 5-year survival probabilities with a 95% confidence interval (95% CI). The relationships between selected clinicopathological features and life status were tested with the  $\chi^2$  test. The influence of selected prognostic factors on the risk of death was analyzed using the Cox proportional hazards models. Univariate and multivariate analyses were interpreted using regression coefficients and hazard ratios with their respective 95% CIs. *P* values < 0.05 were considered statistically significant. All statistical analyses were performed using R (version 3.6.3).

**Results**

In the study group of patients (*n* = 114), the probability of disease-free survival at 1, 3, and 5 years was 0.945 (0.903, 0.989), 0.854 (0.784, 0.930), and 0.808 (0.721, 0.906), respectively. The probability of overall survival at 1, 3, and 5 years was 0.982 (0.958, 1.000), 0.894 (0.832, 0.959), and 0.850 (0.770, 0.939), respectively (Fig. 2). The median survival time based on the longest survival time observed in the data was 8.1 years. There were 12 deaths and 16 cancer relapses in the analyzed group. The most common cause

of death was dissemination of the disease to the liver, bones, and the brain. In all of the deceased, dissemination occurred within 3 years after the diagnosis. In 2 patients, locoregional recurrence occurred in the skin and regional lymph nodes. Four patients are alive with cancer dissemination to the bones and lymph nodes of the mediastinum after the salvage systemic treatment. A significant relationship with life status was observed for clinical stage, use of sentinel lymph node biopsy, use of radiotherapy, and complete pathological regression after neoadjuvant chemotherapy (Table 2). In stages I and II, death occurred in 7% of patients, and in stage III in 36%. In the group with SLNB, death was reported in 6%, and after axillary lymphadenectomy in 20% of patients. Death in the group of patients treated with adjuvant radiotherapy was reported in 25%, and in 1.4% without this form of treatment. Pathological complete regression (pCR) of the cancer after NAC was observed in 52 patients. In this group, death occurred in 4% of patients. In the group without complete cancer regression, death was reported in 16% of patients.

Clinicopathological features were included in the univariate Cox proportional hazard models, the significance of which was *p* ≤ 0.2 in the previous analysis (Table 2). Negative values of regression coefficients indicated relatively better, positive, and relatively worse prognoses in the case of the studied category of the analyzed feature compared to the reference category. Based on univariate models, a significant association with the risk of death was observed for the clinical stage, the type of surgery, the presence of SLNB, and radiotherapy (Table 3). All features presented in Table 3 were qualified for further multivariate analyses. Based on the multivariate Cox model, a significant relationship

**Table 2.** Relationships between vital status and selected clinicopathological characteristics

Characteristic	Alive			Death			P
	n	Row %	Column %	n	Row %	Column %	
Age [years]							0.206
< 55	77	87.5	75.5	11	12.5	91.7	
≥ 55	25	96.2	24.5	1	3.8	8.3	
Cancer type							0.625
NST	100	89.3	98.0	12	10.7	100.0	
Other	2	100.0	2.0	0	0.0	0.0	
Clinical stage (CS)							0.001
I and II	93	93.0	91.2	7	7.0	58.3	
III	9	64.3	8.8	5	35.7	41.7	
Grading (G)							0.547
G1	3	100.0	2.9	0	0.0	0.0	
G2 and G3	99	89.2	97.1	12	10.8	100.0	
Gene mutation							0.126
No	62	86.1	60.8	10	13.9	83.3	
Yes	40	95.2	39.2	2	4.8	16.7	
Neoadjuvant chemotherapy							0.660
No	20	87.0	19.6	3	13.0	25.0	
Yes	82	90.1	80.4	9	9.9	75.0	
Adjuvant chemotherapy							0.139
No	57	93.4	55.9	4	6.6	33.3	
Yes	45	84.9	44.1	8	15.1	66.7	
Type of surgery							0.066
NSM	101	90.2	99.0	11	9.8	91.7	
SSM	1	50.0	1.0	1	50.0	8.3	
Sentinel lymph node biopsy							0.022
No	27	79.4	26.5	7	20.6	58.3	
Yes	75	93.8	73.5	5	6.3	41.7	
Radiotherapy							< 0.001
No	70	98.6	68.6	1	1.4	8.3	
Yes	32	74.4	31.4	11	25.6	91.7	
Complete pathological regression							0.033
No	52	83.9	51.0	10	16.1	83.3	
Yes	50	96.2	49.0	2	3.8	16.7	

NST – no special type, NSM – nipple-sparing mastectomy, SSM – skin-sparing mastectomy

**Table 3.** Univariate Cox proportional hazard model based on selected clinico-pathological characteristics of patients with triple-negative breast cancer

Characteristics	Coef.	Exp. (Coef.)	SE (Coef.)	Lower	Upper	z	P
Age [years]	-0.04	0.96	0.03	0.90	1.02	-1.37	0.170
Clinical stage (CS), CS III vs. CS I and CS II	1.71	5.52	0.59	1.75	17.42	2.91	0.004
Gene mutation, yes vs. no	-1.23	0.29	0.78	0.06	1.33	-1.59	0.112
Adjuvant chemotherapy, yes vs. no	0.79	2.21	0.61	0.66	7.33	1.29	0.196
Type of surgery, SSM vs. NSM	2.35	10.43	1.07	1.27	85.54	2.18	0.029
Sentinel lymph node biopsy, yes vs. no	-1.23	0.29	0.59	0.09	0.92	-2.10	0.036
Radiotherapy, no vs. yes	-2.99	0.05	1.04	0.01	0.39	-2.86	0.004
Complete pathological regression, yes vs. no	-1.28	0.28	0.78	0.06	1.27	-1.65	0.099

Coef. – coefficient, Exp. – exponent, SE – standard error, z – Wald statistic value, Lower/Upper – lower and upper bound of 95% confidence interval, NST – no special type, NSM – nipple-sparing mastectomy, SSM – skin-sparing mastectomy

**Table 4.** The eight-factor Cox proportional hazard model for the triple-negative breast cancer patients

Characteristics	Coef.	Exp. (Coef.)	SE (Coef.)	Lower	Upper	z	P
Age [years]	-0.06	0.94	0.04	0.87	1.01	-1.59	0.112
Clinical stage (CS), CS III vs. CS I and CS II	0.39	1.47	0.69	0.38	5.65	0.56	0.574
Gene mutation, yes vs. no	-2.11	0.12	0.99	0.02	0.84	-2.14	0.032
Type of surgery, SSM vs. NSM	3.19	24.27	1.35	1.71	344.92	2.36	0.019
Sentinel lymph node biopsy, yes vs. no	-0.03	0.97	0.69	0.25	3.74	-0.05	0.962
Adjuvant chemotherapy, yes vs. no	-2.10	0.12	1.20	0.01	1.28	-1.76	0.079
Radiotherapy, no vs. yes	-3.14	0.04	1.34	0.00	0.60	-2.34	0.019
Complete pathological regression, yes vs. no	-3.02	0.05	1.35	0.00	0.68	-2.25	0.025

Coef. – coefficient, Exp. – exponent, SE – standard error, z – Wald statistic value, Lower/Upper – lower and upper bound of 95% confidence interval, NST – no special type, NSM – nipple-sparing mastectomy, SSM – skin-sparing mastectomy

**Table 5.** Final Cox proportional hazard model for the triple-negative breast cancer patients

Characteristic	Coef.	Exp. (Coef.)	SE (Coef.)	Lower	Upper	z	P
Age [years]	-0.05	0.95	0.03	0.89	1.02	-1.45	0.146
Gene mutation, yes vs. no	-1.90	0.15	0.95	0.02	0.96	-2.00	0.046
Adjuvant chemotherapy, yes vs. no	-2.09	0.12	1.06	0.02	0.98	-1.98	0.048
Radiotherapy, no vs. yes	-3.41	0.03	1.20	0.00	0.34	-2.86	0.004
Complete pathological regression, yes vs. no	-2.48	0.08	1.17	0.01	0.83	-2.12	0.034

Coef. – coefficient, Exp. – exponent, SE – standard error, z – Wald statistic value, Lower/Upper – lower and upper bound of 95% confidence interval

with the risk of death was observed for gene mutations, the type of surgery, radiotherapy, and the presence of complete pathological regression (Table 4). The presence of a genetic mutation, complete cancer regression in the pathological examination, and the absence of indications for radiotherapy significantly reduced the risk of death, and skin-sparing mastectomy compared to nipple-sparing mastectomy increased the risk of death. Clinicopathological features (except for types of surgery) were included in further multivariate analyses, the significance of which was  $p \leq 0.2$ . The reason for the exclusion of types of surgery from the further analysis was an uneven distribution of the frequency of the examined features, which affected the reliability of the results, visible in the example of a highly wide and non-diagnostic 95% CI.

Based on the 5-factor (final) Cox model, all included features (except for age) had a significant impact on the risk of death (Table 5). In conclusion, the presence of a genetic mutation, adjuvant chemotherapy, complete pathological regression, and the absence of indications for postoperative radiotherapy were associated with better prognosis. In the analyzed model, age as a key factor taken into account in all time-to-event analyses did not show a significant relationship with the risk of death.

## Discussion

Triple-negative breast cancer is a highly aggressive form of malignancy. TNBC is associated with both a higher and an earlier risk for relapse. Hazard rates

for distant recurrence are the highest for TNBC within the first 3 years following the diagnosis, relapses after 5 years are uncommon, and death is associated with dissemination, as was confirmed in our analysis. The results of treatment in our group are positive. Many women, particularly those with a low stage of cancer, achieved a complete response after chemotherapy, avoided aggressive surgical treatment, and did not need radiotherapy in addition to surgery.

## Systemic treatment

In the analyzed time in our hospital, only chemotherapy was used in relation to the systemic therapy. No monoclonal antibodies or poly-ADP ribose polymerase (PARP) inhibitors which are presently accessible were used [10]. Invariably, an anthracycline- and taxane-based regimen remains the standard of care for TNBC patients. In our group, we used preoperative systemic treatment in 80% of women, but 20% of patients, in whom the cancer was detected in stages IA and IIA (with the tumor less than 3 cm), received chemotherapy after surgical treatment, and the decision of the multidisciplinary team was the surgery upfront. Neoadjuvant chemotherapy allows for the reduction of the volume of the primary tumor and the regional nodes, which can facilitate more options for surgical treatment. Nowadays, preoperative systemic treatment is most commonly applied, even in patients with early-stage disease. However, according to the NSABP B-27 trial, where preoperative or postoperative doxorubicin and cyclophos-

phamide with docetaxel were compared, there was no significant difference in disease-free survival (DFS) or overall survival (OS) [11]. In our study TNBC patients had a worse survival with NAC than with AC. This fact may be related to the low stage of cancer at diagnosis. These findings contrast with those of NSABP B-18, EORTC 10902, and the IBBGS, three large randomized trials evaluating NAC vs. AC. Those trials did not find a difference in survival between breast cancer patients receiving NAC and patients receiving AC. However, there was no selection according to the clinical subtype of breast cancer in those studies. Other prior studies had shown conflicting results in outcomes specifically for TNBC patients treated with NAC vs. AC [12–14]. Knowing that triple-negative breast cancer is significantly sensitive to chemotherapy, we can expect complete pathological regression in many patients. Although pCR patients have better outcomes than non-pCR patients, a number of those with pCR still have disease recurrence and breast cancer-related deaths. Lastly, this study confirms the previously described increasing trend in the use of NAC in TNBC patients [15]. In our group 83% of patients reached pCR and only 4% of them died, in comparison to 16% in whom pCR was not achieved. Since the year 2018, we have been using capecitabine due to the lack of complete regression of the cancer (30 women in our group). Five patients died. In all of them, the cancer was detected in clinical stage III.

### **Surgical treatment**

The choice of surgery remains one of the most difficult issues in the treatment of TNBC [16]. The general trend in breast cancer, including TNBC, is the desire not only for oncological radicalism but also to ensure a good cosmetic result, which is possible with organ-preserving or reconstructive plastic surgery. It should be noted that the choice of method of surgical intervention depends on the decisions of the surgeon and the patient. Study results indicate that women with TNBC who undergo breast-conserving therapy do not have a worse prognosis than those who undergo mastectomy [17, 18]. According to Rippey, 27% of patients refused to undergo organ-preserving surgery in favor of mastectomy, but the patients' choice depends on their understanding of this aspect of treatment [19]. Subcutaneous mastectomy is currently increasingly used as a method of surgical treatment of patients with breast cancer. Psychological aspects are also important in determining eligibility for this method of treatment, and many patients choose this form of therapy also because of the fear of radiotherapy, which is an inseparable part of conserving treatment. However, in patients with triple-negative breast cancer, in whom BRCA mutations are more common than in other biological types of breast cancer, mastectomy

is the recommended method, and patients are rarely treated with breast preservation. The patients from the analyzed group were treated in the years 2013–2020. During that period we observed in our institution an upward trend for subcutaneous mastectomies. The decision to perform a mastectomy was made by the doctor and the patient. During this period the number of subcutaneous mastectomies with immediate reconstruction increased from 2% to 25% of all surgical procedures for women with breast cancer. The proportion of breast-conserving treatment at that time was about 50–60%. We also observed more sentinel lymph node biopsies than axillary lymph node dissections. At present, SLNB is a standard for patients with clinically negative lymph nodes, regardless of the biological subtype of the breast cancer. In the analyzed group, skin-sparing mastectomy was used in only 2 women. The decision to perform a mastectomy with removal of the nipple-areola complex was dictated by the higher stage of the disease and the proximity of the tumor to the skin of the areola and nipple; the distance was several millimeters, and therefore the decision was made to remove the nipple-areola complex for radical treatment. In the univariate analysis, SSM was a prognostic factor but it was not confirmed in the multivariate analysis. The use of axillary lymph node dissection was associated with a worse prognosis. The reason for this was the stage of the cancer and the necessity of more aggressive local treatment. The cancer in all women who died was detected in stages II and III with clinically positive lymph nodes. In 7 of them, axillary lymph node dissection was performed. There has also been a general trend in recent years for the rejection of extensive lymph node dissections in favor of sentinel lymph node biopsy. The condition of the axillary lymph nodes is one of the most important prognostic factors. Currently, the sentinel lymph node biopsy, in many cases, has replaced axillary lymphadenectomy and is also performed in patients after systemic treatment. In the group of 61 patients, a sentinel node biopsy was performed after systemic treatment. Only in one patient, in 1 sentinel lymph node, was cancer metastasis detected. A complete pathological response after neoadjuvant chemotherapy is a positive prognostic factor and, additionally, axillary lymphadenectomy can be avoided. In our study, the majority of patients underwent sentinel node biopsy, with a significant reduction in the toxicity of this surgical treatment. In 52 out of 91 women treated with neoadjuvant chemotherapy, complete pathological regression was achieved, which allowed most patients to undergo the SLNB procedure. Several clinical trials have found that complete axillary lymph node dissection had no significant effect on the overall survival, but reduced the risk of locoregional recurrence [20–22]. Axillary recurrences are very rare, which appears to be the rationale for not commonly using axillary dissection [23, 24].

### BRCA status

Triple-negative breast cancer widely harbors *BRCA* gene mutations, more commonly than in other biological types of breast cancer. For patients with a diagnosed *BRCA* mutation, primary chemotherapy followed by surgery seems to be the most optimal therapy option. Research has shown that the mutation is a factor contributing to the complete pathological regression of cancer [7, 25]. In patients with triple-negative breast cancer and *BRCA* mutation, mastectomy is the recommended method, and patients are rarely treated with breast preservation [7]. In a systematic review, it was found that breast-conserving surgery was associated with a greater rate of ipsilateral breast cancer recurrence in *BRCA* mutation carriers. However, it was not associated with adverse short- and long-term survival outcomes. Breast-conserving surgery should be offered as an option to *BRCA* mutation carriers with proper preoperative counseling [26]. In the analyzed group, 20 patients achieved pCR and only 2 out of 43 patients with mutation died.

### Radiation therapy

Radiotherapy is a valuable treatment method for breast cancer patients. It is particularly important after breast-conserving treatment, but when used in patients after mastectomy, it has a positive effect on local control and overall survival. Indications for radiotherapy occur in patients after mastectomy mainly due to metastases to regional lymph nodes, and the positive role of radiotherapy in TNBC patients has been proved [27–29]. In our group, radiotherapy was used in patients with a high primary stage of cancer. For patients with early-stage disease, there were no indications for irradiation. Forty-three patients were irradiated because of metastases to regional lymph nodes – 10 after adjuvant chemotherapy, and 33 women after mastectomy. Out of 12 patients in our group who died, 11 were post-operatively irradiated, but only in 1 case did we note loco-regional (skin of the thorax) recurrence. What is interesting, in patients in whom mastectomy was the first stage of the treatment, radiotherapy of regional lymph nodes replaced axillary dissection in 9 cases. Patients in whom 1 or 2 sentinel nodes were positive are alive after radiotherapy of regional lymph nodes.

### Conclusions

The results of treatment with subcutaneous mastectomy with immediate reconstruction are positive. The early stage of the cancer is associated with a better prognosis. The effective systemic therapy can be used before as well as after the surgery. Complete pathological regression after systemic treatment, particularly in patients with *BRCA1* mutation, is a good prognostic

factor and can help diminish the range of surgery in the axilla region. In particular, the sentinel node biopsy can be used in most patients even after neoadjuvant chemotherapy. In early cases, regional lymph node irradiation can replace axillary lymph node dissection. However, it is necessary to remember that in women with an early stage of breast cancer, usually we should propose breast-conserving therapy. Nevertheless, very often, despite the early stage of the cancer, women, for various reasons, wish to undergo subcutaneous mastectomy with reconstruction.

### Disclosures

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4. Conflicts of interest: None.

### References

1. Torre LA, Bray F, Siegel RL, et al. Global cancer statistics, 2012. *CA Cancer J Clin* 2015; 65: 87-108.
2. Pourteimoor V, Mohammadi-Yeganeh S, Paryan M. Breast cancer classification and prognostication through diverse systems along with recent emerging findings in this respect; the dawn of new perspectives in the clinical applications. *Tumor Biol* 2016; 37: 14479-14499.
3. Dent R, Trudeau M, Pritchard KI, et al. Triple-negative breast cancer: clinical features and patterns of recurrence. *Clin Cancer Res* 2007; 13: 4429-4434.
4. Sharma P. Biology and management of patients with triple-negative breast cancer. *Oncologist* 2016; 21: 1050-1062.
5. Khosravi-Shahi P, Cabezon-Gutiérrez L, Aparicio Salcedo MI. State of art of advanced triple negative breast cancer. *Breast J* 2019; 25: 967-970.
6. Chaudhary LN, Hope Wilkinson K, Kong A. Triple-negative breast cancer: who should receive neoadjuvant chemotherapy? *Surg Oncol Clin* 2018; 27: 141-153.
7. Tutt A, Tovey H, Cheang MCU, et al. Carboplatin in *BRCA1/2*-mutated and triple-negative breast cancer *BRCAness* subgroups: the TNT Trial. *Nat Med* 2018; 24: 628-637.
8. Tokin C, Weiss A, Wang-Rodriguez J, et al. Oncologic safety of skin-sparing and nipple-sparing mastectomy: a discussion and review of the literature. *Int J Surg Oncol* 2012; 92182. doi: 10.1155/2012/921821.
9. Lanitis S, Tekkis PP, Sgourakis G, et al. Comparison of skin-sparing mastectomy versus non-skin-sparing mastectomy for breast cancer: a meta-analysis of observational studies. *Ann Surg* 2010; 251: 632-639.
10. Gradishar WJ, Moran MS, Abraham J, et al. Breast cancer, version 3.2024, NCCN clinical practice guidelines in oncology. *J Natl Compr Canc Netw* 2024; 22: 331-357.
11. Rastogi P, Anderson SJ, Bear HD, et al. Preoperative chemotherapy: updates of National Surgical Adjuvant Breast and Bowel Project Protocols B-18 and B-27. *J Clin Oncol* 2008; 26: 778-785.
12. Kennedy CR, Gao F, Margenthaler JA. Neoadjuvant versus adjuvant chemotherapy for triple negative breast cancer. *J Surg Res* 2010; 163: 52-57.
13. van der Hage JA, van de Velde CJ, Julien JP, et al. Preoperative chemotherapy in primary operable breast cancer: results from the European Organization for Research and Treatment of Cancer trial 10902. *J Clin Oncol* 2001; 19: 4224-4237.
14. Mauriac L, MacGrogan G, Avril A, et al. Neoadjuvant chemotherapy for operable breast carcinoma larger than 3 cm: a unicentre randomized trial with a 124-month median follow-up. *Ann Oncol* 1999; 10: 47-52.
15. Murphy BL, Day CN, Hoskin TL, et al. Neoadjuvant chemotherapy use in breast cancer is greatest in excellent responders: triple-negative and *HER2+* subtypes. *Ann Surg Oncol* 2018; 25: 2241-2248.

16. Wang J, Xie X, Wang X, et al. Locoregional and distant recurrences after breast conserving therapy in patients with triple-negative breast cancer: a meta-analysis. *Surg Oncol* 2013; 22: 247-255.
17. Fancellu A, Houssami N, Sanna V, et al. Outcomes after breast-conserving surgery or mastectomy in patients with triple-negative breast cancer: meta-analysis. *Br J Surg* 2021; 108: 760-768.
18. Chen QX, Wang XX, Lin PY, et al. The different outcomes between breast-conserving surgery and mastectomy in triple-negative breast cancer: a population-based study from the SEER 18 Database. *Oncotarget* 2016; 8: 4773-4780.
19. Rippy E, Ainsworth R, Sathananthan D, et al. Influences on decision for mastectomy in patients eligible for breast conserving surgery. *Breast* 2014; 23: 273-278.
20. Bromham N, Schmidt-Hansen M, Astin M, et al. Axillary treatment for operable primary breast cancer. *Cochrane Database Syst Rev* 2017; 4: CD004561. doi: 10.1002/14651858.CD004561.pub3.
21. Lyman GH, Temin S, Edge SB, et al. American Society of Clinical Oncology Clinical Practice Sentinel lymph node biopsy for patients with early-stage breast cancer: American Society of Clinical Oncology clinical practice guideline update. *J Clin Oncol* 2014; 32: 1365-1383.
22. Yagata H, Kajiura Y, Yamauchi H. Current strategy for triple-negative breast cancer: appropriate combination of surgery, radiation, and chemotherapy. *Breast Cancer* 2011; 18: 165-173.
23. Kahler-Ribeiro-Fontana S, Pagan E, Magnoni F, et al. Long-term standard sentinel node biopsy after neoadjuvant treatment in breast cancer: a single institution ten-year follow-up. *Eur J Surg Oncol* 2021; 47: 804-812.
24. Barrio AV, Montagna G, Mamtani A, et al. Nodal recurrence in patients with node-positive breast cancer treated with sentinel node biopsy alone after neoadjuvant chemotherapy – a rare event. *JAMA Oncol* 2021; 7: 1851-1855.
25. Clifton K, Gutierrez-Barrera A, Ma J, et al. Adjuvant versus neoadjuvant chemotherapy in triple-negative breast cancer patients with BRCA mutations. *Breast Cancer Res Treat* 2018; 170: 101-109.
26. Co M, Liu T, Leung J, et al. Breast conserving surgery for BRCA mutation carriers – a systematic review. *Clin Breast Cancer* 2020; 20: e244-e250. doi: 10.1016/j.clbc.2019.07.014.
27. Yao Y, Chu Y, Xu B, et al. Radiotherapy after surgery has significant survival benefits for patients with triple-negative breast cancer. *Cancer Med* 2019; 8: 554-563.
28. Azoury F, Misra S, Barry A, et al. Role of radiation therapy in triple negative breast cancer: current state and future directions – a narrative review. *Precis Cancer Med* 2022; 5: 9.
29. He MY, Rancoule C, Rehailla-Blanchard A, et al. Radiotherapy in triple-negative breast cancer: current situation and upcoming strategies. *Crit Rev Oncol Hematol* 2018; 131: 96-101.