



## Surgery After Neoadjuvant Treatment in Young Women with Breast Cancer

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### Abstract

**Objective:** Selection of the type of surgery after neoadjuvant treatment in young patients diagnosed with breast cancer.

**Methodology:** A retrospective evaluation of the personal oncology records of 108 patients diagnosed with breast cancer up to the age of 40 and treated with neoadjuvant therapy at the Oncology Service in Albania from 2010 to 2020 was performed.

**Results:** From 108 female patients up to the age of 40, from 25 cities of Albania treated with neoadjuvant therapy for breast cancer in our Service, most were with locally advanced breast cancer, multifocal and inflammatory breast cancer. Only 4.6% of patients were in the early clinical stage and underwent neoadjuvant therapy to perform conservative breast surgery. Statistical analysis with Kendall's correlation coefficient found some significant links. A significant correlation was found between the type of intervention and the pathological stage ( $p < 0.001$ ); between the type of intervention and PCR ( $p = 0.016$ ); between the type of intervention and relapse ( $p = 0.014$ ).

**Conclusion:** *Conservative surgery followed by radiotherapy is considered safe from the oncological point of view and a good option for mastectomy. Neoadjuvant treatment of breast cancer patients is a "strong weapon" in the hands of surgeons to enable the development of different types of surgery such as conservative, reconstructive, etc. This is so important in patients of that young age.*

**Keywords:** *breast cancer, young ages, neoadjuvant treatment, surgery.*

### **Background:**

About 11% of breast cancer cases occur in women under the age of 45 [1] and 5% of them are under the age of 40 [2]. Every year over 1000 women under the age of 40 die from this disease [2]. Young women suspected of breast cancer should be diagnosed by a multidisciplinary team of specialized physicians and despite the relatively low risk of breast cancer in patients under 40 years of age, any abnormality in breast palpation requires prompt and careful diagnosis through the so-called "Triple test" which includes a physical examination, imaging examination and cyto / histopathological verification [3]. Surgical treatment of breast cancer at younger and older ages is essentially the same. Radical surgery (radical mastectomy, modified radical mastectomy, simple mastectomy, skin preservation mastectomy and areola complex preservation mastectomy) or conservative surgery followed by radiotherapy remain the standard approach to breast cancer treatment in early stages, regardless of age [4].

### **Purpose of the study**

The main purpose of this study is to analyze the surgical treatment of young patients diagnosed with breast cancer who have undergone neoadjuvant treatment.

### **Material and methodology**

This is a retrospective study that utilizes existing data and allows the formation of hypotheses based on the database. The stages of realization of this study took place during 2020.

### **Methods and criteria**

Data for this study were collected from personal medical records of patients in the Oncology Service at the University Hospital Center "Mother Teresa", Albania, from 2010 to 2020. The search of the medical records was done by years in the relevant cabinets in our Service. The selection of the subjects of this study was carried out based on three main criteria:

- Gender: All subjects included in the study are female.
- Age: All patients included in the study are up to 40 years of age.
- Diagnosis and treatment: All patients included in the study underwent systemic neoadjuvant therapy for breast cancer.

### **Data**

Data for this retrospective study were collected from the personal oncology records of female patients up to 40 years of age, diagnosed with breast cancer and treated with neoadjuvant therapy at the Oncology Service at University Medical Center “Mother Teresa” from 2010 to 2020. Age limit of patients reduces the number of subjects included in the study, but being the only public multidisciplinary service and reference center for cancer treatment in Albania we were able to collect data on patients from different cities obtaining a clearer picture of the situation in our country.

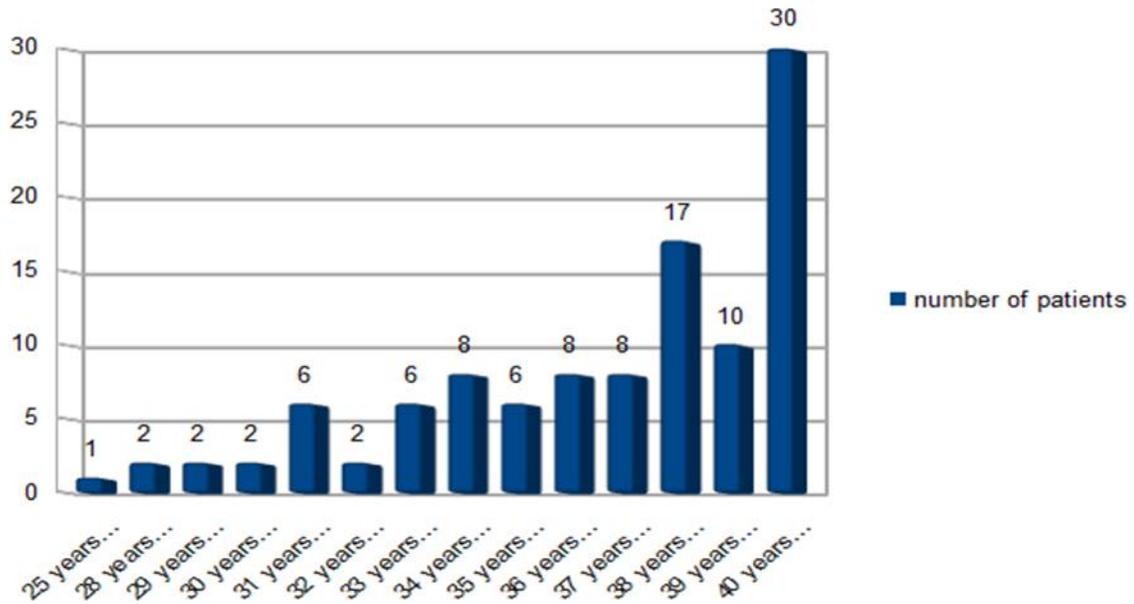
### **Statistical analysis**

The data collected from the oncology files were transferred to the Microsoft-Excel program from where they were then processed in the Statistical Package for Social Sciences, version 25.0. Statistical procedures and techniques applied in the analysis of this data are described in detail below:

- For all categorical variables (nominal including binary/dichotomous and ordinal scale), absolute numbers and corresponding percentages were calculated.
- Random relationships between variables were analyzed through Kendall’s tau correlation technique.
- The presentation of the data was done through simple and composite tables, as well as through graphs of the type bar-diagram, line diagram, etc.
- The values of  $p \leq 0.05$  were considered significant.

### **Results**

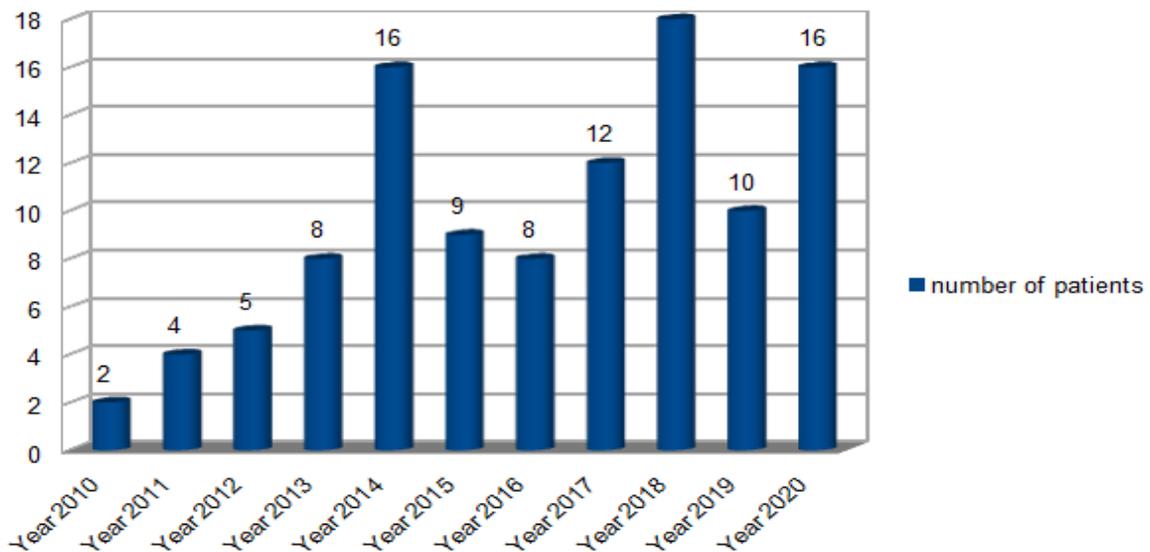
The total number of patients in this study is 108. All patients are female and up to 40 years old. The youngest patient was 25 years old, while the largest number of breast cancer cases was 40 years old. The mean age is 36. The number of patients treated with neoadjuvant therapy by age is shown in figure 1.1.



**Fig. 1.1** Number of patients treated with neoadjuvant therapy by age

Also based on the data, the patients had a mean menarche age of 13.54 years and had performed an average of 2.0 births. Only 5% of patients had a family history of breast and gynecological cancer.

Data were collected from oncology medical records from 2010 to 2020 showing an increase in the number of patients treated with neoadjuvant therapy from year to year and especially the last 5 years. This is a result of improving the multidisciplinary approach to breast cancer treatment in our Service. The number of patients according to the years of study is reflected in the figure. 1.2.



**Fig. 1.2** Number of patients by years of study

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Among the 108 breast cancer patients included in the study, it was found that the majority had left breast involvement, 52% of them. The rest, 47% had affected right breast and only one patient was with both breast cancers at the time of diagnosis. The percentage representation of the diagnosed breast laterality is shown in the figure. 1.3.

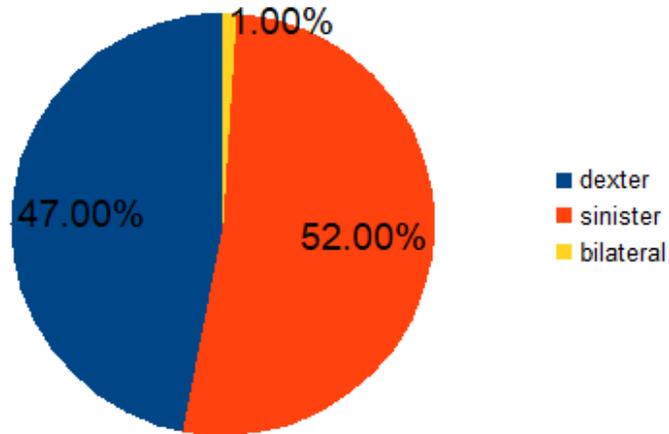


Fig. 1.3 Presentation of diagnosed breast laterality.

Clinical staging of patients was performed through objective examination, inspection and palpation by the surgeon-oncologist and imaging examination, which mostly included ultrasound examination and magnetic resonance imaging of the breast, the latter used especially in recent years, due to the young age of patients in the study. The largest number of patients were with locally advanced breast cancer, multifocal breast cancer and inflammatory cancer because they were candidates for neoadjuvant treatment. Presentation of the number of patients according to the classification of cT, cN and clinical stage at the time of diagnosis are presented in figures 1.4, 1.5 and 1.6, respectively.

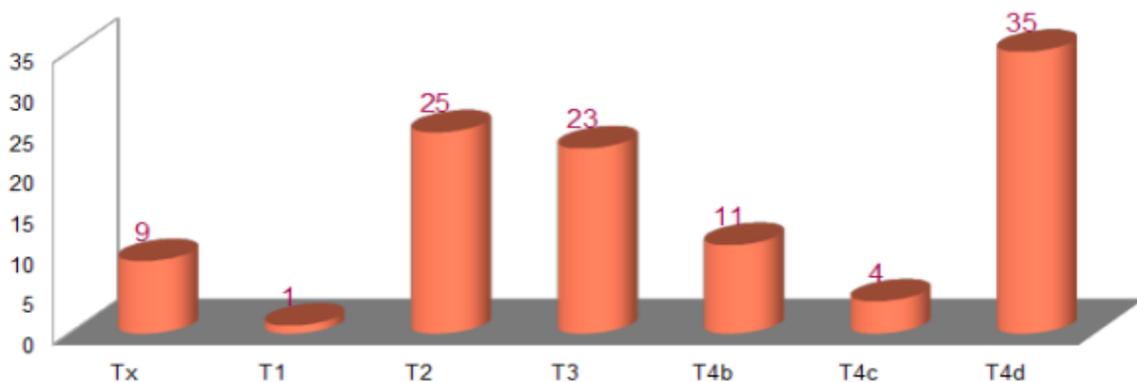
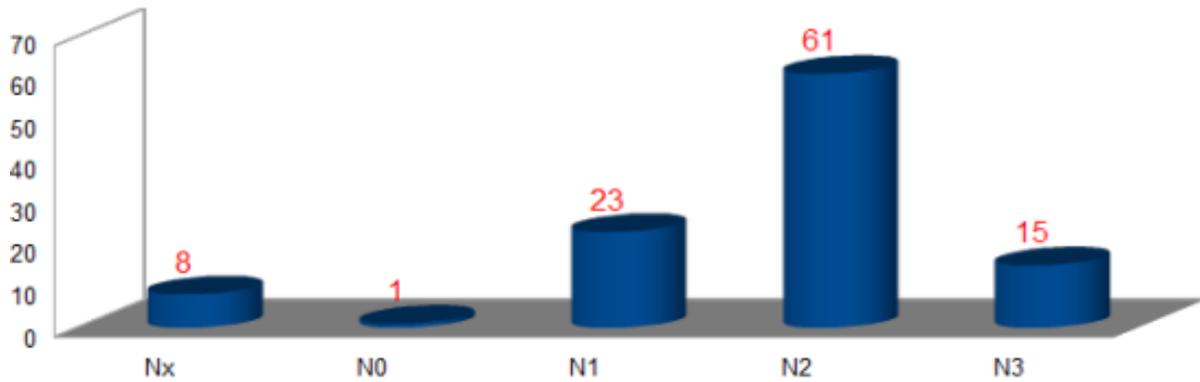
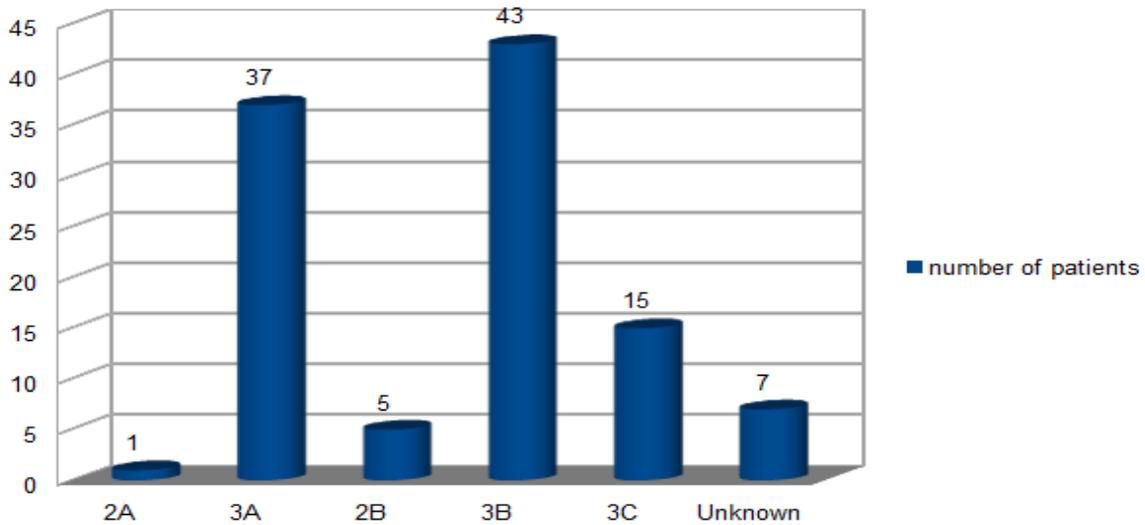


Fig. 1.4 Number of patients according to clinical classification T



**Fig. 1.5** Number of patients according to clinical classification N

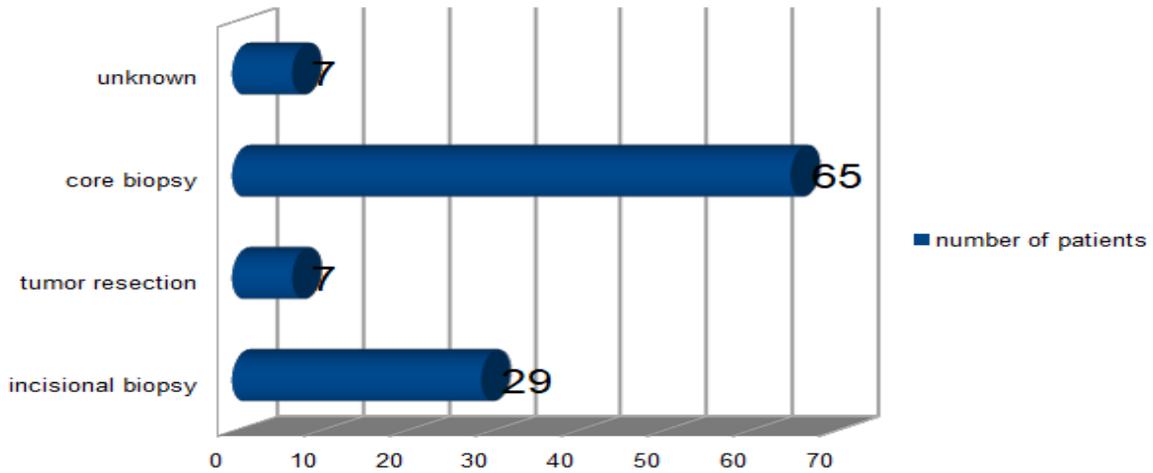


**Fig. 1.6** Number of patients according to the TNM classification

The clinical classification was based on data from the 8th edition of the American Joint Committee on Cancer (AJCC). The largest number of patients were with breast cancer in stage 3B at the time of diagnosis, 43 patients from the total of the subjects in the study. Only for 7 patients, the clinical staging could not be done due to the lack of data in the respective medical records.

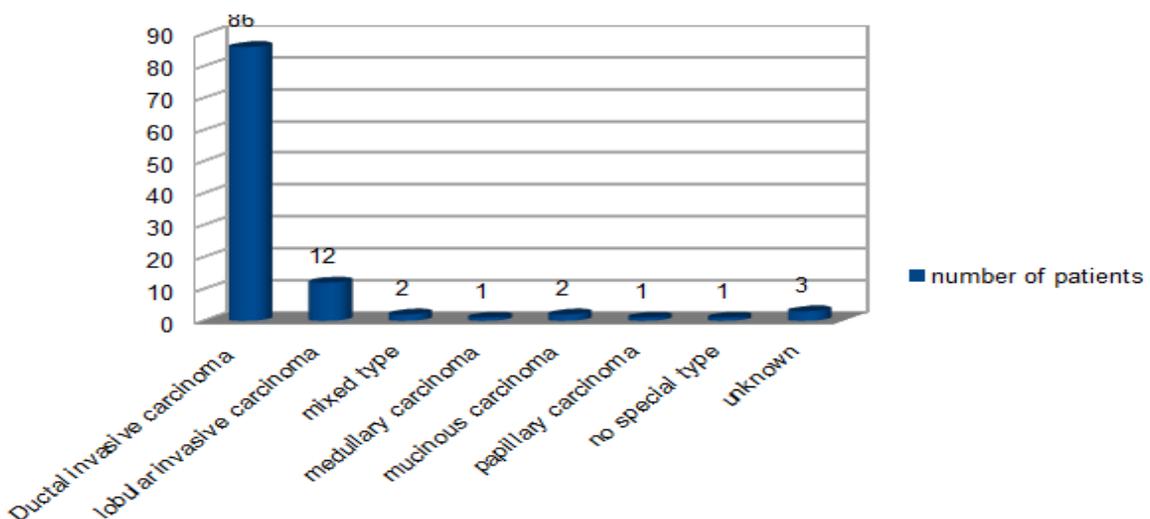
Generally, the medical records document the sampling method used for histopathological verification of the tumor. In our study, we found the use of three different methods: incisional biopsy, core biopsy and tumor resection. The latter was used in only 7 patients, while incisional biopsy in 29 patients. The most used method, especially in recent years was core biopsy which was performed on 65 patients. Lymph nodes are considered pathological through imaging on ultrasound with relevant specifics such as partial or diffuse hypoechogenicity, deformation or disappearance of the hilus, and lymph node cortex thickness

over 3mm. The sampling method for histopathological verification according to the number of patients is shown in the figure. 1.7.



**Fig. 1.7** Establishing histopathological diagnosis according to the number of patients.

The most common histological type was infiltrative ductal carcinoma, in 86 patients, followed by infiltrative lobular carcinoma, mixed carcinoma and some specific types of ductal carcinoma such as medullary, mucinous, papillary. Only in one case, the pathological report confirmed the infiltrative carcinoma of the non-specific type, while for three patients the pathological report could not be found on the medical records before the start of neoadjuvant therapy. Histopathological diagnosis according to the number of patients is illustrated in figure 1.8.



**Fig. 1.8** Histopathological diagnosis before NACT according to the number of patients.

Despite the clinical response to systemic neoadjuvant therapy and the young age of patients in most cases Madden type mastectomy with axillary dissection was performed. Biopsy of the sentinel lymph node was performed in only two patients, one of whom underwent a mastectomy and the other lumpectomy. Information on the type of intervention was obtained from 96 oncology medical records and of the 4 patients were inoperable. Only one patient despite the good clinical response to neoadjuvant therapy refuses to undergo breast surgery. The type of surgical treatment according to the number of patients is reflected in figure 1.9.

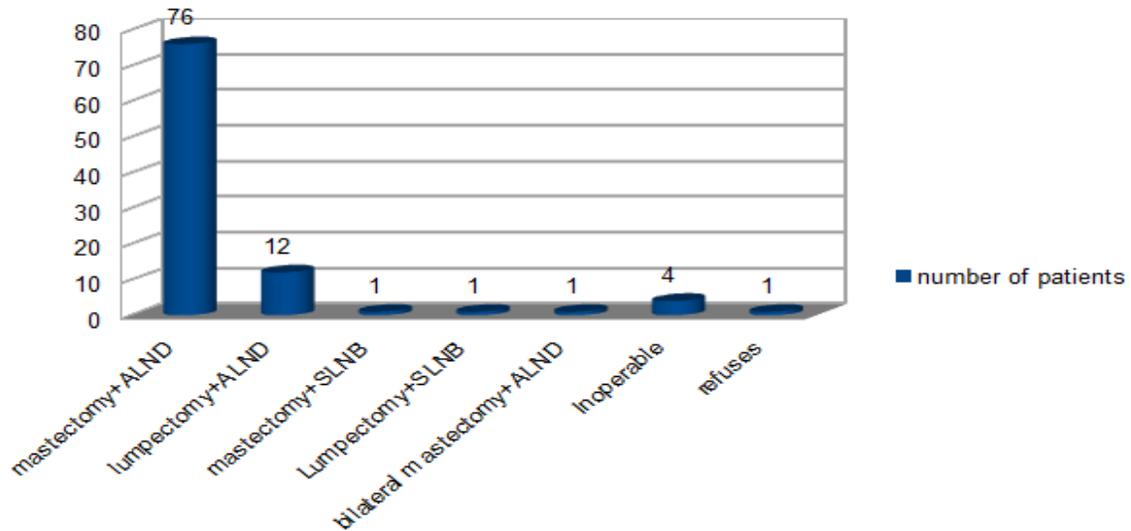


Fig. 1.9 Type of surgical treatment

The final pathological report was obtained in full in 78 patients, while for one patient in the medical record it was possible to obtain information on the pathological stage but not the histological type of breast cancer. In most cases, the final histological diagnosis coincided with the preoperative histological diagnosis. Graphic presentation of the final histological diagnosis as well as ypT and ypN, according to the number of patients who were intervened, are presented respectively in figure 1.10, 1.11 and 1.12.

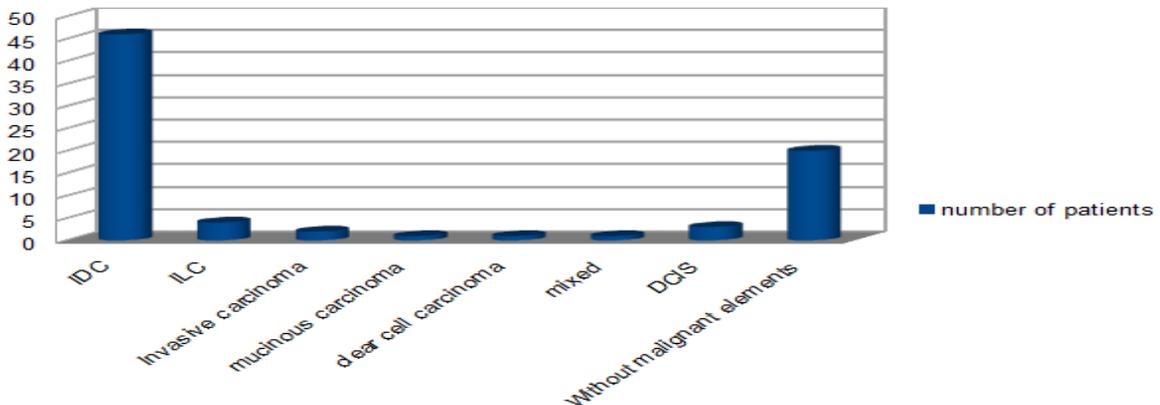
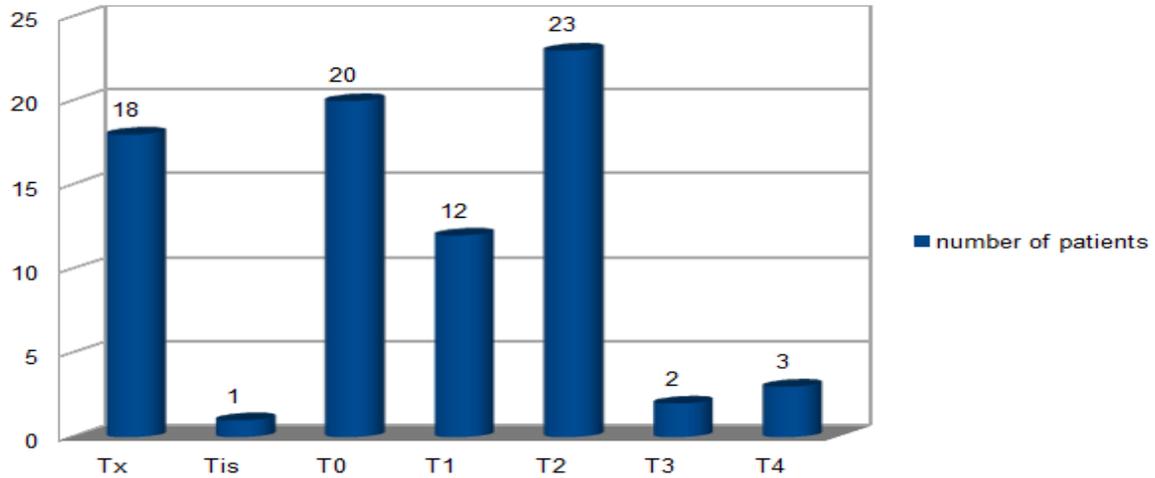
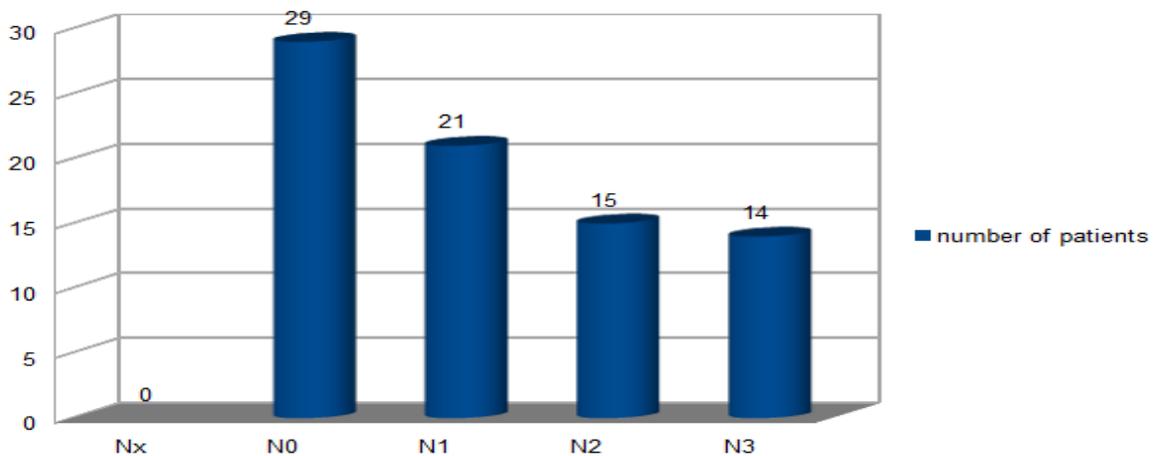


Fig. 1.10 Final histological diagnosis.



**Fig. 1.11** Graphic presentation of ypT according to the number of patients.



**Fig. 1.12** Graphic representation of ypN according to the number of patients.

Among the 79 patients whose oncology records provided information on the pathological staging of ypTNM, 17 of them, 22%, resulted in complete pathological responses after neoadjuvant treatment.

From the statistical analysis no significant relationship was found between vascular invasion and pathological stage ( $r = 0.167$ ,  $p = 0.079$ ). No statistically significant relationship was found between vascular invasion and PCR ( $r = -0.129$ ,  $p = 0.132$ ). Also no significant relationship was found between vascular invasion and disease relapse ( $r = 0.009$ ,  $p = 0.928$ ).

In the statistical analysis of the variables, a significant relationship was found between the type of intervention and pathological stage ( $p < 0.001$ ), between the type of intervention and PCR ( $p = 0.016$ ) and

between the type of intervention and disease relapse ( $p = 0.014$ ), showing that more complete and partial pathological responses translate into conservative breast surgery after neoadjuvant treatment, as well as noting that conservative breast surgery, accompanied by radiotherapy after neoadjuvant systemic therapy is from an oncological point of view safe and a good alternative to mastectomy.

PATHOLOGICAL STAGE	Type of surgery			Total
	No surgery	mastectomy	lumpectomy	
No disease	0	11	6	17
	0.00%	16.20%	50.00%	20.00%
Stage 1	0	23	5	28
	0.00%	33.80%	41.70%	32.90%
Stage 2	0	10	0	10
	0.00%	14.70%	0.00%	11.80%
Stage 3	0	22	1	23
	0.00%	32.40%	8.30%	27.10%
Stage 4	5	2	0	7
	100.00%	2.90%	0.00%	8.20%
Total	5	68	12	85
	100.00%	100.00%	100.00%	100.00%

Table 1

PCR	Type of surgery			Total
	No surgery	mastectomy	lumpectomy	
no PCR	5	66	7	78
	100.00%	85.70%	53.80%	82.10%
PCR	0	11	6	17
	0.00%	14.30%	46.20%	17.90%
Total	5	77	13	95
	100.00%	100.00%	100.00%	100.00%

Table 2

Relapse	Type of surgery			Total
	No surgery	mastectomy	lumpectomy	
yes	5 100.00%	19 24.70%	2 15.40%	26 27.40%
no	0 0.00%	58 75.30%	11 84.60%	69 72.60%
Total	5 100.00%	77 100.00%	13 100.00%	95 100.00%

**Table 3**

**Discussion**

In our study, conservative breast surgery was performed in 14% of patients. However, the statistical analysis found a statistically significant relationship between the type of intervention and the pathological stage ( $p < 0.001$ ), between the type of intervention and PCR ( $p = 0.016$ ) and between the type of intervention and disease relapse ( $p = 0.014$ ), showing that more complete and partial pathological responses translate into conservative breast surgery after neoadjuvant treatment, as well as noting that conservative breast surgery, accompanied by RT after neoadjuvant systemic therapy is oncologically safe and a good alternative to mastectomy.

In our study, the sampling methods for histopathological verification were tumororectomy, incisional biopsy and core biopsy, respectively in 7%, 29% and 64% of patients. Core biopsy was used especially during the second 5 years. In no case, including patients undergoing neoadjuvant therapy for conservative breast surgery, was a clip placed to identify the tumor bed in case of a complete pathological response.

According to a retrospective study [5] involving 410 non-metastatic breast cancer patients treated with neoadjuvant therapy from 1990 to 2005, published in 2007 in the Journal of the American Cancer Society Journals in multivariate analysis concluded that the lack of clip in the tumor bed of patients who underwent conservative surgery after NACT was associated with a higher risk of local recurrence, compared to patients in whom the clip was placed ( $p = 0.02$ ).

In our study histopathological verification after neoadjuvant treatment, in all patients was done only for breast tumor mass, but in no case was histological confirmation of axillary lymph node with FNA performed. Meanwhile, today one of the most developed debates in the field of oncology is: "When is the golden time for performing a biopsy of the sentinel lymph node, before or after neoadjuvant therapy?"

A multi-institutional retrospective study [6] published in The American Journal of Surgery assessed the importance of timing sentinel lymph node biopsy before or after neoadjuvant treatment. Statistical analysis revealed a significant correlation between nodal clinical status and SLNB time. The latter performed before NACT, was successful in patients with clinically negative lymph nodes in 100%, compared to 80.6% when performed after neoadjuvant treatment. This study recommended performing sentinel lymph node biopsy before neoadjuvant treatment for patients with clinically negative lymph nodes and raised concerns about the use of post-neoadjuvant SLNB for clinically positive lymph node patients in presentation due to a high degree of negativity (11%).

### **Conclusion**

Neoadjuvant treatment of breast cancer patients is a "strong weapon" in the hands of surgeons to enable the development of different types of surgery such as conservative, reconstructive, etc. This is so important in patients of that young age.

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