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Research Article

# Triple negative breast cancer: Early stages management and evolution, a two years experience at the department of breast cancer of CHSF

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## Abstract

Breast cancer is the most common cancer in women and is a major public health problem. It is divided into several subtypes, including triple negatives. The general objective of our study is to establish the profile and the management of patients with triple negative breast cancer over a period of 2 years, operated in our department.

During our study period, triple-negative breast cancers accounted for 10% of our population. The most affected age group ranges from 50 to 60. The majority of patients in our sample are pauciparous. In the group of patients who received hormone therapy, it was mainly HRT for 4 to 6 years. 96.77% of patients consulted a health worker within 3 months of the discovery of the signs. Adenopathies are frequently present at the time of diagnosis. 93.54% of the cases have an invasive ductal carcinoma. Triple negative cancers are essentially poorly differentiated. Triple-negative cancer has a high rate of cell renewal. In our study, neoadjuvant chemotherapy is mostly indicated for triple-negative breast cancers ≥ 30 mm at diagnosis and a delayed lumpectomy is then performed in 23.52% of the patients. For tumors of < 30 mm size, a lumpectomy is performed immediately in 76.47% of the patients, followed by adjuvant chemotherapy.

Mastectomy was performed in 45.16% of patients; it was mainly indicated in front of a large tumor size associated with a small breast volume, then multifocal breast tumors. Breast reconstruction was performed in 21.42%. Radiation therapy is indicated in the majority of patients, postoperatively. In our population, 11 patients were proposed to have an oncogenetic survey; it was mainly indicated based on the Manchester criteria in front of a young age and a family history of cancer. There are two BRCA 1 mutations, one BRCA 2 mutation, and one case of absence of mutation. The therapeutic intake in case of a mutation is directed towards a prophylactic bilateral mastectomy and adnexectomy, proposed at the age of 40. Two patients had presented triple negative recurrences of their already treated breast cancer; first case PDL1 positive PD-L1 ≥ 1% treated with immunotherapy combined with chemotherapy (atezolizumab/abraxane) while the second and second PDL1 negative treated with chemotherapy alone.

Despite their low frequency, triple negative breast cancers represent a subgroup marked by pejorative characteristics, a reserved prognosis, with limited treatment options.

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## Introduction

Breast cancer is a malignant tumor that develops with no preservation of the different anatomical and functional structures of the breast. There are different types of breast cancer depending on their initial cells of origin from which they develop. The most common breast cancers (95%) are adenocarcinomas, that develop from the epithelial cells (= carcinoma) of the mammary gland (= adeno). There are also other rare types of breast cancer. Adenocarcinomas most often arise from the cells of the ducts and more rarely from the cells of the lobules of the mammary gland. A distinction is made between cancers in situ and invasive cancers. [1-5].

With approximately 54,000 new cases and 12,000 deaths per year estimated in 2015, breast cancer ranks second among cancers and third among cancer deaths worldwide. However, it is the most common cancer among women in France and represents a major public health problem. The incidence of breast cancer has increased significantly in the last decades [2].

The main risk factors are age, genetic predisposition, a personal history of breast disease and a personal history of high dose chest radiation. Other risk factors are suspected, such as the endogenous hormonal exposures (puberty age, number of children, age at first pregnancy, breastfeeding, overweight/obesity) and the exogenous ones (hormone replacement therapy).

Breast cancer can be discovered at an early stage through the mammography screening. In several countries, there is an organized screening program offered to all women aged between 50 and 74. The incidence of this cancer is, therefore, influenced by the evolution of screening practices [2]. However, there are several subtypes of breast cancer [6,7]. Recent diagnostic advances have made it possible to distinguish the most frequent, hormone-dependent breast cancers, which express estrogen and/or progesterone receptors on their membranes, and are associated with a good response to hormone therapy, and "HER +" cancers "characterized by an overproduction of the HER2 protein. For the latter group, there are today very effective targeted therapies [7]. But 15% of patients have the so-called "triple negative" breast cancer, that is without any known marker on the surface of cancer cells. They have the following characteristics in common [4,6,9].

- Affect younger women.
- Have a higher risk of metastasis
- Poorer prognosis than the other subtypes:
    - Possible resistance to conventional chemotherapy protocols
    - Frequent recurrences within 2 years of the end of treatment.
- Are frequent in the hereditary forms that are associated with mutations in the Breast Cancer oncogenes (BRCA).
- Progress quickly, it is often a cancer of interval (discovered between two tests of control).
- Occur in women not yet concerned by the screening.
- Are more often detected at large sizes. The neoadjuvant chemotherapy is therefore more often used. Triple negative breast cancers are a priority in research, because up to date, there is no effective targeted therapy to treat women suffering from this form of cancer.

We thus initiated this work based on the following hypotheses:

- Triple negative breast cancer has a low frequency and mainly concerns the young population.
- It would be associated with a group of population at risk
- Its prognostic criteria would be severe
- The therapeutic means would be limited to chemotherapy, surgery, and radiotherapy.
- Mutations of oncogenes are frequent.

The general objective of our study is to establish the profile and the management of patients with triple negative breast cancer over a period of 2 years, operated in the gynecology-obstetrics department of the Center Hospitalier Sud francilien, France.

Our specific objectives are as follow:

- To bring out the socio-demographic characteristics of the patients.
- To identify the clinical and paraclinical aspects of triple negative breast cancer
- To describe their histo-prognostic specificities
- To present the treatment modalities

## Method

Our study was done over the period from January 1, 2017 to December 31, 2018, spanning a 2-year period.

Type of study: This is a descriptive retrospective study.

### The population

This study involved a total of thirty-one patients with triple negative breast cancer followed and operated at the gynecology department of the Centre Hospitalier Sud Francilien during the determined period over the study period.

### Inclusion criteria

- Patients with triple negative breast cancer operated during the determined period.
- Patients whose record was completed including the various studied parameters.
- Patients in the non-metastatic stage.

**Non-inclusion criteria**

- Patients with another type of breast cancer.
- Patients with incomplete records.
- Patients with metastatic cancer.

**Sampling technique**

We conducted a comprehensive census of all patient records operated on for triple-negative C.H.S.F. breast cancer over our study period.

### Data collection

**Collection technique:** Our data collection was based on the records of the genecology department, the oncology department, and the pathology department.

**Data collection tool:** To collect our data, we established a fact sheet that was tested corrected and validated.

### Data collection source

- The data were collected from:
- Admission records
- Patient consultation and follow-up sheets
- Operative reports
- Reports of pathology
- Reports of the multidisciplinary Meetings

**Collection team:** The fact sheet was filled out on our own

### Definition and operational aspects of variables

We defined and studied the following variables:

- Frequency
- Demography

Sex, age at diagnosis, Body Mass Index (BMI), age of menarche, menopause, parity, age at the first child birth, breastfeeding and its total duration, hormonal treatments, personal and family history of cancer.

- Clinical issues

o Time between the discovery of the abnormality and the consultation,

o Initial tumor size,

o Tumor site,

o Adenopathy.

- Paraclinical elements

Imaging, ACR grade, histological type, histoprognostic grade, ki67 cell renewal rate

- Therapy

Chemotherapy and tumor size, lumpectomy by tumor size, sentinel lymph node and adenopathies, indications of axillary Lymph node dissection and mastectomy, breast reconstruction, radiotherapy, oncogenetics investigation.

The evaluation of estrogen and progesterone receptors was carried out by an immunohistochemistry technique, with a threshold of positivity established above 10%. Thus, estrogen and/or progesterone receptors are considered negative when their levels are less than 10%.

The expression of HER 2 protein was detected by two complementary methods: immunohistochemistry (IHC), fluorescent in situ hybridization (FISH). A tumor is considered HER 2 negative when immunohistochemistry returns with a scale of 0 or 1+; however, for a result of 2+, the tumor is considered HER 2 negative if FISH is negative.

The sentinel node technique was also performed by two additional methods: colorimetric detection by patent blue injection, and isotopic by injection of a radioactive isotope (Technetium 99), followed by a lymphoscintigraphy, and then intraoperative detection via a probe of the gamma rays that are emitted by the sentinel node.

Oncogenetic surveys were conducted by an onco-geneticist, and positive results were confirmed on a second blood sample.

The data was scanned in THE EXCELL software and then interpreted in THE EPI-INFO 7 software. They were represented in as frequency tables, percentages ($n/\sum n \times 100$ with $\sum$ = the sum of the numbers), and figures.

However, the data were collected and analysed in strict compliance with ethical considerations.

## Results

### Frequency

The following table shows the frequency of triple-negative cancers in the studied population.

Triple negative breast cancers account for 10% of our population (Table 1).

## Demography

**Sex:** The entire population studied was female. Note that three cases of male breast Cancer were managed at our department during the considered period: two in 2017 and one case in 2018. None of them were triple negative.

## Age at diagnosis

Table 2 shows patients by age at the time of diagnosis of breast cancer.

The most affected age group ranges from 50 to 60, with an average age of 56.68 years, and extremes from 28 to 80 years. However, 29.01% of patients with triple negative cancer less than 50.

## Body Mass Index

The following table shows the distribution of patients according to their body mass index (BMI).

The body mass index was calculated by the weight formula (kg) divided by the square of size (meter) and interpreted as follows:

- <18: Under nutrition
- [18-25]: normal weight
- [25-30]: overweight
- ≥ 30: obesity (Table 3)

Out of 31 patients, 19 have a normal BMI, the equivalent of 61.29% of our sample.

**Table 1:** Frequency of triple negative cancers.

| Frequency | *n* | % |
|---|---|---|
| Triple negative Cancer | 31 | 10 |
| other types of cancer | 310 | 90 |
| Total | 341 | 100 |

**Table 2:** Age at Diagnosis.

| Age (years) | *n* | % |
|---|---|---|
| **< 30** | 1 | 3.22 |
| [30-40] | 5 | 16,12 |
| [40-50] | 3 | 9,67 |
| [50-60] | 8 | 25,8 |
| [60-70] | 7 | 22,58 |
| [70-80] | 7 | 22,58 |
| Total | 31 | 100 |

**Table 3:** Distribution of BMI.

| BMI | *n* | % |
|---|---|---|
| < 18 : denutrition | 1 | 3,22 |
| [18-25]: normal weight | 19 | 61,29 |
| [25-30]: overweight | 5 | 16,12 |
| >= 30: obesity | 6 | 19,35 |
| TOTAL | 31 | 100 |

## Age of menarche

Table 4 shows the repartition of patients with triple-negative breast cancer based on the age of their menarche.

58.06% of patients had their menarche between the age of 10 and 13.

## Menopause

The following table presents patients according to their menopausal status.

70.96% of patients are in the postmenopausal period at diagnosis (Table 5).

## Parity

The following table shows the parity of the studied patients. A nulliparous patient is considered to have no parity, while the patients that are primiparous, pauciparous, and multiparous have respectively one, two to three, and more than three parities.

48.38% of patients with triple negative breast cancer are pauciparous (Table 6).

## Age at the birth of first child

The following table shows the distribution of patients by the age of first motherhood.

42.85% of patients had their first delivery between the age of 25 and 30, then 35.71% of them between the age of 20 and 25 (Table 7).

**Table 4:** Breakdown according to the age of menarche.

| Age (years) | *n* | % |
|---|---|---|
| < 10 | 1 | 3,22 |
| [10-13] | 18 | 58,06 |
| [13-16] | 12 | 38,70 |
| [16-19] | 0 | 0 |
| Total | 31 | 100 |

**Table 5:** Repartition by the menopausal status.

| Menopause | *n* | % |
|---|---|---|
| Yes | 22 | 70,96 |
| No | 9 | 29,03 |
| Total | 31 | 100 |

**Table 6:** Distribution based on parity.

| Parity | *n* | % |
|---|---|---|
| Nulliparous | 3 | 9,67 |
| Primiparous | 5 | 16,12 |
| Pauciparous | 15 | 48,38 |
| Multiparous | 8 | 25,80 |
| Total | 31 | 100 |

**Table 7:** Age-based repartition of the birth of first child.

| Age (years) | *n* | % |
|---|---|---|
| [15-20] | 4 | 14,28 |
| [20-25]e | 10 | 35,71 |
| [25-30] | 12 | 42,85 |
| [30-35] | 2 | 7,14 |
| [35-40] | 0 | 0 |
| > 40 | 0 | 0 |
| Total | 28 | 100 |

## Breastfeeding and its total duration

Tables 8 and 9 show the proportion of breastfeeding patients, as well as its duration in months respectively.

20 out of 31 patients were breast-feeding, the equivalent of 64.51%.

30% of the patients breastfed over a period between 9 and 12 months, followed by 25% beyond 24 months.

## Hormonal treatments

The following table shows the repartition of patients based on the use of hormonal treatments (contraceptives, Hormone Replacement Therapy HRT) and the total duration of treatment, in years.

64.51% of patients with triple negative breast cancer did not receive hormone therapy. In the group of patients who received hormonal treatments, it consists mainly of HRT (19.35 %) for 4 to 6 years. Hormonal contraceptives accounts for 16.12% over a period of 2 to 4 years (Table 10).

## Tobacco and alcohol consumption

61.12% of patients do not consume alcohol and tobacco. In the group of patients who use it, it is mainly tobacco at 22.58% (Table 11).

**Table 8:** Repartition by breastfeeding.

| Maternal breastfeeding | *n* | % |
|---|---|---|
| No | 11 | 35,48 |
| Yes | 20 | 64,51 |
| Total | 31 | 100 |

**Table 9:** Breakdown by total duration of breastfeeding.

| Total duration (months) | *n* | % |
|---|---|---|
| [0-3] | 3 | 15 |
| [3-6] | 0 | 0 |
| [6-9] | 1 | 5 |
| [9-12] | 6 | 30 |
| [12-15] | 0 | 0 |
| [15-18] | 3 | 15 |
| [18-21] | 2 | 10 |
| [21-24] | 0 | 0 |
| > = 24 | 5 | 25 |
| Total | 20 | 100 |

**Table 10:** Distribution following the use of hormonal treatments.

| Total duration (years) | Contraceptives | HRT | No treatment |
|---|---|---|---|
| [0-2] | 0 | 0 | 20 |
| [2-4] | 3 | 0 | |
| [4-6] | 1 | 4 | |
| [6- 8] | 0 | 0 | |
| [8-10] | 0 | 2 | |
| > 10 | 1 | 0 | |
| Total | 5 | 6 | 20 |
| % | 16,12 | 19,35 | 64,51 |

**Table 11:** Repartition by Tobacco and Alcohol Use.

| Consomption | Tobacco | Alcohol | No | total |
|---|---|---|---|---|
| *n* | 7 | 5 | 19 | 31 |
| % | 22,58 | 16,12 | 61,12 | 100 |
| Total | 12 | | 19 | 31 |

## Personal history of malignant tumors

The following table 12 divides patients according to the personal history of malignant tumor.

2 out of 31 patients have a personal history of malignant tumors, or 6.45%. It is a controlling breast cancer, and ENT cancer.

## A history of benign breast lesions

Table 13 shows the history of benign breast injury in our patients.

16.12% of patients with triple-negative breast cancer initially developed benign breast lesions. It is essentially the fibroadenomas.

## Family history of 1st and 2nd degree cancer

Table 14 shows the types of cancer in the patient's family: first and second degree.

67.74% of patients with triple-negative cancer have a family history of cancer at the level of first- and second-degree relatives. Mainly, it is breast cancer, colorectal cancer, gastric cancer, endometrial cancer.

## Time between discovery and consultation

We present in the table 15 the time elapsed between the

**Table 12:** Repartition by Personal History of Malignant Tumors.

| Malignant Tumor | Yes Type of tumor | No | Total |
|---|---|---|---|
| | Infiltrating Ductal Carcinoma of controlateral breast = 1 | 29 | 31 |
| | Epidermoïd Carcinoma: epiglottis + esophagus = 1 | | |
| % | 6,45 | 93,54 | 100 |

**Table 13:** Repartition based on history of benign breast injury.

| Atypical Breast Lesion | Yes | No | total |
|---|---|---|---|
| | Breast cyst =1 | 26 | 31 |
| | Intraductal papilloma+ non atypical epithelial hyperplasia of ipsilateral breast =1 | | |
| | Mastosis of controlateral breast = 1 | | |
| | ipsilateral fibroadenoma = 2 | | |
| % | 16,12 | 83,87 | 100 |

**Table 14:** Distribution based on family history of cancer.

| Past family history of cancer | Yes | No | Total |
|---|---|---|---|
| Breast | 7 | 10 | 31 |
| Stomach | 2 | | |
| Kidneys | 1 | | |
| Pancreas | 1 | | |
| Endometrium | 2 | | |
| Thyroïd | 1 | | |
| Ovary | 1 | | |
| Lung | 1 | | |
| Prostate | 1 | | |
| Thyroïd | 1 | | |
| Colorectal | 3 | | |
| % | 67,74 | 32,25 | 100 |

discovery of a breast abnormality and the consultation of the patient (Table 15).

## Initial tumor size

The following table shows the size of the tumor at the time of diagnosis.

At the time of diagnosis, the majority of patients have a tumor larger than 30 mm. The majority of sizes range from 30 to 40 mm (29.03%) and from 50 to 60 mm (22.58%) (Table 16).

## Tumor site

In table 17, we present the seat of tumors according to the different quadrants of the breast.

The upper-outer quadrant of the breast is the most affected by the tumor (38.70%) followed by the union of external quadrants (22.58%) (Table 17).

## Adenopathies

We present in the following table the association of adenopathies with triple negative cancers at diagnosis, as well as the conclusion of pathology.

Adenopathies are frequently associated with triple negative cancer (58.06%) at the time of diagnosis; with a lymph node invasion ($n$ = 14) (Table 18).

**Table 15:** Repartition by the delay that passed until the consultation.

| Total duration (Months) | *n* | % |
|---|---|---|
| 0-3 | 30 | 96,77 |
| 3-6 | 1 | 3,22 |
| 6-9 | 0 | 0 |
| 9-12 | 0 | 0 |
| > 12 | 0 | 0 |
| Total | 31 | 100 |

**Table 16:** Initial tumor size.

| Tumor size (mm) | *n* | % |
|---|---|---|
| < 10 | 1 | 3,22 |
| [10 – 20] | 7 | 22,58 |
| [20 - 30] | 6 | 19,35 |
| [30 - 40] | 9 | 29,03 |
| [40 - 50] | 0 | 0 |
| [50 - 60] | 7 | 22,58 |
| > 60 | 1 | 3,22 |
| Total | 31 | 100 |

**Table 17:** Repartition by the tumor site.

| Tumor site | *n* | % |
|---|---|---|
| UOQ | 12 | 38,70 |
| UIQ | 2 | 6,45 |
| LOQ | 1 | 3,22 |
| LIQ | 2 | 6,45 |
| Junction of UPPER quadrants | 5 | 16,12 |
| Junction of LOWER quadrants | 1 | 3,22 |
| Junction of OUTER quadrants | 7 | 22,58 |
| Junction of INNER quadrants | 1 | 3,22 |
| Total | 31 | 100 |

**Table 18:** Repartition by presence of adenopathies.

| Satellite nodes | Yes | No | Total |
|---|---|---|---|
| Lymph node invasion | 14 | 13 | 31 |
| Negative fine needle biopsy | 4 | | |
| % | 58,06 | 41,93 | 100 |

## Imaging

**Type of imaging:** Table 19 presents the imaging methods used to explore patients.

All patients in our sample received the following imaging methods: mammography, ultrasound, MRI, PET-Scan.

**ACR Grade:** We detail in the table below the grades of lesions found at mammography, according to the classification of the American College of Radiology.

ACR 5, were mainly found (77.41%), followed by ACR 4 (22.58%) (Table 20).

## Preoperative histology

**Histological type:** The following table shows the type of tumor found on pathological anatomy examination of preoperative sampling.

Patients with triple-negative breast cancer have 93.54% infiltrating ductal carcinoma (Table 21).

**Histo-prognostic grade:** We present the histo-prognostic profile of triple negative breast cancers in the following table 22.

**Table 19:** Imaging methods used.

| Imaging | *n* | % |
|---|---|---|
| Mammography | 31 | 25 |
| Ultrasound | 31 | 25 |
| MRI | 31 | 25 |
| PET-Scan | 31 | 25 |
| Total | 124 | 100 |

**Table 20:** Distribution by ACR grade.

| GRADE ACR | *n* | % |
|---|---|---|
| 1 | 0 | 0 |
| 2 | 0 | 0 |
| 3 | 0 | 0 |
| 4 | 7 | 22,58 |
| 5 | 24 | 77,41 |
| Total | 31 | 100 |

**Table 21:** Breakdown by histological type of cancer

| histologic type | *n* | % |
|---|---|---|
| Infiltrating Ductal Carcinoma | 29 | 93,54 |
| Invasive apocrine carcinoma | 1 | 3,22 |
| Invasive pleiomorphic Lobular carcinoma | 1 | 3,22 |
| Total | 31 | 100 |

**Table 22:** Distribution by histo-prognostic grade.

| Grade | *n* | % |
|---|---|---|
| I | 0 | 0 |
| II | 5 | 16,12 |
| III | 26 | 83,87 |
| Total | 31 | 100 |

Triple negative cancers are mainly poorly differentiated, classified as grade III (83.87%), according to Elston-Ellis.

**Ki67 cell renewal rate:** The following table shows the percentage rate of cell renewal, according to the Ki67 coefficient.

Triple-negative cancer has a high rate of cell renewal, ranging from 80% to 100% (38.70%) 60-80% (34.37%) (Table 23).

## Initial tumor size and chemotherapy

Table 24 shows the type of chemotherapy that was indicated based on the size of the tumor at the time of diagnosis.

Neoadjuvant chemotherapy is mostly indicated for triple-negative breast cancers of size - 30 mm at diagnosis.

## Tumorectomy and tumor size

Table 25 shows the indicated immediate and delayed lumpectomies, depending on the size of the tumor.

The lumpectomy is performed immediately in 76.47%, when the size of the tumor is 30 mm; it is deferred in 23.52% for sizes ≥ 30 mm.

## Sentinel lymph node indications according to adenopathies

Table 26 shows the indications of the sentinel node technique based on the presence of satellite adenopathies.

The sentinel node technique was indicated in 45.16%, in the absence of adenopathies. It was recused in 54.83% in the presence of adenopathies.

Indications of the Axillary lymph node dissection:

The following table 27 lists the indications of axillary lymph node dissection.

**Table 24:** Initial tumor size and chemotherapy.

| Tumor size | Neoadjuvant Chemo | Adjuvant chemo | Total |
|---|---|---|---|
| < 30 mm | 0 | 15 | 15 |
| ≥ 30 mm | 16 | 0 | 16 |
| % | 51,61 | 48,38 | 100 |

**Table 25:** indications of lumpectomies depending on tumor size.

| Tumor size | Immediate tumorectomy | Deferred Tumorectomy | Total |
|---|---|---|---|
| < 30 mm | 13 | 0 | 13 |
| ≥ 30 mm | 0 | 4 | 4 |
| % | 76,47 | 23,52 | 100 |

**Table 26:** Sentinel node indications according to adenopathies.

| Adenopathies | sentinel node | | Total |
|---|---|---|---|
| | Yes | No | |
| Yes | 0 | 17 | 17 |
| No | 14 | 0 | 14 |
| % | 45,16 | 54,83 | 100 |

**Table 27:** Indications of axillary curage.

| Indications | *n* | % |
|---|---|---|
| Positive sentinel node | 1 | 5,55 |
| Positive Fine needle lymph node biopsy | 14 | 77,77 |
| Suspicious adenopathies with negative fine needle biopsy | 3 | 16,66 |
| Total | 18 | 100 |

Axillary lymph node dissection is performed in 18 patients (58.06%); and mainly indicated for invaded adenopathies on fine needle biopsy (77.77%).

## Mastectomy indications

Table 28 shows the different indications of mastectomy in our patients.

Mastectomy is indicated in 14 patients; it is essentially done in the case of large tumor size associated with a small breast volume (35.71%), followed by multifocal breast tumors (28.57%).

## Breast reconstruction

In Table 29, we present the frequency of breast reconstructions and their timing in the patient care.

14 patients had a mastectomy. 21.42% had an immediate breast reconstruction ($n$ = 2), deferred ($n$ = 1).

## Radiotherapy indications

Table 30 shows the different indications of radiotherapy, as well as its timing in relation to the surgical procedure

Radiation therapy is indicated in the majority of patients (96.66%), postoperatively ($n$ = 30).

## Oncogenetic survey indications

Table 31 shows the indications of oncogenetic consultations in patients with triple-negative breast cancer.

**Table 28:** mastectomy indications.

| Indications | *n* | % |
|---|---|---|
| Large tumor size and small breast | 5 | 35,71 |
| Multifocal tumor | 4 | 28,57 |
| Carcinomatous mastitis | 2 | 14,28 |
| BRCA gene Mutation | 1 | 7,14 |
| History of controlateral breast cancer | 1 | 7,14 |
| Post-tumorectomy recurrence | 1 | 7,14 |
| Total | 14 | 100 |

**Table 29:** indications of breast reconstructions.

| Breast Reconstruction | Immediate | Deferred | No |
|---|---|---|---|
| ***n*** | 2 | 1 | 11 |
| Total | 3 | | 11 |
| % | 21,42 | | 78,57 |

**Table 30:** Radiotherapy indications.

| Timing | Preop. | Postop. | Total |
|---|---|---|---|
| Neoadjuvant radiotherapy | 1 | 0 | 1 |
| Adjuvant radiotherapy | 0 | 30 | 30 |
| % | 3,33 | 96,66 | 100 |

11 patients received the proposition for an oncogenetic investigation based on the Manchester criteria (Table 32); Indicated mainly in front of a young age and a family history of cancer.

### Oncogenetic survey results and impact in management

The following table presents the results of the oncogenes mutation research, as well as its contribution in the management of the concerned patients.

The oncogenetic survey was proposed in 11 patients. There are two BRCA 1 mutations (20%), one BRCA 2 mutation (10%), and absence of mutation in 40% (Table 33).

The therapeutic intake is directed towards a prophylactic bilateral mastectomy and adnexectomy in the case of mutation.

**Table 31:** Indications of the oncogenetic survey.

| Indications | *n* | % |
|---|---|---|
| Age < 30 Years | 1 | 10 |
| Ages 30-39 and 1 family history of cancer | 4 | 40 |
| Ages 30-39 and 2 family histories of cancer | 2 | 20 |
| Age ≥ 40 and 1 family history of cancer | 4 | 30 |
| Total | 11 | 100 |

**Table 32:** Manchester Scoring System 3.

| Index cases of Cancers AND 1st - 2nd degree relatives | Number (A) | Points (B) | A x B |
|---|---|---|---|
| Breast Cancer F < 36 years | | 11 | |
| Breast cancer F 36-39 years | | 8 | |
| Breast cancer F 40-49 years | | 6 | |
| Breast cancer F 50-59 years | | 4 | |
| Breast cancer F > 59 years | | 2 | |
| Breast cancer M < 60 years | | 13 | |
| Breast cancer M ≥ 60 years | | 10 | |
| Ovarian Cancer < 60 ans (except mucinous) | | 13 | |
| Ovarian Cancer ≥ 60 ans (except mucinous) | | 10 | |
| pancreatic Cancer | | 1 | |
| prostatic Cancer < 60 years | | 2 | |
| prostatic cancer ≥ 60 years | | 1 | |
| Ovarian cancer pathology (index cases OR relatives) | Yes/No | Points (B) | if yes, report B |
| High grade serous | | 2 | |
| Breast Cancer Pathology (index case only) | Yes/No | Points (B) | if yes, report B |
| Grade 3 | | 2 | |
| Grade 1 | | -2 | |
| RO+ | | -1 | |
| RO- | | 1 | |
| Triple negative | | 4 | |
| Intraductal | | -2 | |
| Family information | Yes/No | Points (B) | if yes, report B |
| Adoption or one of the parents is unknown | | 2 | |
| Total | | | |
| if Ashkenazi origin, double the total | | | |
| Score ≥ 12 | confirmed indication | | |
| Score between 9 and 11 | Consult | patrick.benusiglio@aphp.fr | |
| Score < 9 | | | |

**Table 33:** Results and therapeutic impact of the oncogenetic survey.

| Results | *n* | % | Therapeutic Impact |
|---|---|---|---|
| Mutation BRCA 1 | 2 | 18 | Bilateral prophylactic Mastectomy+annexectomy proposed at 40 years+Q6monthes monitoring |
| Mutation BRCA 2 | 1 | 10 | Bilateral prophylacticMastectomy +adnexectomy proposed at 40 years+ Q6months monitoring. |
| No mutation | 4 | 36 | Continuation of the established therapeutic protocol Refusal 3 30 Continuation of the established therapeutic protocol |
| Refusal | 4 | 36 | |
| Total | 11 | 100 | |

### Immunotherapy

The experience of immunotherapy in oncology in our department started a year ago. The patients are screened for immunotherapy. In our series, two patients had presented triple negative recurrences of their already treated breast cancer; first case PDL1 positive PD-L1 ≥ 1% treated with immunotherapy combined with chemotherapy (atezolizumab/abraxane) while the second and second PDL1 negative treated with chemotherapy alone.

## Discussion

### Frequency

During our study period, triple-negative breast cancers accounted for 10% of our population. This result is similar to those found in Europe: Adamo, et al. in Italy [19], Redondo, et al. in Spain [20], Wojcinski, et al. in Germany [21] which are 9.8%, 9.6% and 10.5% respectively. In the U.S.A., Bauer, et al. [24] reports an average frequency of 13.1% of the population.

However, it is found to be more often in Asian countries. Which, et al. in China [22], Widodo, et al. in Indonesia [23], and Krishan, et al. in India [4] find respectively frequencies estimated at 20.3%, 25%, and 27.9% of their studied population; This consists the double of the results achieved in European countries. These data suggest that triple negative breast cancers are more common in Asia, with a peak of frequency in India.

### Sex

In our study, the entire population studied was female. This result is corroborated by Gueye M in Senegal [25], and James, et al. in New Zealand [7] who found in a population of 1390 patients, a 100% female.

### Age at diagnosis

The most affected age group ranges from 50 to 60, with an average age of 56.68 years, and extremes that are from 28 to 80 years. Similar results are found in the city of Tours and in several countries in Europe and America. Indeed, Redondoet al in Spain [20], Wojcinski, et al. in Germany [21], Stead, et al. in the USA [27] find average ages of 54.7 years, 55.9 years, and 58 years, respectively in their populations. In England, Jack, et

al. report higher values, 61 years [28], while in Asia there are lower values than ours. In China, Chen, et al. has an average age of 35.4 years [29], Hashmi, et al. in Pakistan has 48.4 years [26], and Krishan, et al. in India has 49.8 years [4].

However, it is important to note that 29.01% of patients develop triple-negative cancer before the age of 50. In Italy, Adamo, et al. [19], yields a value similar to ours: 32.9%. Higher values are reported by Redondo, et al. in Spain [20], Vona-Davis, et al. in Virginia (USA) [30], Jack, et al. in England [28] who respectively found 51.2%, 44.5% 39.1% of triple negative breast cancers diagnosed before the age of 50.

## Body Mass Index

Out of a total of 31 patients, 61.29% have a normal BMI, 16.12% are overweight and 19.37% are obese. In Louisiana (U.S.A.), Mowad, et al. [32] report 13% of patients with a normal BMI, 23% of overweighed patients, and 64% of obese patients. Shaheenah, et al. in the U.A.E. [33], found 34.3%, 30% and 35.7% of patients with normal weight, overweight, and obesity, respectively. These differences could be explained by the non-similar lifestyle of the patients.

However, it should be noted that a high BMI in non-menopausal women is associated with a significant increase in the risk of triple negative tumors (OR=1.18, IC 95% (0.86-1.64), $p$ = 0.003), while an increase in BMI appears to be a protective factor for Luminal A and B and HER2 tumors in non-menopausal women. Obesity in non-menopausal women decreases exposure to estrogen due to frequent associated anovulation. This would explain the protective effect of obesity on hormone-dependent tumors in comparison to triple negative tumors [3].

However, despite an increase in the frequency of larger and more advanced TNM Tumors, obesity is not associated with a decrease in survival with non-recurrence. This is confirmed by the study of Ademuyiwa, et al. who followed 418 women treated for breast cancer and found no relationship between obesity and overall survival or survival with non-recurrence [34].

## Age of menarche

58.06% of patients had their menarche between the age of 10 and 13.

Note that increased age of menarches would be associated with a decreased risk of triple negative tumor in comparison to other types of tumors. This is shown by Yang, et al. study that was carried out in Poland and included 804 patients with breast cancer, 95 of them have triple negative tumors and 2502 were control patients (OR: 0.78; IC 95% 0.68-0.89, $p$ = 0.0009 compared to Luminal A tumors for example) [35]. The meta-analysis of Barnard, et al. included 38 studies and 27629 patients with 4981 triple-negative ones, found that an advanced age of menarches reduced significantly the risk of triple negative tumor [36].

## Menopausal status

70.96% of patients are postmenopausal when diagnosed in our population.

Stacoffe M in Tours (France) [37], James, et al. in New Zealand [7], Gueye, et al. in Senegal [25] reported rates of 63.8%, 60%, 59.1%, respectively.

## Parity and age of first motherhood

The majority of patients in our sample are pauciparous (43.38%) with a parity of between 2 and 3. 42.85% of patients had their first delivery between the age of 25 and 30. In Senegal, Gueye et al returned to an average parity of 3.6.

Many studies suggest that high parity is associated with an increased risk of triple-negative tumors unlike Luminal A tumors of which multiparity decreases the risk [36]. Phipps et al conducted a case-control study in 2008 and included 2,616 women (1140 breast cancer patients, 78 with triple negative tumors and 1,476 controls). They found that nulliparity, compared to multiparity, would result in a significant decrease in the risk of triple-negative tumors (HR-0.61, IC 95%-0.37-0.97, $p$ = 0.02), while nulliparity would increase the risk of tumors with estrogen receptors (HR=1.35, IC 95%=1.20-1.52, $p$ = 0.02). In multiparous, an increase in the number of pregnancies would result in increased risk of triple-negative tumors (HR for ≥ 3 births compared to a birth = 1.46, IC 95%=0.82-2.63, $p$ = 0.63), while it would decrease the risk of tumors with estrogen receptors (HR=0.88, IC 95%=0.74-1.04, $p$ = 0.06) [38]. Similarly, Millikan, et al. in their case-control study conducted in the United States in 2008, including 1,424 breast cancer patients and 2022 controls, found a significant increased risk of triple negative tumors with the increased number of children while this association was not observed for hormone-dependent tumors [39].

## Breastfeeding and total duration

20 out of 31 patients were breast-feeding, which consists the equivalent of 64.51%. Among them, 30% of patients breastfed over a period between 9 and 12 months, then 25% above 24 months.

The "Collaborative group on hormonal risk factors in breast cancer" has determined that breastfeeding has a protective effect on all types of breast cancer (reduced cancer risk by 4.3% for any year of breastfeeding) [40]. The mechanisms involved in the effect of lactation on gene expression and breast epithelial cells differentiation are not fully understood. They could include the complete differentiation of breast epithelial cells during breastfeeding and the decrease in the duration of estrogen exposure associated with secondary breastfeeding amenorrhea [39]. Barnard, et al. in 2014, conducted a literature review in order to study the associations between known risk factors for breast cancer (especially the hormonal ones) and different molecular subtypes. In their meta-analysis

of 38 studies of 27629 patients, including 4981 triple-negative patients, an increase in breastfeeding duration was associated with a decrease in the risk of triple negative breast cancer (as well as Luminal A and B cancers while this association was not found for Her2 positive tumors) [36].

## Hormonal treatments

64.51% of patients with triple negative breast cancer did not receive hormone therapy. In the group of patients who received it, it was mainly HRT (19.35%) for 4 to 6 years. Hormonal contraceptives account for 16.12% and were used mainly over a 2 to 4-year period. According to the literature, there is a relationship between the development of triple negative breast cancers and exposure to hormonal treatments.

Indeed, Dolle, et al. reported an increase in the risk of triple negative tumors of 4.7 in women under the age of 40 years and who had used oral contraception for more than one year (OR: 4.2; IC 95% 1.9-9.3, $p < 0.001$). The risk was 6.4 times for the women who had started contraception before the age of 18 in comparison with those who had never used contraception [42]. Similarly, Ma et al finds an increased risk of triple negative tumors associated with oral contraceptive use, but only in women aged 45-64 who started oral contraception before the age of 18 [41].

In addition, the "Collaborative group on hormonal risk factors in breast cancer" confirms that the risk of breast cancer is increased in women using hormone replacement therapy and would be exacerbated with its duration. However, the risk disappears after 5 years of usage. In addition, the study indicates that the relative risk of breast cancer among recent users is higher in thin women than those who are high weight. This analysis studied breast cancers as a whole, without the molecular subtype repartition.

Few studies have studied the association between HRT and triple negative tumor [36].

## Tobacco and alcohol consumption

61.12% of patients do not consume alcohol and tobacco. In the group of patients who use it, it is mainly tobacco at 22.58%.

The literature points to a link between tobacco and/or alcohol use and the occurrence of breast cancer in general. Alcohol consumption is a well-established risk factor. For each additional intake of 10 grams of alcohol per day the risk of breast cancer increases by 7%. For tobacco the risk is significantly increased in women who started smoking at a young age or more than 5 years of duration before their first pregnancy at term [36].

However, for the specific case of triple negative cancers, Geoffrey, et al. in the USA studied this relationship among 146,985 women enrolled in the Women's Health Initiative. It included 300 cases of triple negative cancer and 2,479 cases of hormone-sensitive cancer over 8 years. It appeared that smoking and alcohol consumption are not associated with an increased risk of triple-negative breast cancer, but may be modestly associated with an increased risk of breast cancer expressing hormone receptors [43].

## Personal history of malignant tumor and/or benign breast lesions

2 out of 31 patients have a personal history of malignant tumors, which is the equivalent of 6.45%. It consists of a controlateral breast cancer, and ENT cancer. 16.12% of patients with triple-negative breast cancer initially developed atypical breast lesions. It was essentially adenofibromas.

A patient with this type of lesions on a surgical biopsy has an increased risk of developing breast cancer within at least 15 years of diagnosis. Cancer occurs in 40% of cases in the controlateral breast. In the case of atypical ductal hyperplasia, the relative risk is multiplied by 4-5 or even more in cases of mixed atypical hyperplasia (ductal and lobular, RR of 5-6) and lobular carcinoma in situ diagnosed in a woman with a young age and a family history of breast cancer [44].

## Family history of 1st and 2nd degree cancer

67.74% of patients with triple-negative cancer have a family history of first- and second-degree cancer. This is primarily breast, colorectal, stomach, and endometrial cancer.

In a comparative study, Khalil, et al. in Morocco found a family history in 17.4% of cases of triple negative cancers versus 57.6% of non-triple-negative cancers [6]. This difference could be explained by the small size of the triple negative breast cancer sample.

Women with a family history of breast cancer, whether in the maternal or paternal branch, have an increased risk of developing it. For example, a history of first-degree breast cancer (mother, sister, and daughter) increases the relative risk to 2.

Two first-degree history confers a relative risk of 3, and if there is more than 3 (same parental branch, first and second degree) the relative risk is at least greater than 4 and makes the underlying genetic problem to be considered [44].

## Consultation time and tumor size

96.77% of patients consulted a health worker within 3 months of the discovery of the signs of calls on the affected breast and the majority of patients had a tumor larger than 30 mm: 30 to 40 mm (29.03%), then 50 to 60 mm (22.58%) with an average of 25 mm.

Boisserie, et al. in Bordeaux reported an average size of 40 mm, Rosalind, et al. in USA has an average of 32 mm, James, et al. in New Zealand has an average tumor size of 23 mm, while

Samain in Nantes has an average of 18 mm. These results would be strongly influenced by the time elapsed between the appearance of the tumor and the consultation, as well as the various factors of tumor proliferation [5,7,15,45].

## Tumor site

The upper-external quadrant of the breast is the most affected by the tumor (38.70%). Secondly, comes the junction of external quadrants (22.58%).

Boisserie, et al. confirm this high frequency in the upper-external quadrant with 46.6%, followed by the upper-inner quadrant with 17.8% [14].

## Adenopathies

Adenopathies are frequently present (58.06%) at the time of diagnosis of triple negative cancer with a histological invasion of lymph nodes ($n$ = 14).

Similar results are reported by Rosalind, et al. in the USA and James, et al. in New Zealand, 51% and 40% respectively [5,7]. Samain in Nantes describes a lower percentage: 23%, while Gueye, et al. in Dakar reported higher value of 68.1% [25,45]. These differences could be explained by the delay between the appearance of the tumor and the consultation, the histological peculiarities and different factors of cell proliferation.

## ACR Grade

Cancer-suggestive lesions, ACR 5 are mainly found (77.41%) in patients with triple-negative breast cancer. These are followed by ACR 4 (22.58%) lesions.

Woodwork et al report in their studied population the following results: ACR 1 and 2 in 6.4% of cases, ACR 3 in 4.8%, ACR 4 in 58.7%, ACR 5 in 30.2% [14]. Thus, triple negative breast cancers present on imaging in their severe forms.

## Histological type

Patients with triple-negative breast cancer have in 93.54% of the cases, an invasive ductal carcinoma.

James in New Zealand, Gueye, et al. in Dakar, Samain in Nantes, Rosalind, et al. in the USA, Boisserie, et al. in Bordeaux reported in their studied populations frequencies similar to ours, including 88%, 86.4%, 84.5%, 88%, 79% respectively [5,7,25,45].

Invasive ductal carcinoma is therefore the most commonly found histological type in triple negative breast cancers.

## Histoprognostic grade

Triple negative cancers are essentially poorly differentiated, classified grade III (83.87%), according to Elston-Ellis.

Similar values are reported by other authors, including Boisserie, et al. in Bordeaux, James, et al. in New Zealand, Samain in Nantes, Gueye, et al. in Dakar, which objectively frequencies of 72.6%, 79%, 69.1%, 68.2% respectively [7,14,25,45].

## Cell Renewal Rate (Ki-67)

Triple-negative cancer has a high rate of cell renewal, ranging from 80% to 100% (38.70% of the cases) and 6080% to 80% (34.37% of the cases).

This result is corroborated by Rosalind in the USA, which finds a high Ki-67 index in its population in 79% of the patients with triple negative breast cancer [5].

## Chemotherapy and lumpectomy by initial tumor size

In our study, neoadjuvant chemotherapy is mostly indicated for triple-negative breast cancers ≥ 30 mm at diagnosis (51.61%) and a delayed lumpectomy is then performed in 23.52% of the patients. On the other hand, for tumors of < 30 mm size, a lumpectomy is performed immediately in 76.47% of the patients, followed by adjuvant chemotherapy (48.38%).

In the Gueye, et al. series in Dakar, neoadjuvant chemotherapy is indicated in 59% of patients. This high rate can be justified by the high percentage of tumours≥30 mm at diagnosis, also by the average time for consultation which is 11.1 months in its series [25]. Samain in Nantes reports a lower frequency of neoadjuvant chemotherapy in its series: 34.6% in comparison to 65.4% for adjuvant chemotherapy [45].

## Indications of mastectomy and breast reconstruction

Mastectomy was performed in 45.16% of patients; it was mainly indicated in front of a large tumor size associated with a small breast volume (35.71%), then multifocal breast tumors (28.57%). Breast reconstruction was performed in 21.42% of mastectomy patients.

James, et al. in New Zealand, reports in his series a higher frequency of mastectomy: 55% with breast reconstruction performed in 19% of them [7].

## Radiotherapy indications

Radiation therapy is indicated in the majority of patients (96.66%), postoperatively ($n$ = 30).

This result is corroborated by Samin in Nantes which had a frequency of 91%, and by James in New Zealand which reported a frequency of 66% [7,45].

## Oncogenetic survey indications

In our population, 10 patients benefited from an oncogenetic survey; it was mainly indicated in front of a young age and a family history of cancer. Our results are similar to the recommendations of the Curie and Gustave Roussy Institute [15] which define the following criteria as oncogenetic consultation indications:

- 3 (or more) subjects with breast and/or ovarian cancer in first- or second-degree relatives if paternal transmission in the same parental branch
- At least 2 cases of breast cancer in first-degree relatives (or second-degree relatives if transmission is paternal), if one of them is diagnosed before 45-50 years or bilaterally (if the first is diagnosed before the age of 50)
- Breast cancer + ovarian cancer in first- or second-degree relatives
- Ovarian cancer (excluding borderline and germinal tumors) before age 50 or high-grade serous regardless the age
- Breast cancer before age 35 (questionable until age 40)
- Triple negative breast cancer before age 50
- Breast cancer in men
- Other clinical syndromes, cowden's disease or Li Fraumeni syndrome, association of diffuse gastric cancer with infiltrating lobular carcinoma of the breast
- Any other family of a particular nature, multiple primary tumors: take prior advice from the geneticist.

However, there are urgent indications, especially if it can influence the choice of treatment (surgical: mastectomy + immediate breast reconstruction rather than conservative treatment).

### Oncogenetic survey results

The oncogenetic survey was proposed in 11 patients. There are two BRCA 1 mutations (18%), one BRCA 2 mutation (10%), and four cases of absence of mutation (36%). The therapeutic intake in case of a mutation is directed towards a prophylactic bilateral mastectomy and adnexectomy, proposed at the age of 40.

According to the National Cancer Institute [46], patients with a BRCA 1, BRCA 2 gene mutation have a risk of developing breast and ovarian cancer. Thus, depending on the age and the parental project, breast monitoring is proposed starting from 20 years of age based on: clinical examination every 6 months.

Starting from the age of 30, MRI + mammogram/ultrasound if dense breasts every year. Note that MRI is recommended first, to guide other examinations if an abnormality is suspected. The maximum time of 2 months is recommended between examinations, to be carried out if possible in the same structure for optimal synthesis and comparison.

On the other hand, the alternative to breast monitoring is a prophylactic mastectomy with maximum benefit if performed before the age of 40. A time for reflection is essential and its indication is made in the Meeting of Pluridisciplinary Concertation, and the care of the patient is done by a multidisciplinary team.

Concerning the ovarian risk, monitoring is initiated starting from the age of 35 using an annual pelvic trasnsvsaginal ultrasound. Starting from the age of 40 or as soon as the parental project is completed, a prophylactic adnexectomy is proposed after validation in the Meeting of Pluridisciplinary Concertation.

### Immunotherapy

In general 25% of patients suffer from recurrent regional or distant recurrence with a mortality rate that can reach up to 75 %.This issue can be explained by the absence of targeted therapies [46]. Immunotherapy had shown good results not only in improving survival rates but also in maintaining adequate tumor response and had recently obtained approval from the US Food and Drug Administration [47]. Most studies speak about the effect of immunotherapy through cases and controls in the context of an initial treatment for triple negative breast cancer and not treatment of its recurrence. According to Schmid, et al, survival progression-free was prolonged by immunotherapy by 7.4 months compared to 4.8 months for those who had not received it in combination with chemotherapy in advanced triple negative breast cancer [48].

Currently more than 50 clinical trials evaluate pembrolizumab, durvalumab, ipilimuma, nivolumab, tremelimumab as well as azolizumab. Immunotherapy, particularly with drugs that inhibit PD1 and PDL1 (and therefore likely to restore the person's anti-tumor immunity), seems promising in patients with metastatic triple negative breast cancer. The combination of atzolizumab (anti PD-L1) with paclitaxel has given very promising results justifying to evaluate its real effectiveness, compared to standard treatment [49].

Tumors that present a high mutational charge seem to be more immunogenic. Based on this, these tumors would be good candidates for immunotherapy. For patients that present BRCA1 and BRCA2 mutations, anti-parp can be prescribed. Olaparib (Lymparza) was approved at the European level for breast cancers (HER2 negative with BRCA mutation) in patients treated with some meds or when medications are not adapted.

## Conclusion

Breast cancer is the most common cancer in women and is a major public health problem. It is divided into several subtypes, including triple negatives. The subject of our study entitled "Triple Negative Breast Cancer: Early Stages Management And Evolution, A Two Years Experience At The Department Of Obstetrics And Gynecology Of CHSF" has specific objectives to highlight the socio-demographic characteristics of patients, to identify the clinical and paraclinical aspects of triple negative breast cancers, to describe their histo-prognostic specificities and to present the modalities of management.

At the end of this study, we can remember the following:

1. Triple negative breast cancer accounts for a small proportion of all breast cancers and mainly affects the female sex.
2. The age of onset is mostly above 50 years, with an average age of 56.68 years, the majority of patients develop it at menopause. On the other hand, 29.01% of women develop it before the age of 50.
3. A normal BMI is present in 61.21% of patients and would not be a protective factor in non-menopausal women, the same for high parity, oral contraceptive use, alcohol and tobacco use, a personal malignant or familial breast cancer year. Breastfeeding is protective.
4. The average tumor size is 25 mm, despite a period of time to consultation of 3 months. The main tumor site is the upper-outer quadrant with frequent adenopathies at the time of diagnosis.
5. These are mainly invasive ductal carcinomas classified as ACR 5, Elston Ellis grade III, and characterized by Ki-67 high.
6. Management is essentially based on neoadjuvant or adjuvant chemotherapy, coupled with immediate or delayed lumpectomy and radiotherapy, depending on the size of the tumor. The mastectomy is performed in 45.16% of the cases.
7. The oncogenetic survey is carried out in 11 patients in accordance with the recommendations and finds two BRCA1 mutations, one BRCA2 mutation with the proposal of a bilateral prophylactic adnexectomy and mastectomy around 40 years of age. Despite their low frequency, triple negative breast cancers represent a subgroup marked by pejorative characteristics, a reserved prognosis, with limited treatment options. In this way, they are a priority in the eyes of research.

## Informed consent

Informed consent was obtained from all the considered patients in order to publish their cases.

## Ethical considerations

This observational retrospective study respected the ethical issues of honesty and integrity of the reported information, of objectivity and carefulness of the data that corresponds to each patient of the serie.

## Data availability

Centre Hospitalier Sud Francilien, Ile de France, France

# References


1. Anthony G, Renaud S, Emmanuelle CJ. Cancer du sein triple-négatif: caractéristiques histocliniques et moléculaires, prise en charge et perspectives thérapeutiques Bull Cancer. 2013; 100.
2. Portha H, Jankowski C, Cortet M. Tumeurs localisées du sein triple négatives en 2016: définitions et prise en charge Gynécologie Obstetrique & Fertilité. 2016; 44: 492–504.
3. Victoire W, Agnes C, Caroline D. Influence des facteurs hormonaux sur le pronostic des cancers du sein triple négatifs, Gynécologie Obstétrique Fertilité et Sénologie. 2019.
4. Thakur KK, Bordoloi D, Kunnumakkara AB. Alarming Burden of Triple-Negative Breast Cancer in India. Clin Breast Cancer. 2017; 18: 393-399. **PubMed:** https://pubmed.ncbi.nlm.nih.gov/28801156/
5. Rosalind P, Candelaria, Beatriz E, et al. Imaging features of triple-negative breast cancers according to androgen receptor status, Eur J Radiol. 2019; 114: 167–174. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/31005169
6. Ibrahim K, Bendahhou K, Saile R. Antécédent familial et âge de survenue du cancer du sein chez les patientes triples-négatives ou non triples-négatives prises en charge au centre Mohammed VI pour le traitement des cancers, Revue d'Épidémiologie et de Santé Publique 64S. 2016; S137–S161.
7. James M, Dixit A, Robinson B. Outcomes for Patients with Non-metastatic Triple-negative Breast Cancer in New Zealand. Clin Oncol. 2019; 31: 17e24. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/30274766
8. Kallel I, Rebaı M, Khabir A. What common biomarkers characterize a triple-negative profile in breast cancer? Pathologie Biologie. 2015; 63: 224–229. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/26300241
9. Ming Y, Chloé R, Amel R. Radiotherapy in triple-negative breast cancer: Current situation and upcoming strategies. Critical Reviews in Oncology / Hematology.2018; 131: 96–101. **PubMed:** https://pubmed.ncbi.nlm.nih.gov/30293712/
10. UMVF. Anatomie de la glande mammaire. UVMaF. 2011; 21.
11. Kamina P. Anatomie opératoire, gynécologie-obstétrique. Maloine. 2000; 318.
12. Nkondjock A, Ghadirian P. Facteurs de risque de cancer du sein, medecine/sciences. 2005; 21: 175-180.
13. ANAES. Classification en six catégories des images mammograhiques en fonction du degré de suspicion de leur caractère pathologique (en dehors des images construites et des variantes du normal) correspondance avec le système birads de l'American college of radiology (ACR), ANAES/Service des recommandations et références professionnelles. Février. 2002.
14. Boisserie L, Mac G, Debled M. Aspects radiologiques des cancers du sein triple négatifs: à propos de 73 cas, Journal de Radiologie Diagnostique et Interventionnelle. 2012; 93: 196-203.
15. Cottu P, Delaloge S. Cancers et pathologies du sein attitudes diagnostiques et thérapeutiques, protocoles de traitement, Institut Curie & Gustave-Roussy. 2016-2017.
16. Haute autorité de santé, Tumeur maligne, affection maligne du tissu lymphatique ou hématopoïétique Cancer du sein. Institut national du cancer. 2010.
17. Gonçalves A. Chimiothérapie néoadjuvante des cancers du sein HER2-positifs et triplenégatifs. Bull Cancer. 2016; 103: S76–S89.
18. Vijayakrishna K. Gadi E, Davidson. Practical Approach to Triple-Negative Breast Cancer. Am Society Clin Oncol. 2017; 13: 293-300. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/28489980
19. Adamo V, Ricciardi G, Placido S, et al. Management and treatment of triple negative breast cancer patients from the NEMESI study: an Italian experience. Eur J Cancer. 2012; 48: 642867. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/21757335

20. Redondo C, Gago-Dominguez M, Ponte S, Colucci G, Conte P, et al. Breast feeding, parity and breast cancer subtypes in a Spanish cohort. PLoS One. 2012; 7: e40543.
**PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/22792365

21. Wojcinski S, Soliman A, Schmidt J, Makowski L, Degenhardt F, et al. Sonographic features of triple-negative and nontriple-negative breast cancer. J Ultrasound Med. 2012; 31: 1531-1541.
**PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/23011616

22. Qiu J, Xue X, Li R, Wang JD. Clinicopathological features and prognosis of triple-negative breast cancer: a comparison between younger (<60) and elderly (>/¼60) patients. Eur J Cancer Care (Engl) 2016. 25:1065-75.
**PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/26122025

23. Widodo I, Dwianingsih E, Triningsih E, Utoro T, Soeripto. Clinicopathological features of Indonesian breast cancers with different molecular subtypes. Asian Pac J Cancer Prev. 2014; 15: 6109-6113.
**PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/25124582

24. Bauer K, Brown M, Cress R, Parise CA, Caggiano V. Descriptive analysis of estrogen receptor (ER)-negative, progesterone receptor (PR)-negative, and HER2-negative invasive breast cancer, the so-called triple-negative phenotype: a population-based study from the California Cancer Registry. Cancer. 2007; 109: 1721-1728.
**PubMed:** https://pubmed.ncbi.nlm.nih.gov/17387718

25. Gueye M, Gueye S, Mbaye M. Aspects cliniques et pronostiques des cancers du sein triple négatifs à l'unité de sénologie du CHU Le-Dantec de Dakar. J Afr Cancer. 2013; 5: 42-47.

26. Hashmi AA, Edhi MM, Naqvi H, Faridi N, Khurshid A, et al. Clinicopathologic features of triple negative breast cancers: an experience from Pakistan. Diagn Pathol. 2014; 9: 43.
**PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/24581278

27. Stead LA, Lash TL, Sobieraj JE, Chi DD, Westrup JL, et al. Triple-negative breast cancers are increased in black women regardless of age or body mass index. Breast Cancer Res. 2009; 11: R18.
**PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/19320967

28. Jack RH, Davies EA, Renshaw C, Tutt A, Grocock MJ, et al. Differences in breast cancer hormone receptor status in ethnic groups: a London population. Eur J Cancer. 2013; 49: 696-702.
**PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/23058788

29. Chen HL, Ding A, Wang FW. Prognostic effect analysis of molecular subtype on young breast cancer patients. Chin J Cancer Res. 2015; 27: 428-436.
**PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/26361413

30. Vona-Davis L, Rose D, Hazard H, Howard-McNatt M, Adkins F, et al. Triple-negative breast cancer and obesity in a rural Appalachian population Cancer Epidemiol Biomarkers Prev. 2008; 17: 3319-3324.
**PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/19064545

31. Jarroudi A, Abda N, Afqir S. le surpoids est-il un facteur pronostique dans le cancer du sein triple négatif ? revue d'épidémiologie et de santé publique. 2016; 64: S137-S161.

32. Ronny M, Chu Q, Li BDL, Burton GV, Ampil FL, et al. Does obesity have an effect on outcomes in triple negative breast cancer? J Surg Res. 2013; 184: 253-259.
**PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/23768767

33. Shaheenah D, Xiudong L, Jennifer K. Impact of Body Mass Index on Survival Outcome Among Women With Early Stage Triple-Negative Breast Cancer. Clin Breast Cancer. 2012; 12: 364-372.
**PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/23040004

34. Ademuyiwa F, Groman A, O'Connor T, Ambrosone C, Watroba N, et al. impact of body mass index on clinical outcomes in triple negative breast cancer. Cancer. 2011. 117: 4132.
**PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/21387276

35. Yang X, Sherman X, Rimm D, Jolanta Lissowska, Louise A Brinton, et al. Differences in risk factors for breast cancer molecular subtypes in a population based study. Cancers Epidemiol Biomarkers Prev. 2007; 16: 439-443.
**PubMed:** https://pubmed.ncbi.nlm.nih.gov/17372238/

36. Barnard M. Established breast cancer risk factors and risk of intrinsic tumor subtypes, Biochimica et Biophysica Acta. 2015; 1856: 73-85.
**PubMed:** https://pubmed.ncbi.nlm.nih.gov/26071880/

37. Stacoffe M. Etude de l'hétérogénéité des cancers du sein triple négatif et de l'impact de l'infiltration tumorale par les lymphocytes (TILs), des lymphocytes T CD4+, CD8+, des lymphocytes T régulateurs et des macrophages sur le pronostic de 105 patientes traitées en situation adjuvante au CHU de Tours, thèse de médecine, faculté de medecine de tours, Université François-Rabelais, 2016.

38. Phipps A, Malone K, Porter P, Daling JR, Li CI. Reproductive and hormonal risk factors for postmenopausal luminal, HER2-overexpressing and triple negative breast cancer. Cancer. 2008; 113: 1521-1526.
**PubMed:** https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2587413/

39. Millikan R, Newman B, Tse C, Moorman PG, Conway K, et al. Epidemiology of basal-like breast cancer. Breast cancer Res Treat. 2008; 109: 123-139.
**PubMed:** https://pubmed.ncbi.nlm.nih.gov/17578664

40. Collaborative group on hormonal risk factors in breast cancer. Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50302 women with breast cancer and 96973 without the disease. Lancet. 2002; 12: 1059-1069.
**PubMed:** https://pubmed.ncbi.nlm.nih.gov/12133652/

41. Ma H, Wang Y, Sullivan H, Weiss L, Marchbanks PA, et al. Use four biomarkers to evaluate the risk of breast cancer subtypes in the women's contraceptive and reproductive experiences study. Cancer Res. 2010; 70: 575-587.
**PubMed:** https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2807992/

42. Dolle J, Daling J, White E, Brinton LA, Doody DR, et al. Risk factors for triple negative breast cancer in women under the age of 45 years, Cancer Epidemiol Biomarkers Prev. 2009; 18: 1157-1166.
**PubMed:** https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2754710/

43. Kabat GC, Kim M, Phipps AI, Li CI, Messina CR, et al, Smoking and alcohol consumption in relation to risk of triple Negative breast cancer in a cohort of postmenopausal women, Cancer Causes Control. 2012.
**PubMed:** https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3100347/

44. Valeria V, Aurélie A, Pierre O. Cancer du sein : risque génétique, Imagerie de la Femme. 2016; 26: 95-104.

45. Benoit S. Cancer du sein triple négatif: étude rétrospective monocentrique chez 465 patientes prises en charge au centre Renne Gauducheau, thèse de medecine, université de Nantes. 2016.

46. Inca. principales recommandations de prise en charge des femmes porteuses d'une mutation de BRCA 1 ou BRCA 2, Institut National du Cancer. 2009.

47. Steward L, Conant L, Gao F, Margenthaler JA. Predictive Factors and Patterns of Recurrence in Patients With Triple Negative Breast Cancer. Ann Surg Oncol. 2014; 21: 2165-2171.
**PubMed:** https://pubmed.ncbi.nlm.nih.gov/24558065/

48. Vikas P, Borcherding N, Zhang W. The Clinical Promise of Immunotherapy in Triple-Negative Breast Cancer. Cancer Manag Res. 2018; 10: 6823-6833.
**PubMed:** https://pubmed.ncbi.nlm.nih.gov/30573992

49. Schmid S. Adams HS, Rugo A, Schneeweiss CH, Barrios H, et al. Atezolizumab and Nab-Paclitaxel in Advanced Triple-Negative Breast Cancer. N Engl J Med. 2018; 379: 2108-21.
**PubMed:** https://pubmed.ncbi.nlm.nih.gov/30345906/