

Histo-Phenotypic Aspects of Breast Cancer in Women under 40 Years Old, in Yaoundé

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Abstract

Introduction: Breast cancer is the most common cancer in women worldwide, with an increasing incidence. Although it is rare and not much studied in young women, it represents 7% of cases worldwide and often appears more aggressive with a poor prognosis compared to its counterpart in older women. The main objective of our study was to describe the histological and phenotypic aspects of breast cancer in women of age under 40. **Methodology:** We conducted a descriptive and analytical cross-sectional study, with retrospective collection of data over a period of 05 years. All women diagnosed with breast cancer were included and divided into 2 study groups: under 40 years old and over 40 years old. Data were analyzed using SPSS version 23.0 software, compared using the Chi square or Fisher exact test. A p value < 0.05 was indicative of significance. **Results:** We retained 196 files, either 89 for those under 40 and 107 for those over 40. Young patients with breast cancer had a higher stage, grade and tumor size. Lymph node involvement was more observed in women under 40 years (69.6% vs 53.2%). Older women were more likely to be hormone receptor positive (54.2% vs 38.2%); p = 0.018. HER-2 overexpression was higher in women younger than 40 years (39.32% vs 25.23%); p = 0.080 with a high Ki67 proliferation index (30.3% versus 2.8%); p < 0.001. Triple-negative and Her-2 tumors were much more frequent in young women (48.3% vs. 36.4%; p = 0.063) and (17.97% vs. 10.3%; p = 0.125). **Conclusion:** Breast cancer in young women remains more aggressive and is dominated by triple negative and Her-2 phenotypes.

Keywords

Breast Cancer, Young Women, Yaoundé

1. Introduction

Breast cancer is the most common cancer and the leading cause of cancer death among women worldwide [1]. In Cameroon, there were approximately 4170 new cases of breast cancer (20.1%) recorded in 2020, with 2108 deaths [2]. In young women, the definition of breast cancer has been controversial. A “young” woman is considered to be under 35, under 40, or simply premenopausal [3]. Globally, breast cancer in young women accounts for 7% of cases [4]. In Africa, studies have found 18.46%, 8% - 12%, and 18.2% of breast cancer cases in women under 40 in Morocco, Tunisia, and Mali respectively [5] [6] [7]. Although it is rare and little studied in this population, the histological and biological characteristics of infiltrative breast cancers in young women had a worse prognosis: grade 3, hormone receptor negative, Her 2 positive, triple negative compared to the rest of the population [8]. Overall survival was significantly lower in young patients, as were relapse-free survival, locoregional recurrence-free survival and metastasis-free survival [8]. Faced with this growing proportion of breast cancer and its severity in the world, particularly in our environment, we proposed to improve Cameroonian data by conducting this study whose objective was to determine the histological and phenotypic aspects of breast cancer in young woman.

2. Materials and method

Ethical considerations: The study was conducted following the fundamental principles of research as per the Declaration of Helsinki. We obtained ethical clearances from the Institutional Ethics Committee of the University of Douala and the Gynecological-Obstetric and Pediatric Hospital of Yaoundé, as well as a research authorization from the General Hospital of Yaoundé.

Data collection and analysis: We conducted a cross-sectional and analytical study with retrospective data collection over a period of 6 months from January 1 to June 30, 2023. The recruitment period lasted for 5 years from January 1, 2018, to December 31, 2022. We recruited records from the registries of oncological and gynecological consultations and hospitalization reports at the General Hospital and the Gynecological-Obstetric and Pediatric Hospital in Yaoundé. All records of women with breast cancer were included. The diagnosis of breast cancer was confirmed through histopathology and immunohistochemistry. Data were collected using pre-established and pre-texted technical sheets. The variables included sociodemographic data of the population, personal and family history of patients, clinical characteristics of the tumor, anatomopathological

characteristics, treatment modalities, and disease progression. The collected data were recorded on a specific technical sheet and then entered. The data were analyzed using the SPSS (Statistical Package for Social Sciences) software version 23.0. The study population was divided into 2 age groups: Under 40 years and Over 40 years. Qualitative variables were presented in terms of frequencies and percentages and compared using the Chi-square test or Fisher's exact test, with a 95% confidence level (Odds ratio). A p-value < 0.05 was indicative of a statistically significant result. The results were presented in tables generated using Microsoft® Office.

3. Results

Over a period of 5 years, we recruited 89 patients aged under 40 and 107 patients over 40; for a total of 196 cases.

The average age of patients in the 40 and under group was 34.96 ± 4.23 years, ranging from 25 to 40 years; while those over 40 had an average age of 53.66 ± 9.02 years, ranging from 41 to 77 years (**Table 1**). History of mastopathies was more common in women over 40 (6.54% vs 4.49%) without significant difference. Menopause was found in 3.4% of women under 40, compared to 40.2% in women over 40 ($p < 0.001$). Comorbidities were mainly dominated by hypertension, less common in those under 40 (6.7%) compared to women over 40 (22.4%) ($p = 0.002$). Women under 40 had, non-significantly, fewer family history of breast cancer compared to their counterparts, with respective frequencies of 12.2% and 17.8% (**Table 2**).

The two main reasons for consultation were breast nodules (83.1% vs 75.7%; $p = 0.136$) and breast pain (21.3% vs 15.9%; $p = 0.212$) in both study groups. (**Table 2**). Breast size increase (70.8% vs 61.7%; $p = 0.118$) and orange peel skin appearance (44.9% vs 33.6%; $p = 0.071$) were the main physical signs identified and were more common in those under 40 years old. Ulcerations and breast retraction were significantly more frequent in those under 40 years old, with a risk multiplied by 2.7 ($p < 0.05$) (**Table 3**).

The involvement was unilateral in most cases, with a preferential involvement of the left breast in those under 40 years old, with respective frequencies of 60.7% and 54.2% for those over 40 years old. However, bilaterality was significantly more common in women under 40 years old ($p < 0.05$) (**Table 4**). As for the location, the supero-external (68.5% vs 56.1%; $p = 0.050$) and infero-external quadrants (34.8% vs 29.0%) were the most affected. Tumors classified as T4 were the most common: 46.1% vs 40.2% respectively in each group. Lymph node involvement was higher in women under 40 years old with a frequency of 69.6% compared to women over 40 years old, which was 53.2%. Women under 40 years old had a higher percentage of metastases at 24.7%. Stage 4 of the disease was the most represented, at 48.3% and 47.7% respectively. However, the difference observed in the various groups was not significant (**Table 4**).

Table 1. Distribution of women with breast cancer according to age.

Variables	Mean	Standard deviation	Minimum	Maximum
Age ≤ 40 years (N = 89)	34.96	4.23	25	40
Age ≥ 40 years (N = 107)	536.6	9.02	41	77

Table 2. Distribution of women with breast cancer according to personal past history.

Variables	≤ 40 years	> 40 years	OR (95%CI)	P
	N = 89; n(%)	N = 107; n(%)		
Past history of mastopathy	4 (4.49)	7 (6.54)	0.68 (0.19 - 2.42)	0.39
Other cancers				
Cervical cancer	1 (1.1)	0 (0.0)	-	0.454
Menopause				
Yes	3 (3.4)	43 (40.2)	0.05 (0.01 - 0.17)	<0.001
No	86 (96.6)	64 (59.8)	1	
History of hormonal contraception				
Yes	12 (13.5)	11 (10.3)	1.36 (0.56 - 3.25)	0.318
No	77 (86.5)	96 (89.7)	1	
Comorbidities				
HTN	6 (6.7)	24 (22.4)	0.25 (0.09 - 0.64)	0.002
HIV infection	04 (4.5)	6 (5.6)	0.79 (0.21 - 2.90)	0.493
Viral hepatitis	-	6 (5.6)	-	0.025
Diabetes	-	4 (3.7)	-	0.087
Stroke	-	3 (1.5)	-	0.161

Table 3. Distribution of women with breast cancer according to reason for consultation and physical signs.

Variables	≤ 40 years	> 40 years	OR (95% CI)	P
	N = 89; n(%)	N = 107; n(%)		
Reason for consultation				
Breast lump	74 (83.1)	81 (75.7)	1.58 (0.77 - 3.21)	0.136
Breast pain	19 (21.3)	17 (15.9)	1.43 (0.69 - 2.96)	0.212
Axillary nodule	8 (9.0)	7 (6.5)	1.41 (0.49 - 4.05)	0.353
Breast discharge	4 (4.5)	7 (6.5)	0.67 (0.19 - 2.37)	0.383
Screening	1 (1.1)	7 (6.5)	0.16 (0.02 - 1.34)	0.057
Ulceration	4 (4.5)	1 (0.9)	4.98 (0.54 - 4.46)	0.132
Skin/nipple deformation	2 (2.2)	2 (1.9)	1.20 (0.16 - 8.74)	0.617

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Physical signs				
Absence of physical sign	4 (4.5)	7 (6.5)	0.67 (0.19 - 2.37)	0.383
Swelling	63 (70.8)	66 (61.7)	1.50 (0.82 - 2.74)	0.118
Orange peel skin	40 (44.9)	36 (33.6)	1.61 (0.90 - 2.87)	0.071
Ulceration	18 (20.2)	9 (8.4)	2.76 (1.17 - 6.50)	0.015
Retraction	36 (40.4)	28 (26.2)	1.91 (1.04 - 3.40)	0.024

Table 4. Distribution of women with breast cancer according to laterality and clinical stage.

Variables	≤ 40 years	> 40 years	OR (95% CI)	P
	N = 89; n(%)	N = 107; n(%)		
Laterality				
Left	54 (60.7)	58 (54.2)	1.30 (0.73 - 2.30)	0.222
Right	31 (34.8)	49 (45.8)	0.63 (0.35 - 1.12)	0.079
Bilateral	4 (4.5)	-	-	0.041
Stage T				
T1	4 (4.5)	3 (2.8)	1.63 (0.35 - 7.49)	0.399
T2	21 (23.6)	20 (18.7)	1.34 (0.67 - 2.67)	0.253
T3	15 (16.9)	24 (22.4)	0.70 (0.34 - 1.43)	0.214
T4	41 (46.1)	43 (40.2)	1.27 (0.72 - 2.24)	0.247
T undetermined	8 (9.0)	17 (15.9)	0.52 (0.21 - 1.27)	0.109
Stage N				
N0	17 (19.1)	29 (27.1)	0.63 (0.32 - 1.25)	0.125
N1	34 (38.2)	32 (29.9)	1.44 (0.79 - 2.62)	0.142
N2	22 (24.7)	21 (19.6)	1.34 (0.68 - 2.64)	0.246
N3	6 (6.7)	4 (3.7)	1.86 (0.50 - 6.81)	0.265
N undetermined	10 (11.2)	21 (19.6)	0.51 (0.23 - 1.16)	0.079
Stage M				
M0	41 (46.1)	40 (37.4)	1.43 (0.80 - 2.53)	0.139
M1	22 (24.7)	22 (20.6)	1.26 (0.64 - 2.48)	0.300
Mx	26 (29.2)	45 (42.1)	0.56 (0.31 - 1.03)	0.043
Clinical Stage				
Stage 1	3 (3.4)	4 (3.7)	0.89 (0.19 - 4.12)	0.601
Stage 2	16 (18.0)	16 (15.0)	1.24 (0.58 - 2.66)	0.352
Stage 3	19 (21.3)	23 (21.5)	0.99 (0.49 - 1.96)	0.561
Stage 4	43 (48.3)	51 (47.7)	1.02 (0.58 - 1.80)	0.521
Unknown Stage	8 (9.0)	13 (12.1)	0.71 (0.28 - 1.80)	0.318

The invasive ductal carcinoma was the most represented regardless of the group, with a frequency of 96.6% in those under 40 years old versus 94.4% for the rest of the population. The other cancers consisted of lobular carcinoma in situ, invasive lobular carcinoma, mucinous, and cribriform (Table 5). Most patients were classified as SBR 2, with 43.8% in those under 40 years old, compared to 57% in those over 40 years old. However, 39.3% of patients under 40 years old presented significantly ($p = 0.008$) with a grade 3 higher than patients over 40 years old (22.4%), with a confidence interval (OR = 2.24 [1.20 - 4.17]) (Table 5). Hormone receptor positivity was significantly lower in those under 40 years old than in those over 40 years old, at 38.2% and 53.3% (OR: 0.542 [0.3 - 0.96]; $p = 0.018$). Her 2 was overexpressed in 39.32% and 25.23% of cases, respectively, in each group, a significant difference. The Ki67 rate was more significant in those under 40 years old compared to those over 40 years old (30.3% vs. 2.8%), with a risk multiplied by 15 (OR: 15.09 [4.39 - 5.83]; $p < 0.001$) (Table 5). The most common molecular type was Triple Negative (48.3% vs. 36.4%), Her-2 positive tumors were more common in young women (17.97% vs. 10.3%), without significant difference (Table 5).

According to therapeutic modalities, chemotherapy was observed in all cases. Concerning surgery, it was frequent in 62.9% vs 68.2% ($p = 0.265$). Hormone therapy was more practiced among women over 40, 32.7% compared to 23.6%. No statistically significant difference was observed between these two groups therapeutically (Table 6).

In terms of survival, overall, patients under 40 years old had 3 times the risk of dying with a higher mortality rate compared to patients over 40 years old, 48.3% and 22.4% respectively (OR: 3.23 [1.74 - 5.98]; $p < 0.001$). Likewise, they had a significantly lower survival rate compared to those over 40 years old (40.4% vs 57%) $p = 0.015$ (Table 7). The median survival time of those under 40 was lower, 83 months, compared to those over 40, which was 120 months. The difference in survival observed in the two groups was statistically significant according to the Log Rank test or Mantel-Cox test ($p < 0.018$) (Figure 1).

Table 5. Distribution of women with breast cancer according to anatomopathological and immunohistochemical characteristics.

Immunohistochemistry	≤ 40 years	> 40 years	OR (95% CI)	P
	N = 89; n(%)	N = 107; n(%)		
Histological type				
Invasive ductal carcinoma	86 (96.6)	101 (94.4)	1.70 (0.41 - 7.01)	0.348
Others	3 (3.3)	6 (3.6)	0.58 (0.124 - 2.44)	0.5124
Differentiation grade				
SBR unknown	4 (4.5)	6 (5.6)	0.79 (0.21 - 2.90)	0.493
SBR 1	11 (12.4)	16 (15.0)	0.80 (0.35 - 1.83)	0.378
SBR 2	39 (43.8)	61 (57.0)	0.58 (0.33 - 1.03)	0.045
SBR 3	35 (39.3)	24 (22.4)	2.24 (1.20 - 4.17)	0.008

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Hormone receptors				
Positive	34 (38.2)	58 (54.2)	0.542 (0.29 - 0.92)	0.018
Negative	55 (61.8)	49(45.8)	1.91(1.08 - 3.39)	
Her 2				
Positive	35 (39.32)	27 (25.23)	1.92(1.04 - 3.53)	0.025
Negative	54 (60.67)	80 (74.76)		
Ki67				
Significant	27 (30.3)	3 (2.8)	15.09 (4.39 - 51.83)	< 0.001
Low	62 (69.7)	104 (97.2)		
Molecular types				
Luminal A	18 (20.2)	34 (31.8)	0.54 (0.28 - 1.05)	0.048
Luminal B	12(13.48)	23 (21.5)	0.56 (0.26 - 1.22)	0.101
Non-luminal	16 (17.97)	11 (10.3)	1.91 (0.83 - 4.36)	0.08
Triple negative	43 (48.3)	39 (36.4)	1.63 (0.91 - 2.88)	0.063

Table 6. Distribution of the population according totherapeutic modalities.

Therapeutic modalities	≤ 40 years	> 40 years	OR (95% CI)	P
	N = 89; n(%)	N = 107; n(%)		
Chemotherapy				
Yes	89 (100.0)	107 (100.0)	-	-
No	0 (0.0)	0 (0.0)	-	-
Surgery				
No	33 (37.1)	34 (31.8)	1.26 (0.70 - 2.28)	0.265
Radical	49 (55.1)	68 (63.6)	0.70 (0.39 - 1.24)	0.144
Conservative	7 (7.9)	5 (4.7)	1.74 (0.53 - 5.68)	0.264
Radiotherapy				
Yes	18 (20.2)	19 (17.8)	1.17 (0.57 - 2.40)	0.398
No	71 (79.8)	88 (82.2)	1	
Hormone therapy				
Yes	21 (23.6)	35 (32.7)	0.63 (0.33 - 1.19)	0.106
No	68 (76.4)	72 (67.3)	1	

Table 7. Distribution of women with breast cancer according to outcome.

Outcome	≤ 40 years	> 40 years	OR (95% CI)	P
	N = 89; n(%)	N = 107; n(%)		
Deceased	43 (48.3)	24 (22.4)	3.23 (1.74 - 5.98)	<0.001
Alive	36 (40.4)	61 (57.0)	0.51 (0.28 - 0.90)	0.015
Lost of follow-up	10 (11.2)	22 (20.6)	0.48 (0.21 - 1.09)	0.058

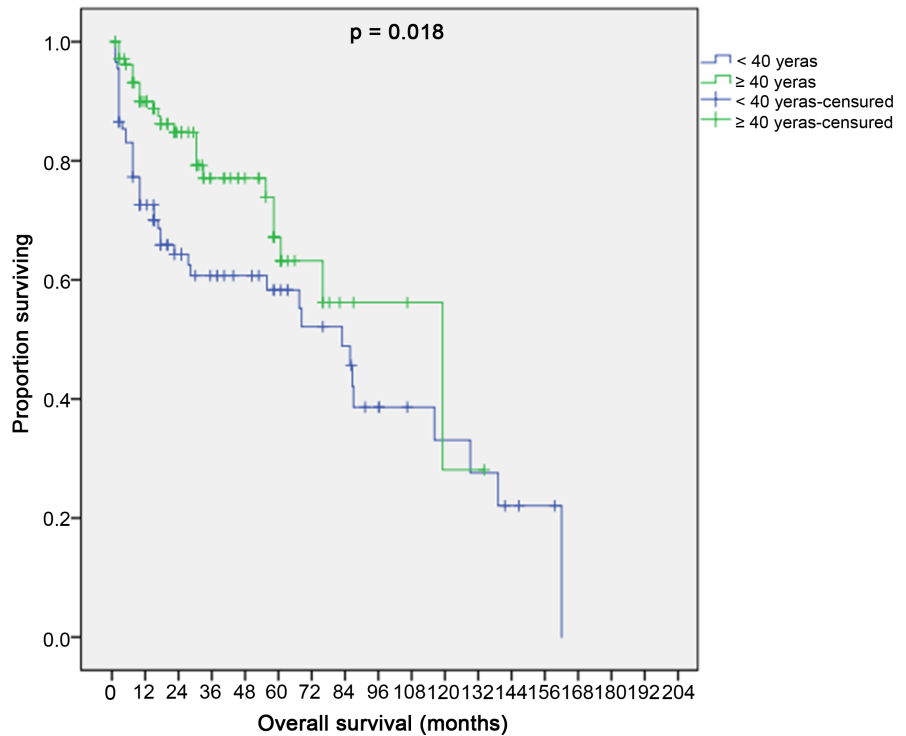


Figure 1. Overall survival of patients.

4. Discussion

Breast cancer in young women is a public health issue in Cameroon as well as worldwide. It presents different characteristics and often appears more aggressive due to their complex histological and biological aspects [9]. In our series, women under 40 years old had higher percentages in terms of tumor size, lymph node involvement, and metastases compared to those over 40. This could be explained by the more intense hormonal action in young women leading to rapid invasion of tumor cells and rapid progression of the disease, compared to those over 40 who are sometimes in premenopausal or menopausal phase. Stage 4 of the disease was the most common, at 48.3% and 47.7% respectively (p = 0.521). These results are similar to those found in Congo in 2020 by Ndounga *et al.*, who also found the disease at late stages in young women [3]. But they differ from those of Eric *et al.* in Croatia in 2018 and Alzaman *et al.* in Saudi Arabia in 2016, who found a predominance of T2 classified tumors in patients under 40 [10]

[11]. Furthermore, stage II of the disease was the most frequent in the study groups [11]. These observed differences could be explained by the delayed consultation of women with breast cancer in our context.

According to the literature data, infiltrating ductal carcinoma represents the most common form of breast cancer (70%) and can occur in both pre- and post-menopausal women. In fact, infiltrating ductal carcinoma was the most represented in our 02 study groups with no significant difference, respectively 96.6% versus 94.4% ($p = 0.348$).

In our study, patients under 40 years old had a higher grade III compared to those over 40 years old: 39.3% versus 22.4%, the difference observed between the two was significant ($OR = 2.24 [1.20 - 4.17]$; $p = 0.008$). This is consistent with the results of Fleurier *et al.* in France, who found a significantly higher grade III in those under 40 years old compared to those over 40 years old (49% and 26%); $p < 0.001$ [8]. This trend was also observed by Eric *et al.* in Croatia and Alzaman *et al.* in Saudi Arabia, who found, respectively, in the different study groups (29.1% versus 17.9%); $p = 0.004$ [10] and (53.2% versus 33.9%); $p = 0.031$ [11].

The most frequent molecular type in both study groups was triple negative, which was more common in women under 40 years old (48.3% vs. 36.4%) with no significant difference [12]. These results are consistent with those found in Croatia (32% vs. 10%) $p = 0.001$ and in several studies conducted in young African women: for example, in Mali, it represented 45.9%; in Togo, it was present in 57.2% in the study by Toukilnan *et al.* [13] and in 37.9% in Cameroon according to a study by Atangana *et al.* on the entire population [14]. The high frequency of triple negative in women under 40 years old could be explained by their young age. Indeed, it has been described in the literature that the young age of patients is a risk factor for aggressive forms of breast cancer. In their study, Schmadeka *et al.* found the same result [15]. However, in some European studies, luminal B and luminal A were more common [8] [9] [10] [11], although triple negative tumors were much higher in young women, 28% vs. 10% ($p = 0.002$) in France [8] and 21.3% vs. 8.1% in Saudi Arabia ($p = 0.046$) [11]. This difference could be attributed to race: black women may have a higher risk of presenting more aggressive tumors compared to white women due to the high frequency of BRCA1 and BRCA2 mutations in the black population.

At the same time, Her-2 tumors were more common in the young population at 17.97% compared to 10.3%. Similar trends had been observed by Ndounga *et al.* (6% versus 0%) [3], Fleurier *et al.* (7% versus 5%; $p < 0.05$) [15], and Alzaman *et al.* (27.7% versus 19.4%; $p = 0.04$) [11]. Young women significantly had a lower percentage of positive hormone receptors (38.2%) compared to women over 40 years old (54.2%). There was a significant difference in the Ki67 proliferation index between young and older women. The rate was higher in patients under 40 years old compared to those over 40 (30.3% versus 2.8%) with a risk multiplied by 15 ($OR = 15.09 [4.39 - 5.83]$; $p < 0.001$). All these differences could indicate the aggressiveness of breast cancer in young women.

In terms of survival, there was a significant difference between our two groups. The survival of young women was lower compared to the rest of the population with an overall survival rate of 40.4% compared to 57%. This rate was lower than that observed in a study carried out in France, where it was 87.7% as compared to 93.4% [8]. This could be due to, first the difference in the technical platform which is more developed in western countries, and also due to diagnosis at the late stage of the disease in our context. Women under 40 had a mortality rate of 48.3%, higher than that of women over 40 (22.4%). The mortality rate was identical to that of Ndounga *et al.* [3] in Congo, 47% in young women compared to 18.2%. This high rate in women under 40 years of age could be due to late diagnosis, absence of hormone receptors making them refractory to endocrine treatment, high histological grade, Her2 overexpression with significant Ki67, more aggressive molecular type.

Limitations: These were mainly due to missing data, either due to incomplete or unfound files, or to patient loss to follow-up.

5. Conclusion

Breast cancer has become a global scourge and represents a public health problem in our environment. It remains more aggressive with a higher mortality rate in women under 40, among whom this cancer is dominated by high-grade infiltrating ductal carcinomas and triple-negative and Her-2 phenotypes.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Appendix: Data Collection Form

- Data collection form number: _____/
- Patient File number: _____/
 - Study Group |_____|: 1) Under 40 years 2) 40 years and older
 - Health facility of follow up |_____|: 1 = HGYP; 2 = HGOPY

A. Socio-Demographic Characteristics

1. **Age at diagnosis (years):** _____
2. **Education Level** |_____|: 1 = None; 2 = Primary; 3 = Secondary; 4 = Superior
3. **Marital status** |_____|: 1 = married; 2 = Single; 3 = Divorced; 4 = Widow
4. **Weight (kg):** _____
5. **Size (cm):** _____
6. **BMI (kg/m²) :** _____

B. Clinical Characteristics

7. Reason(s) for Consultation

- Routine screening (campaign and others) |_____|: 1) Yes; 2) No
 - Breast nodule or swelling |_____|: 1) Yes; 2) No
 - Deformity of the skin or nipple |_____|: 1) Yes; 2) No
 - Breast discharge |_____|: 1) Yes; 2) No
 - Breast pain |_____|: 1) Yes; 2) No
 - Axillary nodule |_____|: 1) Yes; 2) No
 - Vegetative Ulceration |_____|: 1) Yes; 2) No
 - Others (to be specified): _____
 - Date of onset of first symptoms: _____/
8. Date of first consultation: _____/
- Time lapse between both dates (days):** _____/

C. Past History

9. Comorbidities

- HTN |_____|: 1) Yes; 2) No
 - Diabetes |_____|: 1) Yes; 2) No
 - HIV infection|_____|: 1) Yes; 2) No
 - Viral Liver Infection |_____|: 1) Yes; 2) No
 - Heart failure |_____|: 1) Yes; 2) No
 - Stroke |_____|: 1) Yes; 2) No
 - Other comorbidities _____
10. Age of first menstruation: _____/
 11. Age of first pregnancy: _____/
 12. Total number of pregnancies: _____
 13. Parity: _____
 14. Number of preterm babies _____

15. Number of abortions _____

16. Number of living children _____

17. Personal history of mastopathies

- None |_____|: 1) Yes; 2) No

- Fibroadenoma |_____|: 1) Yes; 2) No

- Mastitis |_____|: 1) Yes; 2) No

- Fibrocystic Disease |_____|: 1) Yes; 2) No

- Cyst |_____|: 1) Yes; 2) No

- Other _____

18. Menopause |_____|: 1) Yes; 2) No

19. Contraception |_____|: 1= None; 2 = Oral; 3 = Injectable; 4 = Implant;

5 = Patch; 6 = IUD

If contraception, duration of use (years): _____

20. Breastfeeding |_____| 1) Never; 2) Exclusive; 3) Mixed

If breastfeeding, duration of breastfeeding (in years): _____

21. Personal history of other cancer |_____|: 1 = None; 2 = Cervix; 3 = Ovaries; 4 = Stomach; 5 = Other (to be specified) _____

22. Family history of breast cancer |_____|: 1) Yes; 2) No

If yes, degree of kinship |_____|: 1 = 1st degree; 2 = 2nd degree; 3 = 3rd degree; 4 = Other

23. Family history of other cancers |_____|: 1) Yes; 2) No

If yes, degree of kinship |_____|: 1 = 1st degree; 2 = 2nd degree; 3 = 3rd degree; 4 = Other

D. Clinical

Date of diagnosis: _____

Diagnostic time _____

24. General signs |_____|: 1 = Stage 0; 2 = Stage 1; 3 = stage 2; 4 = stage 3; 5 = stage 4

25. Affected breast(s) |_____|: 1 = Left breast; 2 = Right breast; 3 = Bilateral

26. Location of the tumor:

- Upper outer Quadrant |_____|: 1) Yes ; 2) No

- Upper inner Quadrant |_____|: 1) Yes ; 2) No

- Lower Outer Quadrant |_____|: 1) Yes ; 2) No

- Lower inner Quadrant |_____|: 1) Yes ; 2) No

- Nipple |_____|: 1) Yes; 2) No

- Other _____

27. Skin signs

- No Signs |_____|: 1) Yes; 2) No

- Swelling |_____|: 1) Yes; 2) No

- Orange peel |_____|: 1) Yes; 2) No

- Ulceration |_____|: 1) Yes; 2) No

- Retraction |_____|: 1) Yes; 2) No

- Other skin signs (to be specified) _____

28. Histological type: |_____|: 1 = ductal carcinoma in situ; 2 = lobular carcinoma in situ; 3 = invasive ductal carcinoma; 4 = invasive lobular carcinoma; 5 = tubular carcinoma; 6 = medullary carcinoma; 7 = mucinous carcinoma; 8 = invasive cribriform carcinoma; 9 = endocrine carcinoma of the breast; 10 = metaplastic carcinoma; 11 = apocrine carcinoma; 12 = adenoid cystic carcinoma; 13 = mucoepidermoid carcinoma; 14 = secretory carcinoma; 15 = invasive micropapillary carcinoma; 16 = malignant phyllode tumor; 17 = scirrhous breast carcinoma; 18 = colloid adenocarcinoma

29. Classification |_____| 1 = clinical 2 = pathological

30. Tumor size |_____|: 1 = T0 (no palpable tumor); 2 = T1 (tumor ≤ size 2 cm in diameter); 3 = T2 (2 cm < tumor diameter ≤ 5 cm); 4 = T3 (tumor > size 5 cm in diameter); 5 = T4 (tumor with extension to the wall and/or skin); 6 = Tx (undetermined)

31. Lymph node involvement |_____|: 1 = Absence of lateral lymph nodes (N0); 2 = Presence of motile ipsilateral axillary lymph nodes (N1); 3 = Presence of fixed ipsilateral axillary lymph nodes or subclavicular lymph nodes (N2); 4 = Presence of ipsilateral subclavicular lymph nodes (N3); 5 = Nx (Undetermined)

32. Metastasis |_____|: 1 = Yes ; 2 = No 3 = undetermined

33. Clinical stage of breast cancer at diagnosis |_____|: 1 = Stage 1 (T1N0M0); 2 = Stage 2 (T2N0M0); 3 = Stage 3 (T3N0M0-T4N1M0); 4 = Stage 4 (T4N2M1)

E. Paraclinical Workup

34. Mammography |_____|: 1 = ACR 1; 2 = ACR 2; 3 = ACR 3; 4 = ACR 4; 5 = ACR 5; 6 = ACR 6; 7 = Not done

35. Ultrasound |_____|: 1 = BI-RADS 0 ; 2 = BI-RADS 1; 3 = BI-RADS 2; 4 = BI-RADS 3; 5 = BI-RADS 4; 6 = BI-RADS 5; 7 = BI-RADS 6; 8 = Not done

36. Nature of biopsy sent for pathological examination |_____|: 1 = Breast biopsy; 2 = Lumpectomy; 3 = Mastectomy; 4 = Lymph node dissection; 5 = 3 + 4; 6 = Cytopuncture

37. SBR Classification |_____|: 1 = Grade I 2 = Grade II 3 = Grade III

38. Guildford grading system ----- 1 = grade I 2 = grade II 3 = Grade III

39. Hormone receptors:

- Progesterone |_____|: 1) Present; 2) Absent; 3) Not done

-Estrogen |_____|: 1) Present; 2) Absent; 3) Not done

-Her-2 I-----I: 1) Positive; 2) negative; 3) Not done

-Ki67 |_____|: 1)]0 ; 14%]; 2)]14% ; 30%]; 3) [30% ; 100%]

40. Molecular Types: _____: 1 = luminal A; 2 = luminal B; 3 = Her-2; 4 = triple negative

41. Treatment |_____|:

1 = Chemotherapy 4 = Hormone therapy 7 = 2 + 3
 2 = surgery 5 = 1 + 2
 3 = Radiation therapy 6 = 1 + 2 + 3
If surgery, specify |_____ |: 1) Conservative; 2) Radical
If chemotherapy, specify |_____ | 1) neoadjuvant 2) adjuvant

F. Follow Up

42. 1-year follow up |_____ | A: 1) Complete remission; 2) Partial remission; 3) Progression; 4) Stationary; 5) Lost to follow-up (undetermined); 6) Death

43. Follow up at 2 years |_____ | A: 1) Complete remission; 2) Partial remission; 3) Progression; 4) Stationary; 5) Relapse; 6) Lost to follow-up (undetermined); 7) Death

44. Follow up at 3 years |_____ | A: 1) Complete remission; 2) Partial remission; 3) Progression; 4) Stationary; 5) Relapse; 6) Lost to follow-up (undetermined); 7) Death

45. Follow up at 4 years |_____ | A: 1) Complete remission; 2) Partial remission; 3) Progression; 4) Stationary; 5) Relapse; 6) Lost to follow-up (undetermined); 7) Death

46. Follow up at 5 years |_____ | A: 1) Complete remission; 2) Partial remission; 3) Progression; 4) Stationary; 5) Relapse; 6) Lost to follow-up (undetermined); 7) Death

Global Evolution

47. Death |_____ |: 1) Yes; 2) No; If deceased, date of death _____

48. Relapse |_____ |: 1) Yes; 2) No; If relapsed, date _____

49. Date patient was last seen |_____ |