



# Epidemiology, Diagnosis and Survival of Breast Cancer: Data from the Population-Based Cancer Registry of the City of Parakou from 2017 to 2021

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## Abstract

**Background:** Breast cancer mortality remains high in the majority of developing countries. The Ministry of Health has established two population-based cancer registries in Benin: the first one in Cotonou in 2014 and the second one in Parakou in 2017. However, there is a scarcity of data on breast cancer survival and prognosis in Benin Republic. **Objective:** This study sought to investigate epidemiological, diagnostic, and survival aspects of breast cancer in Parakou, based on data from its population-based cancer registry from 2017 to 2021. **Method:** For descriptive and analytical purposes, we used a retrospective cohort design. From January 24, 2022 to August 31, 2022, data were collected in all health facilities covered by the Parakou population-based cancer registry using an individual questionnaire. Survival and prognosis analysis were performed using KAPLAN MEIER method and David COX proportional hazard model respectively. **Result:** A total of 81 patients have been included in this study. The incidence rate of breast cancer in Parakou was 17.5 per 100,000 person-years with a mortality rate of 2.76 per 100,000 person-years. The median age at diagnosis was 44.50 years with extremes rang-

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ing from 19 to 76 years and a predominance of 40 - 50 years age group. The median survival time was estimated at 30 months with an overall 5-year survival of 47%. Young age at diagnosis (p-value = 0.002) and advanced stage at diagnosis (p-value = 0.000) had a negative impact on survival in women. The combination of surgery and chemotherapy improved survival (p-value = 0.018). **Conclusion:** Breast cancer is still a public health issue in Parakou. It comes out mandatory that resources be made available to make screening, early diagnosis and appropriate treatment of breast cancer affordable.

## Keywords

Breast Cancer, Survival, Cancer Registry, Parakou (Benin Republic)

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## 1. Introduction

Breast cancer is an anarchic cellular proliferation developed at the expense of breast constituents, escaping the laws of tissue homeostasis and triggered by a series of mutations affecting a cell and its clonal descendants [1]. It is a real public health issue worldwide. It is the most frequent cancer in women. According to GLOBOCAN 2020, there will be 2.3 million new cases and 685.000 deaths from breast cancer in women worldwide in 2020. In Africa, breast cancer is the most common cancer and the leading cause of cancer death in women with an estimated mortality rate of 12.1% [2]. In Benin, breast cancer constitutes 32.1% of all women cancers with a mortality rate of 12.1% [3]. Early detection combined with appropriate treatment is the persuasive strategy to allay breast cancer mortality [4]. There is a huge discrepancy between low- and high-income countries. Actually, the substantial challenge in Africa, and in Benin in particular, lies in the early diagnosis of breast cancer. Statistics show that 70% of these cancers are diagnosed at late stages, making the management a serious defiance [5]. Standardized guidelines for the management of breast cancer tailoring treatment to key characteristics of the tumor have been recommended by the National Comprehensive Cancer Network. These key characteristics primarily include stage at diagnosis, and expression of hormone and HER2 receptors. Based on these characteristics, curative treatment should involve a combination of surgery, radiotherapy, hormone therapy, chemotherapy and/or targeted therapy [6]. The Ministry of Health has established two population-based cancer registries in Benin: the Cotonou registry in 2014 and the Parakou registry in 2017. However, there is a scarcity of data on breast cancer survival and prognosis in Benin Republic. For this reason, we proposed to study the situation among women in the city of Parakou.

This study sought to investigate epidemiological, diagnostic, and survival aspects of breast cancer in Parakou, based on data from its population-based cancer registry from 2017 to 2021.

## 2. Method

For descriptive and analytical purposes, we used a retrospective cohort design.

From January 24, 2022 to August 31, 2022, data were collected in all health facilities covered by the Parakou population-based cancer registry using an individual questionnaire. This questionnaire has collected sociodemographic data (age at diagnosis, marital status, occupation, school level, age at menarche, contraception method, parity, age at first pregnancy, baby feeding option and menopausal status), clinical data (reason for medical consultation, the breast affected, the quadrant affected, stage at diagnosis), pathological data (histological type, SBR grade and molecular group), therapeutic data (treatment prior to admission in a specialized setting, conventional options received) and evolutionary data (date at death). Subjects were recruited over sixty (60) months from January 1, 2017 to December 31, 2021. Subject survival was observed over sixty-eight (68) months from January 1, 2017 to August 31, 2022. Entry date for each subject was the incidence date of breast cancer diagnosis. Last news date for each subject was the last call date for alive subjects and death date for deceased subjects. Vital status point date was set to August 31, 2022 for all subjects.

The study population consisted of women residing in Parakou, having consulted in any health facilities covered by the Parakou population-based cancer registry, who had been diagnosed with breast cancer, notified and registered in the registry. Included in this study were: subjects of any age; residing in Parakou for at least 6 months prior to the diagnosis date; diagnosed with a malignant breast tumor, regardless of the diagnosis evidence level (only clinical examination, imaging, cytopathology, and histopathology). Not included in this study were: cases whose medical records could not be located or were not retrievable; and cases of male breast malignancy. We made a nonprobability sampling with exhaustive recruitment of all cases meeting the inclusion criteria during the study period. Then 81 patients have been enrolled in this study. The dependent variable was breast cancer survival time. Survival time represents the time between the diagnosis date and the occurrence of an event. The event we looked for in this study was primarily death. The co-variables were sociodemographic, clinical, pathological, therapeutic and evolutionary variables. Two data collection techniques were used. The first technique was the scanning of patients' medical records. This technique consisted of identifying all patients diagnosed with breast cancer and enrolled in the population-based cancer registry of Parakou, regardless of the diagnosis evidence level. Then, in a second step, this consisted of visiting the health facilities where they had been diagnosed with the disease in order to collect data from their medical records. The second technique was the individual interview of the subjects or their parents. This technique consisted of calling the patients and/or their companions' through the phone number they provided in their records. The aim was to work towards the completion of the information necessary to reach the goal of this study. Data collection was supervised by the Registrar and the Director of the population-based cancer registry of Parakou. It was carried out by a doctoral student in general medicine.

Data analysis was performed with STATA version 16.1 (Stata Corporation, California, USA); and R version 4.2.1 (R foundation for statistical computing,

Vienna, Austria). For survival analysis, we used KAPLAN MEIER method [7]; and the comparison of distributions was performed with MANTEL-COX log-rank test [8], BRESLOW (Generalized Wilcoxon) test [9], and TARONE-WARE test [10]. For prognostic analysis, we implemented David COX proportional hazard model [11]. Variables with a p-value less than 10% in bivariate analysis were considered significant and included in multivariate analysis. In multivariate analysis, a preliminary model was obtained using a stepwise selection algorithm. Risk function graph and Log-Minus-Log graph were used to test proportional hazard assumption. The final model was presented as hazard ratio (HR), 95% confidence interval (CI), and p-value. For this analysis, we used a 5% significance level. Assessment of the model's overall significance and its power was performed based on appropriate parameters.

### 3. Result

#### 3.1. Epidemiological Aspects of Breast Cancer

The population-based cancer registry of Parakou has recorded a total of 81 breast cancer cases between 2017 and 2021. The incidence rate of breast cancer in Parakou city was 17.5 cases per 100,000 person-years with a mortality rate of 2.76 cases per 100,000 person-years. The median age at diagnosis was 44.50 years with extremes ranging from 19 to 76 years and a predominance of 40 to 50 age group. These women were illiterate in 58.02%, married in 82.72% and house-holdwives in 49.38% of cases. Most of them had had their menarche after the age of 12 (59.26%) and had not used any contraceptive method (82.72%). They were multiparous (4 - 5 pregnancies) in 34.57% and grand multiparous (6 or more pregnancies) in 28.40% of cases. They had had their first pregnancy before the age of 30 (79.01%) and had all breastfed their baby. These women were still in their reproductive period in 65.43% of cases (**Table 1**).

**Table 1.** Distribution of participants according to epidemiological characteristics (n = 81).

	Size	Percentage (%)
<b>Age group (years)</b>		
<20	1	1.23
[20 - 30]	6	7.41
[30 - 40]	16	19.75
[40 - 50]	30	37.04
[50 - 60]	19	23.4
>60	9	11.11
<b>Marital status</b>		
Married	67	82.72
Widowed	8	9.88
Single	4	4.94
Divorced	1	1.23
Unspecified	1	1.23

## Continued

<b>Occupation</b>		
Household wife	40	49.38
Shopkeeper	22	27.16
Craftswoman	10	12.35
Civil servant	5	6.17
Retired	3	3.70
Student	1	1.23
<b>School level</b>		
Illiterate	47	58.02
Primary school level	26	32.10
Secondary school level	5	6.17
University level	3	3.70
<b>Early menarche</b>		
Yes	7	8.64
No	48	59.26
Unknown	26	32.10
<b>Contraception method</b>		
No contraception	67	82.72
Oral	7	8.64
Injectable	3	3.70
Other*	4	4.94
<b>Parity</b>		
Nulliparous	4	4.94
Primiparous	6	7.41
Pauciparous	15	18.52
Multiparous	28	34.57
Grand multiparous	23	28.40
Unknown	5	6.17
<b>Age at first pregnancy</b>		
<30 ans	64	79.01
≥30 ans	4	4.94
Unknown	13	16.05
<b>Breastfeeding</b>		
Yes	81	100.00
No	0	0.00
<b>Menopause</b>		
Yes	26	32.10
No	53	65.43
Unknown	2	2.47

\*Other: jadelle contraceptive implant 02, Intra Uterine Device 02.

### 3.2. Diagnostic Aspects of Breast Cancer

Clinically, breast pain was the most frequent reason for medical consultation (62.96%). There was an equitable distribution between the right breast (49.38%) and the left breast (44.44%). The superior-external quadrant was the most affected (45.68%). The disease was mostly diagnosed at an advanced stage (Stage III: 81.47% and Stage IV: 7.41%). Histopathologically, invasive ductal carcinomas of non-specific type (70.45%), SBR grades II (29.55%) and III (31.82%), and triple-negative breast cancers (58.33%) were the most common (Table 2 and Table 3).

### 3.3. Therapeutic Aspects of Breast Cancer

In terms of treatment, more than half of the women in our series (55.56%) had received traditional treatment prior to their admission in a specialized care setting. Of the 81 women in our series, 32 (39.51%) had not received any conventional treatment for breast cancer. Of those who had received conventional treatment,

**Table 2.** Distribution of participants who received breast histopathological examination according to the outcomes (n = 44).

	Size	Percentage (%)
<b>Histological type</b>		
Invasive ductal carcinoma of the non-specific type	31	70.45
Squamous cell carcinoma	5	11.36
Invasive lobular carcinoma	2	4.55
Mucinous carcinoma	2	4.55
Other*	4	9.09
<b>SBR Grade</b>		
Grade I	3	6.82
Grade II	13	29.55
Grade III	14	31.82
Unspecified	14	31.82

\*Other: Medullary carcinoma 01, Sarcocarcinoma 01, Mixed (invasive ductal carcinoma and cribriform) 01, Lymphoma 01.

**Table 3.** Distribution of participants who received breast immunohistochemistry according to molecular groups (n = 12).

	Size	Percentage (%)
<b>Molecular group</b>		
Luminal A	2	16.67
Luminal B	1	8.33
Her 2	2	16.67
Triple-negative	7	58.33

47/49 (65.92%) had received surgery, 18/49 (36.73%) chemotherapy according to the protocol made of 4 FAC (5 Fluoro Uracil-Adriamycin-Cyclophosphamid) and Doxorubicin, 2/49 (4.08%) hormone therapy, 1/49 (2.04%) targeted therapy with Trastuzumab. None of them had received radiotherapy.

Mastectomy with lymphadenectomy was the most frequent surgical procedure (63.83%) and none of the patients had undergone breast reconstruction surgery (Table 4).

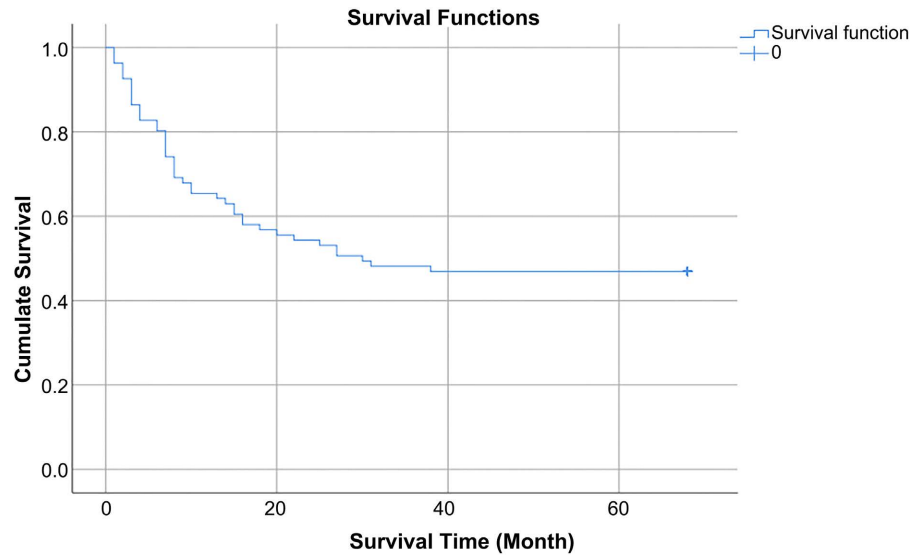
### 3.4. Breast Cancer Survival and Prognosis Analysis

The median survival was estimated at 30 months with an overall 5-year survival of 47% (Figure 1). The 5-year survival rate was 45% for the group treated at the Centre Hospitalier Universitaire et Départemental du Borgou-Alibori (CHUD-BA) and 59% for the Hôpital Saint Jean de Dieu de Tanguiéta (HSJDT) group (Figure 2). Comparison of distributions tests showed that this difference observed between the two groups was not significant (Table 5).

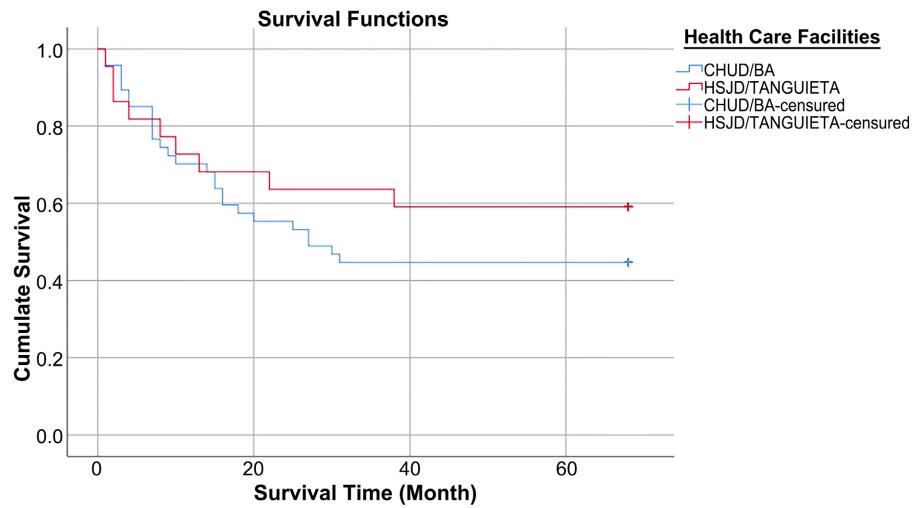
The prognosis analysis model reveals that the risk of death from breast cancer increased with: young age at diagnosis (p-value = 0.002), and advanced clinical TNM stage (p-value = 0.000). Indeed, the risk of death at a given time was 2.59 times higher in the 20 - 30 age group, compared with women aged over 60. In addition, women diagnosed with stage III and IV of the disease were 25.78 and 28.48 times more likely to die at any given time than those diagnosed with stage I disease. On the other hand, the combination of surgery and chemotherapy decreased the risk of death from breast cancer (p-value = 0.018). Actually, the risk

**Table 4.** Distribution of participants according to conventional treatment options (n = 49).

	Size	Percentage (%)
<b>Surgery</b>		
Yes	47	95.92
No	2	4.08
<b>Chemotherapy</b>		
Yes	18	36.73
No	31	63.27
<b>Hormone therapy</b>		
Yes	2	4.08
No	47	95.92
<b>Targeted Therapy</b>		
Yes	1	2.04
No	48	97.96
<b>Radiotherapy</b>		
Yes	0	0
No	49	100.00



**Figure 1.** KAPLAN MEIER curve—Participants probability of survival as a function of time (month).



**Figure 2.** KAPLAN MEIER curves—Probability of survival of CHUD-BA group and HSJD/T group as a function of time (month).

**Table 5.** Comparison of the two groups (CHUD-BA and HSJD/T) based on statistical tests.

Test	Chi-square	Degree of freedom	Significance
Log Rank (Mantel-Cox)	0.874	1	0.350
Breslow (Generalized Wilcoxon)	0.555	1	0.456
Tarone-Ware	0.713	1	0.398

of death was 1.66 times lower in those who received the combination of surgery and chemotherapy than in those who received no conventional treatment (**Table 6**). This model is overall significant (Prob > chi2 = 0.000) and explains only 26.6% of the occurrence of the death event (**Table 7**).



**Table 6.** Factors associated with breast cancer survival in bi- and multivariate analysis by Cox model.

	Bivariate analysis				Multivariate analysis			
	HR	95% IC	p-value	HR	95% IC	p-value		
<b>Age</b>								
≥60	Ref.	.	.	Ref.	.	.		
<20	1	.	.	-43.014	.	.		
20 - 30	1.000	0.112	8.947	0.069	2.595	0.926	4.264	0.002
30 - 40	0.300	0.054	1.669	0.299	-0.054	-1.34	1.232	0.934
40 - 50	0.438	0.092	2.083	0.926	-0.359	-1.539	0.822	0.551
50 - 60	1.083	0.2	5.872	.	-0.506	-1.72	0.708	0.414
<b>Clinical stage</b>								
Stage I	Ref.	.	.	.	Ref.	.	.	.
Stage II	0.950	0.1475	6.122	0.957	1.526	0.66	2.392	0.001
Stage III	6.450	1.822	22.827	0.004	25.785	23.652	27.918	0.000
Stage IV	6.856	0.7212	65.175	0.094	28.489	26	30.977	0.000
<b>Previous treatment</b>								
None	Ref.	.	.	.	Ref.	.	.	.
Medical	1.143	0.257	5.087	0.861	-0.212	-1.645	1.22	0.772
Traditional	5.061	1.702	15.047	0.004	0.304	-0.718	1.327	0.559
<b>Conventional treatment</b>								
No treatment	Ref.	.	.	.	Ref.	.	.	.
Only surgery	0.254	0.0867	0.7489	0.013	-0.532	-1.494	0.43	0.278
Surgery and Chemotherapy	0.125	0.0265	0.588	0.009	-1.66	-3.035	-0.285	0.018
Other*	0.333	0.0401	2.7687	0.309	-1.627	-3.465	0.211	0.083

Other\*: only chemotherapy, Surgery and hormone therapy, Surgery and chemotherapy and targeted therapy.

**Table 7.** Assessment of the model's overall significance and its power.

Prob > chi2	0.000
Pseudo r-squared	0.266

## 4. Discussion

### 4.1. Epidemiological Aspects of Breast Cancer

In our study, the incidence rate of breast cancer in Parakou city was 17.5 cases per 100,000 Person-Years. The French National Cancer Institute (INC) had reported in 2018 a high incidence rate of 100 cases per 100,000 Person-Years [12]. Even higher rates were reported by the Canadian Cancer Registry from 2013 to 2015 in the provinces of Newfoundland-Labrador and Prince Edward Island which were 135.6 cases per 100,000 Person-Years and 127.6 cases per 100,000 Person-Years, respectively [13]. There is considerable variation in breast cancer

incidence across regions. For some authors, this variation in incidence is linked to genetic factors and lifestyle, particularly the high-calorie diet in certain regions of the world [14]. It is important to emphasize aspects related to data collection on cancers from one region to another. Indeed, in some regions, the lack of a good quality population-based cancer registry is a factor of underestimation of cancer incidence [15]. Cancer incidence can also be influenced by factors such as screening policies and access to health care.

In our study, the median age at diagnosis was 44.5 years. This result is comparable to those reported by Kantelhardt *et al.* [16] in Ethiopia, Balekouzou *et al.* [17] in the Central African Republic and Lopes *et al.* [18] in Angola, which were respectively 43, 45.5 and 47 years. A higher median age at diagnosis of 63 years was reported by the French National Cancer Institute (INC) in 2018 [12]. In our study, the apogee of incidence was observed for the 40 to 50 age group. The same trends were also reported by Gnanngnon *et al.* [19] in southern Benin. Indeed, the peak incidence is observed beyond the age of 50 in developed countries [20]. It should therefore be noted that our patients are relatively younger than those in developed countries. Some studies attribute this to the shorter life expectancy observed in developing countries [21]. Others, however, claim that in addition to the already established risk factors for breast cancer, there are factors that may play a unique role in African women, such as: genetic factors, microbiomes, xenoestrogens, use of hair relaxers and skin lighteners [22]. We also believe that the use of antiperspirants, exposure to agrochemicals, stress and many other factors should be reviewed for a more likely hypothesis on the young age at diagnosis of breast cancer in Africa.

#### 4.2. Diagnostic Aspects of Breast Cancer

In our series, breast pain was the most frequent reason for consultation (62.96%). Another study has reported the discovery of a breast mass as the most common reason for consultation [23]. This can be explained by the fact that in the socio-cultural perception of the disease in Parakou, as long as a pain is not really annoying, it does not yet require recourse to health care professionals. A lump that does not cause pain does not therefore require medical attention.

According to El Fouhi *et al.* [24], breast cancer is usually unilateral and affects the left side slightly more often. In contrast to that, in our study, the distribution was almost evenly distributed between the right breast (49.38%) and the left breast (44.44%). Darré *et al.* [25] in TOGO reported the same results as ours with a proportion of 46.22% for the right breast and 44.89% for the left breast. In our study, the superior-external quadrant of the breast was the most affected (45.68%), followed by the retroareolar region (27.16%). The same findings were made by Ranaivomanana *et al.* [26] in Madagascar and El Fouhi *et al.* [24] in Morocco who found respectively 53.23% and 28.7% involvement of the supero-external quadrant. This topographical distribution could be explained by the fact that there is always a greater amount of glandular tissue in the central and supe-

ro-external part of the breast [24].

In our study, 88.88% of breast cancers were diagnosed with an advanced clinical stage (III and IV). The observation is the same in several other developing countries where 65% to 90% of breast cancers are seen in consultation at a late stage [18] [23] [26] [27] [28] [29] [30]. In developed countries, such as Australia and England, 55.9% and 56.8% of breast cancers are diagnosed at a localized stage respectively [31] [32]. Ben Fatma *et al.* [33] claim that, the late diagnosis of breast cancer in developing countries is mainly due to the delay in consultation observed in these countries. Some studies attribute this delay in consultation to illiteracy [34] and to women's reliance on traditional medicine and therapeutic practices related to religious beliefs as their first choice [35]. Indeed, more than half of the women in our series were illiterate (58.02%) and traditional treatment prior to admission was found in 55.56% of cases. Other studies attribute this delay in consultation to lack of awareness [36]. For some authors, the unavailability of screening and diagnostic tests in local health facilities, the long distance to referral centers, the long waiting time for diagnostic tests and the high cost of diagnostic services are to blame [35].

Of the 44 cases diagnosed histopathologically in our series, SBR grades II (29.55%) and III (31.82%) were predominant. Sahraoui *et al.* [37] in Algeria and Kohler *et al.* [38] in Malawi reported high frequencies of grade III SBR. These frequencies were respectively 41% and 49%. In fact, the majority of SBR grades II and III found in our study should be related to the fact that invasive ductal carcinomas of non-specific type were the most represented histological type with a frequency of 70.45%. In fact, invasive ductal carcinomas of non-specific type are frequently associated with undifferentiated high-grade cancers. Molecular groups have prognostic and predictive value for the management of breast cancers [39]. Of the 44 cases diagnosed histopathologically in our series, only 12 had been able to perform immunohistochemistry. That is to say a rate of 27.27%. This result is lower than the 55.3% reported by Guendouz *et al.* [40] in Algeria. This can be explained by the recent introduction of this type of workup in the diagnostic package in northern Benin. It is actually only available at the HSJDT. Of the 12 cases that benefited from immunohistochemistry in our series, the triple-negative subgroup was the most represented with a proportion of 58.33%. The same trend was reported by Aka *et al.* [41] in Côte d'Ivoire and Somé *et al.* [30] in Burkina Faso, who found triple-negative cancer rates of 43.28% and 52.9% respectively. While in Caucasian populations in both North Africa and the United States of America, triple negative cancer rates are lower [42]. Some authors believe that the high rates of triple-negative cancers reported in black women are related to lifestyle choices, particularly dietary habits [43]. Indeed, certain metabolic pathways and biomarkers have been shown to be aberrantly expressed in triple-negative breast cancer in black women [44]. Furthermore, several studies have demonstrated the association of triple-negative cancers with young age at diagnosis [45] [46]. This corroborates the results found in our se-

ries and by some African authors [19] [47]. According to other authors, the high rates of triple-negative cancers reported in developing countries could be due to deficiencies in the pre-analytical treatment of samples. In particular, they accuse the failure to respect cold ischemia times, the lack of fixation or tissue overfixation and the unavailability of quality assurance systems for reagents [48] [49].

### 4.3. Therapeutic Aspects of Breast Cancer

The curative treatment of breast cancer involves a variable combination of surgery, radiotherapy, hormone therapy, chemotherapy and/or targeted therapy [6]. In our series, 39.51% of patients had not received any of these treatment options. Foerster *et al.* [50] in 2019 reported a rate of untreated patients of 38% in a study conducted in two Nigerian regional hospitals; and 18% in the Ugandan national referral hospital. The same authors report a 0% untreated patient rate in Namibia. Cancer treatment is fully subsidized by the Namibian government [50], whereas it is not the case in countries such as Benin, Nigeria and Uganda, where the costs are borne by the patients. The cost of breast cancer management is huge. The majority of patients used traditional practitioners as their first line of treatment (as evidenced in our series), where they exhausted their financial reserves before seeking medical care. Our finding is also consistent with that reported by Joko-Frut *et al.* in 2021, in a multicountry study [51]. Actually, in their study, 50.9% received inadequate or no cancer directed therapy. This authors claim that the access to therapy differed by registry area. Initiation of adequate therapy and early-stage diagnosis were the most important determinants of survival in Sub-Saharan Africa.

The most frequent conventional treatment option in our series was surgical treatment. It is question of the radical Partey procedure with a performance rate of 63.83%. Similar result was reported by Essiben *et al.* [23] in Cameroon with a performance rate of 67.7%. Of the 42 patients who were eligible for chemotherapy in our series, only 18 were able to receive it. This represents a performance rate of 42.85%. This result is lower than those found by Essiben *et al.* [23] in 2013 and Mahjoub *et al.* [52] in 2019 which were respectively 69.2% and 93.97%. Our lower rate should be explained by the fact that a chemotherapy center was recently installed in northern Benin. This is the chemotherapy and ozone therapy section of the HSJDT. Despite the presence of this center, this treatment remains inaccessible to patients for financial reasons.

### 4.4. Breast Cancer Survival and Prognosis Analysis

In our study, the 5-year overall survival rate was 47%. Similar rates were reported by Gnanon *et al.* [53] in southern Benin, Zingué *et al.* [54] in Cameroon, and Galukande *et al.* [55] in Uganda, which were 40%, 43.3% and 51.8%, respectively. A lower rate of 22% was recently reported by Somé *et al.* [30] in Burkina Faso. Except Gnanon *et al.* study, these studies are actually hospital-based registry outcomes. Joko-Frut *et al.* in 2021, in a multicountry study imple-

mented based on data from population-based cancer registries in 10 sub-Saharan Africa (Benin, Congo, Côte d'Ivoire, Ethiopia, Kenya, Mali, Mozambique, Namibia, Uganda, and Zimbabwe), reported a 5-year survival rate of 47.2% (95% CI, 41.1% - 53.1%) [51]. Our survival rate is however much lower than those found in developed countries. Five-year survival rates in these countries are generally above 80%. Indeed, in high and middle income countries, expanded screening programs increasingly adapted to the risk level of each woman and early detection are being implemented to effectively fight breast cancer. In addition, clinical advances in cancer management in these countries over the past five decades have led to a significant improvement in breast cancer survival, particularly with the increasing use of targeted and personalized therapy techniques [56] [57] [58]. The reasons for the low survival rates reported in low-income countries are diverse and include, among others: the low socio-economic level, the unavailability of adequate technical facilities for early detection and appropriate treatment of cancers [59] [60]. The inadequacy of the health systems, and more specifically, the lack of priority for non-communicable diseases [61], should also be mentioned.

In our study, the risk of death from breast cancer increased with an advanced stage at diagnosis. Joko-Frut *et al.* study has evidenced poorest survival rates for patients with metastatic disease irrespective of the therapy received [51]. Our analysis has also evidenced that the risk of death was lower in patients who received the combination of surgery and chemotherapy than in those who received no conventional treatment. This finding is consistent with that reported by Joko-Frut *et al.* [51]. These authors have evidenced that patients with curable breast cancer who received adequate therapy had better overall survival compared with those who received inadequate or no therapy.

## 5. Study Bias

This study encountered some limitations. Indeed, the independence between the observed event (death) and all the censored subjects was not certain. In fact, all the subjects lost to follow-up were excluded alive from the cohort, while some of them had not attended any more medical consultation rendezvous and their contacts were unreachable because they would probably have died at home. The death date of subjects was not always known with accuracy. It was sometimes estimated based on the temporal clues provided by their parents about their death periods. On the other hand, the inclusion period of subjects covered almost the entire observation period of subject survival, so that the last subjects included were observed over a shorter period than the first. The subjects included in this study were judged with the "overall survival rate". This indicator ignores the actual attribution of deaths to breast cancer. According to the model's power parameter, the predictive factors identified explain 26.6% of the death occurrence. In other words, other factors remain to be identified and may not be among our co-variables. In spite of these biases encountered in this study, we believe that it

has good validity and could provide some avenues for action to improve the screening and management of breast cancer in women.

## 6. Conclusion

At the end of this survival study, it appears that breast cancer remains a real public health problem. In the city of Parakou, the incidence rate of breast cancer was 17.5 cases per 100,000 person-years with a mortality rate of 2.76 cases per 100,000 person-years. Young women in their reproductive period are the main victims. Access to diagnosis of certainty and adequate treatment remains difficult. The diagnosis is often made at an advanced stage where the prognosis is already vital. The median survival is estimated at 30 months with an overall survival at 5 years of 47%. Young age at diagnosis and advanced clinical stage are associated with poor survival. However, the combination of surgery and chemotherapy improves survival. It comes out mandatory that resources be made available to make screening, early diagnosis and appropriate treatment of breast cancer affordable.

## Ethical Considerations

This study was conducted in compliance with the legal provisions. The research proposal was submitted to the Local Ethics Committee for Biomedical Research (CLERB) of the University of Parakou, to the dean's office of the Faculty of Medicine of the University of Parakou, to the management staff of the population-based cancer registry of Parakou, and to the administrative authorities of the various health facilities covered by the population-based cancer registry of Parakou. It did not harm the participants. The need for informed consent was waived due to the retrospective nature of the study. However, verbal informed consent was obtained from alive participants or deceased participants' parents prior to the individual interview. In accordance with the legislative provisions in force (Articles L.1121-3 and R5121-13 of the Public Health Code), the persons having direct access to the source data took all the necessary precautions to ensure the confidentiality of the information related to the research. These persons, as well as the main investigator, are subject to professional secrecy.

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## Conflicts of Interest

The authors declare no conflicts of interest.

## References

- [1] Kalluri, R. and Zeisberg, M. (2006) Fibroblasts in Cancer. *Nature Reviews Cancer*, **6**, 392-401. <https://doi.org/10.1038/nrc1877>
- [2] Sung, H., *et al.* (2021) Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA: A Cancer Journal for Clinicians*, **71**, 209-249. <https://doi.org/10.3322/caac.21660>
- [3] Egue, M., *et al.* (2019) Cancer Incidence in Cotonou (Benin), 2014-2016: First Results from the Cancer Registry of Cotonou. *Cancer Epidemiology*, **59**, 46-50. <https://doi.org/10.1016/j.canep.2019.01.006>
- [4] Anderson, B.O., *et al.* (2008) Guideline Implementation for Breast Healthcare in Low-Income and Middle-Income Countries: Overview of the Breast Health Global Initiative Global Summit 2007. *Cancer*, **113**, 2221-2243. <https://doi.org/10.1002/cncr.23844>
- [5] Toure, M., *et al.* (2013) Factors Linked to Late Diagnosis in Breast Cancer in Sub-Saharan Africa: Case of Côte d'Ivoire. *Gynécologie, Obstétrique et Fertilité*, **41**, 696-700. <https://doi.org/10.1016/j.gyobfe.2013.08.019>
- [6] Carlson, R.W., *et al.* (2016) NCCN Framework for Resource Stratification: A Framework for Providing and Improving Global Quality Oncology Care. *Journal of the National Comprehensive Cancer Network*, **14**, 961-969. <https://doi.org/10.6004/jnccn.2016.0103>
- [7] Barker, C. (2009) The Mean, Median, and Confidence Intervals of the Kaplan-Meier Survival Estimate—Computations and Applications. *The American Statistician*, **63**, 78-80. <https://doi.org/10.1198/tast.2009.0015>
- [8] Somes, G.W. (1986) The Generalized Mantel-Haenszel Statistic. *The American Statistician*, **40**, 106-108. <https://doi.org/10.1080/00031305.1986.10475369>
- [9] Gehan, E.A. (1965) A Generalized Wilcoxon Test for Comparing Arbitrarily Singly-Censored Samples. *Biometrika*, **52**, 203. <https://doi.org/10.1093/biomet/52.1-2.203>
- [10] Tarone, R.E. and Ware, J. (1977) On Distribution-Free Tests for Equality of Survival Distributions. *Biometrika*, **64**, 156-160. <https://doi.org/10.1093/biomet/64.1.156>
- [11] Cox, D.R. (1972) Regression Models and Life-Tables. *Journal of the Royal Statistical Society: Series B (Methodological)*, **34**, 187-202.



- <https://doi.org/10.1111/j.2517-6161.1972.tb00899.x>
- [12] Institut National des Cancers (2022) Panorama des cancers en France. [https://www.e-cancer.fr/content/download/336357/4805630/file/01\\_brochure\\_Panorama-2022-V2-@.pdf](https://www.e-cancer.fr/content/download/336357/4805630/file/01_brochure_Panorama-2022-V2-@.pdf)
- [13] Statistics Canada (2015) Table 13-10-0109-01 Cancer Incidence, by Selected Sites of Cancer and Sex, Three-Year Average, Canada, Provinces, Territories and Health Regions (2015 Boundaries).
- [14] Wiseman, M. (2008) The Second World Cancer Research Fund/American Institute for Cancer Research Expert Report. Food, Nutrition, Physical Activity, and the Prevention of Cancer: A Global Perspective: Nutrition Society and BAPEN Medical Symposium on "Nutrition Support in Cancer Therapy". *Proceedings of the Nutrition Society*, **67**, 253-256. <https://doi.org/10.1017/S002966510800712X>
- [15] Thomas, A.S., *et al.* (2017) Breast Cancer in Ghana: Demonstrating the Need for Population-Based Cancer Registries in Low- and Middle-Income Countries. *Journal of Global Oncology*, **3**, 765-772. <https://doi.org/10.1200/JGO.2016.006098>
- [16] Kantelhardt, E.J., *et al.* (2014) Breast Cancer Survival in Ethiopia: A Cohort Study of 1,070 Women: Breast Cancer Survival in Ethiopia. *International Journal of Cancer*, **135**, 702-709. <https://doi.org/10.1002/ijc.28691>
- [17] Balekouzou, A., *et al.* (2018) Histo-Epidemiological Profile of Breast Cancers among Women in the Central African Republic: About 174 Cases. *BMC Cancer*, **18**, Article No. 387. <https://doi.org/10.1186/s12885-018-4256-2>
- [18] Lopes, L.V., *et al.* (2015) Stage at Presentation of Breast Cancer in Luanda, Angola—A Retrospective Study. *BMC Health Services Research*, **15**, Article No. 471. <https://doi.org/10.1186/s12913-015-1092-9>
- [19] Gnangnon, F., *et al.* (2020) Âge du diagnostic des cancers du sein en République du Bénin (Afrique de l'Ouest): Pouvons-nous encore appliquer les standards occidentaux en matière de dépistage? *Revue d'Épidémiologie et de Santé Publique*, **68**, S101. <https://doi.org/10.1016/j.respe.2020.03.027>
- [20] Merviel, P., *et al.* (2011) Existe-t-il encore des facteurs de risque de survenue d'un cancer du sein? *Gynécologie Obstétrique & Fertilité*, **39**, 486-490. <https://doi.org/10.1016/j.gyobfe.2010.10.015>
- [21] Ndamba, J.P., *et al.* (2015) Cancer du sein au Cameroun, profil histo-épidémiologique: À propos de 3044 cas. *The Pan African Medical Journal*, **21**, 2893-2917. <https://doi.org/10.11604/pamj.2015.21.242.7269>
- [22] Brinton, L.A., *et al.* (2014) Breast Cancer in Sub-Saharan Africa: Opportunities for Prevention. *Breast Cancer Research and Treatment*, **144**, 467-478. <https://doi.org/10.1007/s10549-014-2868-z>
- [23] Essiben, F., *et al.* (2013) Diagnosis and Treatment of Breast Cancer in Cameroon: A Series of 65 Cases. *Mali Medical*, **28**, 1-5. <https://doi.org/10.11604/pamj.2020.37.41.21336>
- [24] El Fouhi, M., *et al.* (2020) Profil épidémiologique et anatomopathologique du cancer de sein au CHU Ibn Rochd, Casablanca. *The Pan African Medical Journal*, **37**, Article No. 41.
- [25] Darré, *et al.* (2013) Profil histo-épidémiologique des cancers du sein. A propos de 450 cas observés au CHU de Lomé. *Médecine d'Afrique Noire*, **60**, 53-58.
- [26] Ranaivomanana, M., *et al.* (2021) Aspects épidémio-cliniques des cancers du sein au service d'oncologie de Fianarantsoa, Madagascar de 2011 à 2018. *The Pan African Medical Journal*, **38**, Article No. 264. <https://doi.org/10.11604/pamj.2021.38.264.20031>



- [27] Gnangnon, F., *et al.* (2021) Étude de la survie et des facteurs pronostiques du cancer du sein chez la femme dans deux hôpitaux de référence au Sud du Bénin. *Revue d'Épidémiologie et de Santé Publique*, **69**, S69-S70. <https://doi.org/10.1016/j.respe.2021.04.119>
- [28] Gebretsadik, A., *et al.* (2021) Epidemiological Trends of Breast Cancer in Southern Ethiopia: A Seven-Year Retrospective Review. *Cancer Control*, **28**. <https://doi.org/10.1177/10732748211055262>
- [29] Olaogun, J.G., *et al.* (2020) Socio-Demographic, Pattern of Presentation and Management Outcome of Breast Cancer in a Semi-Urban Tertiary Health Institution. *The Pan African Medical Journal*, **36**, Article No. 363. <https://doi.org/10.11604/pamj.2020.36.363.17866>
- [30] Somé, *et al.* (2022) Breast Cancer in Bobo-Dioulasso, Burkina Faso: Management Outcomes. *Oncologie*, **24**, 173-184. <https://doi.org/10.32604/oncologie.2022.021250>
- [31] Unger-Saldaña, K. (2014) Challenges to the Early Diagnosis and Treatment of Breast Cancer in Developing Countries. *WJCO*, **5**, 465. <https://doi.org/10.5306/wjco.v5.i3.465>
- [32] The ICBP Module 1 Working Group 20, *et al.* (2013) Breast Cancer Survival and Stage at Diagnosis in Australia, Canada, Denmark, Norway, Sweden and the UK, 2000-2007: A Population-Based Study. *British Journal of Cancer*, **108**, 1195-1208. <https://doi.org/10.1038/bjc.2013.6>
- [33] Ben Fatma, L., *et al.* (2018) What Could Be the Reasons of Late Diagnosis of Breast Cancer in Tunisia? *La Tunisie Médicale*, **96**, 665-671.
- [34] Agodirin, O., *et al.* (2021) Determinants of Delayed Presentation and Advanced-Stage Diagnosis of Breast Cancer in Africa: A Systematic Review and Meta-Analysis. *Asian Pacific Journal of Cancer Prevention*, **22**, 1007-1017. <https://doi.org/10.31557/APJCP.2021.22.4.1007>
- [35] Getachew, S., *et al.* (2020) Perceived Barriers to Early Diagnosis of Breast Cancer in South and Southwestern Ethiopia: A Qualitative Study. *BMC Women's Health*, **20**, Article No. 38. <https://doi.org/10.1186/s12905-020-00909-7>
- [36] McKenzie, F., *et al.* (2018) Drivers of Advanced Stage at Breast Cancer Diagnosis in the Multicountry African Breast Cancer—Disparities in Outcomes (ABC-DO) Study: Drivers of Advanced Stage at Breast Cancer Diagnosis. *International Journal of Cancer*, **142**, 1568-1579. <https://doi.org/10.1002/ijc.31187>
- [37] Sahraoui, G., *et al.* (2017) Profil anatomopathologique du cancer du sein dans le cap bon tunisien. *The Pan African Medical Journal*, **26**, Article No. 11. <https://doi.org/10.11604/pamj.2017.26.11.11382>
- [38] Kohler, R. (2015) Pathologically Confirmed Breast Cancer in Malawi: A Descriptive Study: Clinical Profile of Breast Cancer. *Malawi Medical Journal*, **27**, 10-12. <https://doi.org/10.4314/mmj.v27i1.3>
- [39] Ben Gobrane, H., *et al.* (2007) Breast Cancer Prognosis in Salah Azaiez Institute of Cancer, Tunis. *Eastern Mediterranean Health Journal*, **13**, 309-318.
- [40] Guendouz, *et al.* (2011) Cancer du sein de la femme de moins de 35 ans: Étude rétrospective à propos de 612 cas. *Société française de sénologie et de pathologie mammaire La Lettre du sénologue*, 52.
- [41] Aka, E., *et al.* (2021) Expérience africaine monocentrique de la prise en charge personnalisée des cancers du sein à Abidjan: Défis et perspectives. *Gynécologie Obstétrique Fertilité & Sénologie*, **49**, 684-690. <https://doi.org/10.1016/j.gofs.2021.03.001>

- [42] Newman, L.A. and Kaljee, L.M. (2017) Health Disparities and Triple-Negative Breast Cancer in African American Women: A Review. *JAMA Surgery*, **152**, 485-493. <https://doi.org/10.1001/jamasurg.2017.0005>
- [43] Sturtz, L.A., *et al.* (2014) Outcome Disparities in African American Women with Triple Negative Breast Cancer: A Comparison of Epidemiological and Molecular Factors between African American and Caucasian Women with Triple Negative Breast Cancer. *BMC Cancer*, **14**, Article No. 62. <https://doi.org/10.1186/1471-2407-14-62>
- [44] Dean, S.J.R. and Rhodes, A. (2014) Triple Negative Breast Cancer: The Role of Metabolic Pathways. *The Malaysian Journal of Pathology*, **36**, 155-162.
- [45] Raina, V. (2014) Triple-Negative Breast Cancer: An Institutional Analysis. *Indian Journal of Cancer*, **51**, 163-166. <https://doi.org/10.4103/0019-509X.138275>
- [46] Erić, I. (2018) Breast Cancer in Young Women: Pathologic and Immunohistochemical Features. *Acta Clinica Croatica*, **57**, 497-501. <https://doi.org/10.20471/acc.2018.57.03.13>
- [47] Zaki, H.M., *et al.* (2013) Profil épidémiologique et anatomopathologique du cancer du sein au Niger. *Journal Africain du Cancer*, **5**, 185-191. <https://doi.org/10.1007/s12558-013-0274-9>
- [48] Spruessel, A., *et al.* (2004) Tissue Ischemia Time Affects Gene and Protein Expression Patterns within Minutes Following Surgical Tumor Excision. *BioTechniques*, **36**, 1030-1037. <https://doi.org/10.2144/04366RR04>
- [49] Nielsen, T.O., *et al.* (2021) Assessment of Ki67 in Breast Cancer: Updated Recommendations from the International Ki67 in Breast Cancer Working Group. *JNCI: Journal of the National Cancer Institute*, **113**, 808-819. <https://doi.org/10.1093/jnci/djaa201>
- [50] Foerster, M., *et al.* (2019) Inequities in Breast Cancer Treatment in Sub-Saharan Africa: Findings from a Prospective Multi-Country Observational Study. *Breast Cancer Research*, **21**, Article No. 93. <https://doi.org/10.1186/s13058-019-1174-4>
- [51] Joko-Fru, W.Y., *et al.* (2021) Breast Cancer Diagnostics, Therapy, and Outcomes in Sub-Saharan Africa: A Population-Based Registry Study. *Journal of the National Comprehensive Cancer Network*, **19**, 75-85. <https://doi.org/10.6004/jnccn.2021.7011>
- [52] Mahjoub, N., *et al.* (2021) Epidemiological and Anatomopathological Profile of Breast Cancer in the Region of North-West of Tunisia. *La Tunisie Médicale*, **99**, 441-448.
- [53] Gnanon, F., *et al.* (2020) Profil épidémiologique, moléculaire et pronostic du cancer du sein au sud de la République du Bénin. *Revue d'Épidémiologie et de Santé Publique*, **68**, S138. <https://doi.org/10.1016/j.respe.2020.03.077>
- [54] Zingue, S., *et al.* (2021) Epidemiological and Clinical Profile, and Survival of Patients Followed for Breast Cancer between 2010 and 2015 at the Yaounde General Hospital, Cameroon. *The Pan African Medical Journal*, **39**, Article No. 182. <https://doi.org/10.11604/pamj.2021.39.182.26866>
- [55] Galukande, M., *et al.* (2015) Breast Cancer Survival Experiences at a Tertiary Hospital in Sub-Saharan Africa: A Cohort Study. *World Journal of Surgical Oncology*, **13**, 220. <https://doi.org/10.1186/s12957-015-0632-4>
- [56] Sledge, G.W. (2014) Past, Present, and Future Challenges in Breast Cancer Treatment. *JCO*, **32**, 1979-1986. <https://doi.org/10.1200/JCO.2014.55.4139>
- [57] Patel, T.A., *et al.* (2014) Dual HER2 Blockade: Preclinical and Clinical Data. *Breast*

- Cancer Research*, **16**, Article No. 419. <https://doi.org/10.1186/s13058-014-0419-5>
- [58] Criscitiello, C., *et al.* (2014) Immune Approaches to the Treatment of Breast Cancer, around the Corner? *Breast Cancer Research*, **16**, 204. <https://doi.org/10.1186/bcr3620>
- [59] Adesina, A., *et al.* (2013) Improvement of Pathology in Sub-Saharan Africa. *The Lancet Oncology*, **14**, e152-e157. [https://doi.org/10.1016/S1470-2045\(12\)70598-3](https://doi.org/10.1016/S1470-2045(12)70598-3)
- [60] Wadler, B.M., *et al.* (2011) Improving Breast Cancer Control via the Use of Community Health Workers in South Africa: A Critical Review. *Journal of Oncology*, **2011**, H382-H387. <https://doi.org/10.1155/2011/150423>
- [61] Morhason-Bello, I.O., *et al.* (2013) Challenges and Opportunities in Cancer Control in Africa: A Perspective from the African Organisation for Research and Training in Cancer. *The Lancet Oncology*, **14**, e142-e151. [https://doi.org/10.1016/S1470-2045\(12\)70482-5](https://doi.org/10.1016/S1470-2045(12)70482-5)