

Epidemiological, Diagnostic and Therapeutic Aspects of Locally Advanced and/or Metastatic Breast Cancers at the Chu-Mel of Cotonou

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How to cite this paper: Atade, S.R., Dangbemey, P., Klipezo, R., Adjagba, D., Togbenon, D.L., Salifou, K., Hounkpatin, B. and Denakpo, J.L. (2022) Epidemiological, Diagnostic and Therapeutic Aspects of Locally Advanced and/or Metastatic Breast Cancers at the Chu-Mel of Cotonou. *Advances in Breast Cancer Research*, 11, 195-205.

<https://doi.org/10.4236/abcr.2022.114016>

Received: August 5, 2022

Accepted: October 24, 2022

Published: October 27, 2022

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Abstract

Introduction: Breast cancer mortality remains high in most developing countries. Benin Republic does not yet have a technical platform required for the diagnosis and effective management of breast cancer “according to the recommendations”. **Objective:** To study the epidemiological, diagnostic and therapeutic aspects of locally advanced and/or metastatic breast cancers at the Centre Hospitalier Universitaire-de la Mère et de l’Enfant Lagune (CHU-MEL) of Cotonou from 2018 to 2021. **Study Methods:** This was a retrospective cross-sectional study with a descriptive purpose, carried out from January 1, 2018 to September 30, 2021 in the Gynaecology-Obstetrics Section of the CHU-MEL of Cotonou. The study population was patients diagnosed with locally advanced and/or metastatic breast cancers. **Results:** At the end of the study, 63 cases of locally advanced and/or metastatic breast cancer were recorded in 80 cases of breast cancer; a 74.11% prevalence of locally advanced and metastatic breast cancer. The mean age of the patients was 42.6 years. The main reason for consultation was the discovery of a mass in the breast (65.1%). Clinically, an orange peel was noted in 39.6%. Mammography (47.6%) and breast ultrasonography (42.9%) were the reference imaging workups for breast cancer diagnosis. Histopathologically, infiltrating ductal carcinoma (94.1%) was the predominant type with Scarff-Bloom and Richardson (SBR) grade II found in 35.3%. Progesterone and estrogen receptors were present in 42.9%. Mastectomy with axillary node dissection was the surgical treatment performed (80%) after neoadjuvant chemotherapy (39.6%). Only one patient had received radiotherapy. No patient received hormone therapy. **Conclusion:** Locally advanced and metastatic cancers remain a real public health

problem. It is essential that major investments be made in order to improve both their diagnosis and management.

Keywords

Cancer, Breast, Metastasis, Ultrasonography, Mammography

1. Introduction

Breast cancer is a public health problem. It is the most common cancer in women [1]. In 2020, there were 2.3 million women with breast cancer and 685,000 deaths from it worldwide [2].

In Africa, breast cancer is the most diagnosed cancer and the first cause of cancer death in women with an estimated mortality rate of 12.1% [3].

In Benin republic, the observation is the same; breast cancers represent 32.1% of all cancers in women with 12.1% of mortality related to this cancer [4].

The disparities between low and high income countries are considerable. Indeed, the five-year survival rate is over 90% in high-income countries and Africa has the highest mortality rate (12.1%) for breast cancer [2]. It was found in 2013 that the real problem of cancer in Africa is that 70% of diagnosed breast cancer cases are in late stages posing a real problem of therapeutic management [5]. From 2013 to date, is the finding the same? What is the epidemiology of these cancers at the Centre Hospitalier Universitaire de la Mère et de l'Enfant Lagune (CHU-MEL) in Cotonou, Benin Republic? How is the absolute diagnosis made and what are the therapeutic options offered to these patients? The objective of this study was to study the epidemiological, diagnostic and therapeutic aspects of locally advanced and metastatic breast cancers at Cotonou CHU-MEL from 2018 to 2021.

2. Patients and Method

The study was performed at the Centre Hospitalier et Universitaire de la Mère et de l'Enfant-Lagune de Cotonou (CHU-MEL Cotonou). It was a retrospective cross-sectional study with a descriptive purpose, covering all complete medical records of patients carried out from January 1, 2018 to September 30, 2021, in the gynecological and breast oncology section of CHU-MEL for locally advanced and/or metastatic breast cancers. The study population consisted of women who consulted the CHU-MEL for the treatment of a breast tumor. Women whose medical records showed a diagnosis of locally advanced breast cancer, with or without metastasis, were included in our study. Unusable medical records were excluded from the study. An exhaustive recruitment of the notified patients was carried out from the registers of the CHU-MEL of Cotonou. A survey form was used to collect data; these data were collected from the patients' medical records. The dependent variable of the study was the diagnosis of locally advanced breast

cancer. The independent variables were sociodemographic variables, patient history, breast cancer diagnosis variables, and breast cancer treatment variables. Data were entered using KoBoCollect, version 2021.2.4. Data were processed and analyzed using SPSS 26 software. No personal identity of the subjects surveyed was collected and the confidentiality of the personal data collected was respected. In order to do so, numerical characters were used as identification marks for our investigation forms.

3. Results

3.1. Frequence

During the study period, 7038 gynecological consultations were registered; among these we counted 85 cases of breast cancer, 63 of which were locally advanced and/or metastatic, *i.e.* 74.11%. Metastatic breast cancer represented 7.93% ($n = 5$) and locally advanced breast cancer represented 92.07% ($n = 58$).

3.2. Socio-Demographic Characteristics of Patients

The mean age at breast cancer diagnosis was 42.6 ± 15.3 years with extremes ranging from 16 to 75. The age group 40 to 50 was the most represented, *i.e.* 44.4% of the cases. The patients were illiterate (58.7%), shopkeepers (34.9%), married (65.1%) and lived in urban areas (88.89%) (**Table 1**).

3.3. Gynecological and Obstetrical History of Patients

- **Menarche**

The mean age of menarche was 14.6. More than half of the patients (62%) had had their menarche between the ages of 12 and 16. Those who had had their menarche before the age of 12 or after the age of 16 were respectively 5% and 33%.

- **Parity and Breastfeeding**

In the study, 17.5% were nulliparous (no pregnancy), 7.9% were primiparous (1 pregnancy), 41.3% were pauciparous (2 - 3 pregnancies), 20.6% were multiparous (4 - 5 pregnancies), and 12.7% were grand multiparous (6 or more pregnancies).

More than half (60.3%) of the patients had breastfed their baby and for more than 18 months in 63.2%.

- **Oral contraception**

Oral contraception consisting of hormonal pills was used in 14.3% of patients. The duration of use was more than 12 months for 66.7% of patients.

3.4. Medical and Surgical History

More than 2/3 of the patients had no medical (76.2%) or surgical (93.6%) history. High blood pressure and diabetes were the most common medical histories in the proportions of 19.0% and 3.2% respectively, while nodulectomy was found in 3.2% of patients.

Table 1. Distribution of patients with locally advanced and/or metastatic cancer at the CHU-MEL of Cotonou from 2018 to 2021 according to their sociodemographic characteristics.

	Size (n =)	Frequency (%)
Age (years)		
≤19	7	11.1
]19 - 30[	6	9.5
[30 - 40[	7	11.1
[40 - 50[	28	44.4
50 et plus	15	23.8
Provenance		
Urban area	56	88.89
Rural area	7	11.11
School level		
Illiterate	37	58.7
Secondary school	11	17.5
High school	15	23.8
Occupation		
Shopkeeper	22	34.9
Civil servant	18	28.6
Female worker/Craftswoman	13	20.6
Household wife	8	12.7
Secondary school student/High school student	2	3.2
Civil status		
Married	41	65.1
Unspecified	13	20.6
Single	7	11.1
widow	02	3.2

3.5. Diagnosis of Breast Cancer

3.5.1. Reason for Consultation

The main reasons for consultation were breast mass (n = 41; 65.1%), breast enlargement (n = 9; 14.3%), breast pain (n = 9; 14.3%). Patients referred for breast cancer represented 6.3% (n = 4).

3.5.2. General Condition

The general condition of the patients was good in 49.2% (n = 31), intermediary in 20.6% (n = 13) and impaired in 30.2% (n = 19).

3.5.3. Clinical Presentation

Clinically, 39.6% of the patients had an orange peel, 14.3% had skin ulcers, 14.3% had breast retraction, 4.8% had bloody breast discharge, and 1.6% had a flat spot. The tumor was uni-focal in all our patients. In 52.4% the tumor was located in the right breast and the Superolateral quadrant was most affected in 79.4%. The mean size of the tumor at the moment of diagnosis was 8.4 cm with extremes from 4 to 27 cm. It was adherent to the deep plane (100%) and the superficial plane (96.8%). All patients had axillary adenopathy. Troisier nodes were found in 17.5% of patients.

3.6. Workup

3.6.1. Biological Marker

The CA 15-3 marker level was carried out in 3.2% of patients and was high.

3.6.2. Radiological and Ultrasonographic Investigation

Mammography and ultrasonography were performed in 47.6% and 42.9%, respectively. More than half of the tumors were classified ACR 4 on both mammography and ultrasonography. The following **Table 2** shows the distribution of patients with locally advanced and/or metastatic cancer based on radiological and ultrasound scans.

3.7. Histopathology

Patients who had undergone a breast biopsy with histopathological workup were 27%. Biopsy specimens were classified as infiltrating ductal carcinoma (41.2%), infiltrating breast carcinoma (35.3%), infiltrating lobular carcinoma (17.6%) and ductal carcinoma *in situ* (17.6%). Regarding histoprognosis grade, only Scarff-Bloom and Richardson grading scale (SBR) was used. SBR2 was found in 35.3%, SBR 1 in 23.5% and SBR3 in 11.8%. For 29.4% of the biopsies, the histoprognosis grade was not specified.

Table 2. Distribution of patients with locally advanced and/or metastatic cancer at the CHU-MEL of Cotonou from 2018 to 2021 according to their radiological and ultrasonographic explorations.

	Ultrasonography		Mammography	
	Size	Percentage	Size	Percentage
Performance				
No	36	57.1	33	52.4
Yes	27	42.9	30	47.6
Classification				
ACR3	2	7.4	5	16.7
ACR4	16	59.3	18	60.0
ACR5	9	33.3	4	13.3
Unspecified	00	00	03	9.9

In addition, immunohistochemistry was performed in 11.88% of patients; 85% were estrogen receptor positive, 42.9% were progesterone receptor positive and 42.9% were both progesterone and estrogen receptor positive. From the immunohistochemical workup, 50% of the patients were classified as luminal A, and 16.7% as luminal B.

3.8. Extensional Workup

Abdomino-pelvic ultrasonography was performed in 3 patients (4.76%) and in only one of them was liver metastasis found. The thoraco-abdomino-pelvic scanning was performed in 8 patients (12.69%); 5 patients out of 8 had metastasis (2 cases of liver metastasis, 2 cases of lung metastasis, 1 case of liver and peritoneal metastasis).

3.9. Treatment

Surgical treatment was performed in 5 of the 63 patients with an achievement rate of 7.9%. Radical surgery, Patey's mastectomy, was performed in 80% and breast-conserving surgery in 20%. All patients who had undergone surgery had had their lymph nodes removed. Chemotherapy was performed in 8 of the 63 patients, for an achievement rate of 12.7%. It was neoadjuvant in all cases. The protocol based on doxorubicin and cyclophosphamide (AC60) was the most frequently administered in 6 of the 8 cases. Only one of the operated patients received radiotherapy (1.5%). Hormone therapy was indicated in 4 patients. These were patients classified as luminal A ($n = 3$) and luminal B ($n = 1$) but none of them could benefit from this treatment.

4. Discussion

In most African countries, breast cancer is diagnosed at an advanced stage. In our study, advanced stage breast cancers represented 74.11% of all breast cancers. Ranaivomanana *et al.* [6] reported 87% of cancers diagnosed at stage III and IV in Madagascar. The same is true in most developing countries where 30 to 80% of breast cancers are diagnosed at an advanced stage [7] [8] [9]. In developed countries, in contrast, breast cancer is diagnosed at an early stage [9]. In Australia (55.9%) and England (56.8%), more than half of all breast cancers are found at a localized stage [10]. According to Ben Fatma *et al.* [11], the explanatory factors for the delay observed at the moment of consultation in developing countries are the low level of schooling, rural origin, poor socio-economic conditions and the lack of encouragement from the patient's family. As traditional treatment is rooted in the socio-cultural habits of Benin, women refer much more to traditional therapists for breast pathologies as a first line of treatment. All this contributes to the delay at the early diagnosis of breast cancer. Ermiah *et al.* [12] emphasized the importance of the immediate reference to a medical attention, since a patient consulting within three months after feeling symptoms was associated with greater lymph node involvement and a high burden of lo-

cally advanced and metastatic stages. It is necessary to create and intensify breast cancer awareness campaigns in the different media platforms available; for example, by writing short messages on social media, or through awareness campaigns in health facilities and schools [13]. In addition, screening should be routine at all gynecological activities and in most health centers. This is how to reduce the delay in the early diagnosis of this cancer in an underdeveloped country like Benin.

Age is the best known risk factor for breast cancer; however, the incidence rate increases as age increases [2]. In our study, the mean age was 42.6 ± 15.3 with a predominance of cases between 40 and 50. Lokossou *et al.* [14] found in 2017 in Benin a mean age of 48 ± 12.06 for breast cancers. Gueye *et al.* [15] in Senegal reported an age between 35 and 45. In Ghana and Nigeria, the mean age found for breast cancers was 49.19 and 48 [8] [16]. In developed countries, a mean age of 62.3 to 63.3 has been reported [10]. The mean age of breast cancers is lower in developing countries than in developed countries. Some authors attribute this to the life expectancy which is much shorter in developed countries [6]. But dietary habits, sedentary lifestyle, obesity, smoking, exposure to plant protection products, stress and many other factors should be reviewed for a more likely hypothesis on the low mean age of breast cancers in Africa.

According to the literature, breast cancer is usually unilateral and slightly more often affects the left side; it rarely affects both breasts [17]. In contrast to this literature, 52.4% of the patients in our study had right-sided breast involvement. Several other authors have found the same results as ours: Mensah *et al.* [18] 50% right-sided involvement, Diop *et al.* [19] 62.5% right-sided involvement.

Regarding the most affected quadrant, in 79.4%, the superolateral quadrant was affected by the lesion. The same finding was made by Ranaivomanana *et al.* [6] in Madagascar and El Fouhi *et al.* [17] in Morocco where respectively in 53.23% and 28.7% the superolateral quadrant were affected by breast cancer [6] [17]. The usual site is the superolateral quadrant, the other quadrants are less often affected. This topography is explained by the amount of glandular tissue always more present in the central and superolateral part of the breast [17].

In our study, more than half of the patients were unable to perform breast ultrasonography or mammography. This was due to the fact that 58.7% of the patients were illiterate and did not realize the importance of carrying out these workups, which were nevertheless essential. Another aspect of the issue was the very low number of free breast cancer screening campaigns. Advocacy with the relevant authorities for monthly or quarterly breast cancer screening campaigns would help disadvantaged populations to access these services. Screening mammography and ultrasonography allow for earlier diagnosis and lower risk of death from breast cancer [19] [20]. In this sense, free breast cancer screening campaigns by mobile unit: the “mammobile” or “mammobus” would make it possible to reach an isolated female population, in rural areas, several kilometers from specialized radiology centers, but also in “marginalized” urban areas, in

order to guarantee equal access to screening [11].

Our study revealed a predominance of SBR grade II. The same grade was found by several other authors: 55.90% by El Fouhi *et al.* [17], 43.2% by Darré *et al.* [21]. The SBR grade II found in our study is related to the fact that infiltrating ductal carcinoma was the most common histological type found with a rate of 42.2%. In addition to being the most frequent, infiltrating ductal carcinoma is an aggressive tumor. Its aggressiveness is related to a high frequency of undifferentiated cancers (grade II and III) and to a greater tumor insensitivity to hormones (absence of estrogen receptors) [22].

After the diagnosis, extensional workup was required to determine the stage of the disease. The latter has therapeutic and prognostic value.

Unfortunately, due to the difficulty of access to certain imaging tests, in particular the thoraco-abdomino-pelvic CT scan, and due to the limited financial wherewithal of patients and their parents, very few of them manage to carry out these workups, especially when they know that the treatment will be just palliative. A similar observation was made in our study with only 5 (or 4.8%) of our patients having an abdominal ultrasonography and 8 (or 12.7%) having a thoraco-abdomino-pelvic scanning. Subsidizing these workups for patients with breast cancer could ease the burden on patients and their families.

Surgically, radical treatment using the Parthey technique was the only treatment performed in our study (80%). This was also found in the studies of Essiben *et al.* [23] in Cameroon (67.7%) and Yemba *et al.* [24] in Dakar (92.3%). Node dissection was associated with breast surgery in all the patients operated in our study. No patient benefited from the sentinel node technique. This technique, which has become widespread in many developed countries, has made it possible to avoid complete node dissection.

None of the patients in our series had undergone breast reconstruction because this type of surgery is not yet feasible in Cotonou. Lembrouck *et al.* [25] in 2016 reported high rates of breast reconstruction (47.6%). This breast reconstruction is only one aspect of oncoplastic surgery that is not very developed in our country.

Chemotherapy or targeted therapies aim at destroying micro-metastases, reducing the risk of recurrence and death. In our study, of the 25 patients in whom it was indicated, only 8 patients had undergone it, *i.e.* a performance rate of 32%. This result is lower than those found by Essiben *et al.* [23] which is 69.2% and by Mahjoub *et al.* [26] which is 93.97%. Most of the patients in our series did not have access to chemotherapy due to lack of financial wherewithal.

Radiotherapy reduces the absolute risk of locoregional recurrence by 15.7% and the absolute risk of mortality by 3.8% [27]. However, only one patient in our series was able to benefit from this treatment. This can be explained by the non-availability of radiotherapy in Benin Republic, which constrains patients to benefit from this therapeutic option abroad. In addition, the high costs of this treatment explain these low rates. The strengthening of the technical platform by the creation of a nuclear medicine and radiotherapy center in Benin republic

should contribute to the improvement of the accessibility of patients to radiotherapy while reducing the number of medical evacuations abroad [28].

5. Study Bias

It should be noted that this was a retrospective study and, like all such studies, it is limited by the fact that it uses medical records that are sometimes insufficiently informed. This limit means that some variables may sometimes be missing or that their level of collection does not allow a relevant exploitation. But this did not affect the quality of the results.

6. Conclusion

Breast cancers are discovered most of the time at an advanced stage at the CHU-MEL of Cotonou. Locally advanced and metastatic cancers remain a real public health problem. At the CHU-MEL, ultrasonography, mammography and histopathology are used to make the absolute diagnosis. Treatment by surgery, chemotherapy and hormonal therapy is possible but very few patients are able to afford it. Radiotherapy, on the other hand, is not possible on site. It is essential that major investments be made in order to improve both the diagnosis and the management of breast cancers.

Conflicts of Interest

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

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