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Metastatic Breast Cancer Survival in Pointe Noire: Analysis of 30 Cases

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Abstract

Introduction: Breast cancer is the leading cancer and the leading cause of cancer death in women worldwide. About 5% to 10% of breast cancer patients present with metastases. While the 5-year survival of patients with local breast cancer varies around 98.8%, this survival rate drops to around 26.3% for metastatic patients. The objective of this study was to determine the survival of patients with metastatic breast cancer in resource-limited settings. **Patients and Methods:** This was a cross-sectional descriptive study that took place in the Cancer Department of the General Hospital of Loandjili in Pointe Noire during the period from January 1, 2013 to December 31, 2018, for duration of 6 years. 30 records of patients over 18 years of age and with histological evidence who received at least 3 courses of chemotherapy were collected. The variables studied were: age, level of education, socio-economic level, menopausal status, history, WHO status, menopausal status, tumor size, histological type, tumor location, the type of treatment and survival. Survival was calculated by Kaplan Meier method. Fisher's exact test was used to search for correlation between variables. **Results:** The average age was 52.62 ± 10.96 years old. The extremes were 33 years and 75 years old. The most represented level of education was the primary level in 67% of cases. The majority of patients had low socioeconomic status in 50% of cases. The patients were menopausal in 57% of cases. The antecedents of cancer were present in 13% of cases. 50% of patients had a WHO status performance at 2. The tumor size was greater than 2 cm in 77% of cases. The most represented histological type was invasive ductal carcinoma in 93% of cases. The most represented histological grade was Scharff grade III Richardson bloom in 80% of cases. The

most represented metastatic localization was pulmonary in 33% of cases. The metastatic localizations were unique in 47% of cases and multiple in 53% of cases. Anthracycline-based chemotherapy was more used in 53% of cases. Bivariate analysis revealed a correlation between tumor size and number of metastases, $p < 0.05$. The mean patient follow-up time was 22 ± 15.45 months. The median overall survival was 35.35 months. Brain metastases (18.2 months) had a poor prognosis compared to liver metastases (25.4 months). The median survival of pulmonary metastases was 36.5 months, $p > 0.05$. Patients treated with anthracyclines were greater than that of patients treated with taxanes in combination was 26.48 months, $p > 0.05$. **Conclusion:** Metastatic breast cancer remains an incurable disease, its survival remains low despite diagnostic and therapeutic advances that remain difficult to access for our resource-poor developing countries. Patients are treated with conventional chemotherapy (anthracyclines and taxanes). The most common metastases are respectively pulmonary, hepatic and cerebral in our context.

Keywords

Breast Cancer, Metastatic, Survival, Pointe Noire, Congo

1. Introduction

Breast cancer is the leading cancer and the leading cause of cancer death in women worldwide [1] [2]. This condition was diagnosed in women at a frequency of 24.2% and was responsible for nearly 15% of deaths in 2018 [2]. This cancer is also the first diagnosed and the leading cause of cancer deaths in women in developing countries [1]. In these resource-limited settings, breast cancer is often diagnosed at advanced stages and is responsible for poor prognosis [3]. The last two decades have seen major advances in screening, biomolecular diagnosis and therapeutic breast cancer. Despite these advances, metastatic breast cancer remains an incurable disease, therefore the ultimate goal is to prolong overall survival and improve quality of life [4]. Breast cancer can invade the liver, lungs, bones, the brain, the skin and other organs [5] [6] [7]. The metastatic breast cancer is divided in two, on the one hand the primary metastatic cancer known as Novo or synchronous, whose diagnosis of metastasis is made same time as the primary tumor, on the other hand there is secondary metastatic breast cancer or metachronous whose diagnosis of metastasis is made months or years after the diagnosis of the primary tumor [8] [9] [10]. About 5% to 10% of breast cancer patients present with de novo metastases [4] [11] [12] [13]. However, 20% to 50% of breast cancer patients have secondary or metachronous metastases [14] [15]. While the 5-year survival of patients with local breast cancer varies around 98.8%, this survival rate drops to around 26.3% for metastatic patients. In Congo, few studies have been done on the subject. Thus our study aimed to determine the survival of patients with metastatic breast cancer in resource-limited settings.

2. Patients and Methods

This was a cross-sectional descriptive study that took place in the Cancer Department of the General Hospital of Loandjili in Pointe Noire during the period from January 1, 2013 to December 31, 2018, for duration of 6 years. Have been included in our study: all patients over 18 years old; all patients with a complete file that is to say with a histological diagnosis and an extension assessment performed through an abdominal chest CT scan and/or an ultrasound or chest x-ray; all patients diagnosed with primary or de novo breast cancer (synchronous) and secondary or metachronous breast cancer; all patients who received at least 3 courses of chemotherapy [chemotherapy was based on anthracyclines (FAC protocol = 5 fluorouracil, dose 500 mg/m^2, doxorubicin 50 mg/m^2 cyclophosphamide 500 mg/m^2) and taxanes (docetaxel protocol dose 100 mg/m^2)]; all patients with no histological diagnosis were excluded from our study; all men with breast cancer. The variables studied were: Sociodemographic parameters: age, level of education, socio-economic level; Clinical parameters: WHO status performance, menopausal status, tumor size, number of lymph node involvement, metastatic localization of metastasis, number of metastases; Histological type and histological grade; The type of treatment; The survival. The data collection was done from a survey sheet, comprising the different variables studied.

Bivariate analysis was done between size and number of metastasis. The data entry was made from the Excel version 2016 software. Qualitative variables were represented in numbers and percentages. Quantitative variables were represented in numbers and on average. Statistical analysis and data processing were performed by the Excel 2016 software and graphpad Prism version 7 software. The statistical test used was Fisher's exact test for finding correlation between variables. Survival was calculated by Kaplan Meier method. The initial date was the date of diagnosis of metastasis; the point date was the end date of the study. The final event was the occurrence of death. Patients were followed throughout the study period, from January 1, 2013 to December 31, 2018, for a period of 6 years. The comparison of the curves was made by the logrank test. The results were statistically significant for $p < 5\%$.

3. Results

At the end of our study, 30 files of metastatic breast cancer patients fulfilling the criteria of inclusions were collected. The average age was 52.62 ± 10.96 years old. The extremes were 33 years and 75 years old. The most represented age group was the age group from 53 to 62 in 33%, followed by the age group from 43 to 52 (Table 1). The highest level of education was the primary level in 67% of cases followed by the higher level of education in 20% and the secondary level in 13% of cases (Table 2). The majority of patients had a low socio-economic level in 50% of cases; the intermediate socio-economic level and higher were represented in 37% and 17% of cases respectively (Table 3). Patients were menopausal status in 57% of cases (Table 4). We found a history of cancer in 13% of cases (Table 5).

50% of patients had a WHO status performance of 2; 40% of patients had a

performance at 1, 7% of patients had at 0 and 3% of patients had at 1 (Table 6). Tumor size was greater than 2 cm in 77% of cases and was less than 2 cm in 23% of cases (Table 7). The patients had respectively two nodes invaded in 53% of cases and 3 nodes in 27% of cases (Table 8). The most represented histological type was invasive ductal carcinoma in 87% of cases, lobular carcinoma in 10% of cases and a 3% breast sarcoma (Figure 1). The most represented histological grade was grade III of Scharff bloom Richardson in 80% of cases followed respectively by grade II and grade I with respective percentages of 10% and 5%. Metastatic localization the most represented was that of the lungs in 33% of cases (Table 9). The metastatic localization was unique in 47% of cases and multiple in 53% of cases (Table 10). The most widely used chemotherapies were chemotherapy-based anthracyclines in 53% and taxan-based chemotherapy alone or in combination with anthracyclines in 34% of cases. Only one patient had received targeted therapy (Table 11). Bivariate analysis found a correlation between tumor size and number of metastases, the result was statistically significant (Table 12). The mean patient follow-up time was 22 ± 15.45 months. The median overall survival was 35.35 months (Figure 2). The median survival of patients with lung, liver and brain metastases, with the lungs and liver (lungs + liver) associated with the lungs and lymph nodes (lungs + lymph nodes), was respectively 36.5 months, 25.4 months, 18.26 months, 24.3 months, 37.5 months. There was no statistically significant difference (Figure 3). The survival of patients treated with anthracyclines was 36.35 months that of Patients treated with Texan was 26.48 months, the result was not statistically significant (Figure 4).

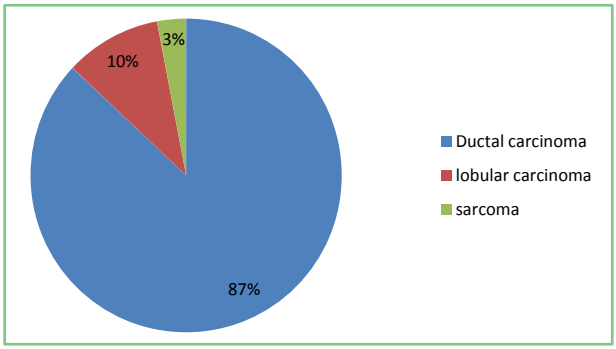

Figure 1. Distribution of patients by histological type.

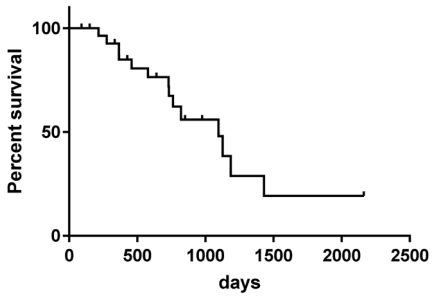

Figure 2. Representation of the survival curve of patients with metastatic breast cancer.

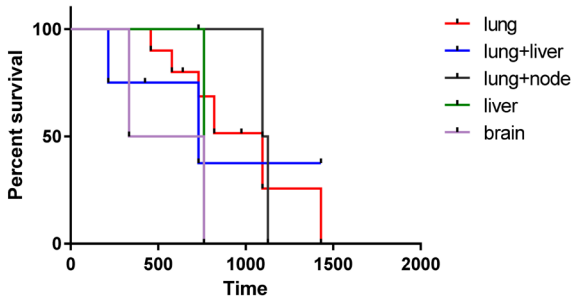

Figure 3. Comparison of survival curves versus metastatic localization. P > 0.05 statistically insignificant.

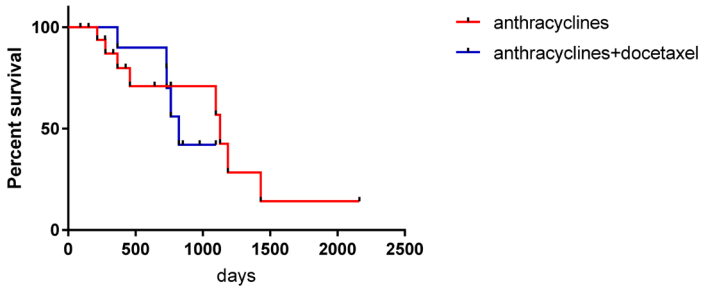

Figure 4. Comparison of survival curves by type of treatment. P > 0.05 non significant results.

Table 1. Distribution of patients according to group age.

Group age	Number	Percentage
33 - 42	5	17%
43 - 52	9	30%
53 - 62	10	33%
63 - 72	4	13%
73 - 82	2	7%
Total	30	100%

Table 2. Distribition of patients according to study level.

Study level	Number	Percentage
Primairy	20	67%
Secondary	4	13%
Superior	6	20%
Total	30	100%

Table 3. Distribution of patients according to socioeconomic level.

Socioeconomic level	Number	Percentage
Low	15	50%
High	11	37%
Intermediate	4	13%
Total	30	100%

Table 4. Distribution of patients according to menopausal status.

Menopausal status	Number	Percentage
No	13	43%
yes	17	57%
Total	30	100%

Table 5. Distribution of patients according to cancer histoty.

Cancer history	Number	Percentage
No	26	87%
yes	4	13%
Total	30	100%

Table 6. Distribution of patients according to performance status of WHO.

Performance status	Number	Percentage
0	2	7%
1	12	40%
2	15	50%
3	1	3%
Total	30	100%

Table 7. Distribution of patients according to tumor size.

Tumor size	Number	Percentage
<2 cm	7	23%
>2 cm	23	77%
Total	30	100%

Table 8. Distribution of patients according to the number of invade nodes.

Nodes number	Effective	Percentage
0	2	7%
1	4	13%
2	16	53%
3	8	27%
Total	30	100%

Table 9. Distribution of patients according to metastatic localization.

Metastatic localization	Number	Percentage
bone + foie	2	7%
brain	2	7%
liver	2	7%
lung	10	33%
lung + node + rachis	3	10%
lung + liver	5	17%
lung + nodes	2	7%
Lung + bone + liver	4	13%
Total	**30**	**100%**

Table 10. Distribution of patients according to number of metastases.

Metastases number	Number	Percentage
Multiple	16	53%
Unique	14	47%
Total	30	100%

Table 11. Distribution of patients according to treatment.

Chemotherapy type	Number	Percentage
Fac	17	53%
fac + taxotere	11	34%
taxotere	2	6%
taxotere + avastin	1	3%
capecitabine	1	3%
Total	32	100%

Table 12. Distribution of patients according to tumor size and number of metastases

	Metastases Number		
Tumor Size	**Unique**	**Multiple**	**Total**
<2 cm	6	1	7
>2 cm	8	15	23
Total	14	16	30

$P < 0.05$ results statistically significant.

The histological grade most represented was grade III of Scharff bloom Richardson in 80% of cases followed respectively by grade II and grade I with respective percentages of 10% and 5%.

4. Discussion

At the end of our study, which took place in the Oncology Department of Loandjili General Hospital in Pointe Noire, we collected 30 cases of women with metastatic breast cancer who met the inclusion criteria of our study. The mean age in our study was 52.62 ± 10.96 years with extremes of 33 years and 75 years. This average age and these extremes are close to those found in the literature [7] [16]. In contrast to the relatively young average age in our study, other studies have found a mean age of 61 years [5] [8]. The most represented age group in our study was the 53-year-old angel slice at age 62 in 33% of cases. These results are in agreement with the literature which explains the presence of metastases during breast cancer, because of the age, the menopause would be a factor favoring the occurrence of metastases as we can observe in our study, that the majority of patients were menopausal in 57% of cases. [16] [17]. The majority of patients in our study had a primary education level in 67% of cases. In the literature the level of study was higher. Although there is no cancer control program that should facilitate access to information on cancer disease but also screening, the level of primary education is a factor contributing to the lack of knowledge about cancer. The cancerous disease, thus allows time for it to spread in several organs. In the Guié *et al.* study in Côte d'Ivoire, only 21% of women over 50 had benefited from breast cancer screening [18]. The socioeconomic level was low in our study and in the majority of African studies since developing countries are poor in the majority of cases [7] [18] [19]. In Africa the management of the cancerous disease is excessively excessive and is the responsibility of the patient and/or the family of the patient, in addition there is no health insurance, the whole making difficult the accessibility specialty services of the disease. The patients were menopausal in the majority (57%) of cases in our study. One study also reports this predominance of postmenopausal women in 77.6% of cases [6]. The antecedents of breast cancer reported in 13% of patients in our study were similar to those of Athanasios kotsakis *et al.* in Greece [6]. The most represented WHO status performance was 0 to 2 in the majority of cases. This result is consistent with the literature [6]. Patients with a tumor size greater than 2 cm, ganglion number greater than two, histological grade III, were the most represented in 77% of cases, 60% of cases and 60% of cases in our study respectively. These results corroborate those of the literature [5] [18] [20]. Tumor size is a prognostic factor for breast cancers also associated with lymph node involvement and histological grade. As all these prognostic factors increase, the risk of metastases is high [12]. Approximately 25% to 30% of patients without lymph node involvement and tumor size greater than 2 cm will develop recurrence in 20 years [21]. Only 2% of patients with a tumor size of less than 1 cm die within 5 years of diagnosis [22]. The number of lymph nodes affected has been correlated with metastatic risk in the literature [23]. Although they are determining factors for the local treatment of breast cancer, these prognostic factors are also determinants for the initiation of adjuvant or complementary treatment. The most represented histological type was invasive ductal carcinoma

in 87% of cases. This result corroborates to the literature [5] [18] [24] [25]. The risk of developing metastases according to the histological type is practically the same, which explains the same treatment between invasive ductal carcinoma and invasive lobular carcinoma [12]. In our study, visceral metastases were most represented by pulmonary metastases in 30% of cases and hepatic metastases in 10% of cases. Bone metastases were represented in association with other metastases in two cases. These results do not corroborate with those of some authors of the literature. Indeed several authors have described the predominance of bone metastases in their series [5] [7] [20], this could probably be explained by an underestimation of bone metastases due to the lack of other balance sheet examinations, such as bone scans and pet scan that are not available in our limited resource context. On the other hand, one study reported the same pulmonary prevalence as in our study [25]. The multiple metastases were the most represented in our study contrary to the literature that reported predominance. Metastatic breast cancer is incurable, under these conditions the goal of treatment is the improvement of the quality of life and the prolongation of survival. Nowadays the advent of targeted therapies and immunotherapy combined with conventional chemotherapy has helped to achieve the goal of these treatments that of improving the quality of life and prolonging survival. Thus, in our study, patients received anthracycline chemotherapy in 53% of cases, continuously or sequentially associated with taxanes in 34% of cases. These results corroborate those of the literature [5] [20] [25]. The absence of health insurance, the high cost of targeted therapies was a limiting factor in the use of these, so only one patient was able to benefit from targeted therapies. The absence of immunohistochemistry for the detection of hormone receptors made it impossible to use hormonal treatment. In our study we observed a positive correlation between tumor size and number of metastases. The number of metastases increased with tumor size. Size is a prognostic factor for breast cancer.

Although small in size with a sample of 30 patients representing approximately the female population of Pointe Noire suffering from cancer and being a hospital study, our study suffered from a few limitations. Indeed in terms of survival, several studies were based on bimolecular characteristics that could not be realized in our context of resource-limited countries. It was the hormonal status, the expression of the Her 2 receptor, which have been necessary elements for the establishment of survival comparisons, especially as they are prognostic and predictive factors apart from other factors such as the performance status of WHO. The hormonal status and expression of Her 2 receptors are still widely used in the therapeutic decision of breast cancer [26] [27] [28] [29]. Our study was based on the median of overall survival, the median survival of patients according to metastatic localization (lungs, liver, lungs + liver, lungs + node and brain). Thus, the median of overall survival in our study was 35.35 months. These results corroborate those in the literature [5] [25]. The median overall survival of patients with metastases to the lungs, liver, lungs + liver, lungs + ganglion, brain in our study were respectively 27.4 months, 25.4 months, 23.3 months,

36.5 months, 18.2 months.

Brain metastases were those with the lowest median survival. Indeed, brain metastases are difficult to access to cytotoxic treatments because of the blood-brain barrier that prevents the passage of anticancer drugs. Moreover, no patient has been able to benefit from a specific local treatment (surgery and radiotherapy). The liver is a common site of metastasis of breast cancer, with bone and lung [30] [31] [32]. Liver metastases in breast cancer patients are a prognostic factor independent of other risk factors [15] [33], since the median survival of patients with breast cancer with hepatic metastasis varies from 4.8 to 15 months [34] [35] [36] [37] [38]. In contrast, breast cancer patients with lung or bone metastases have median survival rates of 9 to 27.4 months [37] [38] and 16.3 to 56 months [37] [39] [40], respectively. The survival of breast cancer patients with cerebral metastases was estimated in the literature between 4 and 16 months [41] [42] [43] [44]. This rate is close to that of our study which was 18.6 months. The median overall survival of anthracycline-treated patients was 36.35 months, while that of taxane and anthracycline-treated patients was 26.48 months. These results were statistically insignificant. In the literature, associations with texanes are superior to those without taxanes [45].

5. Conclusion

Metastatic breast cancer remains an incurable disease, the goal of its treatment is to prolong survival and improve quality of life. Despite the limitations of our study, the survival of patients with metastatic breast cancer remains low. The various advances in diagnosis and therapeutics of recent years are currently difficult to access in developing countries with limited resources. Anthracycline-based chemotherapy remains the basis of treatment. The most frequent metastatic sites are pulmonary, hepatic and cerebral. However, studies with a larger sample are needed to support its observations in our context with limited resources.

Conflicts of Interest

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

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