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Prognosis of Breast Cancer Patients Underwent Surgery in a Developing Country

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Abstract

Background: We aim to review different factors associated with the relapse and the mortality in breast cancer patients in restricted-resource settings over a five-year period. **Method:** A retrospective cohort study including 133 women underwent breast cancer surgery was performed at the Surgical Oncology Unit of the Conakry University Hospital in Guinea. Socio-demographical characteristics, clinical information, treatment and data on relapse and survival were retrieved from medical files. Predictor factors of relapse were analyzed by using univariate and multivariate logistic regression. Factors associated with mortality were analyzed by Kaplan Meier survival and Cox models. **Results:** Breast cancer surgery was conservative in 13 cases (9.8%) and radical in 120 cases (90.2%). Five-year relapse was 33.8% ± 8.0% and the predictor factors of this relapse were age and stage III ($p = 0.005$). The overall 5-year mortality was 42.1% and the risk factors independently associated with death were body mass index ($p = 0.01$), origin of patients ($p = 0.02$), radiotherapy ($p = 0.01$) and cancer relapse ($p = 0.001$). **Conclusion:** The proportions of relapse and death were higher in breast cancer patients. The age and the stage of cancer at the time of surgery were the predictor factors of relapse. Body mass index, origin of patients, radiotherapy and cancer relapse were associated with death.

Keywords

Breast Cancer, Breast Surgery, Prognosis, Developing Countries

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1. Introduction

Cancer is recognized as a critical public health problem in Africa. While communicable diseases continue to burden African populations, it is becoming clear that non-communicable diseases also require the attention of health professionals.

Breast cancer is a major cause of morbidity and can reach high mortality among women. The incidence of this cancer has been progressively increasing worldwide. The number of new cases is estimated at 1.82 million in each year worldwide [1].

In Sub-Saharan Africa, the incidence of breast cancer ranged from 15 to 53 per 100,000 women, which are lower than those in industrialized countries [2]. However, the cancer burden reported for sub-Saharan Africa may be underestimated due to the lack or insufficient awareness, a lack of appropriate diagnosis, poor access to care, limitations in the technical workforce and infrastructure, and low quality of cancer data systems compared to those in high resource countries [3] [4]. In Guinea, the incidence of breast cancer is estimated at 14.5 new cases per 100,000 [5] and breast cancer accounts for over 26% of all cancers at our surgical oncology unit [6].

In developed countries, breast cancer is frequently diagnosed at an early stage allowing conservative treatment and reducing mortality due to this disease. In countries with limited resources, locally advanced breast cancer is still common and has poor prognosis [2] [7] [8]. In sub-Saharan Africa, data on survival of breast cancer patients are limited [9].

Recent advances in the diagnosis (molecular subtypes) and treatment (targeted therapy), allowing to individualize breast cancer treatment, are still poorly available in developing countries [10].

In the present study, we aimed to analyze the predictive factors of relapse and other events that are associated with five-year survival after breast cancer surgery in our restricted-resource settings.

2. Materiel and Methods

2.1. Setting

The study was conducted in the surgical oncology unit of the University Hospital of Conakry, Guinea.

2.2. Study Design and Population

This was a retrospective cohort study on 133 patients with histologically confirmed breast cancer from 2005 to 2012. These patients underwent surgical operation and were followed from November 2005 to February 2014.

2.3. Data Collection

For each patient, data were collected from the date of cancer diagnosis until the end of the follow up, *i.e.* 60 months after surgery. Data included socio-demographical information (age at cancer diagnosis, marital status, profession, residence area) and anthropometric characteristics (body mass index) source of referral (home, hospital), co-morbidities, cancer characteristics (date of diagnosis, pathological statute, molecular subtypes, location of primary cancer, stage), date and type of surgery, other cancer treatment (radiotherapy, chemotherapy). For cancers diagnosed before 2010, the stage at diagnosis was revised according to the TNM classification of the UICC 2010 [10] at the early (stage I-II) and late stage (stage III).

2.4. Surgical Treatment Procedures

Surgical treatment was dependent on the stage at diagnosis. For the breast cancer in the stage I, breast-conserving surgery (BCS) was performed. In stage II, neoadjuvant chemotherapy (NAC) was administrated before BCS or radical breast surgery (RBS). In stage III, RBS was performed after NAC. The RBS applied was a modified Patey's method. NAC was based on a protocol comprising anthracyclines and/or taxanes. After surgery, adjuvant chemotherapy was administered. There is no radiotherapy in our country and patients are referred to the Institute of Cancer Dakar (Senegal) for this. Adjuvant hormonal therapy (tamoxifen) was also prescribed for menopausal women and/or with positive hormone receptors.

2.5. Statistical Analysis

Patients were stratified into two groups: patients experiencing relapse and patients without relapse. Categorical

variables were shown as the frequency and percentage (%), and continuous variables were presented as the median and interquartile range (IQR). Frequency distributions between categorical variables were compared using χ^2 test or Fisher's exact test while continuous variables were compared using the Mann-Whitney test. A multivariable Cox proportional hazards model was used to estimate the Hazard Ratio (HR) and its corresponding 95% confidence interval (CI). Survival distributions were analyzed using the Kaplan-Meier method. For all tests performed, 2-tailed *P* values < 0.05 were regarded as denoting statistical significance. Statistical data were analyzed with statistical package for the social sciences (version 21.0 for Windows, SPSS, Inc., Chicago, IL).

2.6. Ethical Considerations

In this retrospective study, data were collected anonymously and confidentially. Patients signed the consent form for the use of data contained in their records.

3. Results

3.1. Characteristics of Patients

A total of 133 consecutive patients who underwent surgery for a primary breast cancer were included in this study. The median age of patients was 48.0 ± 12.4 years. **Table 1** shows that the patients were mostly the housewives (51.8%) and vendors (9.1%), and about half of them live in Conakry (53.6%), the capital of the country.

Cancer characteristics showed that the main histological type was invasive ductal carcinoma (86 cases or 64.7%), 27 cases of carcinoma no other specified (20.3%), 10 cases of invasive lobular carcinoma (7.5%) and 4 cases of mucinous carcinoma (3.0%).

In 24 cases, according to the hormone receptor status and the Her2 oncogene, the molecular subtypes were luminal A (29.2%), luminal B (8.3%), triple negative (29.2%) and Her 2 positive (33.3%).

Breast cancer surgery was conservative in 13 cases (9.8%) and radical in 120 cases (90.2%). The median time from diagnostic to surgery was 5.0 months (IQR: 3.0 - 7.0). In addition to surgery, 90% of all patients received a chemotherapy and 44.4% a radiotherapy.

Table 1. Socio-demographical characteristics of breast cancer patients who had a surgical management.

Characteristics	Relapse n = 45	Without relapse n = 88	*P*
Age, years	43.4 ± 9.8	50.5 ± 13.0	0.001
Body mass index	26.9 ± 6.0	25.6 ± 4.8	0.37
Menopause	14 (31.8)	52 (59.8)	0.003
Profession			0.21
Vendors	6 (15.4)	10 (12.3)	
House wives	17 (43.6)	47 (58.0)	
Dressmakers	3 (7.7)	6 (7.4)	
Teachers	6 (15.4)	3 (3.7)	
Health workers	3 (7.7)	3 (3.7)	
Engineers	0 (0.0)	3 (3.7)	
Secretaries/administrators	4 (10.3)	9 (11.1)	
Geographical areas			0.38
Conakry and countryside	23 (51.1)	52 (59.1)	
Other country's areas	22 (48.9)	36 (40.9)	
Underlies diseases			
Diabetes mellitus	2 (28.6)	6 (28.6)	1.00
Arterial hypertension	11 (24.4)	20 (22.7)	0.82

3.2. Predictive Factors of Cancer Relapse

Out of all patients, 45 experienced relapse, corresponding to a 60-month relapse rate of 33.8% ± 8.0%. Relapse occurred in the first year after surgery in 9 cases (20.0%), the second year in 18 cases (40.0%), the third year in 12 (26.7%), the fourth year in 0 cases (0.0%), and the fifth year in 6 cases (13.3%). Of the all of these relapses, 2 (4.4%) were local, 4 (8.9%) were loco-regional, 19 (42.2%) were metastatic and 11 (24.4%) were in more sites. The median time from surgery to relapse was 7.0 months (IQR: 3.0 - 15).

Socio-demographic and cancer characteristics in patients who relapsed and those who did not relapse are presented in Table 1 and Table 2 respectively. The median time from diagnosis to surgery was 6 (IQR: 3.5 - 8.5) and 4 months (IQR: 3.0 - 6.0), respectively in the relapse and no relapse patients (P = 0.04). It is worth noting that at the time of diagnosis, the primary cancer was more advanced in patients who experienced relapse. In these patients, cancer was mainly at stage III (P = 0.03). The results of logistic multivariate regression showed that the predictor factors of relapse were age [OR = 0.94; 95%CI (0.92 - 0.99; P = 0.005)], and the stages III and IV of cancer [OR = 6.30; 95%CI (1.72 - 22.97); P = 0.005)]. The body mass index was retained in the model but the association was not statistically significant (OR = 1.10; 95%CI (0.99 - 1.22; P = 0.08).

3.3. Five-Year Mortality

Out of 133 patients, 56 died corresponding to an overall 60-month mortality of 42.1% (95%CI: 33.6% - 50.6%). Mortality was higher in patients with relapse than in patients with no relapse (64.3% vs. 35.7%; P < 0.001). The median time from diagnosis to death was 18.0 (IQR: 11.0 - 29.0) months. The results of the multivariate Cox model showed that the independently factors associated with death were body mass index, origin of patients, radiotherapy and cancer relapse (Table 3).

4. Discussion

Breast cancer is a major cause of morbidity and cancer related mortality among African women. In the current study, we analyzed the factors associated with the occurrence of relapse and mortality of breast cancer patients who underwent surgery in our surgical oncology unit in Conakry, Guinea. Of 276 women with breast cancer followed in that unit, only 50.7% underwent surgery. This could explain the low availability of cancer treatment facilities in low-resource countries. Limited financial resources lead to a suboptimal cancer data collection, as well as a delayed diagnosis and treatment, a common characteristic of many African breast cancer patients [9] [11].

The results showed that breast cancer relapse is the most common. The five-year relapse rate was 33.8%. This high relapse rate could be explained by the young age of the patients, premenopausal status, advanced stage

Table 2. Comparison of the breast cancer characteristics in patients with relapse and without relapse after surgery.

	Relapse n = 45	Without relapse n = 88	*P*
Cancer stage			0.002
Stage I - II	3 (6.7)	27 (30.7)	
Stage III - IV	42 (93.3)	61 (69.3)	
Surgical treatment			0.004
Conservative surgery	0 (0.0)	13 (14.8)	
Radical mastectomy	45 (100.0)	75 (85.2)	
Chemotherapy	41 (91.1)	80 (92.7)	1.00
Radiotherapy	17 (37.8)	42 (47.7)	0.27
Origin of patients			0.77
Hospital	28 (62.2)	57 (64.8)	
Home	17 (37.8)	31 (35.2)	

Table 3. Risk factors independently associated with mortality in breast cancer patients underwent surgery at Donka National Hospital.

	Adjusted HR	95% CI	*P*
BMI	1.10	1.02 - 1.18	0.01
Origin of patients			
Home	Ref		
Hospital	2.14	1.12 - 4.09	0.02
Radiotherapy	0.46	0.25 - 0.88	0.01
Relapse	7.00	3.65 - 13.42	0.001

cancer and radical surgery. Patients who relapsed were younger than patients who did not relapse ($P = 0.001$). Similar data have been reported in previous studies previous data [12]-[14].

The median time from surgery to relapse was 7 months, and over 80% occurred in 3 years after surgery. This is consistent with data of previous studies in the developing countries in which the relapse rate within 5 years was around of 80% [15] [16]. In Finland, the authors found that the median time from surgery to relapse was 27 months [17]. These data suggest that relapse is earlier in low income countries than industrialized countries.

Data showed that in 77.4% of all patients, cancer was at stage III at the time of diagnosis. This suggests that the diagnosis was delayed and this contributed to an increase of the rate of relapse. In fact, 93.3% who experienced a cancer relapse were at stage III.

During the study period, no relapse was noted in patients who underwent breast conserving surgery. Conversely, all cases of relapse occurred in patients with radical breast surgery. Data from several studies showed that there are differences in the risk of relapse and survival but not statistically significant between breast-conserving surgery and radical breast surgery [18] [19]. In a Brazilian study, the recurrence rate after breast-conserving surgery was 6.8% [20].

In this study, almost all of the patients received the chemotherapy. However, the high rate of locoregional and metastatic relapse was higher. This could be explained by the aggressive behavior of tumor.

In our patients, data showed that radiotherapy improves the outcome of locoregional control and reduces the risk of relapse after surgery. Thus, relapse-free survival of locally-advanced breast cancer can reach 87% in patients treated with adjuvant radiotherapy [21]. This suggests that the availability of radiotherapy in the country would be helpful for improving breast cancer survival in developing countries.

The 5-year overall mortality was 42.1% and this was higher in patients who experienced relapse. Previous data showed that the 5-year mortality was from 36% to 38% in Sub-Saharan Africa [22]-[24]. The overall survival and disease-free survival 57.9% and 64.3% respectively are similar to other previous studies performed in the developing countries [25]-[29] (**Table 4**).

The multivariate Cox models showed that the increasing of BMI was an independently factor associated with death. In a meta-analysis, Chan *et al.* [30], showed the associations of obesity with an unfavorable overall and breast cancer survival in pre and post-menopausal breast cancer, regardless of when body mass index is ascertained. These findings suggest that as in developed countries, obesity is a condition to be taken into account in the fight against non-communicable diseases in developing countries as well. Thus regular physical exercise shown to have positive effects in the prevention of breast cancer and in improving the daily life of breast cancer patients [31] must be promoted among African women.

We noted that patients who came from other services of the hospital were at a high risk to death. We believe that patients lose enough time going through the non-specialist services where diagnostic facilities are very limited before reaching an oncology service. In a recent study, we reported that despite the majority of breast cancers are referred to our unit for healthcare professionals, the diagnosis is still late [32]. This could be related to the multiple recourses used by patients before the consultation in specialized oncology services. Gombe Mbalawa *et al.* [33] showed that the late diagnosis of breast cancer was largely attributed to the responsibility of health professionals: the hospital personal, the nurses and physicians who work in private (40.8%) and the medical doctor, specialist or not (25.5%) while the direct responsibility of the patient was weak (24.4%) by ignorance or fear of diagnosis.

Table 4. Comparison of overall survival, disease-free survival and independent prognostic factors for 5-year follow-up of breast cancer in some developing countries.

Studies	Number of cases	Country	OS	DFS	Independent prognosis factors
Our study	133	Guinea	57.9%	64.3%	BMI, Origin of patients, radiotherapy, relapse
Al-Moundhri *et al.* 2004	152	Oman	62%	64%	Axillary node involvement Tumor differentiation
Ben Gobrane *et al.* 2007	470	Tunisia	61%	NA	Surgery, radiotherapy
Gakwaya *et al.* 2008	297	Uganda	56%	NA	Stage
Makanjuola *et al.* 2014	224	Nigeria	24.1%	NA	Treatment (chemotherapy, surgery, radiotherapy)
Ngowa *et al.* 2015	404	Cameroun	30%	NA	Stage

NA: Not available.

Despite the importance of this study and its potential impact on the quality of care for patients with breast cancer in developing countries, it may have some limitations: first, because of the design which was a retrospective cohort study. Somme important data as molecular subtypes were missed in the majority of patients because this test is not carried in our country. Secondly, we cannot be taking into account of socio-economical (education, income) data, because they were not recorded. However, in Guinea, the medical care is not free and there is no almost any health insurance. So, patients pay medical care. Thus, the taken into account of socioeconomical data in the regression would be helpful to the best understand of the determinants of the prognosis after breast cancer surgery. Finally, the sample size was small. Need to be extended in a large study with a high number of samples. However, despite the small size, the power of this retrospective study can be considered as sufficient.

5. Conclusion

The proportions of relapse and death were higher in breast cancer patients. Age and stage of cancer at time of surgery were the predictors of relapse and body mass index, radiotherapy and cancer relapse were associated with death. The improved means of diagnosis and access to other methods of locoregional and systemic treatment provide a better understanding and increase the survival of breast cancer treated in our settings. The findings of this study will be helpful for the physicians in developing countries in better referral of the patients from the cancer management health department. The impact of the study is to provide the first breast cancer survival data in a country with low resources.

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Conflict Interests

No conflict interests.

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