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Original Research Article

Determinants of the survival of patients operated on for breast cancer at the Yaoundé Gyneco-Obstetric and Pediatric Hospital

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ABSTRACT

Background: In Cameroon, breast cancer remains a real public health problem and 5-year survival varies from 30 to 62%. Surgery improves survival. This study was conducted to determine that apart from surgery, what are the determinants of the survival of breast cancer patients at YGOPH.
Methods: This was a descriptive study with historico-prospective collection of data from breast cancer patients at YGOPH (2010-2020). Kaplan-Meier estimated survival and Cox regression looked for factors associated with survival. The origin date was the date of the surgery and the end date was the date of death or the latest news.
Results: The mean age of the 166 patients operated on was 48.27±12.44 years. About 48.2% had stage 4 (T4), 59% had lymph node invasion and 10.8% had metastases. Radical surgery was performed in 92.2% and 20% presented tumor recurrences. The 5-year survival was 62%. Independent factors associated with reduced survival were breast pruritus (HRa=9.74; p=0.004), retroareolar location of the tumour (HRa=2.5; p=0.035), lymph node invasion (HRa=2.66; p=0.008) and tumour recurrence (HRa=7.57; p=0.000).
Conclusions: The 5-year survival was 62%. Factors associated with reduced survival were breast pruritus, retroareolar location of the tumor, lymph node involvement, and tumor recurrence.

Keywords: Breast cancer, Determinant, Operated on, Survival, Yaoundé Gyneco-Obstetric and Pediatric Hospital

INTRODUCTION

Breast cancer is the most common cancer in the world and remains the leading cancer in women with 2,261419 new cases in 2020.[1] It is one of the leading causes of death worldwide. Survival varies widely around the world, it is better in developed countries. There are many factors that determine the survival of breast cancer patients, including sociodemographic, clinical, paraclinical and therapeutic data.[2] In Africa, despite limited screening, diagnosis and treatment, the incidence of breast cancer has almost doubled.[3,4] This cancer ranks first in Africa with a prevalence of 370,015 cases and a mortality of 74,072 deaths in 2018.[3] In Cameroon, breast cancer remains a real public health problem and 5-year survival varies from 30 to 62%. Surgery improves survival. Apart from surgery, what are the determinants of the survival of breast cancer patients at YGOPH? Hence the study rational.

METHODS

This was a descriptive study with retrospective data collection from 166 breast cancer patients at YGOPH from January 1, 2010 to December 31, 2020, i.e. a study period of 11 years.

Any patient whose file did not contain the diagnosis, the date of surgery, and the latest news was excluded. The files were therefore considered unusable because they did not allow for survival calculations.

We completed the missing information, that are, the data relating to survival which were not in the files, directly from the patients or their relatives, through a telephone conversation. The analysis was done using SPSS version 23.0. Kaplan-Meier estimated survival and Cox regression looked for factors associated with survival. The origin date was the date of the surgery and the end date was the date of death or the latest news.

RESULTS

Profile of the patients operated: The age of the 166 patients operated on varied between 20 and 84 years with an average of 48.27±12.44 years. Most were multiparous and 42.2% postmenopausal. The average duration from the first consultation through surgical programming was 9.9 and 6 months respectively. The most frequent reason for consultation was a breast nodule (75.9%). About 48.2% had stage 4 (T4), 59% had lymph node invasion, and 10.8% were metastatic. Invasive ductal carcinoma was more common (91.6%) and grade II more represented (54.2%). Radical surgery was performed in 92.2%. The majority of those operated on (97%) received chemotherapy. Hormone therapy prescribed in 37.3% and radiotherapy performed in 62%. Nevertheless, 20% had tumor recurrences.

Survival assessment

The survival of breast cancer patients who were operated on at 2 years was 79.4%, at 3 years 73.4% and at 5 years 62%. The slope of the survival curve shows that mortality was higher in the first three years and tended to stabilize after this period and to remain constant after the fifth year (Figure 1).

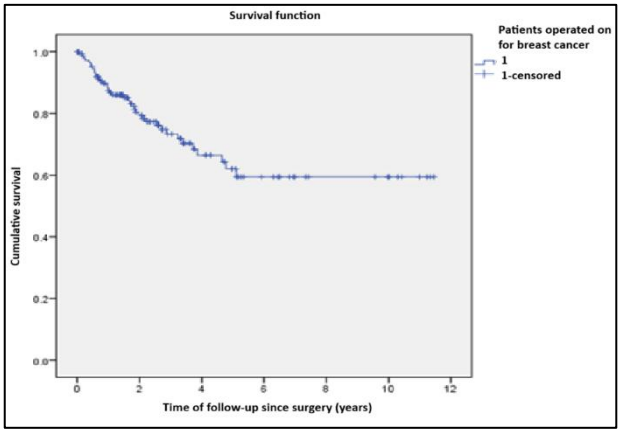

Figure 1: Survival curve of patients operated on for breast cancer (n=166).

Factors associated with survival

Factors associated with prolonged survival of breast cancer surgery patients were investigated in univariate analysis among epidemiological factors (age, level of education, occupation, marital status, religion), clinical (reasons for consultation, clinical signs, location of the tumor, TNM classification), paraclinical (histological type, grade of differentiation, hormone receptors, Her-2) and therapeutic (type of surgery, axillary dissection, chemotherapy, radiotherapy, hormone therapy, recurrence). Among the clinical factors, we were able to observe that operated patients whose reason for consultations was the breast nodule, breast pruritus, had a high risk of death. As well as those with lymph nodes, a retroareolar location of the tumor, bone metastases before surgery, had poor postoperative survival chance. On the other hand, therapeutically, an improvement in survival was observed in women on hormone therapy. However, during follow-up, a reduction in survival was observed in patients who had a tumor recurrence in general and an ipsilateral axillary recurrence in particular (Table 1).

Multivariate analysis of the determinants of prolonged survival of breast cancer surgery patients, according to the Cox model, showed that breast pruritus as a reason for consultation, palpation of lymph node on physical examination, retroareolar location of the tumor and the occurrence of tumor recurrence were statistically significantly associated with a reduction in survival (Table 2).

Table 1: Distribution of survival determinants in operated patients in univariate analysis.

Variables	Death		HR (95% CI)	P value
	Yes (%)	No (%)		
Nodule (symptom)	25 (19.8)	101 (80.2)	2.149 (1.12-4.14)	0.022
Pruritus (symptom)	2 (50)	2 (50)	5.28 (1.22-22.93)	0.026
Lymphadenopathy (sign)	27 (27.6)	71 (72.4)	1.98 (1-3.92)	0.050
Retromamelonal tumor	7 (43.8)	9 (56.2)	2.42 (1.06-5.49)	0.035
Bone metastasis	2 (66.7)	1 (33.3)	6.58 (1.53-28.25)	0.011
Hormone therapy	7 (12.5)	49 (87.5)	0.352 (0.156-0.799)	0.006
Recurrence	19 (63.3)	11 (36.7)	5.59 (2.94-10.66)	0.000
Ipsilateral axillary recurrence	5 (71.4)	2 (28.6)	5.79 (2.23-15.03)	0.000

Table 2: Distribution of survival determinants in operated patients in multivariate analysis.

Variables	Adjusted HR	95% CI		Adjusted p value
Nodule (symptom)	0.71	0.34	1.47	0.353
Pruritus (symptom)	9.74	2.10	45.22	0.004
Lymphadenopathy (sign)	2.66	1.29	5.47	0.008
Retromamelonal tumor	2.5	1.08	5.82	0.035
Bone metastasis	2.44	0.516	11.53	0.260
Hormone therapy	0.51	0.22	1.18	0.114
Recurrence	7.57	3.79	15.12	0.000
Ipsilateral axillary recurrence	1.55	0.53	4.48	0.423

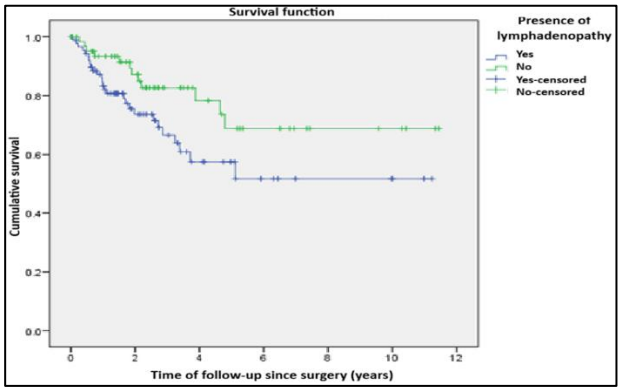

Figure 2: survival curve as a function of the presence of lymphadenopathy.

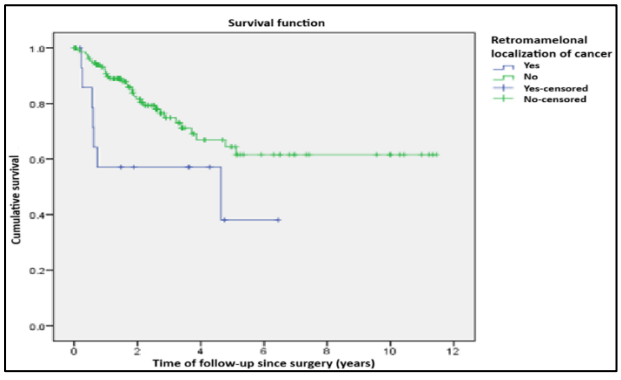

Figure 3: Survival curve according to the retromamelonal localization of the tumor.

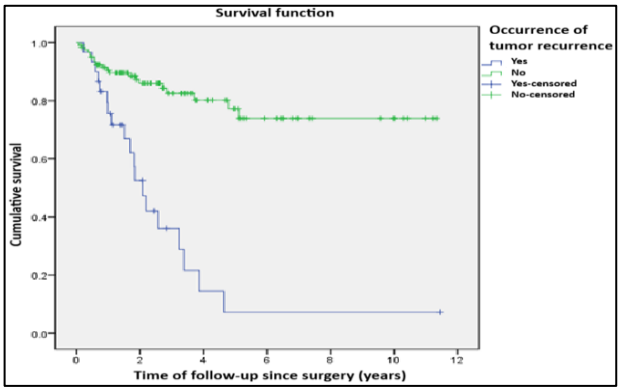

Figure 4: Survival curve as a function of tumor recurrence.

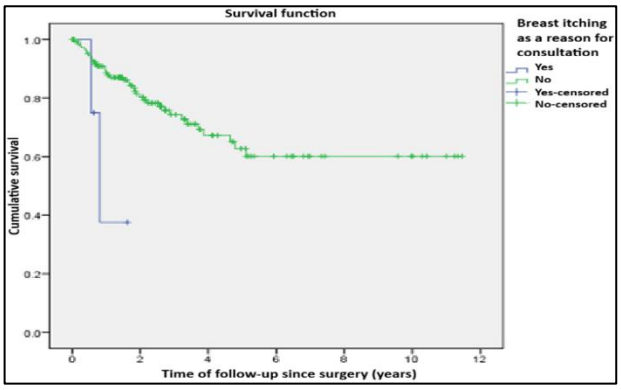

Figure 5: Survival curve as a function of the reason for consultation pruritus.

Comparisons of the survival function curves, as a function of tumor recurrence, pruritus, lymph node and retroareolar location, reveal through their slopes that mortality is higher in the group of those who presented these characteristics in a statistically significant way (p<0.05 values) (Figures 2-5).

DISCUSSION

Factors associated with survival

Factors associated with prolonged survival of breast cancer surgery patients were investigated among epidemiological, clinical, paraclinical, therapeutic factors and according to the onset or not of a recurrence. In multivariate analysis, the independent factors associated with reduced survival were breast pruritus (HRa=9.74; p=0.004), retroareolar location of the tumor (HRa=2.5; p=0.035), lymph node invasion (HRa=2.66; p=0.008), and tumor recurrence (HRa=7.57; p=0.000). However, many other factors have not been associated with survival despite the fact that they were associated with many others, such as: age, tumor stage T, metastases, histological type, hormone and Her-2 receptor expression and the different therapeutic modalities.

Tumor recurrence

Tumour recurrence (HRa=7.57; p=0.000) reduced survival. These results are similar to those observed in Cameroon in 2014 and South Africa in 2018 where the occurrence of locoregional relapse (p=0.046) was associated with a reduction in survival.[5,6] Bollet et al in 2010 thought that when the risk of locoregional recurrence is reduced by 20% at 5 years, overall survival at 15 years is improved by about 5%.[7] They found that the size of isolated breast cancer recurrence seemed to be a prognostic factor for the risk of metastasis and consequently poor survival. The other derogatory factors they found were the early onset of recurrence, i.e. an avearge of 5 to 7 months, which correlates our results where the average time of recurrence in our study population was 5 months.

As a pejorative factor, in the case of recurrences, they reported lymph node recurrence, which best justifies our results wherein an axillary location of the recurrence was associated with a reduction in survival without it being an independent factor associated with survival in multivariate analysis. And finally, Bollet et al found that the absence of hormone receptors and young age at the time of initial treatment (less than 40 years) were also derogatory prognostic factors for locoregional recurrence and therefore poor survival.

However, in our study, neither of the latter two influenced survival because of our small sample size. Seltz et al in 2014, had found that a Ki67 greater than 20% was the only independent negative prognostic factor for locoregional relapse-free survival.[8]

Lymph node invasion

Lymph node involvement (HRa=2.66; p=0.008) was associated with poor survival. Similarly, in Tunisia, clinical lymph node status and metastases at diagnosis (p=0.01) were the significant prognostic parameters reducing overall breast cancer survival.[9] Colzani et al in Sweden found that the mortality rate was very high in the event of lymph node involvement.[10]

Breast pruritus

Patients presenting as a reason for consultation breast pruritus had a poor survival rate (HRa=9.74; p=0.004). However, Togo et al found breast pruritus as the most frequent reason for consultation 35% without however influencing survival.[11] Our result could be explained by the fact that breast pruritus could be a telltale sign of breast carcinoma with skin involvement corresponding to the clinical stage T4b or even T4c. Indeed, when the tumor affects the skin, there is secretion of histamine which is the cause of breast pruritus. This would easily explain why this pattern reduces survival because it is indicative of an advanced stage. However, in many studies, this symptom was not included in the reasons for consultation.

The retroareolar location of the tumor

A retroareolar location of the tumor did not have a good prognosis for survival (HRa=2.5; p=0.035). Tumors with this location tend to spread easily to the entire breast due to their topography and to be more aggressive due to their ductal nature. But even more so, the onset phases of these mammary tumors with retroareolar localization are misleading and can mimic benign pathologies and consequently delay consultation, diagnosis and eventually treatment.

Parameters sought but not associated with survival in our study

Age- young age, less than 30-45 years in the studies by Bollet et al and Colzani et al was associated with poor survival.[7,10] On the other hand, Kemfang et al did not find any difference between the different age groups as is the case in our study.[12] This could be explained by the large proportion of advanced stages in our studies that can worsen the prognosis on the one hand and by a low life expectancy in developing countries on the other hand which could considerably reduce the survival of women in their fifties and over.

The T1 stage in the studies of Kemfang et al in Cameroon and Cubasch et al in South Africa, were a factor in good survival.[6,12] Although no deaths were recorded in the group of patients operated on for stage T1 breast cancer, we did not find a statistically significant difference between the different survival curves according to clinical stage T. Probably due to the small size of our sample.

In Ethiopia, the metastatic stage was associated with poor survival, as in many other studies. This was not proven in our study, perhaps because of the small size of our sample. Indeed, their sample was large, of the 1070 cases, 285 were metastatic, i.e. 26.6% far superior to our study.[13] In addition to the metastatic appearance of the breast tumor, in their study survival was influenced by the histological type of the tumor. Survival was better in ductal carcinoma compared to other histological types.[13]

Cubasch et al found that mortality was higher in the absence of hormone receptors, high overexpression of Her-2 and triple-negative tumors.[6] This had no effect in our study because of the incomplete or absent information concerning the immunohistochemistry results. However, in Sweden, Colzani et al had not also, as in our study, found a difference in the presence or absence of hormone receptors in terms of survival.[10]

The type of surgery done, was found by Kemfang et al to improve survival in favor of conservative surgery where the median survival was 6 years compared to 2 years in the case of radical surgery. This difference would be due to the morbidity and complications related to mastectomy on the one hand and on the other hand to the fact that patients would be at an advanced stage, contra indicating conservative surgery. In our study, no difference was found. However, other authors have found a beneficial effect of mastectomy on survival, such that in 2008, Blanchard et al. found that mastectomy was an independent factor that improved the survival of patients with breast cancer at stage T4.[14] In Cameroon, in 2014, in a cohort of the survival of patients with non-metastatic breast cancer, mastectomy was found to be a factor influencing locoregional relapse-free survival (p=0.042).[5]

As in our study, Kemfang et al did not find a difference in survival in the groups that had undergone radiotherapy sessions or not.[12]

Although we found that hormone therapy improved survival by 0.352 (CI=0.156-0.799; p=0.006) in univariate analysis, it was not significant in multivariate analysis. This could be explained by the fact that hormone therapy would reduce the rates of locoregional recurrence and therefore improve survival, hence the confounding effect.

The outcome of chemotherapy on improving survival is well established. The fact that chemotherapy was not associated with survival in our study would be due to the fact that most (97%) of our patients had undergone chemotherapy sessions.

CONCLUSION

The 5-year survival was 62%. The slope of the survival curve shows that mortality was higher in the first three years and tended to stabilize after this period and to remain constant after the fifth year. Factors associated with reduced survival were breast pruritus, retroareolar location of the tumor, lymph node involvement, and tumor recurrence. Our results suggest increasing screening and early diagnostic activities on the national territory in order to provide early management for these patients.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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