

Clinical, Prognostic and Socio-Economic Aspects of T4 Breast Cancers in Ouagadougou, Burkina Faso: A Retrospective Study

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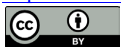
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Abstract

Breast cancers classified T4 according to the TNM code are frequent in Burkina Faso. A better knowledge of these cancers would help to better organize the fight against breast cancer in general. We conducted this study to present the clinical and prognostic aspects of T4 breast cancer in Ouagadougou. It was a descriptive retrospective study based on the medical record of patients received from January 1, 2017 to December 31, 2021 in the cancer department of Yalgado Ouedraogo University Hospital. Patients followed for histologically confirmed breast cancer who were classified in the cT4 category of the TNM code 8e edition were included. We collected a total of 286 patients. Non-salaried patients accounted for 90.56%. In this study, 53.3% of patients lived in urban area and 36.7% in rural area. Menopausal patients accounted for 56.8% of cases. One hundred and thirty-three (46.5%) patients were overweight or obese and 121 (42.3%) patients had a normal weight. The average consultation time, which is the time between the first signs and consultation in a specialized center, was 12 months, with a median of 11 months. According to category T of the TNM code, 19 patients (6.6%) were classified T4d, 176 (61.5%) were classified T4c, 69 (24.1%) were classified T4b and 22 (7.7%) T4a. One hundred and twenty patients (42%) were metastatic. The median overall survival of all patients in our sample was 20 months. In univariate analysis, metastatic status was risk factor for death, while obesity and surgery were protective factors. In multivariate analysis, obesity, surgery and metastatic status were independently associated with survival; obesity and surgery were protective factors. Survival is poor due to advanced stages and difficulties in the management of these cancers. Measures to facilitate access to care would improve the prognosis of these cancers.

Keywords

T4 Breast Cancer, Prognosis, Clinical, Burkina Faso

1. Introduction

Breast cancer is a major health problem in Burkina Faso. It is the first cancer in women and the leading cause of cancer death [1]. The prognosis of this cancer is unfavorable due to the advanced stages at diagnosis. More than 70% of these cancers are diagnosed at stages III and IV [2]. These stages consist mainly of T4 cancers, that is, locally advanced cancers with or without metastases. Breast cancers classified T4 according to the TNM code are a heterogeneous group of breast cancers. They include cancers infiltrating the skin and/or chest wall (T4a, b, c), as well as inflammatory breast cancer [3]. The management of these cancers is an important challenge in this context. Drug treatments, including neoadjuvant chemotherapy and targeted therapies, are the main weapons [4]. Burkina Faso is a country with limited resources. It is characterized by a large social protection deficit with a low capacity of individuals and households to cope with the consequences of unforeseen events (illness, job loss, natural disaster, etc.) [5]. Thus, 40% of total health expenditure is borne by residents, who pay when they go to health centres [6]. The poor population and the inadequacies of the medical platform further affect the prognosis of the disease. Diagnostic means are inaccessible. Treatment is difficult to access due to its high cost, poor populations and lack of health coverage. Treatment regimens are therefore heterogeneous and irregular. Very few studies have focused specifically on T4 breast cancer in this context. A better knowledge of these cancers would help to better organize the fight against breast cancer in general. We therefore conducted this study with the objective of presenting the clinical and prognostic aspects of T4 breast cancer in Ouagadougou.

2. Methods

2.1. Type and Period of Study

We conducted a retrospective study based on the medical record of patients received from January 1, 2017 to December 31, 2021 in the cancer department of Yalgado Ouedraogo University Hospital.

2.2. Patients

Patients followed for histologically confirmed breast cancer who were classified in the cT4 category of the **TNM code 8e edition** [7] were included.

All patients were treated according to the same therapeutic approach with different objectives according to the metastatic status. After consultation with the surgical team, a neoadjuvant treatment was proposed to non-metastatic patients including neoadjuvant chemotherapy, locoregional treatment in case of

satisfactory tumor response and radiotherapy. Hormone therapy was prescribed to patients with hormone receptors positive tumors depending on menopausal status. Trastuzumab was prescribed in case of overexpression of oncoprotein HER2. Palliative treatment was proposed for metastatic cancers, including chemotherapy, hormonal therapy depending on menopausal status and targeted therapy for overexpression of oncoprotein HER2. The response to treatment was evaluated according to RECIST (*Response Evaluation Criteria in Solides Tumors*) criteria.

2.3. Analysis

Patient and disease characteristics were described by mean, median, proportion. Survival was calculated by the Kaplan Meier method by taking as time of participation (in months) the time between the date of diagnosis and the date of the last news. The factors influencing survival were analysed using a proportional risk model (Cox model). A significance threshold of 0.05 was used for all these analyses.

3. Results

From January 1, 2017 to December 31, 2021, we collected a total of 286 patients in the cancer department of Yalgado Ouedraogo University Hospital, meeting the inclusion criteria. The average age of patients was 47 years (standard deviation: 12.9), with extremes of 16 and 99 years. Housewives accounted for 74.5% of cases, followed by civil servants (8%) and traders 6.6%). Non-salaried patients accounted for 90.56%. In this study, 53.3% of patients lived in urban area and 36.7% in rural area. Menopausal patients accounted for 56.8% of cases. One hundred and thirty-three (46.5%) patients were overweight or obese and 121 (42.3%) patients had a normal weight. The average consultation time, which is the time between the first signs and consultation in a specialized center, was 12 months, with a median of 11 months (**Table 1**). The mean tumour size was 8.6 cm. 115 patients had inflammatory breast signs, with skin ulceration in 42 cases. Invasive ductal carcinoma-not otherwise specified was the most common histological type (88%), followed by infiltrating lobular carcinoma (5.6%). Fifty patients, or 17.5% had performed immunohistochemistry. Triple negative cancers accounted for 44% of cases. Luminal subtypes A and B accounted for 28% and 26% of cases respectively. A case of HER2-enriched breast cancer was recorded. According to category T of the TNM code, 19 patients (6.6%) were classified T4d, 176 (61.5%) were classified T4c, 69 (24.1%) were classified T4b and 22 (7.7%) T4a. One hundred and twenty patients (42%) were metastatic. The lung was the most common metastatic site, followed by bone. Therapeutically, neoadjuvant chemotherapy was prescribed to 166 non-metastatic patients. This was a sequential combination of Doxorubicin (60 mg/m², day 1), Cyclophosphamide (600 mg/m², day 1) every 3 weeks for four cycles then 80 mg of paclitaxel per square meter weekly for 12 doses. Among these patients, 124 (43.4%) received at least one cycle of chemotherapy. 77 (62.1%) patients received at least

Table 1. Patients characteristics.

Characteristics	Numbers	Percentages
Residence		
Urban	167	58.4
Rural	119	41.6
Employees		
No	259	90.6
Yes	27	9.4
Weight status		
Lean	32	11.2
Normal	121	42.3
Overweight	68	23.8
Obese	65	22.7
Consultation delay		
<3 months	7	2.4
[3 - 6] months	34	11.9
[6 - 12] months	72	25.2
>12 months	173	60.5
Performance status		
1	110	38.5
2	170	59.4
3	6	2.1
Category T		
T4a	22	7.7
T4b	69	24.1
T4c	152	18.2
T4d	43	50.0
Category N		
N0	23	8.0
N1	135	47.3
N2	105	36.7
N3	23	8.0
Category M		
Non-metastatic	166	58.0
Metastatic	120	42.0

6 to 8 cycles of treatment. Following this chemotherapy, 38 patients underwent radical surgery consisting of a total mastectomy with axillary dissection. Nine patients underwent a clean mastectomy. Eleven (11) patients received radiation therapy after surgery.

The median overall survival of all patients in our sample was 20 months, 95%CI: [16; 24] months. Median overall survival differed significantly according to weight status, metastatic status, performance status, T category (**Table 2**). In univariate analysis, metastatic status were risk factors for death, while obesity and surgery were protective factors (**Table 3**). In multivariate analysis, obesity, surgery and metastatic status were independently associated with survival; obesity and surgery were protective factors (**Table 4**).

Table 2. Median survival by patient characteristics.

Variables	Numbers	Median survival	95%CI	*p-value
Age				
≤40 years	94	19	[13; 27]	0.73
>40 years old	191	21	[16; 24]	
Obesity				
No	153	15	[13; 20]	<0.0001
Yes	132	25	[18; 38]	
Menopause				
No	121	19	[14; 27]	0.8504
Yes	158	21	[16; 25]	
Performance status				
1	110	23	[20; 31]	0.0005
2	169	16	[14; 23]	
3	6	4	[2; -]	
Category T				
T4a	22	24	[11; -]	0.0249
T4b	69	31	[20; 32]	
T4c	52	15	[11; 21]	
T4d	142	19	[15; 24]	
Category M				
No	165	27	[21; 31]	<0.0001
Yes	120	15	[12; 17]	
Surgery				
No	238	27	[14; 20]	<0.0001
Yes	47	35	[30; -]	

95%CI: 95% confidence interval; *Log-rank test.

Table 3. Hazard ratio estimated in cox model based on death due to T4 breast cancer by patients' characteristics (univariate analysis).

Variables	Hazard ratio	Standard deviations	95%CI	p-value
Age				
≤40 years	1			
>40 years old	0.94	0.17	[0.66; 1.33]	0.73
Obesity				
No	1			
Yes	0.46	0.08	[0.32; 0.65]	<0.0001
Employee				
No	1			
Yes	0.76	0.21	[0.43; 1.32]	0.32
Menopause				
No	1			
Yes	1.03	1.79	[0.73; 1.45]	0.85
Performance status				
3	1			
2	0.36	0.18	[0.13; 0.99]	0.05
1	0.21	0.11	[0.76; 0.60]	0.003
Category T				
T4d	1			
T4c	1.33	0.30	[0.86; 2.08]	0.20
T4b	0.67	0.15	[0.43; 1.03]	0.07
T4a	0.59	0.20	[0.31; 1.15]	0.12
Category N				
N3	1			
N2	0.75	0.23	[0.42; 1.38]	0.35
N1	0.43	0.13	[0.24; 0.78]	0.005
N0	0.48	0.19	[0.22; 1.03]	0.06
Metastases				
No	1			
Yes	2.45	0.43	[1.73; 3.46]	<0.0001
Regularity of treatment				
No	1			
Yes	0.78	0.17	[0.51; 1.20]	0.26
Surgery				
No	1			
Yes	0.28	0.08	[0.16; 0.48]	<0.0001

Table 4. Hazard ratio estimated in cox model based on death due to T4 breast cancer by patients' characteristics (multivariate analysis).

Variables	Hazard ratio	Standard deviations	95%CI	p-value
Obesity				
No	1			
Yes	0.57	0.10	[0.40; 0.81]	0.002
Metastases				
No	1			
Yes	2.03	0.36	[1.43; 2.88]	<0.0001
Surgery				
No	1			
Yes	0.38	0.11	[0.22; 0.66]	0.001

4. Discussion

This study evaluates the prognosis of T4 breast cancer in a context of countries with limited resources without university health coverage. Patient characteristics are similar to those of patients in different series in Burkina Faso and other countries in sub-Saharan Africa who share the same socio-economic conditions [8] [9] [10] [11]. Obesity is a risk factor for breast cancer [12]; this could explain the relatively high proportion of obese or overweight women in our study.

More than half of the patients consulted 12 months after the onset of symptoms. This is a delay in consultation that characterizes countries with limited resources [13]. Several factors can be responsible: lack of financial means, socio-cultural habits with traditional treatments in first line, misdiagnosis and insufficient therapeutic management [13]. This results in locally advanced stages of diagnosis. T4 breast cancers correspond to locally advanced breast cancers, metastatic or not. These are cancers of any size that invade the skin or chest wall or have the characteristics of inflammatory breast cancer. Inflammatory breast cancers are a rare anatomoclinic entity described by De Vita as "heat and erythema on more than 50% of the breast surface, often with cutaneous edema associated with erysipelatoid and orange skin appearance. The breast is increased in size with or without palpable mass. The symptoms settled quickly, in less than three months" [14]. These cancers are to be distinguished from neglected breast cancers that have secondarily presented inflammatory signs [15]. In our study, inflammatory breast cancers represent 15% of T4 breast cancers. They represent 1% - 5% of all cancers [16]. Neglected, secondarily inflammatory breast cancers accounted for a third of cases. This is a high proportion, reflecting long delays in consultation and diagnosis.

In terms of diagnosis, these cancers have no pathological particularity except inflammatory breast cancer, which differs according to authors of other cancers [15] [17]. Invasive ductal carcinoma-not otherwise specified was the most fre-

quent histological type in our study. Few patients could benefit from immunohistochemistry because of the high cost of this exploration. Triple negative cancers were the majority. Data from the sub-Saharan literature are variable. Some authors have found a majority prevalence of luminal cancers [10] [18]. The immunophenotypic profile in our study does not seem exploitable because of the small proportion of patients who could benefit from immunohistochemistry. Therapeutically, patients received standardized prescriptions, but were not always able to meet them due to the high cost of drugs.

The median overall survival was 20 months in our study; 5-year survival was 9%. These figures are much lower than those of series of interest to early stage patients. For example, the 5-year survival of patients operated on for all stages of breast cancer is 66.2% in Burkina Faso [8]. In the western series [5] [19] survival is significantly higher than in our study, even in a metastatic situation [20]. This would be explained by the better living conditions and management of patients. There was no significant difference between T4a, b, c and d cancers. Inflammatory breast cancer is considered to have a worse prognosis than non-inflammatory cancers [17]. However, not surprisingly, metastatic status was a risk factor for death. In contrast, operated patients had a better chance of survival as shown by different authors [8] [21]. Similarly, obese patients had a better chance of survival than non-obese patients. This contrasts with the literature. Obesity, in addition to being a risk factor for cancer [12], is a risk factor for death in patients followed for breast cancer [12] [22]. Our results are difficult to interpret due to the heterogeneity of treatments received by patients. The small number of patients who benefited from immunohistochemistry did not allow us to compare survival by different molecular subtypes.

5. Conclusion

T4 breast cancers are very common in Burkina Faso due to delay in consultation. They often present with inflammatory signs and metastases at diagnosis. Given the poverty of populations and the lack of universal health coverage, diagnostic procedures and therapeutic sequences are inadequate and heterogeneous. Survival is poor due to advanced stages and difficulties in the management of these cancers. Measures to facilitate access to care would improve the prognosis of these cancers. Emphasis should be placed on promoting systematic screening and early diagnosis as well as improving the medical facilities.

Conflicts of Interest

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

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