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Burden and Pattern of Metastatic Breast Cancer on Computed Tomography in Cameroon: A Preliminary Assessment

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ABSTRACT

Introduction: *Breast cancer is the most frequent cancer among women in sub-Saharan Africa and the second leading cause of cancer-related deaths. Late diagnosis at advanced stage of disease is a prevailing problem, and the presence of metastatic disease is a significant prognostic factor. The aim of this study was to determine the burden of metastatic breast disease and to describe the pattern of spread in a sub-Saharan African population.*

Methods: *Data was extracted from eligible reports of CT scans of the thorax, abdomen and pelvis (CT-TAP) of patients with histologically proven breast cancer during an 18-month study period. Independent categorical variables were assessed for statistical association with metastatic breast disease, and a Sankey diagram used to illustrate the pattern of metastatic disease.*

Results: *Breast cancer represented 35.84% of all cancers in the study setting. The sex ratio of patients with breast cancer was 1:155 and the median age 41 years (range: 16 to 68 years). Sixty-five percent of the primary cancers occurred at the left breast (101/155) whilst 34.84 % (54/155) occurred at the right. Out of 156 eligible CT-TAP reports assessed, 99 had evidence of either locally invasive, regional or distant tumor spread (63.46%). There was metastatic disease in 65.85% of baseline studies and 63.16% of follow-up scans. Common sites for distant metastatic disease were the pleurae (20.00%), bones (18.71%), lung (16.13%) and liver (11.26%). While left breast cancers were more locally invasive and showed increased tropism for the pleurae and bones, right breast cancers showed increased tropism for the lungs and liver.*

Conclusion: *The burden of metastatic breast disease is high with diagnosis at advanced stage and differential metastatic tropism. Screening and early diagnosis strategies should be given priority, whilst follow-up planning adapted based on anticipated pattern of spread.*

Keywords
Breast cancer, Metastases, Patterns, Computed tomography.

Introduction

Breast cancer is a public health problem worldwide with increasing incidence over the past decades. In 2022, 2.3 million women were diagnosed with breast cancer globally and there were 970,000 related deaths [1]. Breast cancer is the leading cause of cancer in sub-Saharan Africa (SSA) with increasing incidence from puberty until 45 years of age, after which the incidence declines [2]. The peak of breast cancer is estimated to be ten years earlier in many African countries compared to European and American countries [3,4]. Thus, women diagnosed with breast cancer in SSA are relatively younger and late diagnosis at advanced stage of disease is a major concern [5,6]. Despite a reported higher incidence of breast cancer in high-income countries (1 in 12 women *vs*. 1 in 27 women for low income countries), affected women in low-income countries are more likely to die from a breast cancer (1 in 48 *vs*. 1 in 71 for high-income countries [1].

Metastatic disease spread is a leading cause of mortality amongst patients with cancer and it is an important therapeutic and prognostic factor. Some studies have reported on the patterns of spread of breast cancer [7,8]. There remains the need to contribute local data that might improve upon the diagnostic, therapeutic and follow-up strategies, especially imaging surveillance. This knowledge will be vital in the personalization of cancer care tailored to meet the specific needs of people with breast cancer.

Computed tomography (CT) technology is a workhorse in cancer care. Its use ranges from disease diagnosis, assessment of spread, tumor volume assessment prior to radiation therapy, and assessment of disease progression following treatment. CT is often used as a standalone imaging modality for breast cancer assessment or combined with nuclear imaging modalities such as positron-emission tomography (PET) where available. CT can be adequately diagnostic in its own right, and some authors have compared its diagnostic accuracy to hybrid techniques such as PET-CT for the assessment of metastatic breast disease [9]. In one study, bone and distant lymph node metastases were more often reported for PET-CT than CT, while lung and liver metastases were more often reported by CT than PET-CT [9]. Such findings indicate the unique place of CT in cancer care and justify its continuous use in the management of cancer.

This study aspired to describe the burden of metastatic breast cancer and to describe the pattern of spread in a sub-Saharan population in Central Africa. The findings have the potential to foster more advocacy for cancer prevention strategies and improve upon the care of individual patients.

Methods

We extracted and analyzed data from a prospectively collected cancer-imaging database at Cameroon Oncology Center (COC). COC is an integrated cancer care hospital situated in the central African country Cameroon. This hospital is equipped with modern technology for cancer care including a linear accelerator for radiation therapy, an imaging department with multi-slice CT scanner and magnetic resonance imaging, an operating theatre and medical units for surgical interventions and medical treatments, and an international team of healthcare providers. COC also has academic faculty who practice and/or provide consultancy services from universities in Cameroon, the United States of America, Europe and Asia.

Data was extracted over a period of 18 months (July 2022 to December 31, 2023). The University of Buea Faculty of Health Science's institutional review board waived ethical clearance for this study, given that the data was extracted from an existing registry of prospectively collected clinical information. Reports of CT scans of the thorax, abdomen and pelvis (CT-TAP) of patients with a histologically proven breast cancer during the study period were retrieved from the database. Only scans performed at the COC were included in this study as these were the studies with raw images that could be reviewed. For patients who had done more than one CT-TAP scan we considered only the study with metastatic disease or that with the most advanced disease progression (Figure 1). A 16-slice Brilliance Big Bore Philips CT scanner was used to acquire all the images. The standard protocol was multiphasic contrast-enhanced series, with or without a delayed phase. All CT reports and images were archived in an electronic database.

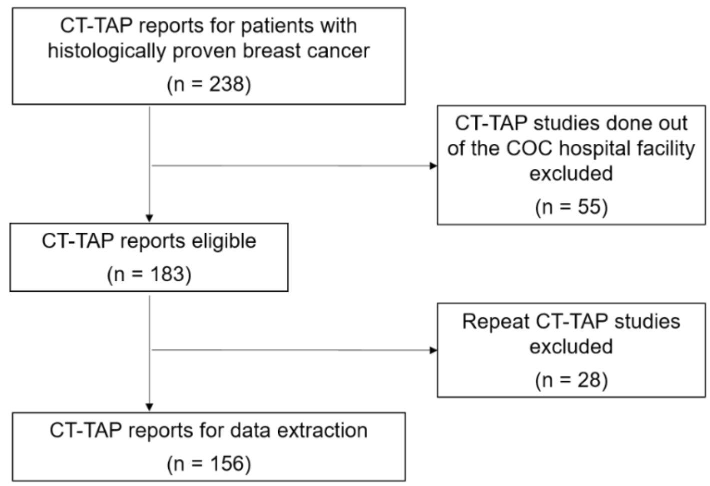

Figure 1: Flow diagram of data extraction procedure.

A standardized form was used to extract information from the reports. Data extracted included age, sex, clinical indication for the scan (noted as either baseline for staging or follow-up), histologic tumor type, breast affected, past and current treatment, and CT findings. Data on CT findings was organized based on the presence of metastatic disease to any of thirteen body organs [10]. CT images in digital imaging communications (DICOM) format were reviewed for verification of the reported metastases across these organs by two radiologists (YO, MM) and the final decision was consensual. Any suspected lesion in a target organ was considered as metastatic disease of the known breast cancer. With respect to the consideration of lymph node metastatic disease, the new Response Evaluation Criteria in Solid Tumors (RECIST) guidelines (version 1.1) was used [11].

Extracted data was transcribed onto a Microsoft Excel® spreadsheet and imported onto the data analysis software (STATA 12MP, STATACORPS, TEXAS, USA). Categorical variables were summarized and presented as counts and percentages whilst the single continuous variable "Age" is presented using the median and the range. Tests for independent statistical associations between the presence of metastatic breast disease and age, the clinical indication side of the primary breast cancer were done using Fisher's exact or *chi*-squared test as appropriate. All *p*-values were two-tailed and the threshold for statistical significance was set at 0.05.

We assessed and presented patterns of metastatic breast cancer disease using a Sankey diagram. Metastatic disease o the different organs from both breasts were presented on the same plot using different colors to differentiate metastases from either the left or the right breast.

Results

Over the 18-month period for the study breast cancer was the most prevalent representing 35.84% of all cancers, followed by cancers of the uterine cervix and prostate gland (Figure 2).

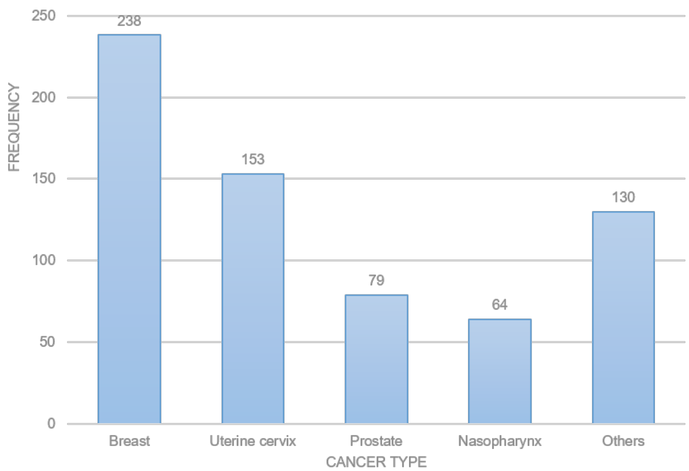

Figure 2: Distribution of cancers at COC during study period.

Breast Cancer Sex and Age Distribution

Out of the 156 CT reports from which data was extracted there was a single male patient aged 66 years old (sex ratio of 1:155). The median age of all the patients was 41 years old (range: 16 to 68 years; interquartile range: 38 to 50 years). The most affected age group was patients aged 40 to 49 years old, with no case observed amongst patients aged 20 to 29 years. Figure 3 shows the age distribution of the patients.

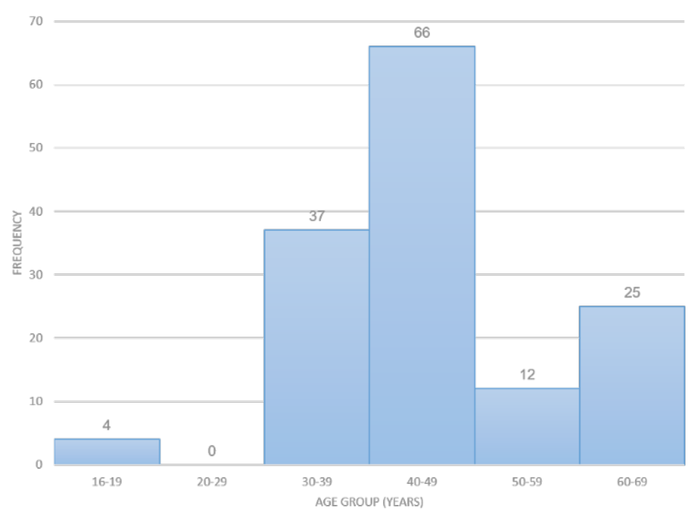

Figure 3: Age group distribution of patients with breast cancer

Anatomical Site of Primary Disease and Clinical Indications

Most of the primary malignancies occurred at the left breast (101 cases, 65.16%), whilst 54 cases (34.84%) occurred at the right breast. Data was not provided on the side of the breast primarily affected for one patient. The main clinical indication for CT-TAP as documented on request forms was for follow-up of treatment (114 cases, 73.55%), with 41 cases (26.45%) for staging.

Metastatic Disease Patterns

There was CT evidence of metastatic breast cancer disease for 99 out of 156 patients (63.46%). Twenty-seven out of 41 (65.85%) baseline (staging) CT-TAP scans showed evidence of metastatic tumor disease, comparable to 72 out of 114 (63.16%) for follow-up CT-TAP scans. Metastatic breast cancer disease was more prevalent for primary cancers of the left breast compared to the right (p=0.001; Table 1).

Table 1: Metastatic breast cancer based on age, affected breast and clinical indications.

	Metastases present *n(%)*	Metastases absent *n(%)*	*p*-value
Indication for CT			0.758
Baseline	27 (65.85)	14 (34.15)	
Follow-up	72 (63.16)	42 (36.84)	
Side of breast			0.009
Right	27 (50.00)	27 (50.00)	
Left	72 (71.28)	29 (28.71)	
Age group (years)			0.001
16-19	4 (100)	0 (0)	
20-29	0 (0)	0 (0)	
30-39	27 (72.97)	10 (27.02)	
40-49	43 (65.15)	23 (34.85)	
50-59	12 (100)	0 (0)	
60-69	10 (40.00)	15 (60.00)	
p-values obtained using Fischer's exact and chi-squared tests			

Local tumor invasion of the chest wall and/or skin (soft tissues) was noted in 62 cases (40%). Lymph node spread was the primary site for regional metastatic disease tropism (82 out of 99 cases, 82.83%), of which there was axillary involvement in 96% of cases. The most common sites for distant metastatic breast cancer disease were the pleurae (20.00%), bones (18.71%), lung (16.13%) and liver (11.26%). Table 2 summarizes the local, regional and distant spread of metastatic breast cancer whilst Table 3 shows nodal involvement.

Table 2: Local, regional and distant spread of breast cancer.

Body organs	Metastasis present, *n(%)*	Metastasis absent, *n(%)*
Lung	25 (16.13)	130 (83.87)
Pleurae	31 (20.00)	124 (80.00)
Nodes	82 (52.90)	73 (47.10)
Liver	17 (11.26)	134 (88.74)
Bone	29 (18.71)	126 (81.29)
Adrenal glands	4 (2.58)	151 (97.42)
Soft tissues	62 (40.00)	93 (60.00)

Table 3: Distribution of nodal breast cancer disease.

Nodal stations	Frequency (%)
Axillary only (bilateral or unilateral)	79 (96.3)
Axillary + Rotter	4 (4.88)
Axillary + internal mammary	7 (8.54)
Axillary + Rotter + Mediastinal	4 (4.88)
Axillary + Rotter + mediastinal + Abdominal	4 (4.88)
Axillary + mediastinal	6 (7.32)
Rotter only	3 (3.66)
Supraclavicular + axillary + Rotter	4 (4.88)

Left breast cancer showed a strong propensity to invade lymph nodes, soft tissues (skin, chest wall, and subcutaneous tissues), pleura and bones. There was less tropism for the lungs and liver, compared to right breast malignancies. Conversely, liver and lung involvement were predominantly from right breast cancer. Figure 4 depicts some metastatic lesions from both right and left cancers. The trend of metastatic disease spread from right and left breast cancers is illustrated in a Sankey diagram (Figure 5).

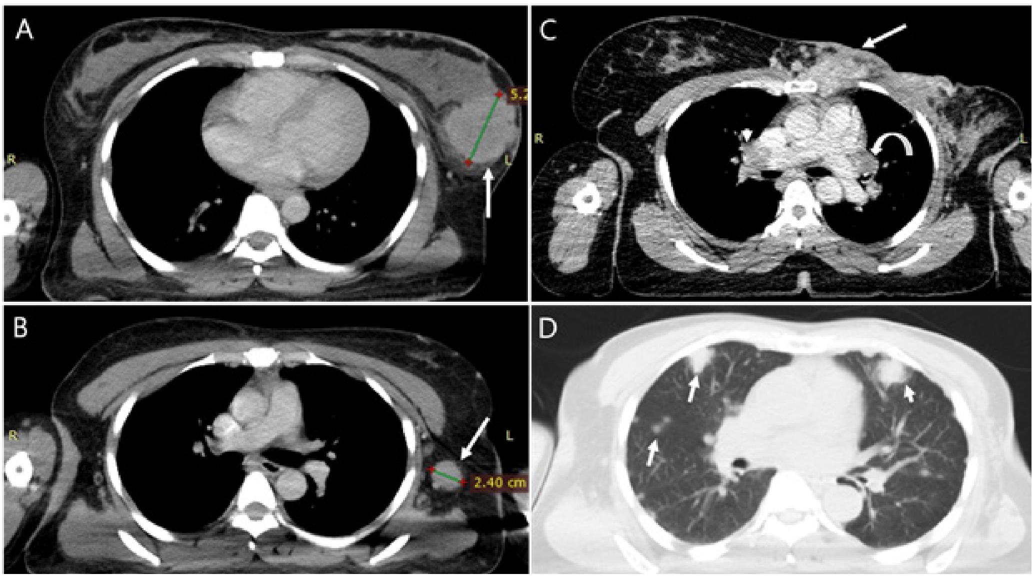

Figure 4: A, B. Contrast-enhanced axial CT of a 40-year-old female with a left breast cancer. In A, there is a huge left breast mass with long axis more than 5cm (white arrow). In B, there is a bulky Berg's level I ipsilateral axillary lymph node (white arrow). C. Axial contrast-enhanced CT of a 44-year-old woman with left breast cancer and history of left mastectomy. There is tumor infiltration of the skin and chest wall (straight arrow), a left hilar lymphadenopathy (curved arrow) and pulmonary embolism at the distal right pulmonary artery (arrowhead). D. Axial CT, lung window of a 53-year-old woman with a left breast cancer. There are multiple solid lung nodules of different sizes in a random distribution

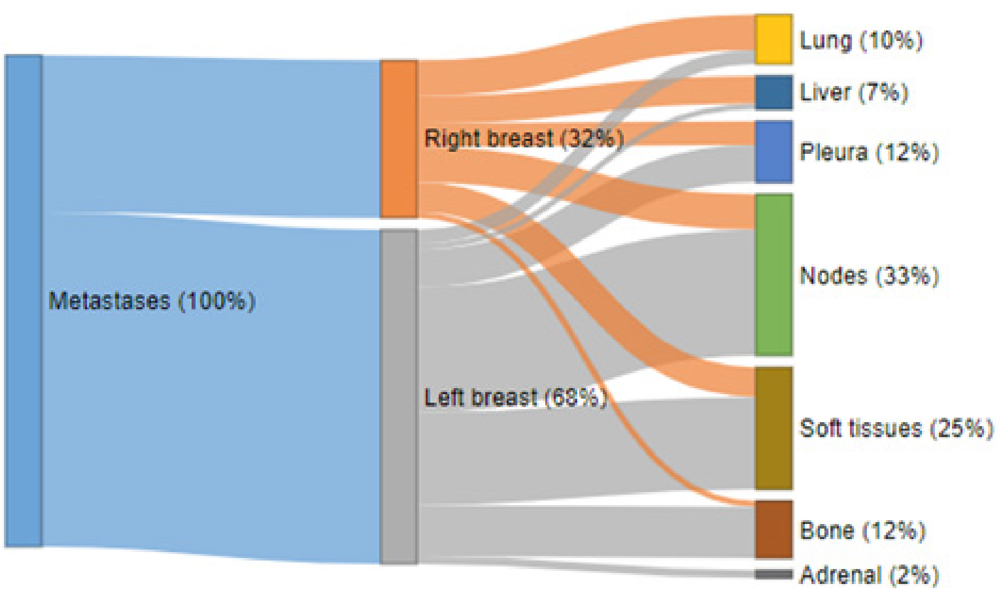

Figure 5: Pattern of spread of metastatic breast disease from the right and left breasts. The nodes in the Sankey diagram are proportionate to number of cases observed.

Discussion

From the findings of this study, breast cancer was the most prevalent cancer, with above 99% of persons affected being females. The female sex is the strongest predictor of breast cancer, and about 0.5-1% of all breast cancers occur in men [1]. The average age of patients with breast cancer in this study was 41 years, with age range from 16 to 68 years old. These findings are similar to previous reports indicating the young age of breast cancer patients in sub-Saharan Africa [2,3].

Most of the primary breast cancers were located at the left breast, indicating a left breast predilection. Several authors reported similar findings [12,13]. More than half of all the patients with breast cancer had some form of spread either local, regional or distant. Evidence of the spread of cancer on imaging is an important factor indicative of poor prognosis. With more than half of the patients having some form of spread at diagnosis, late diagnosis with advanced disease remains an ordeal in this setting.

Invasion of the skin or chest wall was often present, with regional lymph node involvement. The reporting of such findings on imaging affects the treatment planning and protocols, with the use of neo-adjuvant therapy as first line most of the times.

Beyond local invasion, distant sites for tumor disease were the pleurae, bones, lungs and liver in order of decreasing frequency. Patanaphan in 1988 reported the most common sites of metastatic breast disease were the bones, lungs, brain, liver in decreasing frequency [7]. Many years later Wu et al. reported the most common sites of metastatic breast cancer in a very large nationwide cohort to be the bones, lungs, liver and brain in deceasing frequency [8].

There were some disparities in the spread of breast cancer depending on whether the right or left breast was the primary site. Left breast cancers showed more local invasiveness and regional nodal spread compared to the right. Abdou et al. reported a more aggressive biology and poorer outcomes for left breast cancers [12]. However, Amer did not report any difference in survival based on breast cancer laterality [13]. Left breast cancers showed increased tropism for the pleurae and bones and less tropism for the lungs and liver, while right breast cancers showed increased tropism for the lungs and liver. The pattern of spread of breast cancer was reportedly different based on hormonal subtype [8,14-16]. Data on hormonal status of the breast cancers was not routinely provided on CT request forms and hence could not be analyzed.

There was a correlation between the occurrence of cancers in different age groups and metastatic disease. There were more cancer cases in age groups 30 to 39 years and 40 to 49 years with corresponding increase in metastatic disease in these age groups. There was a 100% metastatic disease occurrence at the 50-59 years age group. Chen et al. reported a high proportion of multiple-site metastatic breast disease in patients less than 50 years old and those between 50 and 69 years, compared to those above 69 years of age [17].

This study highlights the high burden of metastatic breast cancer in Cameroon. Late diagnosis remains a major concern, and the population affected is relatively young. Advanced disease stage implies a poor prognosis and in a setting with limited diagnostic and therapeutic options, and prevailing barriers to access available technology, survival is expected to be even lower. Knowledge awareness campaigns and primary prevention strategies are imperative and should be encouraged as these may curb the occurrence of some cases of breast cancers. These usually include minimizing modifiable risk factors of disease. Secondary prevention through regular screening also help detect breast cancers at a very early stage when they are potentially curable. Early diagnosis at the onset of symptoms also stands the chance of detecting breast cancer relatively early with a potentially favorable prognosis.

We further recommend improved government spending for healthcare targeting cancer care, as this will reduce the burden of out-of-pocket expenditures, improve access to care and provide more treatment options. The training of healthcare professionals in cancer management should also be given some priority.

Some limitations to this study were acknowledged and addressed. Metastatic breast disease assessment was limited to the use of contrast enhanced CT. The diagnostic capability of CT is reported to be high in detecting liver and lung metastatic breast disease. However, this accuracy is lower compared to PET-CT for bone and nodal tumor disease [9], and it is likely there might have been underreporting. Moreover, routine CT assessment was usually limited to the thorax, abdomen and pelvic anatomic regions. Studies for other anatomic regions were performed as indicated but these were not linked and analyzed in this study. Furthermore, the criteria to classify a target organ lesion as metastatic disease was based on CT morphologic criteria. However, in the context of a histologically proven malignancy these features would more often than not correlate with a malignancy.

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