Breast Cancer Treatment and Outcomes at Cape Coast Teaching Hospital, Ghana

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| Citation       | Okifo, Oghenefejiro. 2020. Breast Cancer Treatment and Outcomes at Cape Coast Teaching Hospital, Ghana. Doctoral dissertation, Harvard Medical School. |
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Scholarly Report submitted in partial fulfillment of the MD Degree at Harvard Medical School

Date: 8 May 2020

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Scholarly Report Title: Breast Cancer Treatment and Outcomes at Cape Coast Teaching Hospital, Ghana

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Title: Breast Cancer Treatment and Outcomes at Cape Coast Teaching Hospital, Ghana

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Objective: Breast cancer is a recognized major health condition in Ghana, with the incidence rising due to an aging population, socioeconomic development, and an increasingly Westernized lifestyle. Breast cancer treatment and outcomes were analyzed at Cape Coast Teaching Hospital, Ghana.

Methods: A retrospective medical record review of 197 female patients diagnosed with invasive breast cancer was performed. Data collection included operative procedure, postoperative complications, chemotherapy and radiation treatment, pathology and survival. Statistical analysis was performed using SPSS Statistics and included descriptive statistics, Pearson correlation, binary logistic and multinomial regression analysis.

Results: An operative procedure for cure or local control was performed in 106 women and included partial mastectomy (21.7%) and total mastectomy (78.3%). The most common postoperative complication was a surgical site infection (3.8%). Grade 1 cancers were diagnosed in 11.0%, Grade 2 in 43.8%, and Grade 3 in 45.2%. Mean cancer size was 6.5 centimeters (range 1.5 to 20.0 cm). Lymphatic vascular invasion (LVI) was present in 59/125 (47.2%), estrogen receptor status was positive in 31/117 (32.6%), progesterone receptors were positive in 21/117 (22.1%), and Her-2/neu was positive in 29/123 (32.6%). Triple negative breast cancer (TNBC) was identified in 41/89 (46.1%). Stage 3 and Stage 4 cancer patients were twofold more likely to receive neoadjuvant chemotherapy compared with earlier stages (OR= 2.0 95% CI (1.4, 3.0, p<0.001).

Conclusions: Ghanaian women frequently present with advanced stage breast cancer and experience poor outcomes. Public health initiatives should focus on dispelling harmful beliefs that delay women from seeking care. Expansion of the national health care system is needed to support breast cancer screening, diagnostic tests, and treatment.

Keywords: Breast cancer, advanced stage presentation, treatment, Cape Coast, Ghana, Sub-Saharan Africa
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Scholarly Project Question and Role

The purpose of this study is to determine the outcomes of patients diagnosed and treated for breast cancer at the Cape Coast Teaching Hospital in Ghana between 2011 and 2019. This investigation will include two components: a prospective survey of patients attending the Breast Cancer Outpatient Clinic at the RCCH and a retrospective medical record review.

a) The first component of the study will prospectively collect data regarding the reasons women seek medical attention at the Breast Cancer clinic and administer a validated survey that assesses general feelings of well-being and health. In addition to the collection of patient characteristics, chief complaint, family history of breast cancer, clinical and radiographic findings, and recommendations, a validated SF-36 survey that assesses general feelings of well-being and health will be verbally administered. This component of the study is still ongoing and data is currently being collected.

b) The second component of the study will include a review of medical records for presenting symptoms of locally advanced breast cancer, including stage of disease at presentation, utility and results of radiographic studies, histopathologic information, operative procedure performed, operative morbidity and mortality rates, and patient survival outcomes.

Student Role:

I collaborated with Dr. Rosemary Duda to develop a research project analyzing breast cancer outcomes at Cape Coast Teaching Hospital, where Dr. Duda had previously conducted research. We collaborated with Dr. Derek Tuoyire, Dr. Morna, and Anthony Appiah in the design of the study. I applied and received IRB approval from Harvard Medical School, while Dr. Rosemary Duda obtained an IRB from the Cape Coast Teaching Hospital. I traveled to Cape Coast, Ghana in the summer of 2019 to interview eligible patients and review medical records and subsequently compiled the data for analysis. I worked with Dr. Derek Tuoyire, Dr. Morna, and Anthony Appiah at the Cape Coast Teaching Hospital to both identify suitable cases and obtain access to patient records. Dr. Duda conducted the majority of the analysis. Upon returning from Ghana, I wrote and revised the manuscript with feedback from Dr. Duda.
INTRODUCTION:

Previously, communicable diseases took center stage in global health research efforts. However, non-communicable diseases like breast cancer are recognized as an increasingly important burden of disease in African countries. As per the Kumasi Cancer Registry obtained via Globocan, the number of new cases of breast cancer in Ghana represented 20.4% of all cancers in both sexes and 33.6% in females.1 Breast cancer had the highest incidence of new cancers followed by cervical cancer and liver cancer. By region, Western Africa saw 45,157 new cases of breast cancer in 2018 and 20,983 deaths relating to breast cancer.1 Adeloye et al estimated the incidence of breast cancer in Africa as 24.5 per 100,000 person years, which represents an increase from 2000 to 2015.2 This data suggests that not only is breast cancer on the rise, but it represents a significant burden of malignancies in Ghana and other African countries.

Though breast cancer has a lower incidence in women from sub-Saharan African countries compared with women from moderate to high resource countries, there is a higher mortality risk amongst these patients from low-income countries.3 Lower postmenopausal breast cancer incidence rates are thought to be associated with demographics, in particular population age and overall life expectancy. Age is a cumulative risk factor for breast cancer; the life expectancy of Ghanaian women is 64.4 years compared to 79 years in American women.

Protective factors extend from a combination of biological, cultural, and societal influences. African women experience menarche at older ages compared with western women, increased parity, childbearing at earlier ages, and extended postpartum lactation.3 A study
conducted in Accra, Ghana found that the median age of first menstruation of the cohort was 15.5 years and the median age of first menstruation among those aged <20 was 14.5 years. These gynecologic and reproductive patterns lead to fewer ovulatory cycles over a lifetime, and therefore serve as a protective factor against breast cancer.

African breast cancer patients experience a higher morbidity and mortality rate due to multiple factors. Examples include a younger age at presentation, delayed presentation, limited therapeutic modalities, and a potential predisposition to biologically aggressive tumors. In addition, these factors are complicated by larger scale challenges such as poor health infrastructure, incomplete vital registrations, lack of population awareness, delayed health seeking behavior and low levels of female education and empowerment. 2,5,6

Adeloye et. al found that the mean age of populations in both population- and hospital-based breast cancer registries ranged from 30.6 to 60.8 years (median 50.2 years), with over 33% and 81% of population in ages 30-49 years, and 30-59 years, respectively. This was also shown in a 2008 article in Lancet Oncology, which showed that the young age structure of African populations, coupled with rather constant incidence rates in postmenopausal women (by contrast with the increasing rates noted in the developed world) means that the average age at diagnosis in Africa is lower than in American populations and populations of European origin.7 Though the incidence of breast cancer is generally low, breast cancer may in fact be a greater threat in Ghana and other African countries in the upcoming years due to ageing, population growth, and adoption of unhealthy lifestyles especially in the absence of effective public health policies and interventions.2

Ghana does not have a population-based cancer registry, so the rates of breast cancer incidences are estimated from single-institution databases and range from 15.2 to 35 patients per 100,000.8 Previous research conducted in Ghana have demonstrated challenges in the infrastructure that result in late presentations with advanced disease. It has been estimated that fifty percent or more of Ghanaians report to the hospital with advanced disease with the peak age of presentation between the ages of 40-49.9 The standard of care for breast cancer treatment in Ghana is early identification and breast-conserving surgery followed by radiation therapy. However, when patients present with advanced cases, surgical management becomes the primary mechanism of treatment. Other forms of therapy such as chemotherapy, targeted therapy, and hormone therapy vary based on the treatment center.
In addition to challenges in the infrastructure, African and African-American women present with more biologically aggressive tumors. A 2010 study compared the frequencies of ER-negative and triple-negative breast cancers in Ghanaian women, African-American women from the United States, and white Americans and demonstrated that 76% of Ghanaian women were diagnosed with ER-negative cancers compared to 21.9% in white Americans and 36.1% in African-American women. The highest prevalence of triple-negative breast cancers was in Ghanaian women (82.2%). Recently, Ademuyiwa et al evaluated 1104 Cancer Genome Atlas breast cancers and similarly found the triple-negative phenotype as well as the basal subtype to be more frequent in African Americans compared with White Americans (33.3% vs 14.9% and 34.8% vs 16.1%, respectively). The correlation between higher rates of aggressive tumors in African and African-Americans supports the theory of a common genetic predisposition. Not only are there increased rates of aggressive tumors in this population, but the cancer burden may be shifted to women that are younger in age compared to other advanced countries where breast cancer is seen more in the 55- to 64-year old group. Patients with triple-negative breast cancer cannot benefit from treatments such as selective estrogen receptor modulators and aromatase inhibitors or targeted anti-HER2 agents, which limits treatment options to non-targeted chemotherapy and surgical interventions.

Multiple studies have indicated innovative strategies for tackling the high rates of late-stage early-age breast cancer and subsequently low survival rates after treatment. One strategy was tested in a recent study of over 10,000 women who were offered breast cancer screening with the breastlight/breast-i transillumination device. This is an optical device developed by David J. Watmough capable of picking up angiogenesis associated with breast tumors and lesions. This novel screening tool had a sensitivity of 94.4% in detecting breast cancer and is not associated with radiation exposure or tissue compression. Further, it is quick, portable, and a promising tool to enhance early detection screening. Targeted breast education awareness programs are also important to target high rates of late presentation. A study by Clegg-Lamptey et al attempted to shed light on potential reasons for late presentations. The main reason given for delayed presentation was a previous hospital consultation during which only 52% of the 48 women surveyed received a proper diagnosis. Four main causes of both delayed reporting and absconding from treatment included fear of mastectomy, the use of herbal treatment, resort to
prayers and prayer camps, and financial incompatibility. These reasons provide focused points of intervention to optimize breast cancer awareness education.

The purpose of this investigation was to determine the presentation, treatment and outcomes of women with breast cancer in Cape Coast, Ghana, an important regional city.
METHODS:

Study design and population of breast cancer patients in Cape Coast, Ghana

This was a retrospective medical record review conducted at the Cape Coast Teaching Hospital (CCTH), Ghana. The CCTH is a 400 bed referral institution, is the largest medical facility in the central region of Ghana and is the main health care provider for many of the regional coastal communities. All patients diagnosed with breast cancer at CCTH between 2011 and 2019 were eligible for inclusion in the study.
**Data variables**

Documents reviewed included the medical chart, operative records, pathology and radiology reports. Data collection included the patient characteristics gender, age at diagnosis, menopause status, family history, marital status, and town or village of residence. The operative procedure and postoperative complications and radiographic imaging were recorded. Histologic and pathologic features included histologic type, grade, size, stage of disease, and nodal status. Tumor markers included estrogen receptors, progesterone receptors, Ki67 and non-operative management including chemotherapy, anti-estrogen hormonal therapy, and radiation therapy administration therapy were recorded as dichotomous variables.

**Statistical Analysis**

Data were entered into an excel spread sheet and transferred to the IBM SPSS Statistics for Windows, (Professional Analysis Software platform version 26.0, Armonk, NY). Statistical analysis included descriptive statistics for frequency and mean values, Fisher’s Exact Test (FET) (1-sided), chi-square test, Pearson correlation, binary logistic regression analysis and multinomial regression analysis. A p value < 0.05 was considered statistically significant. Correlations were performed using the continuous variable age to determine any significant association with stage of disease, tumor makers, and tumor grade. Binary logistic regression analysis was performed to assess statistically significant associations between operative intervention, chemotherapy and radiation therapy administration and stage of disease.

**Institutional Review Board Approval**

The investigation was approved by the Institutional Review Boards at Harvard Medical School, Boston, MA, USA and the Cape Coast Teaching Hospital, Cape Coast, Ghana. The Harvard Medical School study protocol number is Protocol #: IRB19-0351. The CCTH IRB protocol number is CCTHERC/EC/2019/071.
RESULTS:

Patient characteristics

Charts were available and reviewed for 197 patients diagnosed with breast cancer at Cape Coast Regional Hospital between September 2011 and June 2019. All patients diagnosed with breast cancer in this time interval were women. The mean age at the time of diagnosis was $49.9 \pm 12.9$ years (range 22 – 87 years). The majority of women were 50 years of age or younger (54.6%) at the time of diagnosis. Menopause status was recorded for 156 women; most women were peri-menopausal or post-menopausal at the time of diagnosis (52.3%).

For 84.3% of women, this was the primary presentation of breast cancer. Stage of disease was recorded for 189 patients as shown in Table 1. Metastatic disease was documented at presentation in 38.1%. The majority of women presented with Stage 3 or Stage 4 disease (78.8%). Family history of breast cancer was uncommon. Only 3.0% of women had a known first-degree relative with a breast cancer and 3.6% had a known second-degree family member.

The distribution of breast cancer cases treated at Cape Coast Teaching Hospital is shown in Figure 1. Most of the women resided in the Central Region. The estimated cumulative prevalence of breast cancer cases based upon the study data from 2011 – 2019 is shown in Figure 2.

Pre-operative Evaluation and Surgical Management

The pre-operative evaluation was identified for 185 women and included a mammogram in 98.4% and an ultrasound in 96.8% of women. A total of 192 women had undergone a breast operative intervention. A diagnostic core or incisional biopsy was identified for 44.8% of patients. An operative procedure performed for curative intent or local control was performed in 106 women and included a partial mastectomy (PM) in 21.7% (23/106) or a total mastectomy (TM) in 78.3% (83/106). There was a significant association between diagnostic biopsy only versus a combined PM and TM cohort and increased stage of disease (OR= 1.5 95% CI (1.1, 2.4, p<0.022). An axillary dissection was reported to have been performed in 103 women. Patients with stage 1 to 3 disease were significantly more likely to have undergone an axillary dissection compared with patients with stage 4 disease (OR= 2.6 95% CI (1.7, 4.0, p<0.001).

A post-operative complication was described for 17 of 185 women (9.2%) as shown in Table 2. The most common complication was a surgical site infection (3.8%). The mean length of hospital stay for all admissions was $8.6 \pm 7.4$ days (range 0 to 34 days). A blood transfusion
was administered to 5 (2.8%) women. Often the post-operative hospital stay included administration of chemotherapy. However, there was no significant correlation between length of hospital stay and neoadjuvant chemotherapy administration.

**Non-operative Management**

The frequency of all non-operative treatment modalities by stage is shown in Table 3. Neoadjuvant chemotherapy was administered to 64.5% of patients staged. Advanced stage 3 and 4 cancer patients were two fold more likely to receive neoadjuvant therapy compared with patients with earlier stage disease (OR= 2.0 95% CI (1.4, 3.0, p<0.001). Post-operative radiation therapy was administered more often to earlier stage patients compared with those with advanced stages (OR= 54 95% CI (1.2, 24.7, p<0.031). There was a significant correlation between young age and administration of preoperative radiation treatments (Pearson correlation r= -.175, p=0.02). There was no other significant association between chemotherapy, radiation therapy and oral anti-estrogen medication administration and stage of disease.

**Histopathology**

Histology was available for 164 patients. Invasive carcinoma was the most common malignancy as shown in Table 4. Grade 1 cancers were diagnosed in 11.0%, Grade 2 in 43.8%, and Grade 3 in 45.2%. There was a near even distribution comparing laterality of breast cancer, with 47.7% patients diagnosed with a right breast cancer, 50.3% with a left breast cancer, and 2.1% with bilateral cancer. The upper outer quadrant was the most common site of cancer (32.9%), followed by overlapping sites (20.1%), retro-areolar site (18.8%), upper inner quadrant (11.4%), lower inner quadrant (9.4%), lower outer quadrant (6.7%), and 0.7% nipple areola complex.

Most cancers reported (54.0%) were 5 centimeters (cm) or greater (mean 6.5± 4.0 cm, range 1.5 - 20.0 cm). Estrogen receptor status was positive in 32.6% and progesterone receptor status was positive in 22.1% of cases reported. Her-2/neu was positive in 32.6% of cases and Ki67 was positive in 44.0%. Lymphatic vascular invasion (LVI) was identified in 47.2%. There was no significant correlation between age and histology, histologic grade or stage of disease. There was no significant association between estrogen receptor status, progesterone status, Ki67, LVI and menopause status or age at diagnosis 50 years or younger. However, Her-2/neu was significantly more likely to be positive in premenopausal women compared with a combined group of peri and post-menopausal women (52.4% versus 20.8% respectively, Odds ratio [OR] =
4.20, 95% CI 1.42-12.41, p=0.009). There was no significant association between a positive Her-2/neu status and patients age 50 years or younger.

Tumor marker assessment was available for most patients who had an operative procedure performed. Lymphatic vascular invasion was present in 59/125 (47.2%) tumors, estrogen receptor status was positive in 31/117 (32.6%), progesterone receptors were positive in 21/117 (22.1%), and Her-2/neu was positive in 29/123 (32.6%) tumors. Decreasing age was significantly correlated with positive Her-2/neu cancers (Pearson r=.275, p<0.19). Neither age nor menopause status was significantly associated with any other tumor marker.

A combination of estrogen receptor, progesterone receptor, and Her-2/neu data were all available for 89 patients. Triple negative breast cancer (TNBC) was identified for 41 (46.1%) patients. There was also no statistical significance between TNBC and age, stage of disease, menopause status, histology, size of cancer, total number of positive axillary lymph nodes, time to local recurrence, disease status, and death from breast cancer.

The results of the axillary dissection were available for 87 patients. Positive axillary lymph nodes, ranging from 1 to more than 10, were identified in 77.0 % of 87 patients. Approximately 10% of patients had more than 10 positive nodes identified, as shown in Table 5. No other sites of regional nodes (i.e. cervical, supraclavicular or infra-clavicular lymph nodes) or sites of distant disease (i.e. liver, lung) were reported to be biopsied.

**Treatment Outcomes**

The mean duration of follow-up was 10.8 ± 9.8 months (range 0.3 to 49.31 months). 52 of the initial cohort of 197 patients (26.4%) were reported to be lost to follow-up. Disease status follow up was available for 145 patients as shown in Table 6. A total of 21 patients were reported to have succumbed to breast cancer. The mean duration from time of diagnosis to death was 4.6 ± 4.7 months (range 1 to 15 months). The mean duration from diagnosis to local recurrence after treatment for a curative intent was 13.2 ± 9.4 months (range 3 to 36). The mean time for diagnosis of metastatic disease (n=145) was 14.0 ± 8.0 months (range 5 to 24). The most common sites of metastatic disease included brain, lungs and liver.
DISCUSSION:

Breast cancer is a growing public health concern in Ghana that requires new and effective interventions. This paper provides novel breast cancer outcomes data on women presenting to the Cape Coast Teaching Hospital from September 2012 and June 2019 and will address how focused interventions in this community may lead to earlier breast cancer presentations and improved outcomes.

Clinical Characteristics

The women affected by breast cancer in this study were an average of 49.92 (12.9) years in age compared to the median of 50.2 years and the age range of 40-50 that have been cited in prior studies.2,9 The majority of these women (n=197) were 50 years old or younger and 52.3% of women were peri-menopausal or post-menopausal at the time of diagnosis. In comparison, the median age of breast cancer presentation is 62 in the United States. For 84.3% of women, this was their primary presentation of breast cancer, which suggests that a proportion of these initially present with breast cancer and are lost to follow-up. However, 34.5% of women already had metastatic disease when they initially presented. In addition, 78.8% of the patients included in the study had advanced stage 3 or 4 disease. Prior research has shown that Ghanaian women tend to present at a younger age, a more advanced stage (3 and 4), have larger tumors, and have fewer tumors that are hormone positive.7

Ghanaian women in this study may present with advanced stage disease due to barriers in the diagnostic process and/or delays in seeking care. Some of the barriers in the diagnostic process may include the lack of current national breast cancer screening protocols or countrywide literacy initiatives, limited availability of mammography or ultrasound machines, or out-of-pocket expenses which are incurred with regards to receptor evaluation and definitive treatment.8 In a majority of cases in this study, both a mammogram (98.4%) and an ultrasound (96.8%) was performed prior to biopsy suggesting that diagnostic imaging at the Cape Coast Teaching Hospital was accessible. This suggests that radiographic imaging may be available for screening purposes and should be incorporated into general health care recommendations for women. It is likely that many of the women that received a biopsy only as definitive treatment failed to continue care. Many women were unable to afford chemotherapy and would miss cycles of chemotherapy before returning with more advanced disease. It is also possible that some of
these women presented with advanced disease that made them a poor candidate for other definitive treatments, especially since patients with advanced disease were more likely to undergo a diagnostic biopsy. Only 12% of overall patients underwent a partial mastectomy. Patients with stage 1 to 3 cancer were more likely to undergo an axillary dissection than patients with stage 4 disease, for whom treatment options were limited to palliative options.

There are multiple reasons why women present with advanced stages of disease. Clegg-Lamptey found that some were due to delays caused by previous medical consultations or ignorance or the painless nature of the lump and the fact that the patients thought the lump might disappear. Further, women in Ghana are likely to resort to traditional or spiritual methods of treatment, and when those methods fail they then turn orthodox medical advice. This data signifies that more public education is needed as well as an expansion of the Global National Health Services to cover the costs associated with the diagnostic process and to ameliorate the possibility of defaulting from care.

Cape Coast Teaching Hospital offers chemotherapy on-site, which enhances the ability for patients to access this form of treatment. This was evident in the data showing that 64.5% of patients that were staged received neoadjuvant chemotherapy. Patients with advanced stage 3 and 4 breast cancer were also more likely to receive neoadjuvant therapy compared with patients presenting with earlier stage disease as they were often too advanced to obtain other types of definitive treatments. Post-operative radiation therapy was more difficult to access because it was not offered at Cape Coast Teaching Hospital. The closest hospital that had radiation therapy was Korle Bu Teaching Hospital, which is located approximately 142.6 kilometers in Accra, Ghana. Post-operative radiation therapy was administered more often to patients with earlier stages of breast cancer. The definitive care for patients with early stage tumors was a partial mastectomy in addition to postoperative radiation therapy. At Cape Coast Teaching Hospital, it would be advantageous to create access for radiation therapy either on-site or by providing support for all patients to access radiation therapy at hospitals with that capacity. Other treatments such as tamoxifen and trastuzumab are not available at Cape Coast Teaching hospital, but may be offered at other hospitals.
**Histology and Survival Data**

There is evidence to support that breast cancer presents differently in African and African-American women compared to other populations. In the United States, black females have a lower overall incidence of breast cancer than white females, but are diagnosed with later-stage disease, have shorter survival, and have the highest mortality from breast cancer of all ethnic groups in the USA. In this study, only 3% of women had a known first degree family history of breast cancer and 3.6% had a known second degree family member with breast cancer. Pathology data was limited as many of the women either sought pathology at different institutions or didn’t end up getting pathology once they already had advanced disease. Invasive ductal carcinoma was the most common breast cancer malignancy, with a majority of malignancies being either Grade 2 (43.8%) or Grade 3 (45.2%). This study also found that the most common site of cancer was the upper outer quadrant with 54% of cancers reported as 5 centimeters or greater. Parkin et. al found that “there is little to no evidence for differences in histopathological type, but tumours in black females are of a higher grade, are more often hormone-receptor negative, and more often show characteristics of inflammatory breast cancer than those in white females”. Receptor status data was available for a fraction of the patients, as it is considered an out-of-pocket expense for patients. 46.1% of patients (n=89) in this study were noted to have a triple-negative breast cancer. Estrogen-receptor and progesterone-receptor breast cancers are typically associated with higher survival rates than triple-negative breast cancer. Other factors that are associated with poor survival include lymphatic vascular invasion and axillary node involvement. This study found that lymphatic vascular invasion was present in 47.2% in tumors and positive axillary lymph nodes were found in 77.0% of the 87 patients (OR=2.6 95% CI (1.7, 4.0, p<0.001) who underwent an axillary dissection with nodal status recorded.

In terms of patient survival, the data underestimates how many patients were lost to follow-up and/or eventually passed away from breast cancer. Only 21 patients were reported to have passed away from breast cancer, however that number may actually be much higher as many women return to their home villages if they cannot afford health care, when a mastectomy is recommended or when they may sense the situation is futile. Of those that were known to have succumbed to breast cancer, their disease statuses were so advanced that the mean duration from time of diagnosis to death was 4.6 +/- 4.7 months. Patients presented with metastatic disease to the brain, lungs, and liver the mean time for diagnosis of metastatic disease 14 +/- 8.0
months. 62.9 percent of these patients (n=21) passed away within one month of presenting to the hospital.

**Limitations:**
This study has several limitations. The medical records data available at the Cape Coast Teaching Hospital was often incomplete, especially in terms of pathology data and follow-up information. Data was compiled from electronic and paper records to try to compensate for missing information. In addition, Ghanaian patients that were able to access care at Cape Coast Teaching Hospital are overrepresented in the study. It is likely that the study does not capture the patients in isolated communities or patients that cannot afford to come in to the hospital.

**Conclusion**

*Policy Implications*

This study highlights several targeted and effective points of intervention. The approach would have to be multi-pronged and includes breast cancer education, screening, and resources to address the growing concern of breast cancer in Ghana. Late presentations occurred because many women have low awareness of their risks of developing breast cancer, unavailable screening programs, inaccessible specialized treatment centers, and sociocultural beliefs even amongst educated African women. 17 In addition, earlier studies have documented patients as having many reasons for presenting late to care, including: following the recommendations of non-medical personnel such as religious leaders, fear of medical institutions, and fear of disfiguring surgery. Once women did present, other barriers manifested themselves, including but not limited to financial obstacles in accessing biopsies, chemotherapy, and radiation therapy, and targeted therapy such as tamoxifen and trastuzumab. It appears that there are opportunities for interventions at every stage of the process. Comprehensive breast cancer education with instructions on a breast exam and information on risk factors should be incorporated into education as early as in high-school.

Breast cancer screening should also be tailored to the needs of the population and initiated early. Though many women in this study did have access to mammography, this represents a self-selected population of women that are able to access care. Data collected in 2015 amongst 2301 women found a prevalence of breast cancer screening using mammography
to be 3.6%. A cost-effective analysis of breast cancer screening in Ghana found the most cost-effective intervention would be biennial clinical breast exam screening in women aged 40-69 years combined with treatment of all stages, which would cost $1299 per DALY averted. On the other hand, mammography screening would be a financial burden on Ghana with the need for both equipment and human resources. Ultrasounds may also be a viable solution for women that have difficulty accessing mammography. A study on breast cancer screening in a resource poor country found that the sensitivity and specificity of each imaging modality were assessed with ultrasound yielding a high sensitivity (100%) and low specificity (22%) and mammography having a lower sensitivity than ultrasound (85%), but a much higher specificity (55.5%). Further, they recommend that annual breast cancer screening should start at the age of 30 with an ultrasound as the first-line screening tool in nulliparous women and parous women or both ultrasound and mammography in order to increase accuracy. They also found that ultrasound can be used as a first line of screening in remote areas of the developing world.

There is a significant advancement of breast cancer treatment access in the region served by Cape Coast Teaching Hospital supported by a dedicated surgical staff that provides surgical and medical treatment for breast cancer patients. Long-term goals for the hospital should include a tumor registry for prospective collection of data, social service support to reduce the number of patients lost to follow-up, and complementary medical staff included dedicated radiologists, pathologists, and medical and radiation oncologist. With the exception of the teaching hospitals in Kumasi and Korle Bu, no other Ghanaian facility has all aspects of breast cancer treatment within the same hospital. On a larger scale, financial barriers also exist due to inadequate and incomplete coverage by the National Health Insurance, which makes it difficult to access both diagnostics tests and treatment options and results in a lot of patients to default from treatment.

**Acknowledgement**

I would like to thank Dr. Rosemary B. Duda for her unwavering support and supervision throughout the course of this project. I would also like to thank my collaborators at Cape Coast Teaching Hospital for their guidance and expertise.
Tables:

Table 1. Stage of disease (n=189)

| Stage | Frequency | %    |
|-------|-----------|------|
| 0     | 1         | 0.5  |
| 1     | 5         | 2.6  |
| 2     | 34        | 18.0 |
| 3     | 77        | 40.7 |
| 4     | 72        | 38.1 |
| Total | 189       |      |
Table 2 Post-operative complications (n=185)

| Complication                  | Frequency | % of all complications | Overall Complication Rate |
|-------------------------------|-----------|------------------------|----------------------------|
| Surgical site infection      | 7         | 41.1                   | 3.8                        |
| Seroma, not infected         | 4         | 23.5                   | 2.2                        |
| Seroma, infected              | 1         | 5.9                    | 0.5                        |
| Profuse bleeding from tumor  | 1         | 5.9                    | 0.5                        |
| Swelling                      | 1         | 5.9                    | 0.5                        |
| Surgical site bleeding       | 1         | 5.9                    | 0.5                        |
| Wound ulceration              | 1         | 5.9                    | 0.5                        |
| Wound dehiscence              | 1         | 5.9                    | 0.5                        |
| Total                         | 17        | 100                    | 9.2                        |
Table 3. Non-operative breast cancer management compared with stage of disease at presentation (n=118)

| Stage | Non-operative interventions | | | | | |
|-------|-----------------------------|-------|---------------------|-------|---------------------|-------|
|       | Counts | Neoadjuvant | Post-Operative | Neoadjuvant | Post-Operative | Tamoxifen | Anastrozole |
|       | n | 0 | 0 | 0 | 0 | 1 | 1 |
|       | % | 0 | 0 | 0 | 0 | 100 | 100 |
| 1     | n | 0 | 1 | 0 | 1 | 2 | 0 |
|       | % | 0 | 20.0 | 0 | 25.0 | 40.0 | 0 |
| 2     | n | 16 | 11 | 1 | 1 | 1 | 0 |
|       | % | 48.5 | 33.3 | 3.0 | 3.0 | 2.9 | 0 |
| 3     | n | 52 | 35 | 0 | 1 | 11 | 4 |
|       | % | 68.4 | 46.7 | 0 | 1.4 | 14.7 | 5.3 |
| 4     | n | 50 | 13 | 2 | 0 | 7 | 2 |
|       | % | 73.5 | 18.6 | 3.1 | 0 | 10.0 | 2.9 |
| Total*| n | 118 | 60 | 3 | 3 | 22 | 7 |
|       | % | 64.5 | 32.6 | 1.8 | 1.8 | 11.9 | 3.8 |

*Total is expressed as total number and percent of patients who received the specific therapy from a cohort of 184 patients.
Table 4. Frequency of histologic types of breast cancer (n=164)

| Histology                                   | n  | %  |
|---------------------------------------------|----|----|
| Infiltrating ductal                         | 72 | 43.9 |
| Infiltrating lobular                        | 16 | 9.8 |
| Invasive, Not Otherwise Specified           | 73 | 44.5 |
| Paget’s disease                             | 2  | 1.2 |
| Intraductal carcinoma                       | 1  | 0.6 |
| **Total**                                   | 164| 100|

Table 5. Results of the axillary lymph node dissection (n=87)

| Number of Axillary Lymph Nodes | n  | %  |
|--------------------------------|----|----|
| None                          | 20 | 23.0 |
| 1                             | 16 | 18.4 |
| 2 to 4                        | 21 | 24.1 |
| 5 to 10                       | 22 | 25.3 |
| > 10                          | 8  | 9.2 |
| **Total cases reported**      | 87 | 100 |
Table 6. Disease status of all patients with known follow-up data (n=145)

| Disease Status                                           | n  | %   |
|----------------------------------------------------------|----|-----|
| No evidence of disease                                    | 52 | 35.9|
| Local recurrence alone                                   | 9  | 6.2 |
| Metastatic disease alone                                 | 49 | 33.8|
| Both local recurrence and metastatic disease             | 12 | 8.3 |
| Contralateral breast cancer                              | 2  | 1.4 |
| Dead of disease                                          | 21 | 14.5|
| Total cases reported                                     | 145| 100 |
Figures

Figure 1. Modified WHO Assessment and referral of women with suspected breast cancer at primary health care as part of the package of essential non-communicable (PEN) disease interventions for primary health care in low-resource settings.

Women who present the following persistent and unexplained signs and symptoms should seek consultation at a PHC:

- a) Breast lump, or any change in the shape or consistency of the breast
- b) Breast lump that enlarges and/or is fixed and hard
- c) Other breast problems (i.e. eczematous skin changes, nipple retraction, peau d’orange, ulceration, unilateral nipple discharge – particularly bloody discharge –, lump in the axilla) with or without palpable lump

Assess likelihood for breast cancer

- Assess signs and symptoms (i.e. history, intensity, duration, progression)
- Identify relevant breast cancer risk factors (such as age, family history, previous history of breast cancer, chest irradiation)
- Clinical examination of both breasts, axillae and neck
- Differential diagnosis: benign breast diseases (e.g. fibroadenoma, fibroadenosis, mastitis, abscess, etc.)

Women < 30 years old

- Presenting with a)
  - Invite for follow-up visit after menstrual period
- Follow-up visit: if b) or c)

Women 30 years old and above

- Presenting with:
  - a) + relevant risk factors, or
  - b) or c)
  - Refer immediately to next level

Access to care may be affected by:
- Low population awareness
- Insufficient breast cancer screening
- Proximity to primary health care centers

Triple negative breast cancers are more common in patients of African ancestry.

Breast cancer may present at a younger age in Ghanian women.

Referral centers may be limited based on location. May not have access to imaging and a variety of treatment options.

Note:
Referral of women with small breast lumps may lead to diagnosis of “early breast cancer.”
Figure 2. Modified Breast Cancer Treatment Guidelines adapted from American Cancer Society Guidelines.

- **Ductal carcinoma in situ (DCIS)**
  - Breast-conserving surgery or mastectomy
  - Radiation therapy
  - Hormone therapy

- **Stage 1-3**
  - Breast-conserving therapy or mastectomy
  - Radiation therapy
  - Hormone therapy
  - Targeted therapy
  - Chemotherapy

- **Stage 4**
  - Chemotherapy
  - Hormone therapy
  - Targeted therapy
  - Immunotherapy

- Many Ghanian patients present with advanced Stage 3 or 4 breast cancer, which limits treatment options that are available for local disease.

- Surgery is a mainstay in treatment of advanced disease. Radiation therapy and chemotherapy are available in certain treatment centers. Hormone therapy and targeted therapy are difficult to access.

- Patients presenting with metastatic disease are offered palliative mastectomies and/or palliative chemotherapy.
Figure 3. Distribution of breast cancer cases by location of residence.

This figure shows the residence of the women treated for breast cancer at Cape Coast Teaching Hospital. As expected, most of the residences were in the Central Region but a few, especially in more recent years, were from the Western Region.
Figure 4. Estimated cumulative prevalence of breast cancer by district, Central Region, Ghana 2011-2019

Estimated prevalence of breast cancer cases by district in the Central Region of Ghana. Most of the cases originate in the Cape Coast district and may be influenced by proximity to the Cape Coast Teaching Hospital.
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