Original article

Radiation therapy: A major factor in the five-year survival analysis of women with breast cancer in Lagos, Nigeria

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ABSTRACT

Purpose: This retrospective study was carried out to examine five-year survival from breast cancer cases diagnosed between 2005 and May 2008 in Nigerian women.

Material and methods: Two hundred and twenty-four patients were entered into the study. Five-year survival was evaluated using proportional hazard model proposed by Cox to assess variables such as age of diagnosis, menopausal status, and stage of the disease in the two treatment groups: surgery/chemotherapy or surgery/chemotherapy/radiotherapy.

Results: Findings revealed that the different staging of disease and treatment are independent predictors of disease outcome whereas age of diagnosis and menopausal status although associated with low hazards, are not significant. TNM Stage I (Hazard Ratio = 0.153, 95% CI 0.45–0.51, $P = 0.003$), II (Hazard Ratio = 0.245, 95% CI 0.12–0.46, $P = 0.0001$), and III (Hazard Ratio = 0.449, 95% CI 0.31–0.46, $P = 0.0001$) showed significantly greater survival rates compared to TNM Stage IV for patients receiving surgery/chemotherapy. Similarly, for patients receiving surgery/chemotherapy/radiotherapy TNM Stage II (Hazard Ratio = 0.110, 95% CI 0.02–0.46, $P = 0.003$) and III (Hazard Ratio = 0.238, 95% CI 0.07–0.73, $P = 0.012$) also showed significantly greater survival rates compared to TNM Stage IV. Treatment had a significant impact on survival independent of stage, age, and menopausal status. Patients receiving surgery/chemotherapy/radiotherapy had a significant increase in survival outcome for TNM Stage (II, $P = 0.045$; III, $P = 0.0001$); age groups (40–49, $P = 0.021$; 50–59, $P = 0.016$; 60–69, $P = 0.017$; >70, $P = 0.025$); and menopausal status (premenopausal, $P = 0.049$; postmenopausal, $P = 0.0001$) compared to those receiving surgery/chemotherapy.

Conclusion: The five-year breast cancer survival rate in Lagos, Nigeria 24.1% (54/224) is relatively poor compared to most countries in the world and needs to be improved. Poor survival rates are mainly attributed to late presentation and poor follow-up, hence early detection through breast cancer awareness programs, appropriate logistics and better management of patients through guidelines for the treatment of breast need to be implemented to improve survival.

The major predictors of treatment outcome for breast cancer patients classically are the tumor size and axillary node status, and recently molecular biology of the tumor [1]. Detection of breast cancer at an early stage provides a greater chance of survival. Non-invasive (Stage 0) and early stage invasive breast cancers (Stage I and II) have a better prognosis than later stage cancers (Stage III and IV). The poorer prognosis is for metastatic breast cancer, Stage IV [2].

Unfortunately, most of the breast cancers presented at this tertiary Institution in Nigeria are locally advanced breast cancer, greatly reducing chance of survival. An earlier study has indicated that at the time of presentation Stage III and IV breast cancers accounted for 45.6% and 35% of all breast cancer cases, respectively [3].

The incidence of breast cancer in developing countries including Nigeria is lower compared to developed countries [4]. However, due to poor breast cancer awareness and late presentation, Nigeria shows high mortality rates for breast cancer.

In the absence of an established National screening program for breast cancer as well as the lack of relevant funding for breast cancer diagnosis and treatment, the stage at diagnosis is a reflection of the degree of awareness of the disease in the population.

Beside late presentation, age at diagnosis seems to have an influence on disease outcome. Young women (35–49 yrs) with

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breast cancer have poorer prognosis compared to older women (over 50 yrs) [5]. Additionally, race also has a major influence on disease outcome. Black patients are nearly twice as likely as white patients to die from breast cancer. Black–white differences in breast cancer survival rates have been traditionally attributed to the fact that black women are more commonly diagnosed with less treatable tumor subtypes. Yet others maintain that factors such as poverty, poor medical care, silence, and racial inequities are responsible for high mortality rates [6].

Treatment of Breast Cancer in most Nigerian Hospitals includes surgery, chemotherapy, hormonal therapy and radiotherapy. Surgery can be lumpectomy for breast conserving surgery in early stages of disease or mastectomy with axillary clearance in locally advanced disease. Chemotherapy neoadjuvant is used to downsize the tumor for possible curative surgery and eradication of micro-metastasis or as an adjuvant to eradicate micro-metastasis and prevent systemic recurrence. Radiotherapy is for elimination of postoperative residuals. Most patients also benefit from Hormonal treatment, which for most Institutes is based on evidence suggesting that ER/PR positivity rates in Nigerians are the same as in Western countries [7].

In this study we primarily evaluated the five-year survival rate among women diagnosed with breast cancer at different stages of the disease. Secondly, we assessed the effectiveness treatment in operable breast cancer by evaluating the survival rates among patients who had mastectomy followed by chemotherapy and those who had mastectomy followed by chemotherapy and radiotherapy. Lastly, we evaluated additional factors that are predictive of a five year survival following diagnosis including age at presentation and menopause status.

Materials and methods

Data collection

Data were obtained from breast cancer files from the Lagos State University Teaching Hospital (LASUTH) Cancer Registry from 2005 to May 2008 having obtained informed consent from these patients and LASUTH ethical approval. This Cohort of patients was subsequently followed up for a period of five years. The files of patients which contained their background information were kept and information on health outcomes was recorded once they were noticed. The information collected from patient's files included the following: age at diagnosis, diagnosis, type of treatment received, staging of disease, and menopausal status. This study included 361 patients diagnosed with breast cancer from 2005 to May 2008 for whom pathology information was available.

Treatment policy

The Oncology Clinic of LASUTH where this study was conducted receives breast cancer cases by referral from the surgical clinic following histological confirmation of tissue biopsy and pre-treatment investigations including full blood counts, chest radiograph, and abdominal ultrasonography. The patients at this stage undergo either neoadjuvant chemotherapy for locally advanced breast cancer to downsize the tumor before surgery or receive adjuvant treatment post-operatively. Loco-regional approach to treatment in the reported cases entails surgical removal of the affected breast followed by chemotherapy and radiotherapy. In early stage disease (Stage I and II), surgical treatment was simple mastectomy with axillary clearance. In this form of treatment the breast is removed with overlying nipple and areolar, followed by removal of palpably enlarged axillary lymph nodes for pathological examination and staging of the disease. Toilet mastectomy in locally advanced disease (Stage III) was performed mainly for palliation. Some of our cases in stage I had breast conservative surgery of the nature of lumpectomy followed by local post-operative radiotherapy. This treatment which requires removal of the lump with a good margin of normal breast tissue is generally reserved for early stages of breast cancer and is usually followed up immediately with adjuvant radiotherapy. Combination of chemotherapeutic agents using 6 cycles of Intravenous Adriamycin, Cyclophosphamide (AC) or 4 courses of Intravenous, Adriamycin, Cyclophosphamide was followed by 4 courses of Intravenous Paclitaxel every 3 weeks among others. In the few early stage breast cancer cases, after lumpectomy, a dose of 45 Gy was given to the tumor bed in 18 fractions and 15 Gy was given to the lumpectomy scar in 5 fractions. Post mastectomy radiation treatment to the chest wall and supraclavicular lymph nodes was performed to decrease the risk of loco-regional recurrence in patients with four or more positive lymph nodes and in patients with tumor size > 5 cm. Radiation up to 45 Gy in 18 fractions from Mondays to Fridays (5 days a week) was given to the anterior chest wall (tumor bed), supraclavicular and axillary lymph nodes after mastectomy. The radiation is delivered by cobalt 60 Radiotherapy Machine. 30 Gy in 10 fractions was given for palliative care mainly for bone pain in bone metastasis and metastatic cord compression to relieve the pressure. Hormonal therapy was given using anti-estrogens for all patients.

Data management

Information obtained was stored in a Sony Compatible computer and analyzed using SPSS version 17.0. Information extracted included the following: type of treatment (surgery/chemotherapy or surgery/chemotherapy/radiotherapy), TNM Stage (I, II, III, and IV), age at diagnosis and menopausal status. This study included 361 patients diagnosed with breast cancer from 2005 to May 2008. The records were matched with LASUTH death files from 2005 to 2013. A passive patient status (dead or alive) was employed and patients were followed until May 31st, 2013. Among the initial 361, 99 patients were reported dead due to breast cancer. No deaths were recorded for causes other than breast cancer. 137 patients were lost to follow-up, meaning that 224 patients met the selection criteria and were included in the survival analysis.

Two hundred and twelve patients received chemotherapy and only 12 failed to receive chemotherapy due to both very late stage of disease and intolerance to the treatment. One hundred and seventy-nine patients had surgery while for the remaining 45 there was no record of surgery. This was primarily associated with late stage disease and on occasion patient refusal. Only 91 out of the 224 patients received radiotherapy, although almost double the number of cases were eligible for radiotherapy after undergoing surgery and chemotherapy. However, due to financial constraints in some cases and poor follow-up in other cases, this has led to delays or non completion of the treatment. Two treatment categories were studied: surgery/chemotherapy (108) and surgery/chemotherapy/ radiotherapy (91), while 25 received unknown treatments.

Five age groups were included: <40 (42), 40–49 (61), 50–59 (51), 60–69 (50), and >70 (20).

All four stages of breast cancer were included: Stage I (7), Stage II (19), Stage III (130), and Stage IV (44), while 23 patients had no record of the stage of disease.

Menopausal status was included as follows: premenopausal (97) and postmenopausal (111), whereas 16 patients had no record of menopausal status.

The survival time in months for each of the patients was calculated from the date of diagnosis to the date of death. The major purpose of the analysis was to determine five-year survival from breast cancer. The model included: TNM staging, age group at