

PATTERNS OF BREAST CANCER CHEMOTHERAPY USE AND ADHERENCE TO TREATMENT IN UNIVERSITY COLLEGE HOSPITAL, IBADAN, NIGERIA

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ABSTRACT

The study determined the patterns of chemotherapy use, treatment adherence, and the association between demographics and adherence to chemotherapy. A retrospective study of patients in the Surgical Oncology Division, University College Hospital, Ibadan was conducted after ethical approval with the number UI/UCH/EC/18/0580. Female patients with not < 3 months' history of breast cancer management were included and patients with cognitive impairment and psychiatric disorders were excluded. The data collected were demographics, histology, immunohistochemistry status, chemotherapeutic agent, other therapies, adherence to therapy, and appointments. The data were analyzed with SPSS version 20 for

descriptive statistics and Chi-Square test for inferential analysis. There were hundred patients with a mean of 52.75 ± 12.63 years, most 88(88.0%) were employed and 2(2.0%) had a family history of cancer or breast cancer. About 66 (66.0%) presented with lump and swelling, 17(17.0%) were recurrent breast swelling cases. Many 42(42.0%) were in stage IIIB, 18(18.0%) were in stage 0, while Stage IIA and Stage IIIA were 9(9.0%), and 5(5.0%) were in Stage IV. Also, 54 (54.0%) had an adjuvant, 44(44.0%) neo-adjuvant and 2(2.0%) had both mode of treatment, 55(55.0%) had combination of Cyclophosphamide and epirubicin while 9(9.0%) had combination of Cyclophosphamide, epirubicin & ondasetrim. About 57% were adherent, 16% non-adherent, and 27 % systemic non-adherent to chemotherapy. There was no significant association between types of chemotherapy treatment and the patient's age (P-value= 0.736), stages of breast cancer (P-value = 0.736), level of adherence was not

significantly associated with patient's age (P-value = 0.159), treatment modality (P-value = 0.197) and the stages of breast cancer (P-value = 0.334). Many of the patients were in stage III at presentation, they were mostly placed on combination chemotherapy. There was no significant association between types of chemotherapy treatment or level of adherence and the age of the patient as well as stages of breast cancer.

KEYWORDS: Breast cancer, chemotherapy, adherence, non-adherence, adjuvant, neoadjuvant.

INTRODUCTION

Breast cancer is a global health issue with high morbidity and mortality in cancers affecting women.^[1] The incidence and mortality in the low and middle-income countries (LMICs) are increasing and it is about 30% in sub-Saharan Africa in the last two decades.^[2,3,4] The outcomes of treatment are poor in LMICs due to late presentation and lack of high-quality treatment compare with the United States.^[3] There are over one million incidences of breast cancer diagnosed yearly in females which is over one-third of the estimated annual diagnosis of 4.7million cancer in females as well as the second most common tumor after lung cancer in both sexes thus making it the most prevalent cancer in women in both developed and developing countries.^[5]

However, WHO (2004) said that in breast cancer rates over 85% of the cases cannot be linked to inherited genetic predisposition.^[6] In Nigeria, there are about 100,000 new cases yearly which were predicted to be up to 500,000 cases by 2010. According to Lambo (2007), only 6 laboratories are available to 4 million Nigerian patients requiring radiotherapy thus making about 15% have access to facilities.^[7] Sadly, the survival rate is 85% in the US and a dire 10% in Nigeria.^[8] The occurrence is mostly in the premenopausal period within the 43-50 years mean age and about 15% of the cases occurred in women less than 30 years in Lagos State, Nigeria.^[9]

Predisposition to breast cancer by over 50% of patients is inexplicable despite known risk factors like smoking, obesity, high-fat diets, genetics, family history, and lifestyle modifications.^[10] Besides, lack of signs and symptoms as well as ignorance of women about the high risks of cancer as compared with other diseases is also a contributing factor.^[11]

Nigeria advocated for the health education of women to conduct routine: “Breast Self Examination” (BSE) that can easily reveal changes in the breast that may require further evaluation by the physician.

Chemotherapy is administered to patients intravenously or orally in an outpatient setting. The protocols could be a cycle of three weeks of treatment or more frequent for three to six months. Many women can work while receiving chemotherapy treatment, they only miss a few days at a given period. Neoadjuvant chemotherapy is medicines that are given before surgery and are clinically indicated for patients with large tumor size, an inflammatory component, and high nodal involvement, or for patients that wish to preserve remnant breast tissue^[12] which is the presentation by the majority of patients with breast cancer in Nigeria.^[9,13,] In the past decades, this approach has been beneficial in the treatment of other patients in addition to those with operable early-stage breast cancer. The fundamental change from the adjuvant to the neoadjuvant chemotherapy is the essence of the understanding of tumor kinetics and the supposition of micrometastatic disease present in breast malignancy at the early stages.^[14] Neo-adjuvant therapy includes the combinations of cytotoxic chemotherapy, hormonal therapy, and targeted molecular agents like trastuzumab and pertuzumab but this depends on breast cancer subtype.^[15] In breast cancer treatment, the gold standard for some time now is the surgery thereafter the adjuvant treatment.^[16] However, in more recent times, neoadjuvant treatment has become acceptable for advanced breast cancer management.^[17]

Non-adherence contributes greatly to the drug’s therapeutic effect variability in patients that can elicit poor outcome or therapeutic failure.^[18] Adherence is the extent to which a patient complies with medical advice. In the Nigerian population, there is a paucity of data on the adherence to chemotherapy and its outcome on treatment. Careful evaluation of patient-specific factors is cogent when working up plans for adherence. Awareness of factors like co-morbidities or depression can help in tailoring interventions that are specific to the patient's needs.

Thus, a chemotherapeutic agent's benefits can only be achieved if patients adhere to their use.^[19] In LMICs compliance to chemotherapy by patients is poorer than the advanced countries.^[20,21] DiMatteo et al (2000) opined that non-adherence in patients with depression was high and the risk increased with complex medication regimens.^[22] Patients on multiple medications for cancer treatment or with co-morbid conditions have the burden of following

and adding the new chemotherapy agent to their current medication regimen and lifestyle. This can present additional risks of drug and drug or medication and food interactions. This study hopes to help with reforms in the process of chemotherapy agent administration and also to evaluate the factors associated with compliance for better patient management. The aims are to determine the patterns of chemotherapy use, treatment adherence, and the association between demographics and adherence to chemotherapy in the Surgical Oncology Division, University College Hospital, Ibadan.

METHODOLOGY

Study Design and Setting

There was a retrospective study of the medical records of the histologically confirmed cases of breast cancer patients seen in University College Hospital (UCH), Ibadan, Oyo State. The UCH Ibadan has 56 clinical departments and that runs 96 consultant out-patient clinics per week in 50 subspecialty and specialty areas.

Study procedure

Ethical approval from UCH Institutional Review Board and Administrative permission was obtained from the UCH administration office to work with Medical Record Officer at the Surgical Oncology clinic, UCH to retrieve the case file. The documentation of information according to the format designed was retrieved from the case files.

Non-adherence was defined as an absence for two consecutive doses of chemotherapy. Those excluded as defaulters are patients with dose reduction and/or omission as a result of inadequate hematological profile or poor clinical condition. The patients that missed medications due to impromptu public holidays or other things they could not control, but came the following week also were captured.

Inclusion criteria: were patients with a minimum of three months of breast cancer management history at Surgical Oncology Clinic, UCH, Ibadan.

Exclusion criteria: were patients with cognitive impairment, depression, or psychiatric disorder.

Study instrument

A well-designed data form that captures all the variables for the evaluation of chemotherapy adherence data was used. The variables included were patient demographics, diagnosis,

histology information, immunohistochemistry status, the type of chemotherapeutic agent, the number of courses prescribed, the dosage, and other therapies such as immunological medications. Patients' adherence to therapy and appointments were noted.

Breast cancer is usually described in stages, according to the presence and size of the tumor, and its metastasis in the axillary lymph nodes, and other factors. T refers to the tumor size. For breast tumors, bigger than 2cm changes the T category. N refers to „*node status*,,, which changes as the tumor spreads into lymph nodes. M refers to „*metastasis*,,, which indicates that cancer has spread to places beyond the breast. The TNM classifications were developed by the American Joint Committee on Cancer (AJCC).^[15]

Data analysis

The data collected were entered and analyzed with Statistical Package for Social Sciences (SPSS) version 20 for descriptive statistics and inferential analysis like the Chi-Square test was done for the association of adherence with treatment modality, stages of diseases, and age.

Ethical considerations

The University of Ibadan/University College Hospital Institutional Review Board for ethical review approval was sought and received with number UI/UCH/EC/18/0580. The confidentiality of all information was ensured.

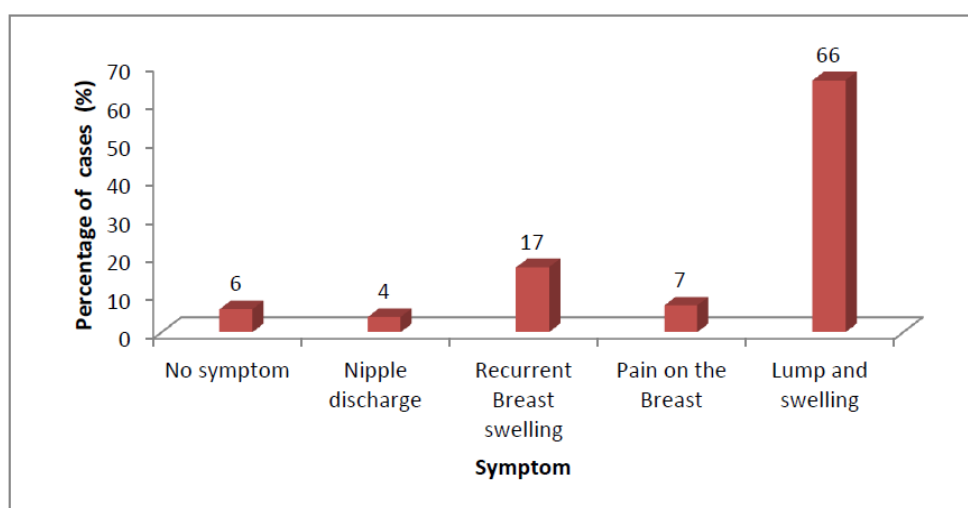
RESULTS

A total of 100 breast cancer cases in females were studied. The ages ranged from 23 to 90 years with a mean of 52.75 ± 12.63 years, one-fifth of the patients were below 40 years of age, with 27(27.0%) and majority 56(56.0%) were between 40-59 years old. Most patients 88(88.0%) were actively engaged and 12(12.0%) being unemployed, student, or retired from active service. Every patient had religious-affiliation, 88(88.0%) were Christian and 18(18.0%) were Muslims. Table 1 showed that 2(2.0%) of the patients had a previous family history of cancer or breast cancer which occurred in the mother or aunt of the patients.

Table 1: Demographic data.

Variables		Frequency	Percentage
Age (years)	<30	1	1.0
	30-39	15	15.0
	40-49	27	27.0
	50-59	29	29.0
	60-69	18	18.0
	70-79	7	7.0
	≥80	3	3.0
Occupation	Unemployed/student	8	8.0
	Selfemployed/ businesswomen	63	63.0
	Civil servant	24	24.0
	Retired	5	5.0
Family history of any cancer	Yes	2	2.0
	No	98	98.0
if a family history of cancer, the person affected	Mother	2	2.0
family history of breast cancer	Yes	2	2.0
	No	98	98.0
if a family history of breast cancer, the person affected	Mother	1	1.0
	Aunty	2	2.0

Figure1 showed that 66(66.0%) presented symptoms of lump and swelling and 17(17.0%) recurrent breast swelling cases. While Figure 2 showed that 42(42.0%) of the breast cancer patients in stage IIIB were in the highest proportion, 18(18.0%) were stage 0, while Stage IIA and Stage IIIA were 9(9.0%) of the cases and Stage IV were 5(5.0%).

**Figure 1: Distribution of symptom at presentations.**

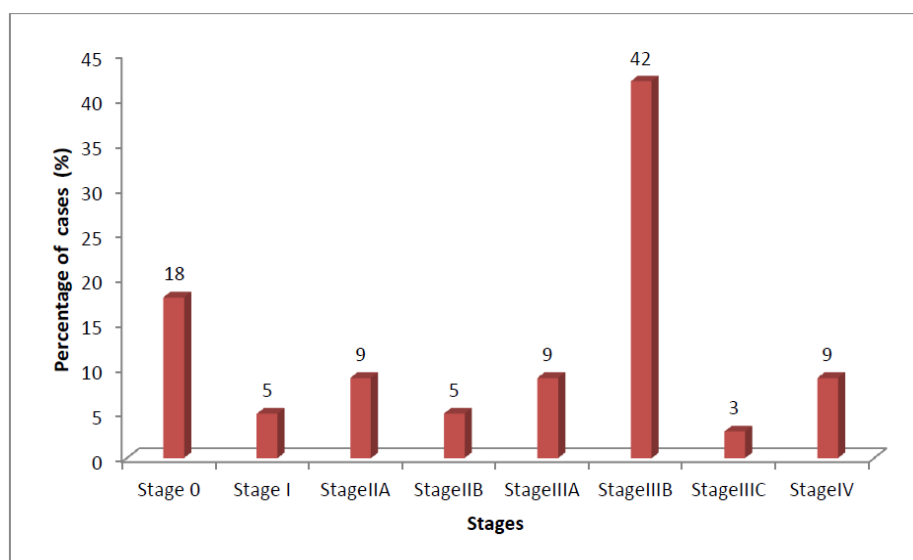


Figure 2: Distribution of Pattern of stages of breast cancer patients.

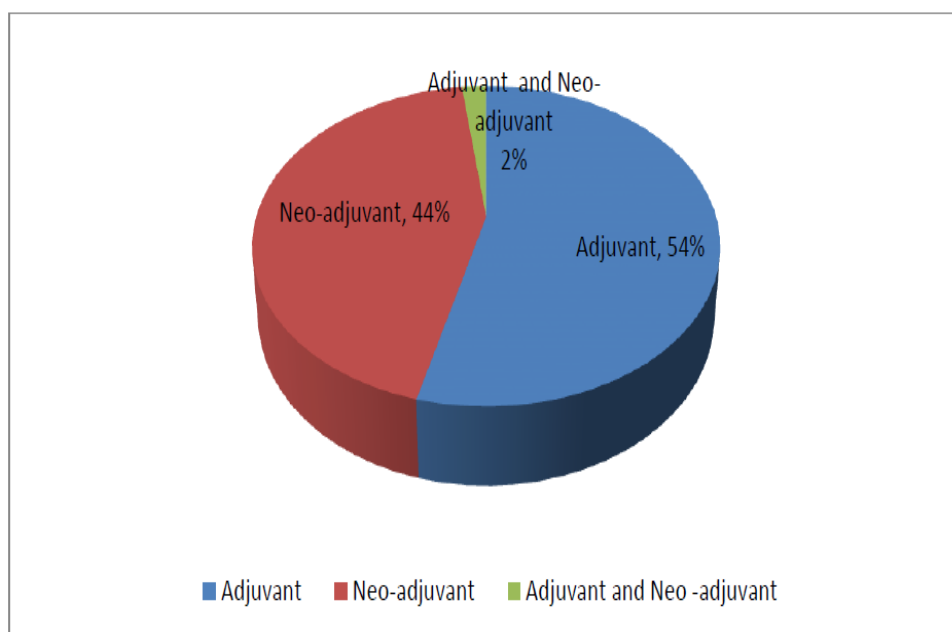


Figure 3: Distribution of treatment modality of breast cancer patients.

Figure 3 above showed that 54 (54.0%) of the breast cancer patients in this study had an adjuvant mode of treatment, 44(44.0%) had the neo-adjuvant mode of treatment and 2(2.0%) had both treatment modality.

Table 2 showed that 55(55.0%) of the breast cancer patients had chemotherapy combination of Cyclophosphamide and epiribicin as the highest proportion in this study, next, is a combination of Cyclophosphamide, epiribicin, and dexamethazone was used by 14(14.0%) of the cases and a combination of Cyclophosphamide, epiribicin & ondasetrim was used by

9(9.0%) of the cases. Figure 4 showed the technical reason for the break-in chemotherapy treatment by 16 breast cancer patients in this study that were classified non-adherent and 27 patients that were classified as systematic non-adherent.

Table 2: Distribution of type of chemotherapy (drugs used).

Types of drugs used	Frequency	Percent
Cyclophosphamide & Epiribicin	55	55.0
Cyclophosphamide , Epiribicin & dexamathazine	14	14.0
Epiribicin & dexamathazine	4	4.0
Ondasetrim, &iv padiclitaxel	7	7.0
Cyclophosphamide & methodrexate	1	1.0
Cyclophosphamide & Adriamycin	2	2.0
Cyclophosphamide, epiribicin & ondasetrim	9	9.0
Incomplete documentation	8	8.0

A bulk of the patients 57(57.0%) in this study were classified adherent and completed every required of chemotherapy while 16% of the cases were non-adherent and 27% of respondents had a break in their chemotherapy. The reasons for non-adherence were; change in clinical condition, financial constraints, strike, and loss to follow up as seen in figure 4.

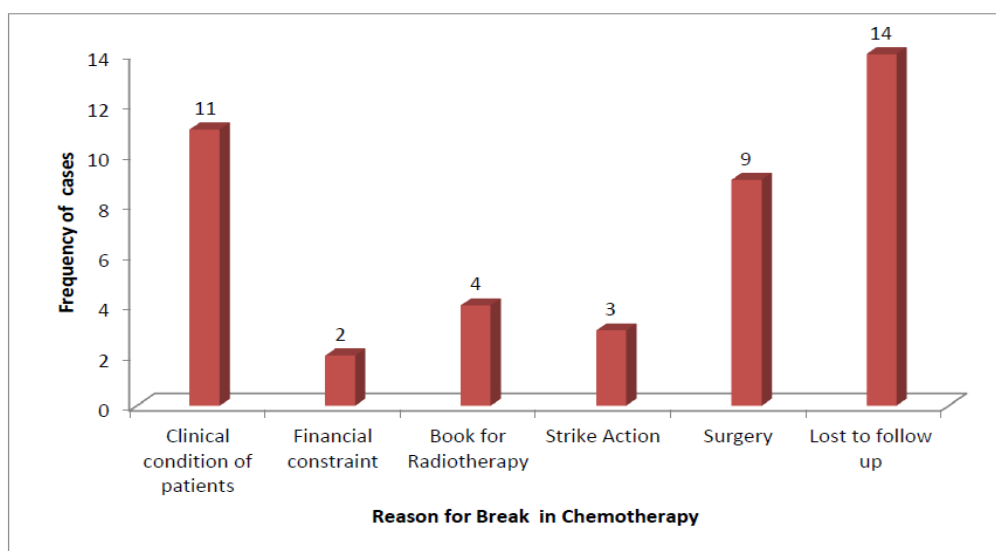


Figure 4: Distribution of reason in break-in chemotherapy.

Table 3 showed that there was no significant association between the age of breast cancer and the type of chemotherapy treatment. (Chi-square =2.034, P-value= 0.736). Also, there was no significant association between the pattern of stages of breast cancer and the pattern of chemotherapy treatment in this study (Chi-square =10.353, P-value = 0.736)

Table 4 showed that level of adherence to treatment with chemotherapy was not significantly associated with stages of breast cancer (Chi-square =15.675, P-value = 0.334) The level of adherence to treatment with chemotherapy was not significantly associated with the type of treatment modality (Chi-square =6.030, P-value = 0.197) Table showed that level of adherence to treatment with chemotherapy was not significantly associated with the age of patients of breast cancer (Chi-square =6.590, P-value = 0.159).

Table 3: Association between pattern stages of breast cancer and the pattern of chemotherapy treatment

Variables		Adjuvantn (%)	Neo- Adjuvantn (%)	Adjuvant and Neo- Adjuvantn (%)	Total	Chi- square	P- value
Stages	stage0	8(44.4)	9(50.0)	1(5.6)	18	10.353	.736
	stage1	4(80.0)	1(20.0)	0	5		
	state11A	7(77.8)	2(22.2)	0	9		
	stage11B	2(40.0)	3(60.0)	0	5		
	Stage111A	6(66.7)	3(33.3)	0	9		
	stage111B	19(45.2)	22(52.4)	1(2.4)	42		
	stage111C	1(33.3)	2(66.7)	0	3		
	Stage IV	7(77.8)	2(22.2)	0	9		
Age (years)	0-39	10(62.5)	6(37.5)	0	16	2.034	.730
	40-59	29(51.8)	25(44.6)	2(3.6)	56		
	≥60	15(53.6)	13(46.4)	0	28		

Table 4: Association between stages of breast cancer and the level of adherence.

		Break in Chemotherapy (%)	Adherencen (%)	Non- adherence (%)	Total	Chi- square	Total
Stages	stage0	3(16.7)	9(50.0)	6(33.3)	18	15.675	334
	stage1	2(40.0)	2(40.0)	1(20.0)	5		
	state11A	2(22.2)	6(66.7)	1(11.1)	9		
	stage11B	2(40.0)	3(60.0)	0	5		
	Stage111A	2(22.2)	5(55.6)	2(22.2)	9		
	stage111B	10(23.8)	29(69.0)	3(7.1)	42		
	stage111C	1(33.3)	1(33.3)	1(33.3)	3		
	Stage IV	5(55.6)	2(22.2)	2(22.2)	9		
Type of treatment	Adjuvant	14(25.9)	30(55.6)	10(18.5)	54	6.030	.197
	Neo- adjuvant	11(25.0)	27(61.4)	6(13.6)	44		
	Adjuvant and Neo- adjuvant	2(100.0)	0	0	2		
Age of patients	<40	6(37.5)	9(56.2)	1(6.2)	16		

	40-59	10(17.9)	36(64.3)	10(17.9)	56	6.590	.159
	≥60	11(39.3)	12(42.9)	5(17.9)	28		

DISCUSSION

This study found that the middle age and elderly women have highest case of breast cancer with one-fifth of them under 40years, which is similar to other studies across Nigeria.^[23,24]

Why the occurrence of breast cancer is mostly in the younger age range in Africa has not been identified. However, it may be connected to the young population of most African nations, but this study could not relate the occurrence to the family history of respondents.

The late presentation to the hospital is a problem that occurs among patients as observed in this study where 42% of the patients were in stage IIIB and 5% were already in Stage IV.

This is similar to other studies that found that late presentation of breast cancer patients cut occurs in many other developing nations.^[25]

The highest presenting symptoms were recurrent swelling and lump growth at the hospital visit for clinical breast examination. This could be a result of poor awareness and low level of organized public enlightenment and screening programmes for breast cancer particularly among women in rural areas in Nigeria. Also, few women practice breast self-examination and clinical breast examination.^[26]

Due to the late presentation, chemotherapy is the mainstay in the management of these patients. Every patient in this study had chemotherapy either as neo-adjuvant or adjuvant or a combination that was used in all the patients and the usual Cyclophosphamide is about 80% of all the cases presented. In this study, the combination of Cyclophosphamide and epirubicin was the highest at 55%, however, they were unavailable and unaffordable for most patients. According to Carlson et al, (2006) and National Comprehensive Cancer Network (NCCN) guidelines, they recommended continuation of chemotherapy till the disease progression in patients with estrogen and progesterone-receptors tumors, symptomatic visceral metastases, or disease refractory to hormonal therapy which provide the potential benefit of prolonging chemotherapy administration.

A significant proportion of the patients are petty traders, civil servants with periodical delayed salaries, found it challenging to afford newly prescribed combination CE

chemotherapy, thus invariably affected their adherence to chemotherapy roster. Indeed, about 16% of patients were non-adherence due to financial constraints. According to Adisa et al, 2008, many patients were unable to obtain and continue the chemotherapy schedule beyond the first of their course.^[19] A similar study at Sussex, UK were 55% of patients were non-adherent to medications either unintentionally or intentionally. Side effects of drugs were the reason for nonadherence in women on Tamoxifen.^[27] In this study, some patients had systematic non-adherence because of other clinical plans and labour industrial disputes while few were intentional non-adherence. However, the level of adherence to treatment with chemotherapy was not statistically significantly associated with patients' age ($p>0.05$). There is conflicting evidence about the role of patient factors in forecasting chemotherapy nonadherence, which makes the association demographic characteristics and non-adherence unclear.^[27] In this study, the association between level of adherence to treatment was not significant with stages of the breast cancer ($p>0.05$) and with the type of treatment modality ($p>0.05$) This is similar to the study that found that there was no association between nonadherence and disease stage and treatment-related symptoms.^[28]

CONCLUSION

Many of the patients were in stage III at presentation, they were mostly placed on a combination of Cyclophosphamide and epirubicin chemotherapy. There was no significant association between types of chemotherapy treatment or level of adherence and the age of patients as well as stages of breast cancer.

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