TREATMENT OF BREAST CANCER IN ACCRA: 5-YEAR SURVIVAL

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SUMMARY

We studied 145 patients most of them with locally advanced breast cancer (LABC) disease over an 8-year period to assess two-and-five-year survival using currently available treatment modalities.

All patients were given Tamoxifen. Combination chemotherapy-adriamycin based was given to those who could afford it. They all underwent mastectomy and axillary clearance whenever possible.

The incidence of the disease peaked at the ages 35-45years and above 65years. There was a prolonged time interval between awareness of lump and presentation at hospital. Two-and-five-year overall survival (OS) and disease free survival (DFS) were 63.9%; 25.3% and 54.2%; 19.3% respectively irrespective of the treatment modality. A significant advantage of treatment with chemotherapy over no chemotherapy was observed in the 2year disease free survival group (p=0.0039). Mortality within the first two years of treatment was highest in patients who failed to respond to chemotherapy.

We concluded that this is a poor result and that public health measures to create awareness, promote early detection and encourage early presentation are some of the ways to reduce mortality from breast cancer disease in this country.

Keywords: Breast cancer, Locally advanced, Survival.

INTRODUCTION

The treatment of breast cancer disease has undergone changes over the years. The radical mutilating surgery has given way to present day breast conservation.

In the 1940's, 5-year survival rate of locally advanced breast cancer (LABC) disease was reported at 3% after radical surgery[1]. The introduction of radiotherapy added no survival advantage and only minimal improvement in the local disease control. This was however negated by treatment-related morbidity[2]. This failure of loco-regional treatment alone, even in Stage I disease led to the realization that micrometastasis-the ultimate cause of death in breast cancer patients, occurs in most patients before clinical diagnosis is made. Extensive local treatment may, therefore, not affect the final outcome. A systemic adjuvant therapy – chemo or hormonal therapy-that attacks the micrometastasis is, therefore, indicated. This was demonstrated in node positive patients by Fisher et al[3] and Bonnadona et al[4] who reported 73.9% 5-year survival using chemotherapy. Freis' introduction of induction (neo-adjuvant) chemotherapy as part of multimodality treatment saw an improvement in local disease control and overall survival when compared with historical controls[5]. The advent of mammographic screening for breast carcinoma in the "at risk group" has seen earlier detection of both invasive and non-invasive breast cancer with consequent better prognosis[6]. Rosen et al reported 91% 10-year disease free survival in patients with 1cm diameter lesion treated by surgery alone[7].

It is against this encouraging background of progressive reduction of mortality in breast cancer disease that this prospective study was carried out to assess the overall 5-year survival of breast cancer patients on one surgical unit of the Korle Bu Teaching Hospital (KBTH) where the vast majority of patients present with advanced disease and are often unwilling to accept mastectomy.

MATERIAL AND METHODS

The study covers breast cancer cases seen by one general surgical unit in Korle Bu Teaching Hospital from January 1990 to December 1998. Those who initially accepted mastectomy as part of the treatment were included in the study (some patients failed to turn up when told that treatment would involve loss of the breast). The diagnosis of breast cancer was made by history and clinical examination, and confirmed by fine needle aspirate cytology (FNA-C) and rarely by excision biopsy when

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the diagnosis was in doubt. There were few cases referred to us with diagnosis already confirmed by excision/incision biopsies.

All patients were given Tamoxifen. Except in very few cases (two) when tumour size was less than 2cm, all patients with no contraindication to chemotherapy were advised to have induction chemotherapy-adriamycin based before surgery to be followed by post-operative chemotherapy if they could afford it. Those who had no induction chemotherapy either had had excision biopsy elsewhere or had tumours less than 2cm in its widest diameter when induction chemotherapy was adjudged unnecessary. Drug regimen and dosage were as reported elsewhere[8].

All patients had total mastectomy plus axillary clearance where possible. Those patients with inoperable tumours and who could not afford chemotherapy were given only Tamoxifen. No patient in this study had radiotherapy. The facility was not available. Eleven cases of early breast cancer (<5cm in diameter) patients were included in this analysis.

RESULTS

One hundred and forty five (145) patients were studied with an age range of 23 to 85years and a mean of 47years. There were 142 females and 3 males. The age distribution is as shown in figure 1 and relative specific age incidence based on the projection of 1984 Ghana population census is as shown in figure 2.

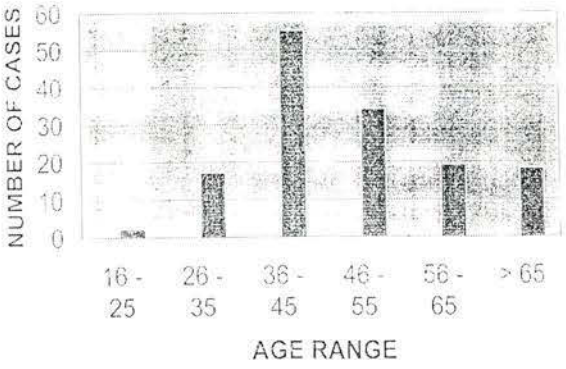

Figure 1 Age distribution

Fifty-three patients (36%) had been aware of their breast lump for greater than 1year duration before reporting to a doctor. Only 16% were seen within the first four weeks of lump awareness.

Thirteen patients had a positive first-degree family history of breast carcinoma. One male patient had lost two sisters and the mother to the disease and a female patient had lost two sisters.

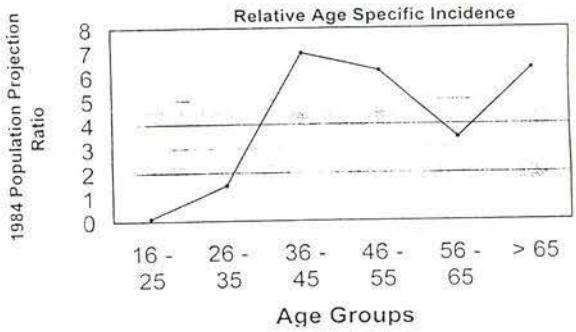

Figure 2 Relative age specific incidence

There were six bilateral tumours. Their mean age was 41.8years. Most patients had involvement of the skin overlying the breast and 12 ulcerated cases confessed to the use of herbs. Five patients spent time with the herbalist and one went into a church house. Only 18 (12.4%) of the study group had tumours less than 5cm in the widest diameter and eleven of those were included in this analysis. There were 115(79.3%) patients with clinically palpable nodes.

Thirty-two patients were lost to follow-up before the end of two years. Of these 29 had only Tamoxifen, ten had one or two cycles of chemotherapy and three had surgery. They were not included in the analysis. Another twenty who had been followed up for less than 2years were also excluded, leaving 83 patients for analysis.

Table 1 shows overall and disease free survival at 2years and 5years for all patients.

Table 1 Two and five year survival rate

Survival	2years	5years
OS	53(63.9)	21(25.3)
DFS	45(54.2)	16(19.3)

Key: OS: Overall Survival
DFS: Disease Free Survival
Percentages in brackets

Tumour response to chemotherapy was assessed in 31 of the 49 patients who had adjuvant chemotherapy. Survival was compared amongst responders, non-responders and those who had no chemotherapy.

Table 2 Comparing chemotherapy Vs No chemotherapy

	Survival	2years	5years
Chemotherapy 49	OS	34(69.4)	12(24.5)
	DFS	33(67.3)	10(20.4)
No Chemotherapy 34	OS	19(55.9)	9(26.5)
	DFS	12(35.3)	6(17.6)

X^2 test: 2yrs DFS p.0.0039

Table 3 Survival in responders, non-responders and no chemotherapy.

	2years Survival	5years Survival
Responders 21	18(61.9)	6(28.6)
CHEMOTHERAPY		
Non-responders 10	2(20)	1(10)
NO CHEMOTHERAPY 34	19(55.9)	9(26.8)

DISCUSSION

Breast cancer in West Africa has been reported to reach the highest incidence ten years earlier than in the Causcasian[9]. This may not indicate that the disease is commoner in the younger age group but rather a reflection of the population distribution. The relative age specific rate of incidence in this study showed two peaks 36-45years and >65years (figure 2). With the expected improvement in life expectancy, it may just be a question of time when the age incidence of the disease will be the same as in the advanced countries.

The true incidence of breast cancer disease in Ghana is not known. The reasons for this are multifactorial and include inadequate health delivery facilities and poor record keeping; also the unwillingness of many patients to seek medical help because of ignorance and poverty. It is estimated that about 200 new cases are currently seen in KBTH each year, most of them locally advanced.

Osteen (1994) reported that 7% of newly recognized breast cancer disease in America are locally advanced (tumour >5cm)[10]. Eighty-eight percent of patients in this study group had tumours greater than 5cm in diameter putting them in a category of "incurable disease" by definition. The currently preferred treatment strategy for such cases is the multimodal approach, which include systemic chemo/hormonal therapy, surgery and radiotherapy. Relapse-free and overall survival is heavily dependent on the stage of the disease at diagnosis even with the best chemotherapy combination currently available.

The biologic diversity of locally advanced breast cancer disease and the fact that there are 13 possible combinations of the current TNM staging system[11] make comparison of treatment-end results difficult. But Hortobagyi's[12] 48.9% 5year survival in stage III B disease using the multimodality approach is at wide variance with our 25% 5-year survival rate. The younger age of our patients with its attendant low ER & PR positivity rate[13,14], the large size of the tumours seen here with a high incidence of lymph node involvement[15] and the probably high proliferation fraction and poor nuclear and histological grade all contribute to this poor overall result.

Comparing treatment results of chemotherapy and no chemotherapy using the X^2 test, there was significant advantage for the former only in the 2-year disease free survival (p=0.0039) as has been widely reported for locally advanced breast cancer disease[12,15,16].

At the end of the first two years, 38%, 80% and 44% deaths were recorded in responders, non-responders and those who had no chemotherapy respectively (Table 3). It would appear that chemotherapy suppresses the innate immunity in the non-responders thus accelerating their death. Our observation was that responders do so with the first two cycles of chemotherapy. This suggests that local treatment must be effected if no objective response is detected after the first two cycles. This way, the metastatic rate of histologically unstable tumour cells would be reduced.

When chemotherapy and surgery were used to treat patients with positive lymph nodes, lesion less than 2cm in diameter were reported to have 33% 20-year disease free survival as opposed to 28% survival for the no chemotherapy group. Lesions greater than 2cm had 31% and 21% survival rates respectively for the same time period and, the greater the number of nodes involved the worse the prognosis[17]. This is a clear indication that though chemotherapy prolongs life, the magnitude is heavily dependent on the stage of the disease.

Most of our patients who had chemotherapy died from liver involvement with ascites but no local disease recurrence. This may support the view that the liver being a major detoxifying organ, has a high de novo P-glycoprotein content – the efflux

pump for substances the body adjudges toxic to itself and hence the unresponsiveness of liver secondaries to currently available chemotherapeutic agents.

The emergence of haemopoietic growth factors and autologous bone marrow transplantation after high dose chemotherapy and the development of new chemotherapeutic agents like the taxels which can attack P-glycoprotein-induced resistance gives hope to long-term survival.

Whilst breast cancer disease cannot be prevented as of now, it is obvious from this study that health education is needed to facilitate early presentation. Screening by both physical and mammographic examination will certainly help to detect the disease early and so reduce mortality from breast cancer disease as had been shown in the Malmo breast screening trials[18].

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