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Original Article

BREAST CONSERVATION IN BREAST CANCER: A BANGLADESH EXPERIENCE

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Abstract

Background: Breast cancer is one of the most common cancers in Bangladeshi women. Breast sacrificing treatment is still now the common practice in our country. Now a day's breast conservative treatment is the standard treatment of breast cancer without compromising the survival.

Objective: To observe local recurrence and distant metastasis free survival and overall survival of patients with breast cancer.

Methods: Between January 1996 and December 2010, breast conserving treatment was carried out in 237 female patients with breast cancer in different Institutions of Bangladesh. Clinical staging was recorded by physical examination, relevant investigations as well as surgical records. Revised breast conserving surgery was carried out in those who had positive surgical margins or palpable disease. The patients with large but operable cancer or locally advanced cancer were treated by neoadjuvant chemotherapy followed by breast conserving surgery. Systemic adjuvant therapy (chemotherapy and or hormone therapy) and adjuvant radiotherapy were given in all patients. After completion of treatment, the patients were followed up with a standard protocol and data were compiled and analysed.

Results: Among 237 patients who underwent breast conserving therapy 13 patients were excluded from the study for various reasons. Total 224 female patients with breast cancer who followed all the treatment schedules and attended for regular follow up were included in the study. They were between 22- 74 years of age, mean age 42.35 years; pre-menopausal 152 (68%). Sixty five percent (146 patients) was localized cancer (T1-2N0M0), 31.6% was regional cancer (T1-3N1M0), five cases were locally advanced stage (T4bN1-2M0) and two metastastatic cancer (T2-3N1M1). All most all (98%) were Infiltrating duct cell carcinoma except four which were Intraductal carcinoma in situ (IDIS). Estrogen and progesterone receptors were positive in 57% , HER2 positive (+++) in 24% of Patients. Lumpectomy/quandrentectomy with/without axillary clearance was done in 158 patients, revised breast conserving surgery in 53 cases, mastectomy in 8 cases and only biopsy done but no surgical treatment in five cases.Chemotherapy was given in 192 patients (86%); adjuvant 122 cases and neoadjuvant 70 cases. Hormone therapy in 182 patients. Radiotherapy: in 222 cases. Follow up period was 4 years to 19 years, median 10 years. Overall survival (OS) and disease free survival (DFS) was 84% and 70% respectively. Local recurrence occurred in 14(6%) cases and distant metastasis in 54 cases (24%).

Conclusion: Breast conserving treatment was satisfactory for appropriate case selection and optimized therapy. Survival was no way worse than breast sacrificing treatment.

Keywords : Breast cancer, Breast conservative treatment,Radiotherapy Chemotherapy and Hormone therapy in the treatment of breast cancer

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Introduction:

Breast conserving surgery (BCS) was introduced in the early 1980s as an alternative, less invasive surgical approach for the treatment of breast cancer.Breast conserving surgery plus radiation therapy is called breast conserving therapy (BCT) which refers to breast conserving surgery (BCS) followed by moderate-dose radiation therapy (RT) to eradicate any microscopic residual disease. The goals of BCT are to provide the survival equivalent of mastectomy, a cosmetically acceptable breast, and a low rate of recurrence in the treated breast.

The adoption of breast conservation has benefited for the early breast cancer (stage I and stageII) patients. Furthermore, the improved cure rates in breast cancer have increased the emphasis on maximizing the quality of life for breast cancer survivors. A major goal of breast cancer locoregional therapies should be organ preservation, which permits survivors to maintain normal breast anatomy and sensation. Studies have demonstrated that breast conservation positively impacts patient well-being and quality of life. Breast-conservation therapy is generally reserved for patients with tumors smaller than 4 cm. However, more important than absolute tumor size is the relationship between tumor size and breast size. The tumor must be small enough, in relation to the size of the breast, to permit the tumor to be resected with adequate margins and acceptable cosmesis. In patients with invasive breast cancer in which the tumor to breast size ratio is unfavorable, the use of preoperative chemotherapy may decrease the tumor size sufficiently to permit breast-conservation therapy.Neoadjuvant chemotherapy is being used increasingly in the management of patients with breast cancer, especially locally advanced cases.Such treatment is administered with the aim of of reducing the size of the primary tumor to increase the possibility of breast-conserving treatment (BCT)[1]. Long-term follow-up of patients from several large, randomized controlled trials has demonstrated equivalent overall survival in patients undergoing mastectomy compared with BCS[2-5].

In Bangladesh, breast conserving therapy is not yet commonly practiced as the most of the patients present at advanced stage; moreover radiotherapy facilities are not adequate. However breast conserving therapy is being tried in different institutes of Bangladesh since 1996 in small scale. This study shows the results of nineteen years experience on breast conservation therapy in Bangladesh perspective.

Methods:

Between January 1996 and December 2010, breast conserving treatment was carried out in patients with breast cancer in different Institutions of Bangladesh. Diagnosis was made by FNAC/ Core biopsy/ incision/ excision biopsy of the lesions and routine histopathology immediately after breast conserving surgery. Clinical staging was done by physical examination, relevant investigation as well as surgical records. Revised breast conserving surgery had been done in those who had positive surgical margin or palpable disease. The patients with large but operable breast cancer or locally advanced cancer were treated by neoadjuvant chemotherapy followed by breast conserving surgery. Adjuvant chemotherapy and or hormone therapy were given after surgery in most of the cases. Adjuvant radiotherapy was given after completion of four cycles of chemotherapy. Further adjuvant chemotherapy was carried out with anthracycline based chemotherapeutic agents with or without trastuzumab in relevant cases. Systemic adjuvant hormone therapy with tamomixfen or letrozole were continued after completion of surgery, chemotherapy and radiotherapy. The adjuvant treatments were given sequentially. Those with resections margins very close (<5mm), were treated with adjuvant radiotherapy within 4-6 weeks of surgery. After completion of treatment, the patients were advised to attend followed up three monthly for first two years, six monthly for next three years and yearly after five years. Physical examination, laboratory investigation, six monthly breast-ultrasonography and yearly mammography were done. Yearly gynecological examination was done. Data were compiled and analyzed.

Results:

Between January 1996 and December 2010, breast conserving therapy was given in female patients with

breast cancer. Two hundred twenty four patients were eligible for the study. Their age range was 22- 74 years, mean age 42.35 yrs; 152 (68%) were premenopausal. Sixty five percent (146 patients) was localized cancer (T1-2N0M0), 31.6% was regional cancer (T1-2N1M0), five cases were T4bN1-2M0 and two T2N1M1. All most all (98%) were Infiltrating duct cell carcinoma except four which were Intraductal carcinoma in situ (IDIS). Fifty seven percent was hormone receptor positive and 24% Her2 positive. Lumpectomy or quandrentectomy with or without axillary dissection was done in 158 patients. Revised breast conserving surgery was carried out in 53 cases. Mastectomy was needed in 8 cases and only biopsy without definitive surgical treatment was done in five cases. Chemotherapy was given in 192 patients (86%); adjuvant 122 cases and neoadjuvant 70 cases. Hormone therapy was given in 182 patients. Radio therapy was given in 222 cases. Total 237 patients were included for breast conserving treatment. Six cases refused revised surgery, five cases did not attend for radiotherapy and two cases were absconded after two cycles of chemotherapy. The eligible cases were 224.

All patients attended for follow up. Follow up period was 4 years to 19 years, median 10 years. Overall survival and disease frees survival were 82% and 70% respectively. Thirteen patients (5%) developed local recurrence. Distant metastasis occurred in 53 patients (23%).

Table-I

Patients demography and baseline Characteristics (n=224)

Age in years (Range, Mean)	22-74 (42.35)
Premenopausal	152 (68%)
Literacy	212 (95%)
Economically solvent*	208(93%)
Performance status (WHO Grade)[6]	0-1
Left breast	116 (52%)
Right breast	108 (48%)
Histopathology	
• Ductal Carcinoma in Situ (DCIS)	4 (2%)
• Infiltrating duct cell carcinoma	220 (98%)
According to TNM classification[7]	
• T1-2 N0M0 (Localized)	146 (65.28%)
• T1-T3N1M0 (Regional)	71(31.6%)
• T4bN0-N1-2M0 (locally advanced)	5 (2.23%)
• T2N1-2M1 (Metastatic)	2 (0.89%)
Patients with receptors status and axillary nodal status	•
ER /PR Positive 140	76 (54%)
• HER2 Postive 103	28 (29%)
• Axillary node positive 164	58(35%)

*Economically solvent: who can bear the expense of most of the treatment.

Table II

Multimodal treatment given sequentially

Surgery (n=224)		Radiotherapy (n=222)		Chemotherapy (n=192)	Hormone therapy (n=182)
BCS	158	Photon	128	Adjuvant 122	Tamoxifen
Revised BCS	53				
Mastectomy	8	Photon and electron boost	94	Neoadjuvant 70	Letrozole Or Tamoxifen only or Letrozole only
Only biopsy	5				

BCS=Lumpectomy/quadranectomy with/without axillary clearance

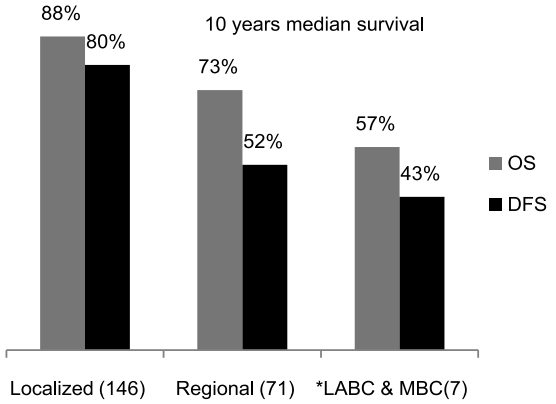
Photon=Externmal beam therapy 45-50Gy by Cobalt60/Linac. Electron boost=10-12Gy by linac.

Chemotherapy=Antracycline combination-115, Antracyclin+Taxol-69, Antracyclin+Taxol+Herceptin-8

Figure 1

Survival of breast cancer after breast conserving therapy;T1-2 N0M0(Localized),

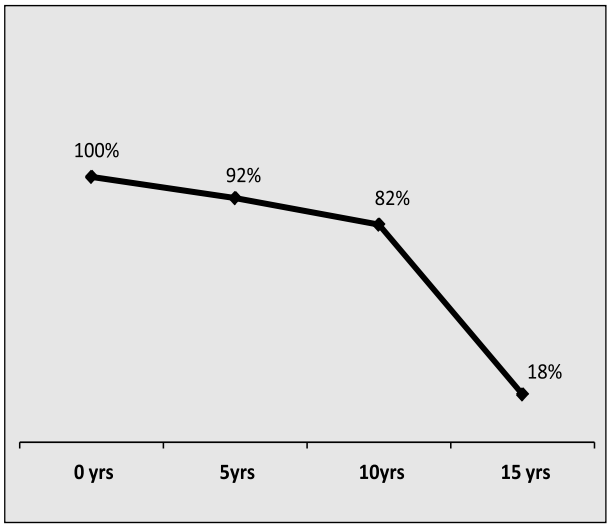
T1-T3N1M0 (Regional), T4bN0-N1-3M0/M1 (locally advanced Breast Cancer and Metastatic breast cancer).Follow up period 4years to 19 years; median 10 years.



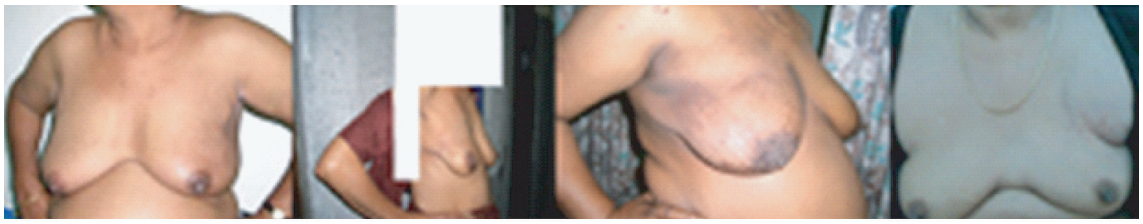
*LABC=Locally advanced breast cancer, MBC=metastatic breast cancer, OS=Overall survival, DFS=Disease Free survival

Figure 2

Total 224 breast cancer patients were treated by breast conserving therapy. Out of them 206patients (92%) survived 5 years, 185 patients (82%) survived 10 years and 41 patients (18%) reached 15 years.



Early breast cancer



19 yrs survivor 16 yrs survivor 10 yrs survivor 12 yrs survivor

Locally advanced breast cancer

Before Chemotherapy | After Chemotherapy | After Surgery | After Radiotherapy | After 10 years

Table-III

Result of Treatment after breast conserving therapy. Median survival was 10 years.

	OS	DFS	DM	LR	LR &DM
Localized (146)	129(88%)	118(80%)	25(17%)	3(2%)	0
Regional(71)	52(73%)	37(52%)	24(34%)	8(7%)	2(3%)
LABC &MBC (7)	4(57%)	3(43%)	4(57%)		
Total(n=224)	185(82.58%)	158(70.53%)	53(23.66%)	11(5%)	2(.89%)

Overall Survival (OS) 185 (82%), Disease Free Survival (DFS) 158 (70%), Distant Metastasis (DM) 54(23%)

Local Recurrence (LR) 13(6.%)

Discussion:

Breast-conservation therapy is established as a standard-of-care loco-regional treatment for early stage (stages I and II) breast cancer. In Bangladesh breast sacrificing treatment is the common trend.

This study is an experience on the breast conserving therapy in 224 breast cancer patients of Bangladeshi women treated in 15 years (1996 to 2010). Of them 176 cases (65%) were localized disease (stage I and stage II) and 76 patients (31%) were with movable breast lump and axillary lymph node involvement (regional). Only five cases were with locally advanced stage and two had metastatic cancers (single bone metastasis) (Table I).

Inadequate surgical margins represent a high risk for adverse clinical outcome in breast-conserving therapy (BCT) for early-stage breast cancer. The majority of studies report positive resection margins in 20% to 40% of the patients who underwent BCT[8]. In the present study, revised surgery had been done for suspected residual and positive surgical margins in 53 cases (40%) out of 132 cases who had attended after some sort of surgery. Five cases needed mastectomy for inadequate breast tissue and other three for local recurrence (Table 2). One case recurred after three years of treatment. Mammography showed small growth in affected breast after 10 years in another case and mastectomy was done on patient's wilingnes but histopathology report showed only fibrosis, no malignancy. The 3rd case recurred after two months of breast conserving surgery. This patient had local recurrence even after mastectomy. In five cases, only biopsy were taken; three cases were locally advanced breast cancer and two patients were elderly patients not fit for any type of surgery.

In this study, adjuvant Radiotherapy was given in 222 cases; of them 128 cases were treated by photon (X-ray or gamma ray) and 92 patients by photon and electron boost. Local recurrence occurred in 14 patients (6.30%) out of 222 cases (table 3)10-years overall survival was 88% and73% and local recurrence was 2% and 10% in localized and regional cancer respectively (Figure 1 and Table 3).Use of post-operative radiotherapy after BCS was associated with significant improvements in local control and survival; 10-year loco-regional recurrence-free-survival was 90.8% with postoperative radiotherapy vs. 77.6% with surgery alone ($p<0.001$).10-year overall survival rates were 55.2% with surgery alone vs. 82.2% following postoperative radiotherapy ($p<0.001$)[9].

One hundred ninety two patients (85%) were treated by anthracycline based chemotherapy; of them neoadjuvant chemotherapy was given in 70 cases and adjuvant chemotherapy in 122 cases. Hormone therapy with tamoxifen and letrozole was added in 182 cases (Table 2). Five years and 10 years survival was 92% and 80% respectively and 18% patients reached 15 years (Figure 2).10 years disease free survival of localized cancer (without regional lymph node involvement detected clinically) was 88% but disease free survival in regional cancer dropped to 52% (Figure 1). Because according to risk such as triple negatives, HER2 positive appropriate adjuvant chemotherapy could be given. Cancer Research U.K shows one year, five years and ten years female breast cancer survival is 96%, 86% and 78% respectively; survival vary according to stages and age groups[10,11].

Among five locally advanced breast cancer(LABC) patients who were treated by neoadjuvant chemotherapy, three patients showed complete response; of them two patients refused further surgery, treated by radiotherapy and hormone therapy. One patient survived 18 years and other patient six years. Partially responded LABC were treated by quadrenectomy and axillary clearance followed by radiotherapy and hormone therapy. One of them survived 11 years. So locally advanced breast cancer patients out of five cases three survived 5 years and one 11 years and other patient 18 years. Though LABC at 5 and 10years, event free survival was 25% and 7%, and overall survival was 52% and 31%, respectively[12]. In our study two breast cancer patients with single bone metastasis (vertebra) were included. They were treated by conventional surgery, chemotherapy and loco regional radiotherapy and hormone therapy along with radiotherapy to bony lesion and bisphosphonate regularly. One of them survived 15 years.

All our patients presented with lump. They were diagnosed and treated in different centers of the country. There were limitations for evaluation of the disease by radiology and imaging, in assessing the receptor status and limited chemotherapy and radiotherapy treatment facilities. In spite of these breast conservative treatment was given is most of the cases. Local recurrence was 6% that was within acceptable limit. Distant metastasis occurred in 54 cases.

Conclusion:

Our experience in breast conserving therapy in patients with breast cancer in Bangladesh perspective was satisfactory for appropriate case selection and optimized therapy. Survival was no way worse than breast sacrificing treatment. More attention should be given for risk assessment and systemic therapy to reduce distant metastasis and to improve survival.

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