Original Article

Outcome of Wire localized Lumpectomies in Breast Cancer Following Neoadjuvant Chemotherapy

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Abstract

Objective: To evaluate the clinical outcome of our breast cancer patients who had non-palpable lesions following neoadjuvant chemotherapy and required wire localized lump excision. Apart from survival outcome; specimen size was calculated and results compared to published literature.
Study Design: A retrospective analysis.
Place and Duration: Shaukat Khanum Memorial Cancer Hospital, Lahore from August 2005 to December 2011.
Methodology: A retrospective analysis of consecutive series of patients treated at Shaukat Khanum Memorial Cancer Hospital with breast conservation after wire localization for non-palpable breast cancer following neoadjuvant chemotherapy. The records were reviewed for patient, radiological, histological and surgical characteristics. Tumor volume was calculated from the pathological specimen size. Data was analyzed using SPSS Version 19.0. Kaplan-Meier curves were used for survival analysis.
Results: A total of 194 were included in the study. The mean age was 44yrs (Range 22-78yrs). Complete pathological response was seen in 65 patients. After the first excision 90.2% of the patients had negative margins. Seventeen patients underwent re-operation of which 7 had re-excision alone and 8 required completion mastectomy. The mean resected specimen volume was 634.72 cm3. Loco-regional recurrence occurred in 13 (6.7%) cases and distant recurrence was seen in 36 (18.6%) cases. Out of these, 6 patients had both local and distal recurrence. The median survival was 44 months (SD 17.16).
Conclusion: Our patients present at advanced stages which makes neo-adjuvant chemotherapy an integral part of their management. Wire guided localization of non-palpable tumors following downsizing is an effective and feasible technique with good surgical outcome.
Key Words: Breast cancer, Neoadjuvan Chemotherapy.

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Introduction

Breast cancer is the most common cancer among women worldwide. It affects women of all ages and the lifetime risk of developing invasive breast cancer is 12-13% in USA. Southeast Asia comprises one the highest rates of breast cancer. Lack of epidemiological studies pertinent to this subcontinent has resulted in poor control of the disease. Surgery for breast cancer has changed dramatically over the past few decades. Breast-conserving therapy was introduced in the 1970s. The introduction of the

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sentinel node procedure for nodal staging has avoided the morbidity of axillary lymph node dissection in the majority of patients. Several trials have demonstrated comparable results with regard to disease-free and overall survival between mastectomy and BCT combined with radiotherapy, and the latter has become the standard of care for early-stage breast cancer. According to national guidelines, 75% of breast cancer patients are suitable for BCT. The main advantage of BCT over mastectomy is the preservation of the breast with improved cosmetic outcomes. [1-4]

Breast cancer and its treatment have many adverse side-effects, which may be both physical and psychological. The cosmetic result is also a major determinant of psychological distress. [5]

Studies have reported satisfactory cosmetic results in only 60-80% of patients, with cosmetic failure rates up to 40%. Overall, a large volume of resected breast tissue is the major determinant of a poor cosmetic outcome. [6,7]

Higher risks of local recurrence have been shown only with evident involvement of the tumor on the inked resection margins. Therefore, there is no need to excise a tumor with a large volume of adjacent breast tissue.[8]

Wire-guided localization of non-palpable tumors is standard of care across the world. However, with the advent of newer techniques namely radio-guided occult lesion localization, radioactive seed localization and intraoperative ultrasound guided resection wire-guided localization is losing popularity. In our setup, this is a cost-effective and feasible method with acceptable surgical outcomes.

Methodology

A retrospective analysis of consecutive series of patients treated at Shaukat Khanum Memorial Cancer Hospital with breast conservation after wire localization for non-palpable breast cancer following neo-adjuvant chemotherapy from August 2005 to December 2011. The records were reviewed for patient, radiological, histological and surgical characteristics. Tumor volume was calculated from the pathological specimen size. Data was analyzed using SPSS Version 19.0. Kaplan Meier curves were used for survival analysis. The main endpoints were incidence of positive margins after initial breast conservation surgery, rate of local and distant recurrence, evaluation of resected specimen volumes and variable effecting survival.

All but one patient had neo-adjuvant chemotherapy for invasive breast cancer resulting clinically in a non-palpable breast lump requiring image guided localization. One patient had a small mucinous tumor that required wire localization but did not receive chemotherapy.

DCIS alone and localization of benign lesions or calcifications were not included. Patients with advance disease requiring mastectomy, inflammatory carcinoma, those having metastatic disease and male patients were excluded.

The localization was performed using either stereotactic or ultrasound guidance according to size of non-palpable lesion and discretion of the radiologist. Wire localization was done on day of surgery.

Results

A total of 194 were included in the study. Patient characteristics are presented in Table I.

The mean age was 44yrs (Range 22-78yrs). Age distribution is shown in Figure 1. Family history of breast cancer was present in 24.7% of the patients. Over 80% of the patients presented in Stage 2 with an average tumor size of 29.74mm. Figure 2 shows the percentage of patients in each stage at presentation. All patients following neo-adjuvant chemotherapy had a good partial or complete response radiologically. Stereotactic localization was performed in 129 (66.5%) cases whereas ultrasound guided wire localization was performed in 45 (33.5%) cases.

Table I: Patient Characteristics

Patient Characteristics	n (194)	%
(Median) (Range)	44	22-78
Family History		
POSITIVE	48	24.74
NEGATIVE	146	75.26
Clinical Stage at Presentation		
STAGE I	11	5.67
STAGE IIA	59	30.41
STAGE IIB	98	50.52
STAGE IIIA	24	12.37
STAGE IIIC	2	1.03
Tumor Size at Presentation		
(Mean) (Range) mm	29.74	5-55

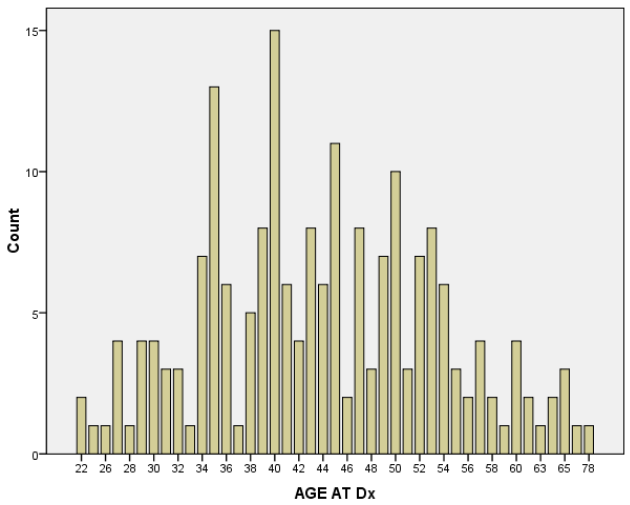


Figure 1: Age distribution at time of diagnosis

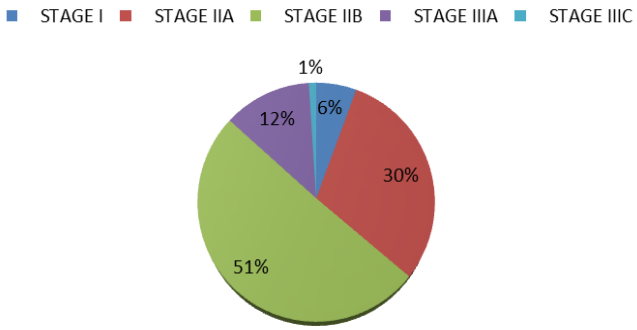


Figure 2: Clinical stage at presentation

Tumor characteristics are presented in Table II. Ninety-five percent of the tumors were invasive ductal with 10% of all tumors having associated DCIS. The majority of the patients presented with T2 tumors (85.05%) and with grade III tumors (63.92%). Axillary lymph node dissection was performed with 140 (72.2%). Almost 70% of these patients had no nodal metastasis detectable on final histopathology. Receptor positivity was present in almost half the patients. Her2neu positive patients comprised 27.32% whereas Her2neu was negative in 53.09% of the cases. There were 38 (19.59%) patients in whom Her2neu status was either unknown or equivocal.

Surgical outcomes are presented in Table III. Complete pathological response was seen in 65 patients in the following stages: Stage I – n= 1, Stage IIA – n=18, Stage IIB – n=35, Stage IIIA – n=10, stage IIIC – n=1. Over 50% of patients with complete pathological response belonged to Stage 2B. After the first excision 90.2% of the patients had negative margins. Seventeen patients underwent re-operation of which 7 had re-excision alone and 8 required completion mastectomy. One patient refused completion mastectomy. The mean resected specimen volume was 634.72 cm.[3]

Twelve patients underwent additional margin excision on the basis of per-operative findings at the initial surgery. Three of these patients had positive margins on final pathology. One patient ended up in a mastectomy due to multiple positive margins in the additional tissue sent for histopathology. One patient underwent a second procedure for re-excision of margins and one patient did not undergo re-excision of deep margin which was at 1mm on final pathology.

Table II: Tumor characteristics

Tumor Characteristics	n (194)	%
Method of Localization		
Stereotatic	129	66.49
Ultrasound	65	33.51
Histological Subtype		
Invasive ductal	185	95.36
Invasive lobular	6	3.09
Associated DCIS	19	9.79
Other	3	1.55
Pathological Tumor Stage		
T1 a/b	8	4.12
T1 c	21	10.82
T2	165	85.05
T3	3	1.54
Pathological Tumor Grade		
GRADE I	1	0.52
GRADE II	61	31.44
GRADE III	124	63.92
Not Known	8	4.12
Axillary Dissection Performed	140	72.17
Pathological Nodal Stage		
N0	135	69.59
N1	25	12.89
N2	25	12.89
N3	9	4.64
Receptor Status		
ER (Positive) (Negative)	100 (51.55%)	94 (48.45%)
PR (Positive)(Negative)	93 (47.94%)	101 (52.06%)
H2N (Positive)(Negative)	53 (27.32%)	103 (53.09%)
H2N (Not Known/Equivocal)	38(19.59%)	

Loco-regional recurrence occurred in 13 (6.7%) cases and distant recurrence was seen in 36 (18.6%) cases. Out of these, 6 patients had both local and distal recurrence. The median survival was 44 months (SD 17.16).

Survival analysis revealed significant survival advantage in patients presenting at early stage of their disease (p=0.024). There was a significantly better survival in patients with negative axillary lymph nodes. This advantage held true for patients who presented with a clinically negative axilla (p=0.005) and even more so in those patients who became node negative following chemotherapy as reported in final pathological report (p=0.001).

Table III: Surgical outcomes

Surgical Outcomes	n (194)	%
Complete Pathological Response		
STAGE I	1	0.52
STAGE IIA	18	9.28
STAGE IIB	35	18.04
STAGE IIIA	10	5.15
STAGE IIIC	1	0.52
Margins		
Positive	19	9.79
Negative	175	90.21
Re-Operation		
Re-Excision	7	3.61
Mastectomy	8	4.12
Refused mastectomy	1	0.52
Recurrence		
Locoregional	13	6.70
Distant	36	18.57
Both	6	3.09
Specimen Volume (Mean) (Range) cm^3	634.72	83.80- 3628.54
Median survival (months)	44	SD 17.16
Survival benefit in early presentation	P=0.03	

Triple negative tumors, complete pathological response or positive margins following initial surgery did not have any significant impact on survival.

There was a significant decrease in overall survival for patients who presented at a very young age less than 30 years and those who presented at over 60 years (p=0.012).

Discussion

Neo-adjuvant chemotherapy is considered standard of care in locally advanced breast cancer. It is also employed for downsizing the tumor in order to make the patient eligible for breast conservation. Up to 80% of cases experience a clinical response and up to 24% of cases can have complete response especially when taxanes are used.[9] When surgery is performed, the lumpectomy volume is based upon the clinical and radiographic extent of disease after delivery of the neo-adjuvant chemotherapy.

A requirement for successful breast conservation surgery is a careful preoperative planning with proper localization of the lesion, especially in non-palpable breast lesions.[10] Techniques to localize the lesion include; wire-guided localization, radio-guided occult lesion localization (ROLL), carbon marking, intraoperative ultrasound-guided localization, cavity shave margins, and biopsy markers.

Wire guided localization of non-palpable tumors is a simple and cost-effective method. It is associated with some disadvantages due to which it is losing popularity. The common pitfalls of this technique include wire dislodgment, patient discomfort, and necessity of radiological and surgical cooperation to allow localization on the day of surgery. Clear margins obtained with this method are reported to be 70.8 - 87.4%. [11-13]

As the Scandinavian study proposes in its ‘plea for wire-guided localization’, excellent results can be obtained with breast conserving surgery for non-palpable lesions using this technique.[14]

Recently The Society of Surgical Oncology (SSO) and American Society for Radiation Oncology (ASTRO) multidisciplinary expert panel has developed guidelines on margins for breast-conserving surgery with whole-breast irradiation in stage I and II invasive breast cancer. The Panel recommended that negative margins (no ink on tumor) optimize ipsilateral breast tumor recurrence. Wider margins widths do not significantly lower this risk. The routine practice of obtaining wider negative margin widths is not indicated.

In our study margin width, less that 2mm was considered positive. Following the current recommendations, the rate of re-excision/ mastectomies can be reduced further.

A major component of breast conservation surgery is optimal resection to gain oncological clearance with a cosmetically acceptable outcome. Large studies have reported poor cosmetic outcomes in 20-40% of patients after breast conservation, with volume of

resected tissue being the major determinant. Our resected volumes were considerably large. It has been shown that resected volumes exceeding 85cm^3 results in poor cosmetic outcome. Our mean specimen volume was 634.72cm.^{3} One major difference in specimen volumes is associated with the extent of excision. At our institution, it is common practice to resect down to the chest wall. In the studies mentioned about 1cm of tissue is excised around the tumor. Again, excessive tissue dissection is unnecessary and negative margins should be aimed for. Intra-operative ultrasound-guided surgery has been proposed to guide smaller resection volumes with acceptable margins and good cosmetic results.[15]

Systemic therapies reduce both risks of distant metastases and of local recurrence, and it is proposed that loco-regional recurrence could be more correlated with biological features of the tumor. Early presentation is the key to improving survival. Only 6% of our patients presented in Stage 1 disease. Whereas according to SEERS data over 60% of their patients present with localized disease.[16] Our patients presented with a mean tumor size of almost 3cm. Patient education and better health facilities are required to encourage early presentation. National screening programs need to be aimed for.

Conclusion

Our patients present at advanced stages which makes neo-adjuvant chemotherapy an integral part of their management. Wire guided localization of non-palpable tumors following downsizing is an effective and feasible technique with good surgical outcome.

With pre-operative planning and precise localization of the tumor, women can be spared extensive tissue resection to allow better cosmetic results and optimum psychological outcome. Per-operative ultrasound can be incorporated to reduce specimen volume by targeted excision.

In our setup education and raising awareness about breast cancer is paramount to achieving goals such as early detection and improved survival.

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