

Original article:

Evaluation of 1cm Resection Margin as “Safety Margin” by Paraffin section in Lumpectomy for Breast Cancer

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ABSTRACT:

Background: The goal of breast conservation surgery is to completely remove the identified cancer while preserving adequate breast tissue to achieve an acceptable cosmetic result.

Objectives: To evaluate the effectiveness of wide local excision with 1cm resection margin with axillary sampling or dissection for early breast cancer without frozen section facility.

Methods: This was a prospective histopathological study designed to evaluate the resection margins among wide local excision (WLE) specimens with early breast cancer treated by mastectomy with axillary dissection up to level 2. Fifty female patients with stage 1&2 Breast Cancer were selected by purposive sampling. Lumpectomy specimen was oriented & marked for margins and sent for histopathology to assess the resection margin status.

Results: Maximum women 58.0% were postmenopausal. 68.0% had upper outer quadrant followed by lower outer quadrant 16.0%. Clinical TNM staging were observed maximum 50.0% T2N0 followed by 32% were T2N1. Resection margin was positive in 3 cases, 2 positive in lateral margin and 1 in medial margin. FNAC findings of the breast carcinoma patients, maximum (70.0%) patients had ductal cell carcinoma (DCC). Most common histopathological findings were invasive duct cell carcinoma 45(90.0%). Pathological TNM staging were observed maximum 38.0%. Among 3 cases who had positive 1 cm resection margin, 1(33.3%) patients had TNM staging (pathological) T2N1, 1(33.3%) T1N2 and 1(33.3%) patient had T2N3. A p value was <0.05, that was statistically significant.

Conclusion: Lumpectomy with 1 cm resection margin is a standard surgical procedure in the management of early stage breast cancer.

Keywords: Breast Cancer, Resection Margin.

INTRODUCTION

Breast carcinoma is the most common cancer in women and also leading cause of cancer related deaths. Fortunately mortality rates are declining in breast cancer- a change attributed to an ongoing multidisciplinary approach to management of the disease. This approach includes use of diagnostic imaging for early detection in appropriate patients. Upon pathological or histological diagnosis of breast cancer, most patients undergo surgical resection and

further pathological evaluation of breast and lymph node tissue followed by additional therapy such as radiation and/or systemic therapy as indicated to reduce the risk of disease recurrence.

Conservative surgery followed by breast irradiation has replaced modified radical mastectomy as preferred treatment for early stage breast cancer. Public education and proactive screening programs have contributed to early detection of small tumors in a greater percentage of women.¹ Stage 1 & stage 2 breast cancers are early cancers that are not fixed to the skin or muscle. If lymph nodes are involved, they are not fixed to each other or to underlying structure.² The aim of Breast conserving surgery (BCS) is to excise all invasive and in situ cancer and to achieve long term disease control whilst at the same time minimizing local morbidity and ensuring a good cosmetic result. BCS as effective as mastectomy in terms of disease free outcome and overall survival but confers the advantages of better cosmesis, less psychological morbidity, improved body image, sexuality and self-esteem.³ The choice in unifocal cancers is determined by a balance between tumour size and breast volume. Clinical and pathological factors also influence patient selection for BCS because of their impact on local recurrence. These include young age (under 35 years), an extensive in situ component associated with an invasive tumour, grade 3 histology and the presence of lymphatic/vascular invasion.^{4,5, 6-19} The preoperative diagnosis of cancer determined by clinical examination, imaging and fine needle aspiration cytology.

This was despite the fact that those with involved or close margins received high doses of radiotherapy than patients with clear margins in almost half of these series. There is no suggestion that patients with narrow margins (<2mm) have a worse rate of local recurrence than those with wider margin (2-5mm).²⁰ A recent review of all literature concludes that wider margins do not equate with an improved rate of local control.²¹ Lagios and Silverstein have suggested that if margins are clear of DCIS by 1cm, radiotherapy is unnecessary. Other studies have also shown that providing the disease is excised (> 1mm) wider excisions do not improve local control.^{22,23}

The study aims to assess the rationality of WLE with 1cm gross margin as effective operative treatment for early breast cancer without frozen section facility & evaluate the effectiveness of the procedure to achieve negative resection margin in histopathology of specimen.

MATERIALS AND METHODS

It was a prospective observational study, conducted in Department of Surgery, Holy Family Red Crescent Medical College & Hospital, Dhaka; from January 2016 to June 2016. The objective was to evaluate the effectiveness of wide local excision with 1cm resection margin with axillary sampling or dissection for early breast cancer without frozen section facility. 50 female patients was selected by purposive sampling method. Those with T1, T2 (tumor size <4cm), N0, N1, M0, T2 (tumor size >4cm) in large breast was included. Those with stage 3 and 4 breast cancer, pregnant or unwilling to participate was excluded. Breast cancer was cytologically confirmed by FNAC. Informed consent was obtained from each participant. At enrollment, each patient was provided an identification number after clinical examination followed by imaging (ultra-sonogram / mammogram) and then FNAC to confirm the pathology. Wide local excision specimen was obtained after mastectomy and axillary dissection. Lumpectomy specimen was oriented & marked for margins and sent for histopathology to assess the resection margin status. The aims and objective of the study along with procedure, methods, risk and benefits of the study was explained to the patient in an easily understandable local language and then informed written consent was taken from each patient. Ethical

clearance was taken from Ethical Review Committee of the institution. Every precaution was taken to protect the anonymity of the subjects. They had the freedom to withdraw at any time. The collected information was collected, coded, revised, compiled and then analyzed by using the software SPSS (Statistical Package for Social science): version 22.0 (IBM), Chicago, Illinois. The qualitative data were presented as number and percentages while the quantitative data were presented as mean, standard deviations and ranges.

RESULTS

This present hospital based prospective observational study in 50 female patients with stage 1 & 2 breast cancer were included at the Department of Surgery, Holy Family Red Crescent Medical College & Hospital, Dhaka in a period of six months, different observations are shown as below-

Table 1 Distribution of the patients by demographic factors (n=50)

Demographic factors	Frequency	Percentage (%)
Age		
< 35 years	6	12.0
> 35 years	44	88.0
Total	50	100.0
Mean±SD	49.26±9.56	
Range	32-69 years	
Parity		
Multipara	38	76.0
Unipara	10	20.0
Nallipara	2	4.0
Total	50	100.0

Table 2 Distribution of the patients by site of tumour (n=50)

Site of tumour	Frequency	Percentage (%)
Upper outer quadrant	34	68.0
Lower outer quadrant	8	16.0
Upper inner quadrant	1	2.0
Lower inner quadrant	7	14.0
Total	50	100.0

Table 3 Site, size of tumor and clinically suspicious lymph nodes (TNM) in patients with early breast cancer (n=50)

TNM (clinical)	Frequency	Percentage (%)
T1N0	4	8.0
T1N1	5	10.0
T2N0	25	50.0
T2N1	16	32.0
Total	50	100.0

Table 4 Distribution of the study patients by staging of breast carcinoma (n=50)

Stage	Frequency	Percentage (%)
Stage I	6	12.0
Stage II	44	88.0
Total	50	100.0

Table 5 Distribution of the patients by FNAC findings (n=50)

FNAC findings	Frequency	Percentage (%)
DCC	35	70.0
IDCC	11	22.0
Papillary ductal carcinoma	2	4.0
DCIS	2	4.0
Total	50	100.0

Table 6 Distribution of the patients by core biopsy findings (n=50)

Core biopsy findings	Frequency	Percentage (%)
IDCC (NOS)	12	92.3
Infiltrating papillary ductal carcinoma	1	7.7
Total	13	100.0

Table 7 Distribution of the patients by histopathological findings (n=50)

Histopathological findings	Frequency	Percentage (%)
Invasive duct cell carcinoma (Not otherwise specified)	45	90.0
Ductal carcinoma in situ (high grade)	2	4.0
Invasive cribriform carcinoma	1	2.0
Malignant phylloides	1	2.0
Ductal carcinoma in situ (Comedo type)	1	2.0
Total	50	100.0

Table 8 Distribution of the patients by histopathological TNM staging (n=50)

TNM (Pathological)	Frequency	Percentage (%)
T1N0	3	6.0
T1N1	3	6.0
T2N0	19	38.0
T2N1	15	30.0
TisN0	3	6.0
T1N2	2	4.0
T2N3	2	4.0
T2N2	2	4.0
Not defined	1	2.0
Total	50	100

Table 9 Distribution of the patients by resection margin status of lumpectomy specimen (n=50)

1 cm resection margin	Frequency	Percentage (%)
Negative	47	94.0
Positive	3	6.0
Total	50	100.0

Table 10 Distribution of the positive resection margin status of lumpectomy specimen (n=3)

Resection margin status	Frequency	Percentage (%)
Medial	1	33.3
Lateral margin	2	66.7
Total	3	100.0

Table 11 Association of age of the patients with 1 cm resection margin of lumpectomy specimen (n=50)

Age group	1 cm resection margin status		P value
	Positive	Negative	
≤ 35 years	1(33.3%)	5(10.6%)	0.241 ^{ns}
> 35 years	2(66.7%)	42(89.4%)	
Total	3(100.0%)	47(100.0%)	

Data were expressed as frequency and percentage

Data were analyzed by Chi-square test, ns= not significant

Table 12 Association of menopausal status with 1 cm resection margin of lumpectomy specimen (n=50)

Menopausal status	1 cm resection margin status		P value
	Positive	Negative	
Premenopause	3(100.0%)	18(38.3%)	0.036*
Postmenopause	0	29(61.7%)	
Total	3(100.0%)	47(100.0%)	

Data were expressed as frequency and percentage

Data were analyzed by Chi-square test, *= significant

Table 13 Association of location of tumour with 1 cm resection margin of lumpectomy specimen (n=50)

Location of tumour	1 cm resection margin status		P value
	Positive	Negative	
Upper outer quadrant	2(66.7%)	32(68.1%)	0.699 ^{ns}
Lower outer quadrant	0(0.0%)	8(17.0%)	
Upper inner quadrant	0(0.0%)	1(2.1%)	
Lower inner quadrant	1(33.3%)	6(12.8%)	
Total	3(100.0%)	47(100.0%)	

Data were expressed as frequency and percentage

Data were analyzed by Chi-square test, ns= not significant

Table 14 Association of stage of tumour with 1 cm resection margin of lumpectomy specimen (n=50)

Stage of tumour	1 cm resection margin status		P value
	Positive	Negative	
Stage I	0(0.0%)	6(12.8%)	0.509 ^{ns}
Stage II	3(100.0%)	41(87.2%)	
Total	3(100.0%)	47(100.0%)	

Data were expressed as frequency and percentage

Data were analyzed by Chi-square test, ns= not significant

Table 15 Association of grade of tumour with 1 cm resection margin of lumpectomy specimen (n=50)

Grade of tumour	1 cm resection margin status		P value
	Positive	Negative	
Grade I	0(0.0%)	9(20.0%)	0.307 ^{ns}
Grade II	1(33.3%)	24(53.3%)	
Grade III	2(66.7%)	12(26.7%)	
Total	3(100.0%)	47(100.0%)	

Data were expressed as frequency and percentage

Data were analyzed by Chi-square test, ns= not significant

Table 16 Association of TNM staging (clinical) of tumour with 1 cm resection margin of lumpectomy specimen (n=50)

TNM staging (clinical)	1 cm resection margin status		P value
	Positive	Negative	
T1N0	0(0.0%)	4(8.5%)	0.537 ^{ns}
T1N1	1(33.3%)	4(8.5%)	
T2N0	1(33.3%)	24(51.1%)	
T2N1	1(33.3%)	15(31.90%)	
Total	3(100.0%)	47(100.0%)	

Data were expressed as frequency and percentage

Data were analyzed by Chi-square test, ns= not significant

Table 17 Association of TNM staging (pathological) of tumour with 1 cm resection margin of lumpectomy specimen (n=50)

TNM staging (pathological)	1 cm resection margin status		P value
	Positive	Negative	
T1N0	0(0.0%)	3(6.4%)	0.047
T1N1	0(0.0%)	3(6.4%)	
T2N0	0(0.0%)	19(40.4%)	
T2N1	1(33.3%)	14(29.8%)	
TisN0	0(0.0%)	3(6.4%)	
T1N2	1(33.3%)	1(2.1%)	
T2N3	1(33.3%)	1(2.1%)	
T2N2	0(0.0%)	2(4.3%)	
Not defined	0(0.0%)	1(2.1%)	

Data were expressed as frequency and percentage

Data were analyzed by Chi-square test, ns= not significant

DISCUSSION

This is a prospective type of observational study for evaluation of 1cm surgical resection margin in lumpectomy for early breast cancer. The mean age of the patient was 49.26±9.56 years, ranged from 32-69 years. The most represented age more than 35 years (88.0%). A study done by Kim et al.²⁵ reported the age of the patients ranged from 27 to 73 years, maximum (86.3%) age more than 35 years, which is similar to our study.

Lumpectomy is the most common surgery for invasive breast cancer.²⁶ It is performed in 60-75% of new breast cancer cases each year and has been in use for 30 years. Also called breast-conserving surgery, lumpectomy removes the cancerous tumor while preserving as much of the breast as possible.²⁷ In an attempt to preserve the size of the breast, however, a doctor may accidentally leave behind a small amount of cancer. During a lumpectomy, surgeons remove the cancer, along with some surrounding normal breast tissue. They then send the surgically removed tumor and surrounding rim of healthy tissue to a pathology lab. A pathologist will examine the tumor and breast tissue under a microscope, and if no cancer cells are found near the edges of the healthy tissue, it is called a clear margin.²⁷

In current study, the 1 cm resection margin status of the lumpectomy specimen was observed in 3 cases (6.0%) positive. 2 cases positive in lateral margin and 1 case positive in medial margin. Kim et al.²⁵ reported resection margin was positive in 10 cases (1.6%). Moschetta et al. (2015)⁴² observed 110 (83%) negative margins and 22 (17%) positive margins were found on US.

The prevalence of positive tumor margins in lumpectomies from published data varies widely, ranging from 4% to 31%.^{28,29,30,31} Some literature seem to suggest that there is no relationship between size of the primary tumor, histologic grade, nodal involvement, and positive margins.^{32,33,34,35} Contrary to this view, other studies found tumor size, grade, and nodal involvement to be associated with positive margins and increased risk of local recurrence.³⁷⁻⁴⁰ Lumpectomy has been performed in Bangladesh over last few years as a standard management option for the treatment of early breast cancer in some tertiary level hospital . To the best of our knowledge there is no study that has evaluated the safety of lumpectomy as a surgical option for the treatment of early breast cancer. However, Der et al. (2013) in their study “Positive malignant margins in clinically diagnosed and excised benign breast lumps” found that 321 (11.0%) out of 2,917 excised breast lumps were malignant and that 142 (44.0%) had positive tumor margins.³⁸

In present study showed FNAC findings of the breast carcinoma patients (70.0%) patients had ductal cell carcinoma (DCC), 22.0% patients had invasive ductal cell carcinoma (IDCC), 4.0% patients had papillary ductal carcinoma and 4.0% patients had DCIS. Moschetta et al. (2015) detected invasive ductal carcinoma in (73%) cases, invasive lobular carcinoma in (24%), mucinous carcinoma in (3%).

In current study, most of the patients 88.0% were stage-II and 12.0% patients had stage I. In the USA, 58% of patients with stage I breast cancer and 36.2% of patients with stage II breast cancer underwent BCS.¹⁰

In present study, among 50 breast cancer patients, clinical TNM staging maximum 50.0% T2N0 followed by 32% were T2N1, 10.0% patients were T1N1 and 8.0% patients were T1N0. Maximum 68.0% had upper outer quadrant followed by lower outer quadrant 16.0%, lower inner quadrant 14.0% and only 2.0% upper inner quadrant. Maximum (70.0%) patients had ductal cell carcinoma (DCC), 22.0% patients had invasive ductal cell carcinoma

(IDCC), 4.0% patients had papillary ductal carcinoma and 4.0% patients had DCIS. 13 patients had done core biopsy. 12(92.3%) patients were IDCC (NOS) and rest 1(7.7%) patients had infiltrating papillary ductal carcinoma. out of 50 breast cancer patients, pathological TNM staging were observed maximum 38.0% T2N0 followed by 32% were T2N1, 6.0% patients were T1N1. Kim et al. (2005)²⁵ demonstrate according to the 1997 American Joint Committee on Cancer (AJCC) tumor staging system, 454 cases (74.3%) were T1 stage and 157 cases (25.7%) were T2 stage. One hundred and thirty-eight cases (22.6%) had lymph node metastasis and the number of involved lymph nodes was less than 4 in 113 cases (18.5%), 4–9 in 18 cases (2.9%) and more than 9 in seven cases (1.1%). Three hundred and sixty-seven cases had stage I disease (60.1%), 193 cases had stage IIA disease (31.6%) and 51 cases had stage IIB disease (8.3%). The tumor histology showed 523 cases (85.6%) with invasive ductal cell carcinoma, 23 cases (3.8%) with invasive lobular carcinoma and 65 cases (10.6%) were other histologic a types of cancer.²⁵

In present study, the width of surgical resection margin in specimen was 1.0 cm. We found significant association ($p=0.03$) between 1 cm resection margin and menopausal status, pathological TNM staging ($p=0.04$). We did not find significant association between 1 cm resection margin and age at diagnosis, location of tumour, stage of tumour, tumour grade, clinical TNM stage. This finding is similar to some published literature that did not find significant positive association between the size of primary tumors with positive margins and the other tumor variables.^{34,35,36} A similar study done by Der et al. (2014)²⁹ was found significant association ($p=0.009$) between positive resection margin and grade of the tumors and did not find significant association between positive margin and age at diagnosis, histological type, TNM stage, and positive lymph nodes. Other studies found tumor size, grade, and nodal involvement to be associated with positive margins.^{37-40,44,45} Wider margins remove a larger volume of tissue which has deleterious effects on cosmesis, body image and problems with sexuality. Surgeons should operate on the basis of best evidence 1 cm resection margin is safe and acceptable.

CONCLUSION

Our study shows that 6.0% of all lumpectomies have 1 cm resection positive tumor margins, a figure that is comparable to those of other studies. Tumors with positive margin in this study were T2 and common in premenopausal women. The safety of wide local excision as a standard surgical option for early stage breast cancer management has been evaluated. We have defined what constitutes a positive and a negative margin and why tumor clearance rather than just a “negative” margin is important in eliminating residual disease. Thus lumpectomy with 1 cm circumferential resection margin is a standard surgical procedure in the management of early stage breast cancer.

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