

OUTCOMES FOLLOWING MASTECTOMY IN TERMS OF LOCAL RECURRENCE AND EFFECT OF POST-MASTECTOMY RADIATION THERAPY ON RECURRENCE IN BREAST CANCER

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ABSTRACT

Background: Recurrence after a mastectomy occurs locally or at distance. These recurrences are of importance as they have a marked impact on the survival, psychology, and morbidity of the subject who underwent the mastectomy.

Aim: The present trial was carried out to evaluate distant and local recurrence after mastectomy in subjects with breast cancer, and the effect of PMRT on recurrence. Also, the impact of nodal status, hormone status, and status of margins on this recurrence was assessed.

Methods: The status of the nodes including the number of nodes evaluated, number of positive nodes, and nodal grade, hormone receptors for estrogen, progesterone, and Herceptin, along with the number of Herceptin was assessed in the study. The data collected were subjected to statistical evaluation and results were formulated.

Results: PMRT was received by 26 subjects (83.8%) in recurrence cases and 6 subjects (54.5%) in the non-recurrence group with a p-value of 0.380. In invasive group, the hormone receptor status was positive in 58% (n=18), 64.5% (n=20), and 16.12% (n=5) for progesterone, estrogen, and Herceptin respectively.. In invasive tumors, positive margins after surgery were seen in 2 subjects (6.89%), negative, equal, close, and were seen in 65.5%, 3.44%, and 6.89% subjects respectively. Concerning node status, 0 staging was in 5% non-invasive recurrence cases, 14% invasive recurrence cases who received radiation therapy, and in 4% subjects with invasive tumors with recurrence who did not receive radiation therapy.

Conclusion: The present study suggests that subjects who undergo radiation therapy after mastectomy shows lesser rates of recurrence compared to those without any post-mastectomy radiation therapy.

Keywords: Breast Cancer, mastectomy, Post-mastectomy radiation therapy, hormone receptor status, surgical margins.

Keynote: Despite safe delivery of PMRT, effective chemotherapeutic measures, and advanced surgical techniques, evidence of local recurrence following mastectomy still needs to be explored. The impact of nodal status, hormone receptor status, and margins on distant and local recurrence following mastectomy also should be further evaluated to identify potential candidates for PMRT.

INTRODUCTION

Recurrence after a mastectomy is a common phenomenon observed. This recurrence can either be seen locally or at distance. These recurrences are of importance as they have a marked impact on the survival, psychology, and morbidity of the subject who underwent the mastectomy. However, the recurrence rate post-mastectomy has varied results as mentioned previously in the literature.¹ Various studies, done previously in the literature report a recurrence of 4% to 32%. These results show a very low as well as high recurrence rate post-mastectomy.²

These differences in the studies reported in the literature regarding locoregional recurrence after mastectomy limits the assessment of risk and benefits of advising prophylactic therapy for locoregional recurrence. Local, as well as distant recurrence following the mastectomy, is known to be affected by various factors including hormonal status, margin status, nodal status, and/or radiation therapy after mastectomy (PMRT).³ ASCO (The American Society of Oncology) recommends Post Mastectomy Radiation Therapy for subjects who presented with either Grade III tumors or had 4 or more positive axillary Lymph nodes. However, ASCO has no recommendation for PMRT in subjects with less than 4 positive lymph nodes or in subjects who are considered low-risk such as those with no positive lymph node.⁴

Various studies conducted in the late 90s and 2000 show high advantages of PMRT following mastectomy in terms of preventing local and distant recurrence. These advantages include significant improvement in survival rates and a marked reduction in local and distant recurrence after PMRT. However, these studies were not accepted widely as they had no information regarding tumor staging and lymph node involvement.⁵ One study showed radiation therapy after mastectomy in pre-menopausal subjects who also underwent chemotherapy; resulted in very low local recurrence of 9% with high survival, and 323% recurrence in subjects who did not undergo PMRT.⁶

Concerning hormone receptors, in subjects with breast cancer, it was seen that the negative status of hormone receptors, particularly for progesterone and estrogen, has increased the risk of local recurrence in breast cancer subjects.⁷ For surgical margins, positive and close margins are found to be associated with a higher risk of local recurrence following mastectomy in subjects with breast cancer. Results were opposite in cases with negative margins, where negative margins were associated with a significantly lower risk of local recurrence following mastectomy.⁸

However, despite safe delivery of PMRT, effective chemotherapeutic measures, and advanced surgical techniques, evidence of local recurrence following mastectomy still needs to be explored. The impact of nodal status, hormone receptor status, and margins on distant and local recurrence following mastectomy also should be further evaluated to identify

potential candidates for PMRT.⁹ Hence, the present trial was carried out to evaluate distant and local recurrence after mastectomy in subjects with breast cancer, and the effect of PMRT on recurrence. Also, the impact of nodal status, hormone status, and status of margins on this recurrence was assessed.

MATERIALS AND METHODS

The present trial was carried out to evaluate distant and local recurrence after mastectomy in subjects with breast cancer, and the effect of PMRT on recurrence. Also, the impact of nodal status, hormone status, and status of margins on this recurrence was assessed. The present trial included 42 females who underwent mastectomy for breast cancer. The study subjects were within the age group of 27 years to 58 years with a mean age of 35.7 years. The study included subjects irrespective of prior history of mastectomy. The data for the study was collected from the medical reports of the institution. After obtaining ethical clearance from the Ethical committee of the institute, pathological and medical records of the included subjects were obtained.

The exclusion criteria for the study were patients who at the time of surgery were positive with metastasis at the distant site. In subjects who underwent mastectomy for both the breasts were considered as two different cases.

The parameters extracted from the medical and pathological records of the study subjects were: demographic characteristics of the subjects including their age, diagnosis, laterality, surgery type, size of the tumor, and histological finding. The status of the nodes including the number of nodes evaluated, number of positive nodes, and nodal grade (histological and nuclear) was examined. Also, hormone receptors for estrogen, progesterone and Herceptin, along with Herceptin were assessed in the study. The status of radiation therapy, recurrence type, and surgical margins were evaluated from the medical records. For subjects who lacked any necessary information were contacted to complete information as far as possible.

For assessment and evaluation purposes, local recurrence was considered in cases with recurrence to the axilla and similar side of the chest wall which was operated on and underwent a mastectomy. The recurrence beyond the axilla and to the contralateral side of the chest was considered as a distant recurrence for the present study. The data regarding the use of additional therapies were also considered. The data collected were subjected to statistical evaluation and results were formulated.

RESULTS

The present trial was carried out to evaluate distant and local recurrence after mastectomy in subjects with breast cancer, and the effect of PMRT on recurrence. Also, the impact of nodal status, hormone status, and status of margins on this recurrence was assessed.

Of the total 42 females assessed, all met the inclusion criteria. The subjects in whom clear information was not available regarding the local or distant metastasis were not included as part of the trial. More evidence of recurrence was seen in subjects where more invasions were seen compared with subjects with non-invasive breast cancers. This can be attributed to the fact that no additional and adjuvant therapies are usually given with the mastectomy. Hence, these cases usually don't report for follow-up sessions. No difference in the recurrence based

on adjuvant radiation therapy, the status of the lymph nodes, and demographic characteristics were seen as shown in Table 1.

The present trial included 42 females who underwent mastectomy for breast cancer. The study subjects were within the age group of 27 years to 58 years with the mean age of 35.7 years. For right side involvement, 48.38% (n=15) subjects had recurrence, and for left side 51.61% (n=16) had recurrence with the p-value of 0.576. The most common nodal status seen was N-0 in cases of recurrence as well as non-recurrence; the p-value was 0.712. T-1 was the most common tumor staging found with 39.7% (n=12) in recurrence cases and 36.3% (n=4) in non-recurrence cases with the p-value 0.05. 80.6% (n=25) cases were invasive in recurrence group, and only 36.3% (n=4) in non-recurrence group (p-value= 0.412). PMRT was received by 26 subjects (83.8%) in recurrence cases and 6 subjects (54.5%) in non-recurrence group with the p-value of 0.380. In invasive group, the hormone receptor status was positive in 58% (n=18), 64.5% (n=20), and 16.12% (n=5) for progesterone, estrogen, and herpectin respectively. These values were respectively negative in 29% (n=9), 19.35% (n=6), and 61.29% (n=19) subjects and were not known in 12.9% (n=4), 16.12% (n=5), and 22.58% (n=7) subjects. The p-values respectively for progesterone, estrogen, and herpectin group were 0.541, 0.675, and 0.814.

The present study also evaluated the treatment patterns for invasive and non-invasive tumors. The results regarding it are depicted in Table 2. These results showed that there were 29 invasive tumors and 13 non-invasive tumors. In invasive tumors mastectomy was done for 13.79% subjects (n=4), modified mastectomy in 15 subjects (51.72%), whereas, in non-invasive tumors, mastectomy was done in 46.1% subjects (n=6), and in 5 subjects modified mastectomy was performed. In invasive tumors, positive margins after surgery were seen in 2 subjects (6.89%), negative, equal, close, and were seen in 65.5%, 3.44%, and 6.89% subjects respectively. In non-invasive tumors, surgical margins were negative and close in 69.23%, and 7.69% of subjects. No positive or equal margins were seen in the non-invasive group.

The rate of recurrence concerning the post-mastectomy radiation therapy in invasive and non-invasive tumors was also assessed in the present study. These results were related to the status of lymph nodes, tumor staging, surgical margins, and hormone receptor status. These results are depicted in Table 3. Concerning node status, 0 staging was in 5% non-invasive recurrence cases, 14% invasive recurrence cases who received radiation therapy, and in 4% subjects with invasive tumors with recurrence who did not receive radiation therapy. Surgical margins were positive in 6% of non-invasive recurrent tumors, negative in 4%, 3%, and 2% of non-invasive recurrence cases, invasive recurrence with radiotherapy, and invasive recurrence without radiotherapy respectively. In invasive tumors without PMRT and recurrence, 1%, 3%, and 8% had a tumor of stage 1, 2, and 3 respectively. In grading invasive tumors without PMRT and recurrence, 6% and 3% had a tumor of Grade 1 and 2. Hormone receptor status was positive for progesterone in 2% of subjects and negative in 3% of subjects who did not receive PMRT and showed recurrence. For estrogen, hormone receptor status was negative in 9% of subjects without radiation therapy and recurrence. For Herceptin, hormone receptor status was negative in 2% of subjects with invasive tumors showing recurrence and who did not receive radiation therapy after mastectomy.

DISCUSSION

The present trial was carried out to evaluate distant and local recurrence after mastectomy in subjects with breast cancer, and the effect of PMRT on recurrence. Also, the impact of nodal status, hormone status, and status of margins on this recurrence was assessed.

The present study showed a low local recurrence in subjects after mastectomy with invasive as well as non-invasive tumors. Concerning node status, 0 staging was in 5% non-invasive recurrence cases, 14% invasive recurrence cases who received radiation therapy, and in 4% subjects with invasive tumors with recurrence who did not receive radiation therapy. Surgical margins were positive in 6% of non-invasive recurrent tumors, negative in 4%, 3%, and 2% of non-invasive recurrence cases, invasive recurrence with radiotherapy, and invasive recurrence without radiotherapy respectively. In invasive tumors without PMRT and recurrence, 1%, 3%, and 8% had a tumor of stage 1, 2, and 3 respectively. These findings were consistent with the study by Voduc et al¹⁰ in 2010 and by Kyndi et al¹¹ in 2008 where authors concluded similar results.

In grading invasive tumors without PMRT and recurrence, 6% and 3% had a tumor of Grade 1 and 2. Hormone receptor status was positive for progesterone in 2% of subjects and negative in 3% of subjects who did not receive PMRT and showed recurrence. For estrogen, hormone receptor status was negative in 9% of subjects without radiation therapy and recurrence. For Herceptin, hormone receptor status was negative in 2% of subjects with invasive tumors showing recurrence and who did not receive radiation therapy after mastectomy. These findings were in agreement with the study by Voduc et al¹⁰ in 2010 and by Kyndi et al¹¹ in 2008, where authors reported that high local and distant recurrence was associated with the negative hormone receptor status for estrogen and progesterone. Authors also showed that negative status for progesterone was significant for local recurrence, whereas, negative Herceptin status was significant for distant spread.

The present study also evaluated the treatment patterns for invasive and non-invasive tumors. These results showed that there were 29 invasive tumors and 13 non-invasive tumors. In invasive tumors mastectomy was done for 13.79% subjects (n=4), modified mastectomy in 15 subjects (51.72%), whereas, in non-invasive tumors, mastectomy was done in 46.1% subjects (n=6), and in 5 subjects modified mastectomy was performed. In invasive tumors, positive margins after surgery were seen in 2 subjects (6.89%), negative, equal, close, and were seen in 65.5%, 3.44%, and 6.89% subjects respectively. In non-invasive tumors, surgical margins were negative and close in 69.23%, and 7.69% of subjects. No positive or equal margins were seen in the non-invasive group. The lymph nodes found positive in these cases showed more than 8 lymph nodes were examined in 44.82% (n=13) in subjects with invasive tumors and only 1 subject (7.69%) in non-invasive tumors. These findings were following the study by Wallgren et al¹² in 2003 where similar findings regarding margins of the surgery, lymph nodes, and type of surgery incorporated were comparable to our study.

Concerning the node status, the findings were per the study by Mc Donald et al¹³ in 2009 where authors found 17% positive lymph nodes associated with the local recurrence. Also, the study by Floyd et al¹⁴ in 2006 had similar results where 7.6% of lymph nodes were positive in local recurrence cases.

CONCLUSION

The present study suggests that subjects who undergo radiation therapy after mastectomy shows lesser rates of recurrence compared to those without any post-mastectomy radiation therapy. Hence, the administration of the adjuvant post-mastectomy radiation therapy needs to be considered while treating breast cancer surgically. However, the present study has few limitations including a smaller sample size and a short monitoring period. Also, few patients had no follow-up and more comprehensive insight is needed into a distant recurrence. Limited data were available in the medial and pathological records were another limitation of the present trial.

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TABLES

Parameter	Positive Recurrence	No Recurrence	p-value
Total Subjects (n=42)	31	11	
Age			
25-35 years	7	3	0.742
36-45 years	12	4	
46-55 years	8	2	
>55 years	4	2	
Involved Side			
Right	15 (48.38%)	4 (36.36%)	0.576
Left	16 (51.61%)	7 (63.63%)	
Nodal Status			
0	18 (58.06%)	5 (45.4%)	0.712
1	6 (19.35%)	2 (18.1%)	
2	2 (6.45%)	1 (9%)	
3	1 (3.22%)	1 (9%)	
Not known	4 (12.9%)	2 (18.1%)	
Tumor Staging			
Carcinoma In situ	6 (19.35%)	3 (27.2%)	0.05
1	12 (39.7%)	4 (36.3%)	
2	10 (32.25%)	2 (18.1%)	
3	2 (6.4%)	1 (9%)	
4	1 (3.22%)	1 (9%)	
Not known	0	0	
Nature of Tumor			
Invasive	25 (80.6%)	4 (36.3%)	0.412
Non-Invasive	6 (19.35%)	7 (63.63%)	
Post-mastectomy Radiation Therapy (PMRT)			
Received	26 (83.8%)	5 (45.4%)	0.380
Not-received	5 (16.12%)	6 (54.5%)	
Hormone Receptor Status			
Progesterone Receptor Status			
Positive	18 (58%)	1 (9%)	0.541
Negative	9 (29%)	1 (9%)	

Not-known	4 (12.9%)	9 (81.8%)	
Estrogen Receptor Status			
Positive	20 (64.5%)	2 (18.1%)	0.675
Negative	6 (19.35%)	3 (27.2%)	
Not-known	5 (16.12%)	6 (54.5%)	
Herceptin Receptor Status			
Positive	5 (16.12%)	1 (9%)	0.814
Negative	19 (61.29%)	1 (9%)	
Not-known	7 (22.58%)	9 (81.8%)	

Table 1: Characteristics of Tumor and subjects in invasive and non-invasive group

Treatment Rendered	Invasive Tumors (n=29)	Non-Invasive Tumors (n=13)
Type of Surgery		
Mastectomy	4 (13.79%)	6 (46.1%)
Mastectomy with negative node biopsy	8 (27.58%)	5 (38.46%)
Modified Mastectomy	15 (51.72%)	1 (7.69%)
Not-known	2 (6.89%)	1 (7.69%)
Status of Surgical Margins		
Positive	2 (6.89%)	0%
Negative	19 (65.5%)	9 (69.23%)
Equal	1 (3.44%)	0%
Close	2 (6.89%)	1 (7.69%)
Not-determined	5 (17.24%)	3 (23%)
Status of Lymph Nodes		
Not-examined	1 (3.44%)	2 (15.38%)
≤8 nodes	13 (44.82%)	7 (53.84%)
>8 nodes	13 (44.82%)	1 (7.69%)
Not-determined	2 (6.89%)	3 (23%)

Table 2: Treatment characteristics of the treated invasive and non-invasive tumors

Parameter	Non-Invasive Tumors	Invasive tumor with radiation therapy	Invasive tumor without radiation therapy
Node Staging			
0	5%	14%	4%
1	-	-	-
2	-	-	-
3	-	-	-
Surgical Margins			
Positive	6%		
Negative	4%	3%	2%
Close			6%
Equal			10%
Tumor Staging			

In situ	4%		
1			1%
2			3%
3			8%
4		17%	
Tumor Grading			
1			6%
2	4%		3%
3	5%	5%	
Hormone Receptor Status			
Progesterone Receptor Status			
Positive			2%
Negative	17%	8%	3%
Not-known	3%		
Estrogen Receptor Status			
Positive		2%	
Negative	18%	3%	9%
Not-known	3%		
Herceptin Receptor Status			
Positive			
Negative	3%	5%	2%
Not-known			

Table 3: Recurrence in study subjects for invasive and non-invasive tumors related to post-treatment radiation therapy.