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Original Article

Benefit of Post-mastectomy Radiotherapy for Breast Cancer Patients with T1-2 and 1-3 Positive Axillary Lymph Node

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Abstract

Background: Post-mastectomy irradiation is suggested in T1-2 and 1-3 positive axillary nodes. In Thailand, there is no consensus of radiotherapy in this group of patients.

Patients and Methods: Medical records of breast cancer patients with T1-T2, 1-3 axillary nodal metastasis and underwent modified radical mastectomy or total mastectomy with positive sentinel node biopsy were reviewed. Disease free survival (DFS) and overall survival (OS) were compared.

Results: There were 66 patients received radiotherapy and 92 patients did not receive radiotherapy. Survival analysis revealed that there was no significant difference in DFS and OS between the two groups. Subgroup analysis showed that radiotherapy in hormone receptor negative patients tended to result in better DFS.

Conclusion: The benefit of radiotherapy in T1-2 with 1-3 positive axillary nodes is not clear, however, selection of the patient to receive radiotherapy might result in better survival.

Keywords: breast cancer, radiotherapy, mastectomy, node positive

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BACKGROUND

The principle of breast cancer treatment comprises of locoregional and systemic control of the disease. Advances in adjuvant systemic treatment, chemotherapy, hormonal therapy, and targeted therapy significantly improve outcome of breast cancer treatment. The extent of surgery for node positive breast cancer patients was reduced from radical mastectomy to Patey mastectomy and now modified radical mastectomy with excellence outcome^{1,2}. Radiation to chest wall and regional lymph nodes warrants better outcome in women with positive axillary nodes after mastectomy and axillary dissection³⁻⁷. Radiotherapy after modified radical mastectomy in the patients with 1-3 positive axillary lymph nodes had shown survival advantage⁸. However, absolute benefit might be smaller in the patients with low risk of recurrence.

In Thailand, the availability of radiotherapy hinders the patients to access the treatment. Considerable proportion of breast cancer patients with 1-3 axillary nodes positive did not receive radiotherapy. In this study, we aimed to evaluate the benefit of post-mastectomy irradiation in breast cancer patients with 1-3 axillary nodes positive.

PATIENTS AND METHODS

Patients

The patients were recruited from the Division of Head Neck and Breast Surgery, Department of Surgery, Faculty of Medicine, Siriraj Hospital from January 2000 to December 2011. Medical records of breast cancer patients with T1-T2, 1-3 axillary nodal metastasis and underwent modified radical mastectomy or total mastectomy with positive sentinel node biopsy were reviewed. The patients who did not complete systemic treatment, loss to follow up, or had contraindication for radiotherapy were excluded. This study was approved by Siriraj ethical committee (certification of approval number si216/2017).

Statistical analysis

Continuous parameters were compared using non-parametric (Mann-Whitney) test. Distribution of categorical parameters were analyzed by Pearson Chi-square statistics or Fisher's exact test. Linear-by-linear association test was used to analyze ordinal parameters.

Disease free survival (DFS) and overall survival (OS) among the patients with and without radiotherapy were compared by Log-rank test. The survival curve was estimated by Kaplan-Meier method. The p -value of <0.05 was considered as statistical significant.

RESULTS

A total of 158 patients were enrolled. There were 66 patients received radiotherapy and 92 patients did not receive radiotherapy. Mean age at diagnosis was slightly higher in non-radiation group but not significant different. Higher proportion of radiation was found in premenopausal patients, 3 positive axillary nodes, and in the patients who received chemotherapy (Table 1). Only one chest wall recurrence was occurred in radiation group. In non-radiation group, 2 chest wall and 1 axillary recurrences were occurred. Sixteen distant metastasis was observed in non-radiation group, while 8 distant metastasis was occurred in radiation group. There was no significant difference regarding local recurrence and distance metastasis between radiation and non-radiation groups. There were 14 and 5 deaths were occurred in non-radiation and radiation group, respectively.

Survival analysis revealed that there was no significant difference in DFS between the two groups ($p=0.77$) (Figure 1). Subgroup analysis showed that in hormone receptor negative breast cancer patients, radiotherapy tended to result in better DFS, while in

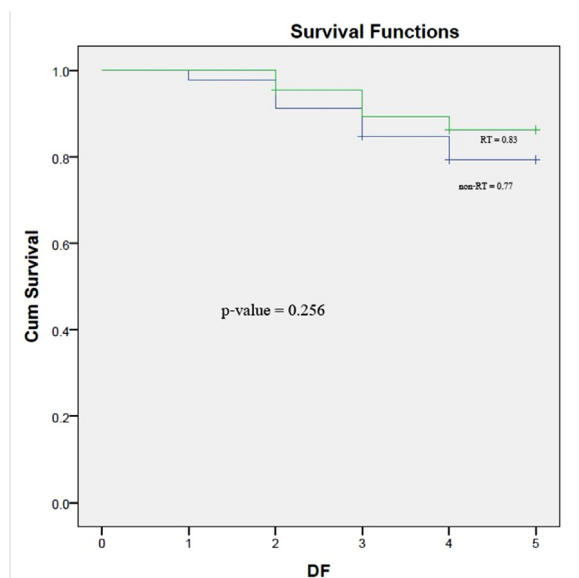


Figure 1 DFS by radiotherapy status among all patients.

Table 1 Characteristics of breast cancer patients according to radiotherapy status.

	No radiation, n=92	Radiation, n=66	p-value
Age, years, mean±SD	53.10±11.03	50.97±11.11	0.123 ^a
Menopausal status			
Premenopause, n(%)	40 (43.5)	40 (60.6)	0.034
Postmenopause	52 (56.5)	26 (39.4)	
Tumor size, mm			
mean±SD	24.97±10.25	27.73±11.14	0.151 ^a
Median (min-max)	24.00 (4.00-45.00)	25.00 (1.00-50.00)	
Number of positive node(s), n(%)			
1	54 (58.7)	28 (42.4)	0.020 ^b
2	24 (26.1)	19 (28.8)	
3	14 (15.2)	19 (28.8)	
Staging, n(%)			
T1N1	25 (27.2)	15 (22.7)	0.526
T2N1	67 (72.8)	51 (77.3)	
Histologic type			
Invasive ductal carcinoma	80 (87.0)	59 (89.4)	0.569 ^c
Invasive lobular carcinoma	4 (4.3)	4 (6.1)	
Other	8 (8.7)	3 (4.5)	
Histologic grading			
1	5 (6.3)	6 (10.2)	0.589
2	50 (63.3)	33 (55.9)	
3	24 (30.4)	20 (33.9)	
Angiolymphatic invasion			
Absence	61 (66.3)	55 (83.3)	0.017
Presence	31 (33.7)	11 (16.7)	
Estrogen receptor			
Negative	28 (30.4)	21 (31.8)	0.853
Positive	64 (69.6)	45 (68.2)	
Progesterone receptor			
Negative	36 (39.1)	28 (42.4)	0.677
Positive	56 (60.9)	38 (57.6)	
HER-2			
Negative	73 (79.3)	53 (80.3)	0.883
Positive	19 (20.7)	13 (19.7)	
Chemotherapy			
No	17 (18.5)	2 (3.0)	0.003
Yes	75 (81.5)	64 (97.0)	
Hormonal therapy			
No	25 (27.2)	23 (34.8)	0.301
Yes	67 (72.8)	43 (65.2)	

^anon-parametric test^blinear-by-linear association^cFisher's exact test

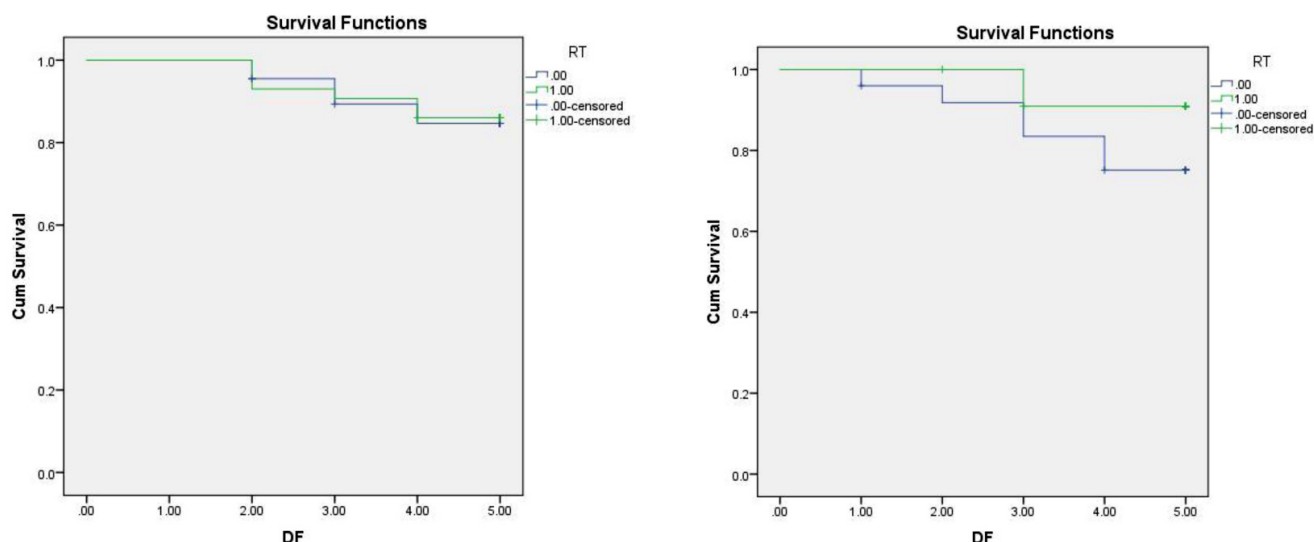


Figure 2 DFS by radiotherapy status. Left panel: hormone receptor positive breast cancer. Right panel: hormone receptor negative breast cancer.

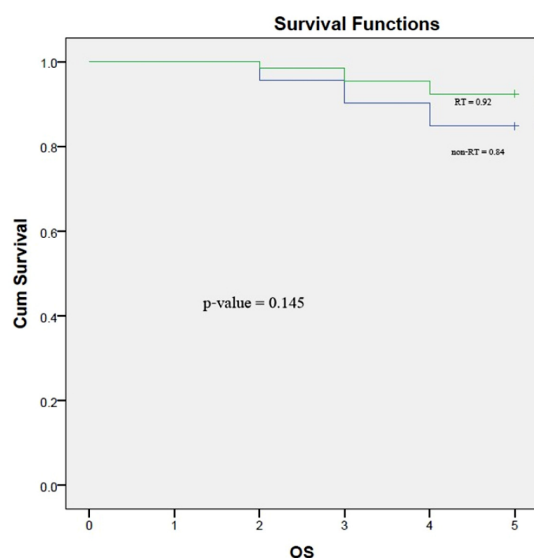


Figure 3 OS by radiotherapy status.

hormone receptor positive patients, similar DFS was observed (Figure 2). No significant difference was found in OS between the two groups (Figure 3).

DISCUSSION

In this study, we evaluated the benefit of post-mastectomy radiotherapy for breast cancer patients with T1-T2 and 1-3 positive axillary nodes and found no significant difference in DFS and OS between the two groups of patients. Higher proportion of the

patients with premenopausal status and higher number of nodes involved received radiotherapy. This might be due to concerning of locoregional recurrence in this group of patients. The extent of axillary node involvement indicates prognosis of the patients. The benefit of radiotherapy in axillary micrometastasis and isolated tumor cells is minimum and can be omitted⁹. In the patients with macrometastasis, the benefit of radiotherapy is significant. In the patients with 1-3 nodes positive, 15-year survival benefit was improved from 48% to 57% in the presence of radiotherapy. This benefit was emphasized in 4 or more nodes positive (12% vs 21%)¹⁰. EBCTGC meta-analysis also confirmed this effect⁸. Small sample size and short follow-up time leads to inadequate power to prove the benefit in this current study. The retrospective nature of this study might result in selection bias of the patients (eg. high risk patients received radiotherapy).

We found that hormone receptor negative breast cancer patients might be benefit from post-mastectomy irradiation. Hormone receptor positive patients have favorable tumor biology and can achieve long-term disease control during and after completion of hormonal therapy. This reduces the benefit of radiotherapy in this group of patients. Post-mastectomy irradiation should be considered in T1-T2, 1-3 positive axillary nodes with high risk features such as negative hormone receptor status.

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บทคัดย่อ ประโยชน์ของรังสีรักษาในผู้ป่วยมะเร็งเต้านมขนาดไม่เกิน T2 และมีการกระจายไปยังต่อมน้ำเหลืองรักแร้ 1-3 ต่อมน

ภูมิพัฒน์ ภูมิสวัสดิ์, ดุลยพัฒน์ สงวนรักษา, พรชัย โอเจริญรัตน์

สาขาศัลยศาสตร์ศีรษะ คอ และเต้านม ภาควิชาศัลยศาสตร์ คณะแพทยศาสตร์ศิริราชพยาบาล

ความเป็นมา: การให้รังสีรักษาเป็นการรักษาที่แนะนำสำหรับผู้ป่วยมะเร็งเต้านมขนาดไม่เกิน T2 และมีการกระจายไปยังต่อมน้ำเหลืองรักแร้ 1-3 ต่อมน อย่างไรก็ตาม ยังไม่มีข้อสรุปของประโยชน์ที่ชัดเจนสำหรับผู้ป่วยกลุ่มนี้ในประเทศไทย

ผู้ป่วยและวิธีการ: เก็บข้อมูลจากเวชระเบียนของผู้ป่วยมะเร็งเต้านมขนาดไม่เกิน T2 และมีการกระจายไปยังต่อมน้ำเหลืองรักแร้ 1-3 ต่อมน ได้รับการผ่าตัดเต้านมออกทั้งหมดและเลาะต่อมน้ำเหลืองรักแร้ ทำการเปรียบเทียบอัตราไม่มีโรคย้อนกลับเป็นซ้ำและอัตราการรอดชีวิตของกลุ่มที่ได้รับและไม่ได้รับรังสีรักษา

ผล: ผู้ป่วย 66 ราย ได้รับรังสีรักษาในขณะที่ผู้ป่วย 92 ราย ไม่ได้รับรังสีรักษา ไม่มีความแตกต่างอย่างมีนัยสำคัญของอัตราไม่มีโรคย้อนกลับเป็นซ้ำและอัตราการรอดชีวิตระหว่างสองกลุ่ม การวิเคราะห์กลุ่มย่อยพบว่า การให้รังสีรักษามีแนวโน้มลดการกลับเป็นซ้ำได้ในกลุ่มที่ไม่มีตัวรับฮอร์โมน

สรุป: ประโยชน์ของรังสีรักษาในผู้ป่วยกลุ่มนี้ยังไม่ชัดเจน อย่างไรก็ตาม ในผู้ป่วยบางรายอาจได้รับประโยชน์ เช่นกลุ่มที่ไม่มีตัวรับฮอร์โมน
