Treatment Outcomes after Breast Conserving Therapy in Breast Cancer Patients in Faculty of Medicine, Vajira Hospital: a 10-Year Retrospective Study

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Abstract

Objective: To study the 5 and 10-year survival rate and prognosis factors in breast cancer patients receiving breast conservative treatment (BCT).

Methods: A retrospective descriptive analysis of BCT patients who were treated in Radiation Oncology unit, Department of Radiology, Faculty of Medicine Vajira Hospital between 2009 and 2019. The Kaplan-Meier method was used for survival analysis. The authors analyzed association of patients and tumor characteristics with survival using the log-rank test and Cox models.

Results: A total of 158 BCT patients were included. Five-year overall and disease-free survivals were 100% and 97.8%, respectively, with 10-year overall survival and disease-free survival were 100% and 95.7%, respectively. Numbers of positive nodes more than 4 (HR of 10.25; 95% CI:1.66-63.18) are significantly prognostic factors related to recurrence.

Conclusions: Breast cancer patients who were treated with BCT had a favorable long-term survival outcome. Survival rates did not change much between 5 and 10 years. The important prognostic factor affecting disease-free survival was axillary lymph node metastasis.

Keywords: breast cancer, BCT, long-term out come

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ผลการรักษาของผู้ป่วยมะเร็งเต้านมที่ได้รับการรักษาแบบสงวนเต้านม ในคณะแพทยศาสตร์วชิรพยาบาล: การศึกษาย้อนหลัง 10 ปี

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บทคัดย่อ

วัตถุประสงค์: เพื่อศึกษาอัตราการปลอดโรค และอัตราการรอดชีวิต ที่ 5 ปี และ 10 ปี รวมถึงปัจจัยที่มีผลต่อการพยากรณ์โรคในผู้ป่วยมะเร็งเต้านมที่ได้รับการรักษาแบบสงวนเต้านมที่คณะแพทยศาสตร์วชิรพยาบาล

วิธีดำเนินการวิจัย: ทำการศึกษาย้อนหลังในผู้ป่วยมะเร็งเต้านมที่ได้รับการรักษาแบบสงวนเต้านมที่คณะแพทยศาสตร์วชิรพยาบาล โดยเก็บข้อมูลในผู้ป่วยที่รักษาครบตั้งแต่ปี 2552 ถึง 2562

ผลการวิจัย: ผู้ป่วยมะเร็งเต้านมที่รักษาด้วยการสงวนเต้านมทั้งหมด 158 คน อัตราการรอดชีวิต และอัตราการปลอดโรค ที่ 5 ปี เท่ากับร้อยละ 100 และ 97.8 ตามลำดับ อัตราการรอดชีวิต และอัตราการปลอดโรค ที่ 10 ปี เท่ากับร้อยละ 100 และ 95.7 การแพร่กระจายของโรคมะเร็งไปที่ต่อมน้ำเหลืองมากกว่า 4 ต่อม นับว่าเป็นปัจจัยสำคัญในการพยากรณ์โรคที่สำคัญต่ออัตราการปลอดโรค (HR = 10.25; 95% CI:1.66-63.18)

สรุป: ผู้ป่วยมะเร็งเต้านมที่ได้รับการรักษาแบบสงวนเต้านม อัตราการรอดชีวิตค่อนข้างคงที่ระหว่าง 5 ถึง 10 ปี ปัจจัยพยากรณ์โรคสำคัญที่มีผลต่ออัตราการปลอดโรคคือ การแพร่กระจายของโรคมะเร็งมาที่ต่อมน้ำเหลือง

คำสำคัญ: มะเร็งเต้านม, การรักษาแบบสงวนเต้านม, ผลการรักษาระยะยาว

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Introduction

Breast cancer is the most commonly diagnosed cancer and the leading cause of cancer-related deaths in women worldwide including Thailand, with global trends indicating rising rates of incidence and mortality[1-3]. Breast cancer treatment is multidisciplinary. The treatment of breast cancer includes the treatment of local disease with surgery, radiation therapy, or both, and systemic treatment with chemotherapy, endocrine therapy, biologic therapy, or combinations of these. The need for and selection of various local or systemic therapies are based on several prognostic and predictive factors. These factors include tumor histology, clinical and pathologic characteristics of the primary tumor, ALN status, tumor ER/PR content, tumor HER2 status, multi-gene testing, presence or absence of detectable metastatic disease, patient co-morbid conditions, patient age, and menopausal status[4-7].

Multiple randomized trials with follow-up of up to 20 years have demonstrated that breast-conserving therapy (BCT) is equivalent to mastectomy in on overall survival and recurrence rate as primary breast local treatment in stage I and II breast cancer women[8-13].

BCT consists of breast-conserving surgery (BCS) plus radiation therapy in the breast area. BCS refers to an operation that aims to remove all cancer while avoiding a mastectomy. Other terms for this operation include lumpectomy, wide local excision, segmental resection, tylectomy, and quadrantectomy. BCT has been increasingly accepted as an alternative to mastectomy in specific patients, as it provides tumor removal while maintaining an acceptable cosmetic outcome, fewer complications, and a better quality of life.

We aimed to evaluate the long-term treatment outcomes and associate factors with the prognosis of breast cancer patients receiving BCT at the Faculty of Medicine, Vajira Hospital.

Methods

The study was approved by the Ethics Committees of the institution (COA O84/2561). Patients diagnosed with pathologically proven breast cancer and were treated with BCT between 2009 and 2019 in the Department of Radiology Faculty of Medicine, Vajira Hospital were retrospectively evaluated. Inclusion criteria were patients who had treated with BCT and completed all treatment. Patients were excluded if they had a history of other cancer or an underlying disease that affects survival, or a history of previous irradiation to the thorax or, a piece of insufficient information. The characteristics features of the patient, tumor, and details of treatment were collected from the patient's medical record.

All patients were treated with BCS, which consists of breast-conserving surgery (BCS) plus radiation therapy in the breast area. After BCS, base on staging, grading, margin, receptor status, and age, high-risk patients who had an indication for systemic therapy went to received adjuvant systemic treatment. The chemotherapy regimen, adjuvant hormonal therapy, and the use of targeted therapy were delivered at the discretion of the oncologist involved in each case. We staged all patients by the 2010 TNM classification system (AJCC 7)[14].

For radiation therapy, the entire breast was treated to a total dose of 50-50.4 Gray (Gy) in 5-6 weeks with medial and lateral tangential fields. Patients were treated once a day, 5 days a week with a daily fraction size of 1.8–2 Gy. The breast tissue extent and treatment coverage of breast tissue were determined clinically. Wedges were the only form of compensation used. An axillary field was added if there were four or more nodes positive. Boost dose was delivered in this select group of women, a total dose 10-15 Gy in 5-7 fractions. The authors also reviewed the duration of delivered radiotherapy after surgery.

All patients were followed up to receive a physical examination every 3 months during the first 2 years then every 6 months until death. The primary outcomes was set as 5-year and 10-year overall survival (OS). The secondary outcomes was set as 5-year and 10-year disease-

free survival (DFS), prognostic factors for survival. OS was obtained from the first day of treatment to the date of death from all causes or last follow-up. DFS was calculated from the first day of treatment until the date of disease progression, recurrence, or right-censored at the time of the last follow-up.

Statistical analysis was performed with SPSS statistical analysis for Windows version 22.0 (IBM Corp, Armonk, NY). DFS and OS were analyzed by the Kaplan Meier method and were compared between groups with the log-rank test. A value of $p<0.05$ was considered statistically significant. Multivariate analysis was performed using Cox proportional hazards regression analysis in a foreword stepwise manner with a p-value of 0.05 as inclusion.

Results

A total of 158 patients were included in the study. The median follow-up times were 6.03 years (range, 1.3 to 16.86 years). The patient characteristics are shown in Table 1. The median age at diagnosis was 47 years (range, 25 to 86 years). The majority of patients (60.8%) were older than 45 years. In 64.6% of the cases, the primary surgical treatment was wide excision and 51.3% had axillary node clearance for lymph node clearance. Negative margins were achieved by surgery in 88.6% of cases, with the remainder of margins positive (8.2%) or unknown (3.2%). Stage I, II, and III were found in the following frequency: 51.3%, 41.1% and 7.6% respectively. Tumor size was smaller than or equal to 5 cm in 96.9% (n = 153). Invasive ductal carcinoma (IDC) was most commonly found, 93% (n = 147) with invasive lobular carcinoma (ILC) only 3.8% (n = 6). Sixty-seven percent of patients had well or moderately differentiated tumors. The detailed histologic evaluation identified the presence of 20.3% of lymphatic or vascular invasion, 67.1% of positive estrogen receptor (ER), 62% of positive progesterone receptor (PR), 20.9% of positive human epidermal growth factor receptor 2 (HER-2) and 25.9% of ≥ 14% proliferative index of Ki-67. Mean and median total radiation dose (initial dose plus boost dose to tumor bed) were 61.45 Gy and 65 Gy (range, 47-66 Gy). Eighty-nine percent of cases had a boost dose, usually with electrons (3/4). Regional lymph node irradiation was performed for 52 patients (32.9%). Chemotherapy was given to 74.1% of patients, most commonly adriamycin/cyclophosphamide. Seventy-five percent of all patients received endocrine therapy and four percent of all patients received targeted therapy.

Table 1:
Patient, tumor and treatment characteristics

Characteristics	n (%)
Age (years)	47 (25-86)
Age group	
< 45	62 (39.2)
≥ 45	96 (60.8)
LN dissection type	
Axillary node clearance	81 (51.3)
Sentinel node procedure	77 (48.7)
Margin status	
Negative	140 (88.6)
Positive	13 (8.2)
Unknow	5 (3.2)
Histologic type	
Ductal	147 (93)
Lobular	6 (3.8)
Others	5 (3.2)
Tumor grade	
Grade I	27 (17.1)
Grade II	78 (49.4)
Grade III	50 (31.6)
Unknow	3 (1.9)
Lymphovascular invasion	
Not present	110 (69.6)
Present	32 (20.3)
Unknow	16 (10.1)

Table 1:
Patient, tumor and treatment characteristics (Continued)

Characteristics	n (%)
ER status	
Negative	43 (27.2)
Positive	106 (67.1)
Unknow	9 (5.7)
PR status	
Negative	48 (30.4)
Positive	98 (62.0)
Unknow	12 (7.6)
Her-2 status	
Negative	93 (58.9)
Positive	33 (20.9)
Unknow	32 (20.2)
Ki67 Index	
< 14 % proliferation index	36 (22.8)
≥ 14 % proliferation index	41 (25.9)
Unknow	81 (51.3)
T stage	
T1	87 (55.1)
T2	66 (41.8)
T3	4 (2.5)
T4	1 (0.6)
N stage	
N0	121 (76.6)
N1	25 (15.8)
N2	10 (6.3)
N3	2 (1.3)
Stage	
I	81 (51.3)
II	65 (41.1)
III	12 (7.6)
Tumor bed boots radiotherapy	
No	18 (11.4)
Yes	140 (88.6)

Table 1:
Patient, tumor and treatment characteristics (Continued)

Characteristics	n (%)
Chemotherapy	
No	41 (25.9)
Yes	117 (74.1)
Endocrine therapy	
No	40 (25.3)
Yes	118 (74.7)
Target therapy	
No	152 (96.2)
Yes	6 (3.8)

Five-year overall and disease-free survivals were 100% and 97.8%, respectively, with 10-year overall survival and disease-free survival were 100% and 95.7%, respectively as presented in Figure 1.

On univariate analysis, the factors that affected the DFS were the number of involved axillary lymph nodes more than 4 (p= 0.011) and Her-2 positive (p= 0.03). However, on multivariate analysis, only the number of involved axillary lymph nodes more than 4 (Hazard ratio (HR) of 10.25; 95% CI:1.66-63.18) affected the DFS as shown in Table 2.

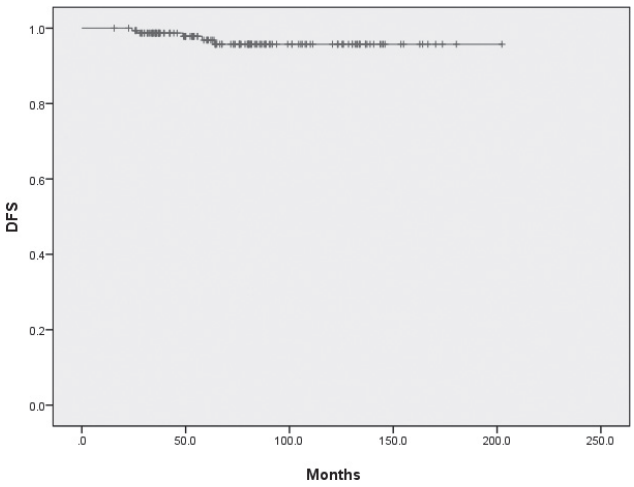

Figure 1: Disease-free survival of breast conservative treatment

Table 2:

Factors affected DFS: univariate and multivariate analysis

Characteristics	Univariate analysis			Multivariate analysis		
	p-value	HR	95%CI	p-value	HR	95%CI
Age (<45 years vs. ≥45 years)	0.384	0.46	(0.08-2.76)			
Axillary surgery (SLNB vs. AXND)	0.247	70.55	(0.53-94441.70)			
Margin status (negative vs. positive)	0.637	0.09	(0.00-1594.89)			
Histologic type (IDC vs. other)	0.945	0.91	(0.06-15.05)			
Histologic grade (I&II vs. III)	0.221	194.87	(0.42-898581.77)			
LVI (not preset vs present)	0.173	3.91	(0.55-27.79)			
Hormonal status (negative vs. positive)	0.34	0.39	(0.05-2.73)			
Her-2 status (negative vs. positive)	0,030	1.99	(1.07-3.69)	0.06	2.11	(0.97-4.26)
Ki 67 index (< 14 % vs. ≥ 14 %)	0.625	56.29	(0.00-584759614.12)			
Tumor size (≤5 cm vs. >5 cm)	0.785	0.047	(0.00-167.80)			
Number of positive nodes (<4 vs. ≥4)	0.011	10.3	(0.72-61.79)	0.012	10.25	(1.66-63.18)
Tumor bed boost (no vs. yes)	0.719	0.67	(0.07-6.00)			
Chemotherapy treatment (no vs. yes)	0.819	1.29	(0.14-11.57)			
Hormonal Rx (no vs. yes)	0.509	0.55	(0.09-3.28)			
Targeted therapy treatment (no vs. yes)	0.818	0.05	(0.00-10.11)			

Discussion

In the present study, the authors focused on the patients-tumor characteristics and outcomes of breast cancer patients treated with BCT. BCT has been increasingly treated as an alternative to mastectomy in specific patients, as it provides tumor removal while maintaining an acceptable cosmetic outcome, fewer complications, and a better quality of life. The 5-year and 10-year DFS rates in our study were 97.8% and 95.7% whereas the 5-year and 10-year OS rates were 100% and 100%. These rates were in the ranges which were reported in the NSABP B06[8] and another studies[9-13]. The long-term analysis of this study demonstrated that the DFS and OS were rather stable after 5 years. Several studies reported a recurrence rate in the range between 3-22%[11-15] that was consistent with this study of 3 percent recurrence rate.

An increasing number of studies have shown improved overall survival among women treated with BCT regardless of cancer phenotype compared with mastectomy[11-17]. Lagendijk M et al. showed that BCT roughly 25% better OS than mastectomy[16]. This was consistent when comparing the OS of BCT in this study with the mastectomy in a study the authors had previously reported[18]. Our results further support the hypothesis that BCT might be the preferred choice for breast cancer patients when both BCT and mastectomy are a suitable treatment options.

Another important aspect of the BCT was the identification of the risk factors for disease recurrence. Several studies have suggested that young age is a risk factor for recurrence[19-23], whereas other have not[24-25]. We did not find that younger age associated with disease recurrence in our study.

Lymph node status was the main prognostic factor that affects the outcome of breast cancer. NSBP trials[8] showed patients with four or more node metastases had significantly worse DFS than those who had no node metastases or to three-node metastases. The present result was similar to the above-mentioned reports.

Several reports have suggested that the histologic features: aggressive cell type, high tumor grade, present LVI, large tumor size, positive margin, poor histochemistry status and adjuvant treatment may contribute to the increased recurrence rates[20-21,26-28]. We did not encounter aggressive cell type, high tumor grade, present LVI, large tumor size, positive margin, poor histochemistry status, and adjuvant treatment as described in some studies associated with a higher recurrence rate.

Conclusion

BCT being at least equivalent in outcome to MRM achieves good long-term survival with reduced local morbidity. Patients who are suitable for BCT should be advised that BCT is the best treatment option for them. The treatment should be decided upon according to the risk of relapse for the patient and the possibility of improved disease control and survival by the treatment. In our study, the number of involved lymph nodes was the important prognostic factor affecting disease-free survival. Therefore, patients with positive lymph nodes should be treated aggressively and patients without risk factors may require less aggressive treatment.

Ethics approval

This study was conducted with the approval of the institutional review board of the Faculty of Medicine Vajira Hospital, Navamindradhiraj University (COA 084/2561).

Disclosure statement

The authors report no conflict of interest.

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References

1. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 2015;136(5):359–86.
2. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68(6):394-424.
3. Virani S, Bilheem S, Chansaard W, Chitapanarux I, Daoprasert K, Khuanchana S, et al. National and subnational population-based incidence of cancer in Thailand: assessing cancers with the highest burdens. Cancers 2017;9(8):180. doi: 10.3390/cancers9080108.
4. Goldhirsch A, Wood WC, Gelber RD, Coates AS, Thürlimann B, Senn HJ. Meeting highlights: updated international expert consensus on the primary therapy of early breast cancer. J Clin Oncol 2003;21(17):3357-65.
5. Colleoni M, Gelber S, Coates AS, Castiglione-Gertsch M, Gelber RD, Price K, et al. Influence of endocrine-related factors on response to perioperative chemotherapy for patients with node-negative breast cancer. J Clin Oncol 2001;19(21):4141-9.
6. Hayes DF. Markers of increased risk for failure of adjuvant therapies. Breast 2003;12(6):543-9.
7. Allred DC, Harvey JM, Berardo M, Clark GM. Prognostic and predictive factors in breast cancer by immunohistochemical analysis. Mod Pathol 1998 ;11(2):155-68.
8. Fisher B, Anderson S, Bryant J, Margolese RG, Deutsch M, Fisher ER, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N Engl J Med 2002;347(16):1233-41.
9. Darby S, McGale P, Correa C, Taylor C, Arriagada R, Clarke M, et al. Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10,801 women in 17 randomised trials. Lancet 2011;378(9804):1707-16.
10. Arriagada R, Lê MG, Rochard F, Contesso G. Conservative treatment versus mastectomy in early breast cancer: patterns of failure with 15 years of follow-up data. Institut Gustave-Roussy Breast Cancer Group. J Clin Oncol 1996;14(5):1558-64.

11. Veronesi U, Cascinelli N, Mariani L, Greco M, Saccozzi R, Luini A, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. N Engl J Med 2002;347(16): 1227–32.
12. Voogd AC, Nielsen M, Peterse JL, Blichert-Toft M, Bartelink H, Overgaard M, et al. Differences in risk factors for local and distant recurrence after breast-conserving therapy or mastectomy for stage I and II breast cancer: pooled results of two large European randomized trials. J Clin Oncol 2001;19(6):1688–97.
13. Poggi MM, Danforth DN, Sciuto LC, Smith SL, Steinberg SM, Liewehr DJ, et al. Eighteen-year results in the treatment of early breast carcinoma with mastectomy versus breast conservation therapy: The National Cancer Institute Randomized Trial. Cancers 2003;98(4):697–702.
14. Edge SB, Compton CC. The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. Ann Surg Oncol 2010;17(6): 1471–74.
15. van Dongen JA, Voogd AC, Fentiman IS, Legrand C, Sylvester RJ, Tong D, et al. Long-term results of a randomized trial comparing breast-conserving therapy with mastectomy: European Organization for Research and Treatment of Cancer 10801 trial. J Natl Cancer Inst 2000;92(14): 1143-50.
16. Lagendijk M, van Maaren MC, Saadatmand S, Strobbe LJA, Poortmans PMP, Koppert LB, et al. Breast conserving therapy and mastectomy revisited: Breast cancer-specific survival and the influence of prognostic factors in 129,692 patients. Int J Cancer 2018;142:165-75.
17. Johns N, Dixon JM. Should patients with early breast cancer still be offered the choice of breast conserving surgery or mastectomy? Eur J Surg Oncol 2016;42(11):1636-41.
18. Tantivatana T, Chongthanakorn M, Rongsriyam K, Katanyoo K. Treatment outcomes and prognostic factors of patients with breast cancer: a retrospective review. J Med Assoc Thai 2009;92(8):1084-93.
19. Stotter AT, McNeese MD, Ames FC, Oswald MJ, Ellerbroek NA. Predicting the rate and extent of locoregional failure after breast conservation therapy for early breast cancer. Cancer 1989; 64(11):2217-25.
20. Kurtz JM, Spitalier JM, Amalric R, Brandone H, Ayme Y, Bressac C, et al. Mammary recurrences in women younger than forty. Int J Radiat Oncol Biol Phys 1988;15(2):271-6.
21. Recht A, Connolly JL, Schnitt SJ, Silver B, Rose MA, Love S, et al. The effect of young age on tumor recurrence in the treated breast after conservative surgery and radiotherapy. Int J Radiat Oncol Biol Phys 1988;14:3-10.
22. Calle R, Vilcoq JR, Zafrani B, Vielh P, Fourquet A. Local control and survival of breast cancer treated by limited surgery followed by irradiation. Int J Radiat Oncol Biol Phys 1986;12(6):873-8.
23. Borger J, Kemperman H, Hart A, Peterse H, van Dongen J, Bartelink H. Risk factors in breast-conservation therapy. J Clin Oncol 1994;12(4): 653-60.
24. Mate TP, Carter D, Fischer DB, Hartman PV, McKhann C, Merino M, et al. A clinical and histopathologic analysis of the results of conservation surgery and radiation therapy in stage I and II breast carcinoma. Cancer 1986; 58(9):1995-2002.
25. Solin LJ, Fowble B, Schultz DJ, Goodman RL. Age as a prognostic factor for patients treated with definitive irradiation for early stage breast cancer. Int J Radiat Oncol Biol Phys 1989;16(2):373-81.
26. Anscher MS, Jones P, Prosnitz LR, Blackstock W, Hebert M, Reddick R, et al. Local failure and margin status in early-stage breast carcinoma treated with conservation surgery and radiation therapy. Ann Surg 1993;218:22-8.
27. Spivak B, Khanna MM, Tafra L, Juillard G, Giuliano AE. Margin status and local recurrence after breast-conserving surgery. Arch Surg 1994;129(9): 952-7.
28. Smitt MC, Nowels KW, Zdeblick MJ, Jeffrey S, Carlson RW, Stockdale FE, et al. The importance of the lumpectomy surgical margin status in long term results of breast conservation. Cancer 1995;76(2):259-67.