Breast-conserving treatment versus mastectomy in T1-2N0 breast cancer: which one is better for Indonesian women?

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Abstrak

Latar belakang: *Tujuan penelitian ini adalah untuk membandingkan hasil pengobatan antara penggunaan pengobatan konservasi payudara (*breast conserving therapy*, BCT) dan mastektomi pada pasien kanker payudara T1-2N0.*

Metode: *Penelitian retrospektif ini dilakukan pada pasien kanker payudara T1-2N0 yang menerima pengobatan antara Januari 2001 dan Desember 2010 di Departemen Radioterapi Rumah Sakit Cipto Mangunkusumo dan* Jakarta Breast Center. *Hasil akhir penelitian ini adalah kesintasan (OS), kekambuhan lokal (LR), kanker payudara kontra lateral (CBC), metastasis jauh (DM), dan* disease free survival *(DFS).*

Hasil: *Diantara 262 pasien yang memenuhi kriteria, 200 (76,3%) pasien menjalani BCT sedangkan 62 (23,7%) pasien menjalani mastektomi. Tidak ada perbedaan antara kelompok BCT dan mastektomi dalam hal kesintasan 5 tahun (5-year-overall-survival) 5-Y OS (88,2% vs 86,7%, p = 0,743), LR (7,4% vs 2,7%, p = 0,85), CBC (3,4% vs 5,3%, p = 0,906), DM (17,7% vs 37,7%, p = 0,212), dan DFS (78,5% vs 60,7%, p = 0,163). Dalam analisis multivariat, grade 3 dikaitkan dengan OS lebih buruk (HR 2,79, 95% CI 1,08-7,21, p = 0,03) dan DFS (HR 2,32, 95% CI 1,06-5,06). Wanita premenopause dikaitkan dengan risiko penurunan DM (HR 0,37, 95% CI 0,17-0,80) dan DFS (HR 0,38, 95% CI 0,19-0,78).*

Kesimpulan: *BCT dan mastektomi menunjukkan hasil yang sama dalam hal OS, LR, CBC, DM, dan DFS.* ***(Med J Indones. 2012;21:220-4)***

Abstract

Background: This study aimed to compare the treatment outcomes between the use of breast-conserving treatment (BCT) and mastectomy for T1-2N0 breast cancer patients.

Methods: This study retrospectively reviewed T1-2N0 breast cancer patients who received treatment between January 2001 and December 2010 at Department of Radiotherapy Cipto Mangunkusumo Hospital and Jakarta Breast Center. The endpoints of this study were overall survival (OS), local recurrence (LR), contra-lateral breast cancer (CBC), distant metastasis (DM), and disease-free survival (DFS).

Results: Among the 262 eligible patients, 200 (76.3%) patients underwent BCT while 62 (23.7%) patients underwent mastectomy. There were no differences between BCT and mastectomy groups in 5-Y OS (88.2% vs 86.7%, p = 0,743), LR (7.4% vs 2.7%, p = 0.85), CBC (3.4% vs 5.3%, p = 0.906), DM (17.7% vs 37.7%, p = 0.212), and DFS (78.5% vs 60.7%, p = 0.163). In multivariate analysis, grade 3 was associated with worse OS (HR 2.79; 95% CI 1.08 – 7.21, p = 0.03) and DFS (HR 2.32; 95% CI 1.06 – 5.06). Premenopausal women were associated with decreased risk of DM (HR 0.37; 95% CI 0.17 – 0.80) and DFS (HR 0.38; 95% CI 0.19 – 0.78).

Conclusion: BCT and mastectomy showed similar outcome in terms of OS, LR, CBC, DM, and DFS. ***(Med J Indones. 2012;21:220-4)***

Keywords: *Breast-conserving treatment, mastectomy, outcomes*

Breast cancer is the second most common cancer around the world with 1.38 million new cases diagnosed in 2008. While in Indonesia, this cancer is the most common cancer with 39.381 new cases diagnosed with 20.052 deaths in 2008.[1] Because in the last decades more screening programs were performed, more breast cancers were detected at early stage.[2]

Breast-conserving treatment or mastectomy are the treatments of choice for early stage breast cancer.[3,4] Both modalities provide similar treatment outcomes in terms of overall survival, loco-regional recurrence, and quality of life.[5-7] Nevertheless, the use of BCT is not uniform in various countries. For example in the Netherlands, 80% of patients underwent BCT.[8] In contrary, only 30% of patients underwent BCT in Hong Kong.[9]

In Indonesia, breast-conserving therapy or mastectomy are the standard therapies for early stage breast cancer. However, the results of treatment in Indonesia have yet to be evaluated. This study aims to compare the overall survival, recurrences, and disease-free survival between BCT and mastectomy for early breast cancer.

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This study is important to give recommendation for daily clinical practice.

METHODS

This is a retrospective cohort study on breast cancer patients undergoing treatment at the Department of Radiotherapy Cipto Mangunkusumo Hospital and Jakarta Breast Center between January 2001 and December 2010. The inclusion criteria were women of all ages, clinical stages T1-2N0 AJCC, histologic type of adenocarcinoma. The exclusion criteria were relapse cases with co-morbidities, non-compliance to the planned treatment or progressive disease during radiotherapy. The endpoints of this study were overall survival, local recurrence, contra lateral breast cancer, distant metastasis, and disease-free survival. Data analysis was using chi square test for patient characteristics, while Kaplan-Meier with log rank test for survival analysis. Multivariate analysis of prognostic factors was using Cox regression test.

RESULTS

A number of 262 patients were included in this study, more than seventy-five percent of patients undergoing breast conserning treatment (BCT). Eleven of 200 patients who underwent BCT obtained concurrent chemotherapy. Definitive radiation therapy after breast-conserving surgery is given using two-dimensional tangential technique, three-dimensional conformal techniques, or fields in the field technique covering the entire breast with doses of 50 Gy followed by a booster to tumor bed using external radiation or brachytherapy implants. Loco-regional radiation therapy was given if there was involvement of more than three positive lymph nodes, pathologically.

Table 1. Characteristics of patient with breast cancer (n = 262)

Variable		BCT n (%)	Mastectomy n (%)	p
Age	< 40 years	40 (20)	3 (4.8)	0.006
	≥ 40 years	160 (80)	59 (95.2)	
Menopause	Pre menopause	121 (61.4)	19 (3.6)	< 0.001
	Post menopause	76 (38.6)	43 (69.4)	
Site	Right	105 (52.5)	34 (54.8)	0.747
	Left	95 (47.5)	28 (45.2)	
Tumor Size	T1	56 (28.4)	14 (22.6)	0.366
	T2	141 (71.6)	48 (77.4)	
pN	Negative	128 (69.2)	33 (60)	0.203
	Positive	57 (30.8)	22 (40)	
Histology	Ductal invasive	163 (81.5)	47 (75.8)	0.326
Margin status	Negative	155 (95.1)	28 (90.3)	0.248
	Close – positive	8 (4.9)	3 (9.7)	
Grade	1 – 2	117 (82.4)	29 (68.3)	0.061
	3	25 (17.6)	13 (31.7)	
LVSI	Positive	21 (70)	14 (73.7)	0.781
ECE	Positive	14 (36.8)	11 (78.6)	0.008
ER	Negative	94 (52.8)	27 (45.8)	0.348
	Positive	84 (47.2)	32 (54.2)	
PR	Negative	91 (51.1)	30 (51.7)	0.937
	Positive	87 (48.9)	28 (48.3)	
Her-2	Negative	111 (63.1)	31 (55.4)	0.302
	Positive	65 (36.9)	25 (44.6)	
Radiation therapy		200 (100)	20 (32.2)	< 0.001
Adjuvant chemotherapy		102 (51)	34 (54.8)	0.597
Hormonal therapy		66 (33)	26 (41.9)	0.198
Trastuzumab		14 (7)	7 (11.5)	0.289

pN = pathological nodes, LVSI = lymphovascular space invasion, ECE = extra capsular invasion, ER = estrogen receptor, PR = progesterone receptor

In the mastectomy group, the most common surgical technique was modified radical mastectomy (60%) followed by radical mastectomy (36.8%) and simple mastectomy (3.2%). Twenty of 62 (32.3%) patients received post mastectomy radiation therapy.

The group who underwent BCT had more patients with age less than 40 years (20% vs 4.8%, p = 0.006) and more premenopausal patients (61.6% vs 30.6%, p < 0.001) compared with the mastectomy group. However, the latter group had more tumors with extra capsular extension (78.6% vs 36.8%, p = 0.008) than BCT group. Tumor location and size, pathologic involvement of lymph nodes, histological type, surgical margin, grade, LVSI, hormonal and Her-2 status, use of adjuvant systemic therapy such as chemotherapy, hormonal, and trastuzumab did not differ between the two groups (Table 1).

In both groups there was no significant differences in the five year overall survival, local recurrence, contra lateral breast cancer, distant metastasis, and disease-free survival (Table 2). On univariate analysis, factors affecting the overall survival is tumor size, pathology lymph node involvement, and grade. Whereas in the multivariate analysis, grade was the only an independent prognostic factor (Table 3).

Table 2. Comparison of treatment outcomes between BCT and mastectomy (%)

Endpoints	Years	BCT	Mastectomy	p
Overall survival	5	88.2	86.7	0.835
Local recurrence	5	7.4	2.7	0.850
Contra-lateral breast cancer	5	3.4	5.3	0.906
Distant metastasis	5	17.7	37.7	0.212
Disease free survival	5	78.5	60.7	0.163

p value obtained from Kaplan Meier with log-rank test

Fifty-two of 259 (16.2%) patients had recurrence, 45 patients (17.4%) had distant recurrence (metastasis), ten patients (3.9%) experienced recurrence in the contra lateral breast. Local and regional recurrence occurred in twelve and two patients each (4.6% and 0.8%).

On univariate analysis, prognostic factors for the occurrence of distant metastases were menopausal status, tumor size, grade. Whereas in the multivariate analysis, menopausal status was an independent prognostic factor for metastasis. The prognostic factors for disease-free survival were grade and menopausal status in both univariate and multivariate analysis (Table 4).

Table 3. Prognostic factors analysis for treatment outcomes

Variable		OS	Recurrences			DFS
			LR	CBC	DM	
Treatment	BCT Mastectomy	0.835	0.850	0.906	0.212	0.163
Age	< 40 years ≥ 40 years	0.161	0.566	0.527	0316	0.691
Menopause	Pre menopause Post menopause	0.180	0.583	0.748	0.009	0.006
Tumor size	T2 T1	0.038	0.316	0.183	0.033	0.430
pN	Positive Negative	0.031	0.797	0.498	0.061	0.241
Margin	Negative Close-Positive	0.799	0.532	0.672	0.196	0.176
Grade	3 1 – 2	0.003	0.294	0.259	0.038	0.030
LVSI	Positive Negative	0.338	0.515	0.114	0.838	0.705
ER	Negative Positive	0.134	0.826	0.737	0.922	0.613
PR	Negative Positive	0.300	0.796	0.253	0.181	0.203
Her-2	Negative Positive	0.250	0.558	0.773	0.295	0.360

pN = pathological nodes, LVSI = lymphovascular space invasion, ER = estrogen receptor, PR = progesterone receptor

Table 4. Multivariate analysis using cox regression model

	HR	95% CI	p
Overall survival			
T2 vs T1	2.338	0.51 – 10.65	0.272
pN positive vs negative	1.634	0.66 – 4.08	0.293
Grade 3 vs 1 – 2	2.796	1.08 – 7.21	0.033
Distant metastasis			
Pre vs post menopause	0.366	0.17 – 0.80	0.012
T2 vs T1	1.524	0.57 – 4.05	0.398
Grade 3 vs 1 – 2	2.211	0.95 – 5.14	0.065
Disease free survival			
Pre vs post menopause	0.379	0.19 – 0.78	0.008
Grade 3 vs 1 – 2	2.323	1.07 – 5.06	0.034

DISCUSSION

During the last thirty years, treatment for early-stage breast cancer has shifted from mastectomy to BCT. Between 1980 and 2004, the use of mastectomy at the Mayo Clinic dropped from 91% to 36%.[10] In four of the nine Dutch Comprehensive Cancer Centers, the majority of early-stage breast cancer patients received BCT (87-99%).[8] However, in Hong Kong as well as in Sabah Malaysia, the use of BCT was only 30% and 22.5%, respectively.[9,11]

BCT is more widely used in patients with younger age (≤ 40 years). In the Dutch Comprehensive Cancer Center, patients with age older than 75 years are associated with decreased use of radiotherapy compared to patients younger than 55 years (OR 0.4; 95% CI from 0.4 to 0.5).[10] The same result has been obtained from research in the U.S.A.[12]

Definitive radiation therapy decreased local recurrence after lumpectomy from 39.2% to 14.3% in a study conducted by the NSABP B-06.[13] Meta-analysis conducted by the EBCTCG showed that radiotherapy after breast-conserving surgery decreased local recurrence within 5 years and mortality in 15 years by 19% and 5.4%.[14]

Several studies have shown that breast conserving therapy and mastectomy provided equivalent survival. The study from North Carolina showed that mastectomy and BCT gives the same 5 year-survival-rate (94.8% and 96.7%, HR 1.33 95% CI 0.86 to 2.05).[15] Rapiti et al reported that the 10 years survival in patients who underwent BCT and mastectomy did not differ significantly (HR 0.69; 95% CI 0.46 to 1.03).[16] A study in Korea showed that 10 year overall survival in patients receiving BCT and mastectomy were 91.96% and 91.01% (p = 0.127).[17] EORTC 10.801 study reported that the 10 year-survival-rate is similar between mastectomy and BCT (66% vs 61%, p = 0.1).[18] The 20 years follow-up showed that there was no difference in term of overall survival between mastectomy and BCT for early stage breast cancer (41.2% and 41.7%, p = 1.0).[19] This study also proved similar result in terms of overall survival. We found that the prognostic factors for overall survival were tumor size, pathologic lymph node involvement, and grade.

Several studies reported that local recurrence occurred more of ten in patients who received BCT compared to mastectomy. EORTC reported that 5 and 10 years loco regional recurrences were higher in BCT group than mastectomy (11.8% and 19.7% vs 9.8% and 12.2%, p = 0.0097).[18] Veronessi et al reported that the incidence of local recurrence in 20 years on breast conservation therapy group was higher than mastectomy (8.8 ± 3.2% vs 2.3 ± 0.8, p < 0.001).[19] A randomized study in Europe showed that local recurrence in the BCT group was higher than mastectomy.[20] Meta-analysis reported that there were no differences in terms of 3, 5, 15, and 20 years loco-regional recurrences between BCT and mastectomy group. But for 10 year, loco-regional recurrence was higher in BCT than mastectomy (OR 1.55; 95% CI 1.05 to 2.30).[6] In this study, 5 year local recurrence in patients who underwent BCT was higher than mastectomy but not statistically significant. This is similar to a study in Korea, where 23 patients (3.8%) in the BCT and 22 patients (2.1%) in the mastectomy group had local recurrence (p = 0.081).[17]

In general, radiotherapy is not associated with an increased risk of contra-lateral breast cancer. The risk of contra-lateral breast cancer after radiotherapy is associated with the increase of follow-up. At follow-up for five years, radiotherapy was not associated with risk. However, after five years, radiotherapy is associated with slightly increased risk of contra-lateral breast cancer (1.14, 95% CI 1.03 to 1.26).[21] Incidence of contra-lateral breast cancer for 5, 10, 15, 20 years in patients receiving radiotherapy is 2.9%, 6.5%, 10.2%, and 13.4%, whereas in patients not receiving radiotherapy it is 3%, 6%, 8.9%, and 11.8%.[22]

In this study, there were no significant differences in patients undergoing BCT compared with mastectomy. This is probably due to lack of follow-up time.

Distant metastases in patients who underwent BCT or mastectomy did not differ significantly. Voogd et al reported that the incidence of distant metastasis for 5 and 10 years in patients with early stage breast cancer after BCT were 24% and 34% while mastectomy were 24% and 32% (p = 0.36).[20] Research in Korea showed that

5 years distant metastasis after BCT and mastectomy were 9.7% and 12.4%, respectively. In these patients, 59.2 to 69.4% received adjuvant chemotherapy and 50.1 to 53.6% received hormonal therapy.[17] EORTC study showed that the 10 years distant metastasis in patients receiving BCT and mastectomy were 26.8% and 26.7% respectively (p = 0.24).[18] Veronessi reported in patients with T1N0 breast cancer during follow-up of 20 years that the rates of distant metastases in patients with breast conserving therapy and mastectomy were 23.3% and 24.3%.[19] This current study provided similar results between two group. Factors that influence metastasis are among others menopausal status, tumor size and grade.

In conclusion, the treatment options for early stage breast cancer (T1-2N0) can be either BCT (breast-conserving surgery followed by definitive radiation therapy) or mastectomy depending on patient preference because both treatment modalities gave similar outcomes. In patients who expect the preservation of the breast, breast-conserving therapy can be considered. Whereas in patients who want to avoid radiotherapy, a mastectomy may be considered. Prospective studies with large numbers of subjects are needed to find out the role of prognostic factors, treatment efficacy for recurrence both local and contra lateral breast cancer, as well as the effect of systemic therapy to reduce distant metastases.

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