A Multicenter Retrospective Cohort Study on Long-Term Outcomes after Partial Mastectomy in Japan

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Abstract

Background: With recent advances in breast cancer treatment, changes in local recurrence and survival following breast-conserving surgery (BCS) are also anticipated over time. Techniques for BCS vary across countries, and anatomical differences among ethnic groups may influence patterns of local recurrence risk. Objective of this study: To investigate the recent rates of local recurrence and prognosis following BCS in Japan using multi-institutional real-world data, with a particular focus on identifying trends and risk factors for local recurrence through comparison with historical data. Methods: This multicenter retrospective cohort study included 8,897 breast cancer patients who underwent BCS between January 2014 and December 2018 at 25 participating institutions across Japan. Data on patient demographics, surgical details, pathological factors including margin status, adjuvant therapy, and outcomes were collected. The primary endpoint was local recurrence rate. Secondary endpoints included distant recurrence rate, overall mortality, and breast cancer-specific mortality. Local recurrence rate (LRR), disease-free survival (DFS) and overall survival (OS) were estimated by Kaplan-Meier analysis; Results: Median follow-up was 6.6 years. In the overall population (N=8,897), Clinical stages at diagnosis were Stage 0 (n=918:10.3%), Stage I (n=4,539:51.0%), Stage II (n=2,566: 28.8%), and Stage III (n=360:4.0%). 5 year LRR, DFS and OS were 2.0%(1.7-2.3: 95%CI), 94.1%(93.6-94.6: 95%CI) and 97.8%(97.4-98.1: 95%CI), respectively. 10 year LRR, DFS and OS were 4.6%(3.6-5.5: 95%CI), 86.2%(84.1-88.3: 95%CI) and 94.1%(93.1-95.1: 95%CI), respectively. Potential risk factors for local recurrence are younger age of onset, tumor size, high Ki-67 , LV invasion, lack of adjuvant therapy (Table 1). Adjuvant systemic treatment was suggested to contribute to a reduced risk of local recurrence in all subtypes. Conclusions: Our recent data suggest that outcomes of BCS in Japan have improved compared to the past. As a growing number of new systemic therapies continue to be introduced each year, it is crucial to incorporate contemporary data—rather than relying solely on historical studies—when considering optimal surgical strategies.

Introduction

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Techniques for BCS vary across countries, and anatomical differences among ethnic groups may influence patterns of local recurrence risk.

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Methods

Study Design Retrospective, multi-institutional cohort study

Study Population January 1, 2014 ～ December 31, 2018

Patients who underwent BCS Stage 0–III breast cancer 25 institutions in Japan

Clinical/pathological data collection through medical record review

Outcomes: Local recurrence, disease-free survival, overall survival

Kaplan–Meier method/log-rank test Cox proportional hazards model

Results

Patient characteristics N=8897

Age	mean	SD
20-97	57.1	12.9
	N (%)	
<40	523 (6.4)	
40-49	2204 (27.0)	
50-59	2041 (25.0)	
60-69	1846 (22.6)	
70≦	1562 (19.1)	

	N (%)
Sex	
Female	8897 (100)
Ethnicity	
Asian	8882 (99.8)
White	10 (0.1)
Hispanic	4 (0.0)
N/A	1 (0.0)

	N (%)
ER	
Null <1%	1000 (11.2)
Weak 1%-9.9%	174 (2.0)
Posi 10%≦	7328 (82.4)
N/A	395 (4.4)
PgR	
Null <1%	1694 (19.0)
Weak 1%-9.9%	580 (6.5)
Posi 10%≦	6226 (70.0)
N/A	397 (4.5)
HER2	
Negative	6903 (77.6)
Positive	880 (9.9)
N/A	1114 (12.5)
Ki-67	
<20%	4407 (49.5)
20%≦	3032 (34.1)
N/A	1458 (16.4)

Surgical margin status

	N (%)
Margin	
Negative	8246 (92.7)
Positive	649 (7.3)
N/A	2 (0.0)

	N (%)
T	
is	1173 (13.2)
0	102 (1.1)
1	5289 (59.4)
2	2201 (24.7)
3	83 (0.9)
4	41 (0.5)
N/A	8 (0.1)
N	
0	6778 (76.2)
1	1406 (15.8)
2	170 (1.9)
3	78 (0.9)
N/A	465 (5.2)
Stage	
0	918 (10.3)
I	4539 (51.0)
II	2566 (28.8)
III	360 (4.0)
N/A	514 (5.8)

	N (%)
subtype	
ER(+)HER2(-)	6249 (70.2)
ER(+)HER2(+)	597 (6.7)
ER(-)HER2(+)	282 (3.2)
ER(-)HER2(-)	650 (7.3)
N/A	1119 (12.6)
Grade	
I/II	6320 (71.0)
III	1448 (16.3)
N/A	1129 (12.7)

Treatment information

	N (%)
Chemotherapy	
Yes	2772 (31.1)
Neoadjuvant	1238 (13.9)
Adjuvant	1534 (17.2)
No	6125 (68.9)
Endocrine therapy	
Yes	6519 (73.3)
No	2378 (26.7)
Radiation	
Yes	7710 (86.7)
Boost (+)	2282 (25.6)
No	1187 (13.3)

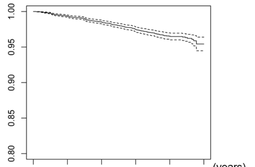
Prognostic outcomes

Median f/u period: 6.6 years

- **Local recurrence rate**
  - 5y : 2.0 % (1.7 – 2.3)
  - 10y: 4.6 % (3.6 – 5.5)
- **Disease-free survival rate**
  - 5y : 94.1 % (93.6 – 94.6)
  - 10y: 86.2 % (84.1 – 88.3)
- **Overall survival rate**
  - 5y : 97.8 % (97.4 – 98.1)
  - 10y: 94.1 % (93.1 – 95.1)

(95%CI)

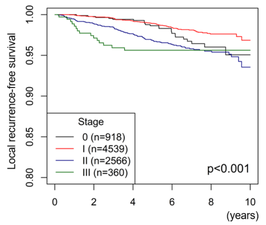
Local recurrence-free survival



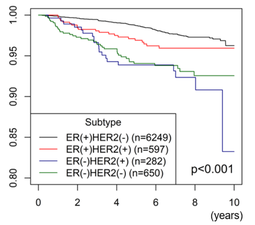
years	0	2	4	6	8	10
# at Risk	8897	8260	7517	5339	2363	117
# Event	0	37	36	33	16	5

Local recurrence-associated factors

Stage

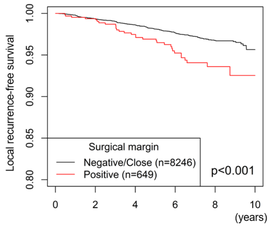


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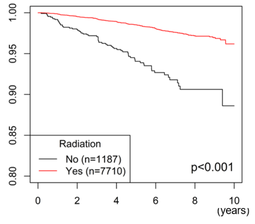


Local recurrence-associated factors

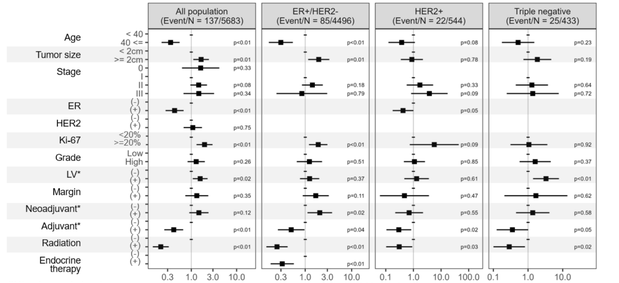
Margin status



Radiation



Local recurrence risk factors: Multivariate analysis



*LV:lympho-vascular invasion,
Neoadjuvant: neoadjuvant chemotherapy, Adjuvant: adjuvant chemotherapy

-: reference, blank: not used variable

Discussion

- **In this recent real-world data from Japan [2014-18]**
  - 10 year-LRR 4.6%, DFS 86%, OS 94%
- **Local recurrence rates in comparison with historical data**

	Study period	Country	MFU*	Local recurrence rate
This study	2014-2018	Japan	6.6 y	4.6% (10y)
AFT-RWD[1]	1997-2010	US	4.7 y	6.2% (10y)
EBCTCG[2]	1970-1990	MA*	9.5 y	7.7% (10y)
Mansfield[3]	1982-1994	US	3.3 y	15% (10y)
EORTC[4]	1980-1986	EU	13.4 y	20% (10y)* Mostly T2
NSABP B-06[5]	1976-1984	US	20.7 y	14.3% (20y)

*MA; meta-analysis, MFU; median follow-up period

0 5 10 15 20 (%)

Potential risk factors for local recurrence

・younger age of onset ・tumor size ・high Ki-67 ・LV invasion ・lack of adjuvant chemo/RT

Adjuvant systemic treatment was suggested to contribute to a reduced risk of local recurrence in all subtypes

ER+/HER2- invasive cancer Local recurrence: High ⇑ --- NAC Low ⇓ --- Adjuvant systemic therapy

Conclusions

Our recent data suggest that outcomes of BCS in Japan have improved compared to the past. As a growing number of new systemic therapies continue to be introduced each year, it is crucial to incorporate contemporary data—rather than relying solely on historical studies—when considering optimal surgical strategies.

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