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Clinicopathological characteristics, surgical management, and outcomes of mammary Paget's disease: 552 cases from a Japanese nationwide cancer registry

Sakiko Maruya
Institute of Science Tokyo
Toshiyuki Ishiba
ishiba.t.222d@m.isct.ac.jp

Institute of Science Tokyo
Hiraku Kumamaru
Yokohama City University Graduate School of Data Science
Takaaki Konishi
National Cancer Center
Naoko Kinukawa
Yokohama City University Graduate School of Data Science
Tomoyuki Aruga
Institute of Science Tokyo
Naruto Taira
Kawasaki Medical School

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Clinicopathological characteristics, surgical management, and outcomes of mammary Paget's disease: 552 cases from a Japanese nationwide cancer registry

Sakiko Maruya[1], M.D.; Toshiyuki Ishiba[1], M.D., Ph.D.; Hiraku Kumamaru[2], M.D., Sc.D.; Takaaki Konishi[3,4], M.D., Ph.D.; Naoko Kinukawa[2], Ph.D.; Tomoyuki Aruga[1], M.D., Ph.D.; Naruto Taira[5], M.D., Ph.D.

[1] Department of Breast Surgery, Institute of Science Tokyo, 1-5-45 Yushima, Bunkyo-ku, Tokyo, Japan

[2] Department of Health Data Science, Yokohama City University Graduate School of Data Science, Yokohama, Japan

[3] Division of Health Services Research, Institute for Cancer Control, National Cancer Center, 5-1-1 Tsukiji, Chuo-ku, Tokyo, Japan

[4] Department of Breast and Endocrine Surgery, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo, Japan

[5] Department of Breast and Thyroid Surgery, Kawasaki Medical School, 577 Matsushima, Kurashiki City, Okayama, Japan

Corresponding author

Toshiyuki Ishiba

Tel: +81-3-5803-5261

E-mail: ishiba.t.222d@m.isct.ac.jp

Address: 1-5-45 Yushima, Bunkyo-ku, Tokyo 113-8519, Japan

ORCIDs

Sakiko Maruya: 0009-0005-2308-7449

Toshiyuki Ishiba: 0000-0002-8709-4972

Takaaki Konishi: 0000-0002-9538-4419

Naruto Taira: 0000-0003-4266-1117

Abstract

Purpose

Mammary Paget's disease (MPD) is a rare breast cancer characterized by the presence of Paget cells within the epidermis of the nipple–areolar complex. Traditionally, mastectomy has been the standard surgical treatment for MPD. However, outcomes following mastectomy and breast-conserving surgery (BCS) remain unclear. We investigated clinicopathological characteristics and survival outcomes of MPD using a Japanese nationwide registry.

Methods

Patients undergoing surgery for MPD between 2004 and 2018 were identified from the Japanese National Clinical Database–Breast Cancer Registry. We defined patients with an invasive component ≤1 mm (pTis/pT1mi), cN0, cM0 as "MPD-defined patients" based on the Japanese General Rules for Clinical and Pathological Recording of Breast Cancer. Clinicopathological characteristics were compared between the mastectomy and BCS groups. Disease-free survival (DFS) was evaluated using Kaplan–Meier analysis and a univariable Cox proportional hazards model.

Results

Among 552 MPD-defined patients, 541 had available surgical information (mastectomy, n= 388 ; BCS, n = 153). Twelve DFS events occurred. Local recurrence occurred in 2/388 patients (0.5%) after mastectomy and 3/153 patients (2.0%) after BCS. The 5-year DFS rates were 97.3% (95% confidence interval [CI], 94.9–98.6%) for mastectomy and 97.7% (95% CI, 93.0–99.3%) for BCS. The difference was not significant (log-rank p = 0.78). The unadjusted hazard ratio for BCS versus mastectomy was 1.20 (95% CI, 0.33–4.44).

Conclusion

MPD-defined patients showed favorable outcomes. No significant difference in DFS was observed between the mastectomy and BCS groups. BCS may be an acceptable treatment option for carefully selected patients with MPD.

Keywords

Paget's disease; Breast-conserving surgery; Mastectomy; National Clinical Database; Registry study

Introduction

Mammary Paget's disease (MPD) is a rare form of breast cancer, accounting for approximately 1% to 3% of all cases [1]. It is characterized by the presence of Paget cells within the epidermis of the nipple–areolar complex and typically presents with clinical symptoms such as nipple erythema or erosion [2–4]. Although MPD often involves ductal carcinoma in situ (i.e., PD-DCIS) or invasive carcinoma (i.e., PD-IDC), less than 10% of cases exhibit only nipple lesions [5, 6].

Surgical resection is the standard initial treatment for MPD. Traditionally, total mastectomy has been the standard approach because of the high incidence of multifocal lesions and occult invasive components [7–10]. Recent studies, however, have demonstrated that breast-conserving surgery (BCS) followed by radiotherapy can achieve local control and survival outcomes comparable to those of mastectomy [1, 11, 12]. Furthermore, the National Comprehensive Cancer Network (NCCN) guidelines present multiple surgical options, including mastectomy, BCS, and central lumpectomy (e.g., nipple-areolar complex excision), based on the extent of disease assessed by preoperative magnetic resonance imaging (MRI) [13]. However, although MRI facilitates preoperative lesion localization [3, 14, 15] and has enabled the selection of BCS, nationwide data on the characteristics and outcomes of patients undergoing different surgical approaches for MPD in Japan are limited [3, 14, 15].

Therefore, this study aimed to characterize patients with MPD and surgical treatment patterns in Japan and to compare outcomes between mastectomy and BCS using data from a nationwide registry.

Patients and Methods

Data source

This study was conducted using data from the National Clinical Database–Breast Cancer Registry (NCD-BCR), a nationwide registry in Japan. The Japanese Breast Cancer Society initiated a breast cancer registry in 1975, which transitioned to a web-based system in 2004 and was subsequently integrated into the National Clinical Database in 2012. The NCD-BCR collects detailed clinicopathological and treatment information on newly diagnosed breast cancer cases from institutions across Japan [16]. As of April 2024, the registry included 5,679 institutions and 14,920 departments, with a cumulative total of approximately 28.48 million surgical cases.

The NCD-BCR collects information on patient characteristics, clinicopathological characteristics, recurrence, and survival through a web-based system. Patient characteristics included age, sex, and body mass index (BMI). Clinicopathological characteristics included clinical tumor category (cT), clinical nodal category (cN), clinical distant metastasis category (cM), pathological invasive tumor size, immunostaining status (estrogen receptor [ER], progesterone receptor [PgR], and human epidermal growth factor receptor 2 [HER2]), nuclear grade, surgical information (type of primary surgery, axillary procedures, and surgical margin status), and use of chemotherapy and radiotherapy. Information on surgical margin status was available only for cases registered from 2015 onward. TNM classification was recorded according to the 7th edition of the Unio Internationalis Contra Cancrum staging system [17].

The NCD-BCR conducts follow-up surveys to collect prognostic information at 5, 10, and 15 years after registration. The follow-up data include recurrence status, the date of recurrence, the site of first recurrence (ipsilateral conserved breast, ipsilateral axillary lymph nodes, other ipsilateral locoregional sites, or distant organs), survival status, and, for patients who died, the date and cause

of death (breast cancer, other causes, or unknown). For patients who were alive, the date of the last confirmed follow-up was recorded.

Participants

From the NCD-BCR, we identified patients who underwent breast cancer surgery for MPD between 2004 and 2018 and had available data on cT, cN, cM, neoadjuvant therapy, and five-year follow-up; these patients were defined as MPD-registered patients. MPD included PD, PD-DCIS, and PD-IDC with an invasive component measuring ≤1 mm, according to the 18th edition (2018) of the General Rules for Clinical and Pathological Recording of Breast Cancer of the Japanese Breast Cancer Society [18]. To improve diagnostic accuracy, we defined eligible patients (i.e., MPD-defined patients) as those who met all of the following criteria: (i) an invasive component measuring ≤1 mm in greatest dimension (pTis or pT1mi), (ii) no clinical nodal or distant metastasis (cN0 and cM0), and (iii) no neoadjuvant therapy.

Variables and outcomes

First, we summarized the patient and clinicopathological characteristics of MPD-registered and MPD-defined patients to characterize the overall population registered as MPD in the NCD-BCR. Patient characteristics included age, sex, and BMI. Clinicopathological characteristics included type of primary surgery (mastectomy or BCS), clinical tumor category (Tis/0/1 or T2/3/4), clinical nodal category (N0 or N1/2/3), clinical distant metastasis category (M0 or M1), pathological invasive component (≤1 mm or >1 mm), immunostaining status (ER, PgR, and HER2), and nuclear grade. Hormone receptor (ER and PgR) expression was considered positive if at least 1% of tumor cell nuclei showed staining on immunohistochemistry (IHC). HER2-positive status was defined as an IHC score of 3+, or an IHC score of 2+ with positive fluorescence in situ hybridization (FISH).

HER2-negative status was defined as an IHC score of 0 or 1+, or an IHC score of 2+ with negative FISH. HER2 status was defined according to the 2018 American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) guidelines [19].

Second, we compared characteristics between the mastectomy and BCS groups among MPD-defined patients. Patients without information on surgical type were excluded. The invasive component was categorized as no invasion (0 mm or pTis) or microinvasion (>0 to ≤1 mm; pT1mi). Eligibility was based on clinical nodal status (cN0), whereas Table 2 presents postoperative pathological nodal status (pN). Because the NCD-BCR has no specific category for central lumpectomy, such procedures were included in the BCS category.

The primary outcome was disease-free survival (DFS), which was evaluated among MPD-defined patients with known surgical type. DFS events were defined as breast cancer recurrence or death from any cause. The date of surgery was used as the origin for calculating DFS.

Statistical analysis

Categorical variables were compared using the chi-square or Fisher's exact test. Continuous variables were compared using the Wilcoxon rank-sum test. Continuous variables are expressed as the median and interquartile range. DFS curves were estimated using the Kaplan–Meier method, and comparisons between the two surgical groups were performed using the log-rank test. A univariable Cox proportional hazards model was used to estimate the hazard ratio (HR) and 95% confidence interval (CI) for DFS comparing BCS with mastectomy. Subgroup analyses were performed according to radiotherapy use, HER2 status (positive or negative), and age (<68 years or ≥68 years). All statistical tests were two-sided, and a p value of <0.05 was considered statistically significant. No adjustment for multiple comparisons was performed. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

Results

The NCD-BCR included 533,000 breast cancer cases registered between 2004 and 2018 with available five-year follow-up data. We identified 1,531 patients as MPD-registered, of whom 552 met the criteria for MPD-defined patients (pTis/pT1mi, cN0, cM0, and no neoadjuvant therapy). The mastectomy group included 388 patients, and the BCS group included 153 patients. Eleven patients with unknown surgical procedure type were excluded from the comparison (**Figure 1**).

Table 1 summarizes the characteristics of the MPD-registered patients (n = 1,531) and the MPD-defined patients (n = 552). Among the MPD-registered patients, 54 (3.5%) had clinical nodal metastases, and 3 (0.2%) had clinical distant metastases at diagnosis. Among the 319 MPD-defined patients for whom HER2 status was available, 257 (80.6%) had a HER2 IHC score of 3+.

Table 2 summarizes the characteristics of patients in the mastectomy and BCS groups. The mastectomy group was significantly younger than the BCS group (median, 67 vs. 71 years; $p = 0.002$). Compared with the BCS group, axillary procedures were significantly more frequently performed in the mastectomy group ($p < 0.001$), whereas the mastectomy group was less likely to have positive or close surgical margins ($p < 0.001$) or receive radiotherapy (0.8% vs. 32%; $p < 0.001$). No significant differences were observed in the other variables between the two groups. Although all MPD-defined patients were clinically node-negative (cN0), pathological nodal involvement (pN1–3) was identified postoperatively in eight patients.

Among MPD-defined patients, 12 DFS events (12/541; 2.2%) were observed. Of these, nine were in the mastectomy group and three were in the BCS group. In the mastectomy group, two patients developed local recurrence (2/388; 0.5%), six patients developed distant metastases, and one patient died of other causes. In the BCS group, all three DFS events were local recurrences (3/153; 2.0%).

The estimated 5-year DFS rates were 97.3% (95% CI, 94.9–98.6%) in the mastectomy group and 97.7% (95% CI, 93.0–99.3%) in the BCS group. Kaplan–Meier analysis showed no significant difference in DFS between the groups (**Figure 2**, log-rank p = 0.78). The unadjusted HR for BCS versus mastectomy was 1.20 (95% CI, 0.33–4.44; p = 0.78).

Among patients who received radiotherapy (n = 52), no DFS events were observed in either the mastectomy group (0/3) or the BCS group (0/49), and therefore statistical comparison was not applicable (**Figure 3a**). In contrast, all 12 DFS events were observed among patients who did not receive radiotherapy (n = 484). No significant difference in DFS was observed between the two groups (9/381 vs. 3/103; **Figure 3b**, log-rank p = 0.74).

Subgroup analyses according to HER2 status and age also showed no significant difference in DFS between the two groups. Among patients with HER2-negative tumors, no DFS events were observed in either group (0/21 vs. 0/14), precluding statistical comparison (**Supplementary Figure 1a**). In contrast, among patients with HER2-positive tumors, DFS events were observed in 8 patients (6/202 vs. 2/74; log-rank p = 0.94) (**Supplementary Figure 1b, c**). Similarly, among patients aged <68 years, DFS events were observed in 6 patients (5/197 vs. 1/61; log-rank p = 0.65) (**Supplementary Figure 1d, e**). Among patients aged ≥68 years, DFS events were observed in 6 patients (4/190 vs. 2/92; log-rank p = 0.96) (**Supplementary Figure 1f, g**).

Discussion

In this nationwide registry-based study, we identified 552 MPD-defined patients from 1,531 MPD-registered patients. The prognosis of the MPD-defined patients was favorable, with only 12 events observed. The 5-year DFS rates (>97%) observed in both groups indicated favorable outcomes among carefully selected patients with MPD. No significant difference in DFS was

observed between the mastectomy and BCS groups; however, the small number of events limited the ability to detect differences between the surgical groups.

MPD includes PD, PD-DCIS, and PD-IDC [1, 5, 6]. Although MPD is generally an early-stage, non-metastatic disease [5, 6, 10], a subset of MPD-registered patients had clinical nodal or distant metastases at diagnosis. This finding may suggest that the pathological definition of MPD has not been uniformly recognized in clinical practice in Japan, as international guidelines (e.g., the NCCN guidelines) do not define MPD as a single pathological entity [13]. The definition of MPD in the General Rules for Clinical and Pathological Recording of Breast Cancer of the Japanese Breast Cancer Society was revised from the 18th edition (2018) to the 19th edition (2025). In the 18th edition, MPD was defined as PD, PD-DCIS, and PD-IDC (i.e., MPD with an invasive component ≤1 mm), whereas the 19th edition (2025) defines MPD as a lesion confined to the nipple–areolar complex containing Paget cells, including PD, PD-DCIS, and PD-IDC [18, 20]. Based on the 18th edition, we limited the MPD-defined population to patients with MPD with an invasive component ≤1 mm (pTis or pT1mi), no clinical nodal or distant metastasis, and no neoadjuvant therapy. The 1-mm threshold corresponds to the T1mi definition in the TNM classification and represents a clinically reasonable cutoff. These observations suggest that applying a clinically appropriate case definition is important when analyzing MPD using nationwide registry data. Such an approach may also facilitate comparisons across future registry-based studies despite differences in pathological classification.

A high proportion of MPD-defined patients had HER2-positive tumors, consistent with previous reports [5, 10]. The biological implications of HER2 overexpression in MPD remain unclear. The high frequency of HER2 positivity raises the possibility of a role for anti-HER2 therapy; however, the clinical impact of anti-HER2 agents in MPD remains difficult to assess because the present study focused on MPD with minimal invasive components.

Kaplan–Meier analysis demonstrated no significant difference in DFS between the mastectomy and BCS groups, presumably due to the small number of events. Although the present findings did not establish equivalent efficacy between BCS and mastectomy, BCS might offer an acceptable treatment option in selected patients with MPD with minimal invasive components. Unlike BCS for general breast cancer, BCS for MPD generally requires resection of the nipple–areolar complex. Therefore, treatment selection should consider not only oncological safety but also cosmetic outcomes, surgical margins, postoperative radiotherapy, and patient preference. As MRI is widely used in Japan to identify the extent of breast cancer (e.g., intraductal components and multifocal or multicentric disease), MRI may facilitate the preoperative selection of BCS [3, 21, 22].

Previous large-scale studies have reported comparable survival outcomes between BCS followed by radiotherapy and mastectomy in patients with MPD, including a population-based analysis of more than 5,000 patients and a meta-analysis of more than 24,000 patients [1, 11]. A prospective study reported favorable local control with BCS followed by radiotherapy despite a small sample size (n = 61) [7]. In contrast, a meta-analysis of retrospective studies involving 685 patients suggested that mastectomy may provide better local control than BCS; however, postoperative radiotherapy was not routinely administered across the included studies (19%–100% of cohorts underwent radiotherapy) [12].

Based on the results of the present study, we consider that BCS followed by radiotherapy may achieve oncological outcomes comparable to those of mastectomy in patients with MPD, similar to the standard management of general breast cancer [13].

Radiotherapy was administered in 32% of the BCS group. This proportion appears lower than that typically observed in standard breast cancer management (approximately 75–95% [23, 24]), although radiotherapy is routinely recommended after BCS in various clinical guidelines [13, 22]. Clinicians' judgment that MPD with minimal invasive components carries a low risk of recurrence

may have reduced radiotherapy use. Previous studies of local control after BCS followed by radiotherapy for MPD have demonstrated inconsistent results [1, 11, 12]. A meta-analysis reported a higher risk of local recurrence after BCS than after mastectomy; however, variation in radiotherapy use across the included studies may have influenced the observed outcomes [12]. In contrast, more recent studies have suggested that radiotherapy after BCS for MPD may be associated with improved local control [1, 11]. In the present study, no DFS events were observed among patients who received radiotherapy, consistent with previous reports. Although the impact of radiotherapy could not be definitively determined because of the limited number of patients and DFS events, the absence of DFS events in patients who received radiotherapy following BCS is consistent with previous reports and current clinical guidelines. Therefore, radiotherapy may be considered in accordance with clinical guidelines when BCS is selected for patients with MPD.

Significant differences between the two groups were observed in age, axillary procedures, surgical margin status, and radiotherapy. The mastectomy group was significantly younger than the BCS group. Younger patients are generally more likely to undergo mastectomy than BCS, which may reflect concerns about recurrence, genetic risk, and the availability of immediate reconstruction [25, 26]. In addition, younger patients may prefer mastectomy and reconstruction because MPD requires resection of the nipple–areolar complex, which can cause major breast deformity even after BCS [27]. Regarding axillary procedures, axillary lymph node dissection may be omitted in BCS even with one or two positive lymph nodes according to clinical trial findings [28], whereas dissection is generally performed during mastectomy for patients with positive nodes [13]. The higher likelihood of close or positive margins in the BCS group than in the mastectomy group was consistent with findings in general breast cancer [29]. In addition, radiotherapy was more likely to be administered after BCS than after mastectomy, in accordance with standard treatment [13].

Several limitations should be acknowledged. First, the NCD-BCR does not include detailed information on factors influencing treatment selection, such as indications for surgery and radiotherapy, or preoperative imaging findings, including MRI. In addition, six distant recurrences were recorded despite restricting the cohort to patients with pTis/pT1mi disease. The NCD-BCR does not provide sufficient detailed information to independently verify individual recurrence events or determine their clinical context. Therefore, these findings should be interpreted cautiously. Second, this study primarily compared DFS between patients who underwent mastectomy and those who underwent BCS. However, important differences in baseline characteristics were observed between the two groups, including age, axillary surgery, surgical margin status, and use of radiotherapy; therefore, treatment allocation was not randomized, and confounding cannot be excluded. Accordingly, these findings should be interpreted as indicating that appropriately selected patients undergoing BCS achieved excellent oncological outcomes, rather than as evidence of equivalent efficacy between BCS and mastectomy. Third, the number of cases and DFS events was small. This limited the statistical power to detect differences in DFS between the two groups and precluded reliable multivariable Cox proportional hazards regression analysis. Multivariable Cox analysis was considered statistically unreliable because only 12 DFS events occurred, providing fewer than 10 events per variable.

In conclusion, patients with MPD with minimal invasive components had favorable outcomes after surgery. No statistically significant difference in DFS was observed between the mastectomy and BCS groups; however, the small number of events and wide confidence interval precluded a definitive comparison of the two surgical approaches. This nationwide registry study provides large-scale real-world data on surgical treatment patterns and outcomes of MPD.

Supplementary information

Supplementary Figure 1 is provided as Online Resource 1.

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Statements and declarations

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Competing interests

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SM and TK declare no competing interests.

Author contributions

SM, TI, and TK conceived and designed the study. HK and NK analyzed the data. TK supported HK in preparing the data request. SM interpreted the data and prepared the first draft of the manuscript. TI and TK supervised manuscript preparation. All authors approved the concept of this study and critically revised the manuscript. All authors have read and approved the final version of the manuscript.

Data availability

The data that support the findings of this study are not openly available due to the nature of the clinical data used. The clinical data are derived from the registry, which is not an open database. The data were accessed by a designated statistician through an application process approved by academic societies. Therefore, we are unable to share the original clinical data.

Ethics approval

This study was approved by the Ethics Committee of the Institute of Science Tokyo (approval No. M2024-036-01).

Consent to participate

Informed consent was not required due to the retrospective nature of the study.

Consent to publish

Not applicable.

Figure legends

Fig. 1 Flow diagram of patient selection from the Japanese National Clinical Database–Breast Cancer Registry

Abbreviations: NCD, national clinical database; MPD, mammary Paget's disease; BCS, breast-conserving surgery

Fig. 2 Kaplan–Meier curves of disease-free survival in mammary Paget's disease-defined patients

(a) Overall view of the survival curves; (b) enlarged view of the survival curves.

Abbreviation: BCS, breast-conserving surgery

Fig. 3 Kaplan–Meier curves of disease-free survival in mammary Paget's disease-defined patients stratified by radiotherapy

(a) Patients who received radiotherapy; (b) patients who did not receive radiotherapy; (c) enlarged view of panel (b).

Abbreviation: BCS, breast-conserving surgery

Supplementary fig. 1 Kaplan–Meier curves of disease-free survival in the mammary Paget's disease-defined patients stratified by human epidermal growth factor receptor 2 (HER2) status or age

(a) HER2-negative patients; (b) HER2-positive patients; (c) enlarged view of panel (b); (d) patients aged <68 years; (e) enlarged view of panel (d); (f) patients aged ≥68 years; (g) enlarged view of panel (f)

Abbreviation: BCS, breast-conserving surgery

Fig. 1

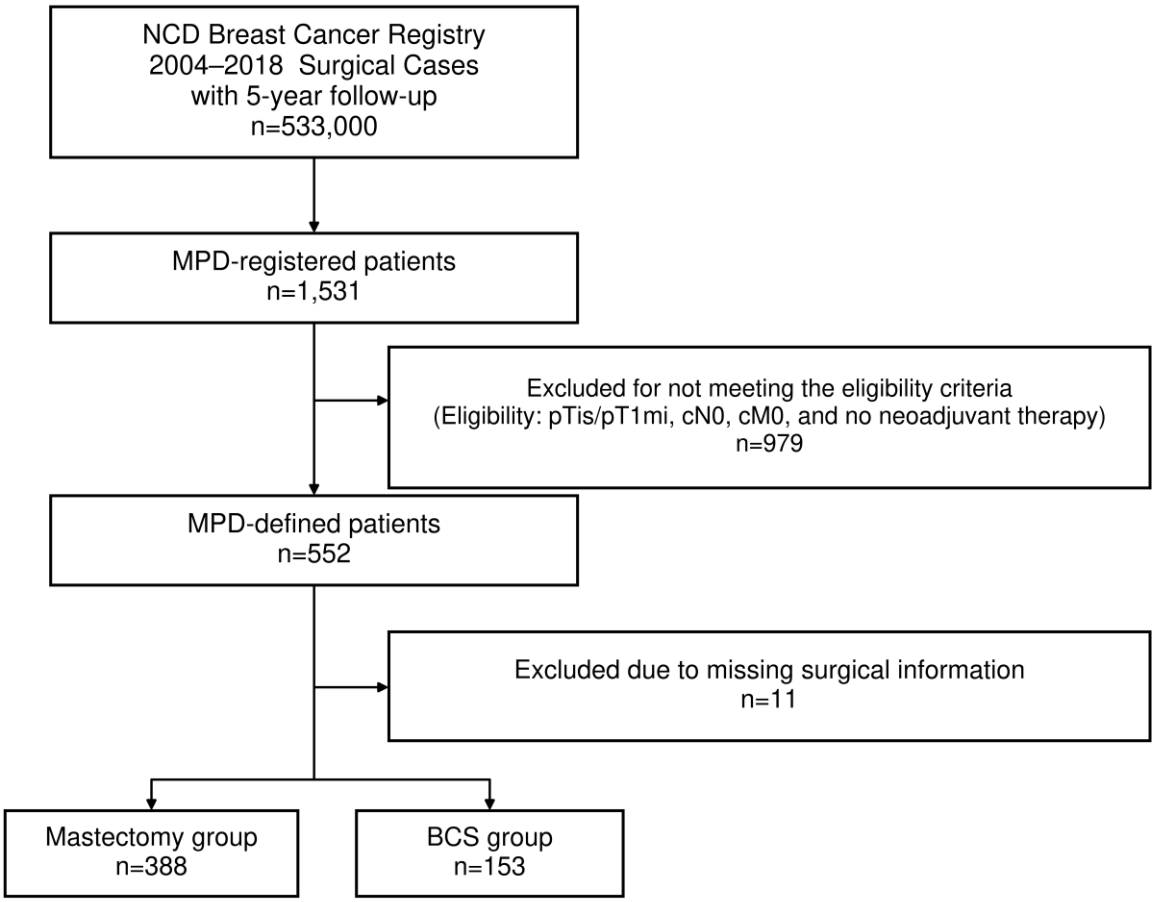
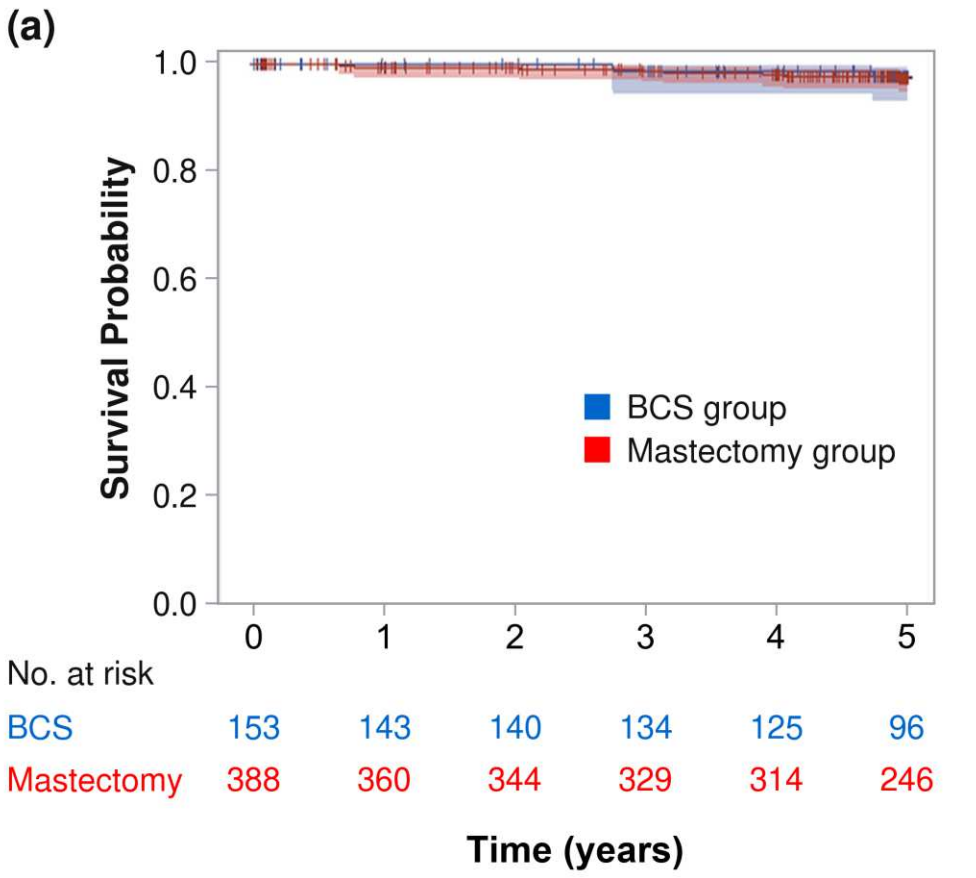

NCD Breast Cancer Registry
2004–2018 Surgical Cases
with 5-year follow-up
n=533,000
MPD-registered patients
n=1,531
Excluded for not meeting the eligibility criteria
(Eligibility: pTis/pT1mi, cN0, cM0, and no neoadjuvant therapy)
n=979
MPD-defined patients
n=552
Excluded due to missing surgical information
n=11
Mastectomy group
n=388
BCS group
n=153

Fig. 2


(a)
Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
BCS group
Mastectomy group
0
1
2
3
4
5
No. at risk
BCS 153 143 140 134 125 96
Mastectomy 388 360 344 329 314 246
Time (years)

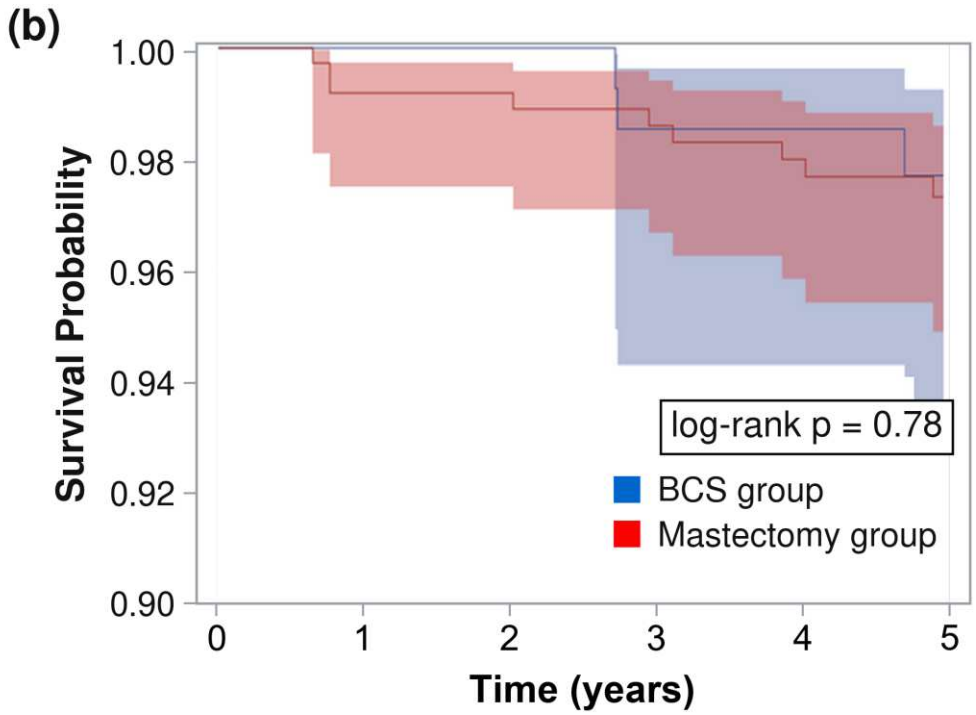
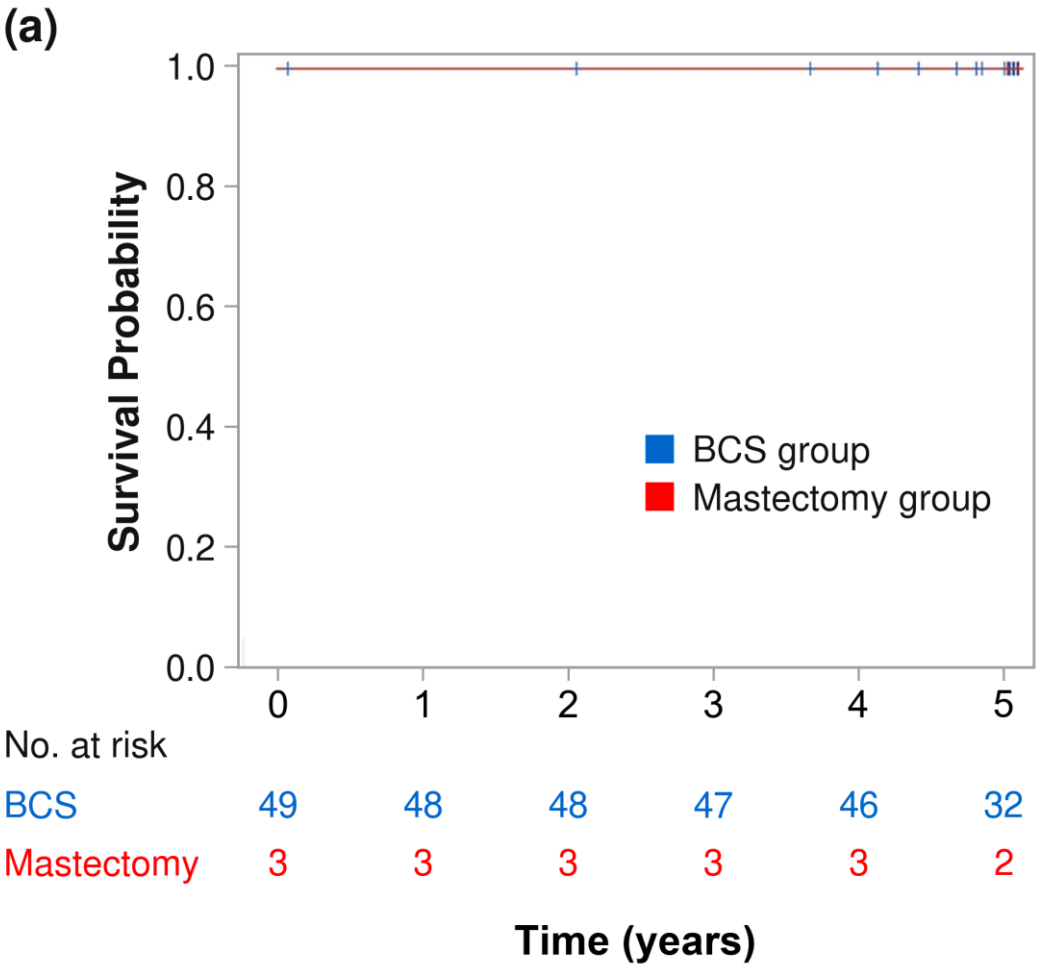
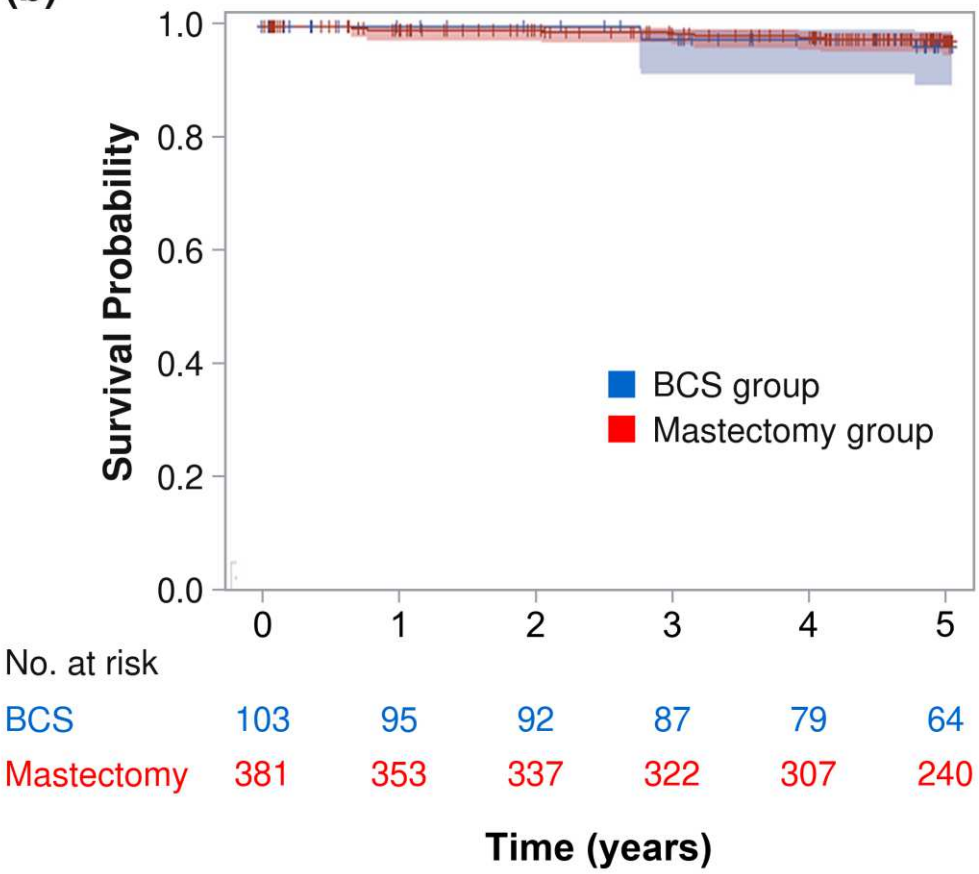

(b)
Survival Probability
1.00
0.98
0.96
0.94
0.92
0.90
log-rank p = 0.78
BCS group
Mastectomy group
0
1
2
3
4
5
Time (years)

Fig. 3


(a)
1.0
0.8
0.6
0.4
0.2
0.0
Survival Probability
BCS group
Mastectomy group
0
1
2
3
4
5
No. at risk
BCS 49 48 48 47 46 32
Mastectomy 3 3 3 3 3 2
Time (years)

(b)



No. at risk

BCS	103	95	92	87	79	64
Mastectomy	381	353	337	322	307	240

Time (years)

(c)

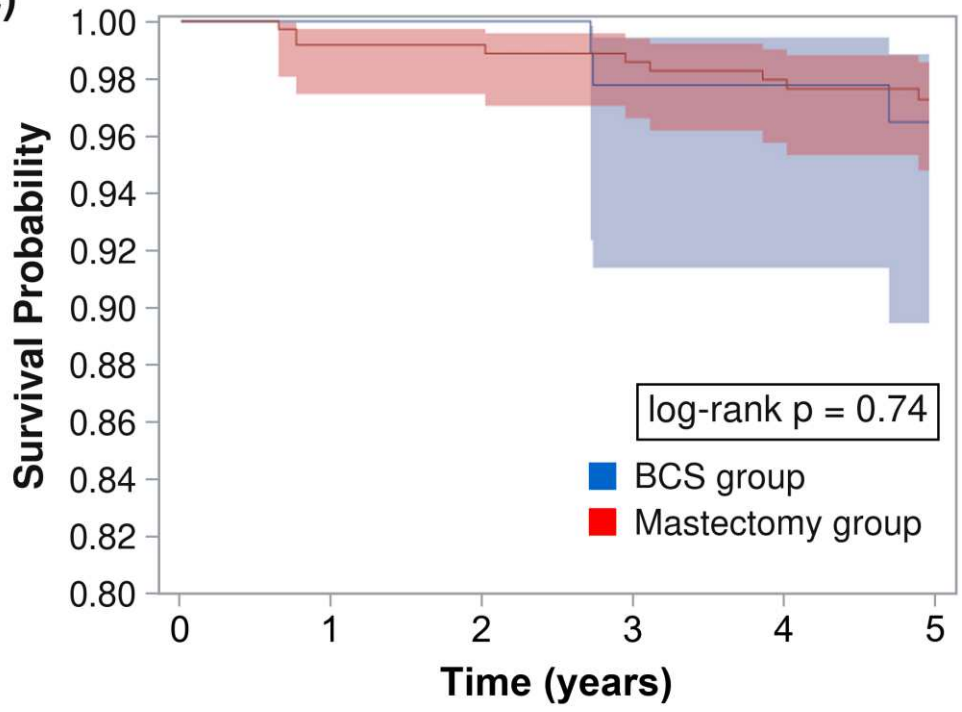


Table 1. Characteristics of MPD-registered patients and MPD-defined patients

	MPD-registered patients (n=1531)		MPD-defined patients (n=552)	
Age, years	67	(59–75)	68	(61–75)
Body mass index, kg/m^2	21.9	(19.8–24.3)	22.1	(19.8–24.3)
Female sex	1516	(99.0)	550	(99.6)
Surgery				
Mastectomy	1087	(71.0)	388	(70.3)
Breast-conserving surgery	403	(26.3)	153	(27.7)
Other	14	(0.9)	0	(0.0)
Unknown	27	(1.8)	11	(2.0)
cTis/T0/T1	1362	(89.0)	552	(100.0)
cN0	1477	(96.5)	552	(100.0)
cM0	1528	(99.8)	552	(100.0)
Pathological invasive component				
≤1 mm	616	(40.2)	552	(100.0)
>1 mm	595	(38.9)	0	(0.0)
Unknown	320	(20.9)	0	(0.0)
Estrogen receptor status				
Positive	274	(17.9)	95	(17.2)
Negative	929	(60.7)	335	(60.7)
Unknown	328	(21.4)	122	(22.1)
Progesterone receptor status				
Positive	156	(10.2)	52	(9.4)
Negative	1054	(68.8)	376	(68.1)
Unknown	321	(21.0)	124	(22.5)
HER2 status				
0	93	(6.1)	28	(5.1)
1+	47	(3.1)	6	(1.1)
2+	88	(5.7)	28	(5.1)
3+	689	(45.0)	257	(46.6)
Unknown	614	(40.1)	233	(42.2)
Nuclear grade				
1	80	(5.2)	18	(3.3)
2	111	(7.3)	40	(7.2)
3	191	(12.5)	70	(12.7)
Unknown	1149	(75.0)	424	(76.8)

Data are presented as the median (interquartile range) or number (%).

Abbreviations: MPD, mammary Paget's disease; HER2, human epidermal growth factor receptor 2; cT, clinical tumor category; cN, clinical nodal category; cM, clinical distant metastasis category.

Table 2. Characteristics of the mastectomy and breast-conserving surgery groups in MPD-defined patients

	Mastectomy (n=388)	BCS (n=153)	p value
Age, years	67 (60–74)	71 (63–78)	0.002
Body mass index, kg/m^2	22.1 (19.8–24.3)	22.2 (20.0–24.3)	0.73
Female sex	386 (99.5)	153 (100)	0.37
Pathological invasive component			0.53
No invasion (0 mm or pTis)	383 (98.7)	152 (99.3)	
Microinvasion (>0 to ≤1 mm)	5 (1.3)	1 (0.7)	
Unknown	0 (0.0)	0 (0.0)	
Estrogen receptor status			0.12
Positive	66 (17.0)	28 (18.3)	
Negative	243 (62.6)	83 (54.2)	
Unknown	79 (20.4)	42 (27.5)	
Progesterone receptor status			0.17
Positive	38 (9.8)	12 (7.8)	
Negative	271 (69.8)	97 (63.4)	
Unknown	79 (20.4)	44 (28.8)	
HER2 status			0.20
0	14 (3.6)	12 (7.8)	
1+	5 (1.3)	1 (0.7)	
2+	17 (4.4)	11 (7.2)	
3+	187 (48.2)	64 (41.8)	
Unknown	165 (42.5)	65 (42.5)	
Nuclear grade			0.18
1	13 (3.4)	5 (3.3)	
2	31 (8.0)	9 (5.9)	
3	57 (14.7)	13 (8.5)	
Unknown	287 (74.0)	126 (82.4)	
Axillary procedures			<0.001
No	50 (12.9)	58 (37.9)	
ALNS	13 (3.4)	2 (1.3)	
SLNB	311 (80.2)	91 (59.5)	
SLNB→ALND	1 (0.3)	0 (0.0)	
ALND	13 (3.4)	2 (1.3)	
Pathological nodal category			0.50
N0	332 (85.6)	96 (62.7)	
N1, N2, N3	7 (1.8)	1 (0.7)	
Unknown	49 (12.6)	56 (36.6)	
Surgical margin status			<0.001
Positive margin	3 (0.8)	2 (1.3)	
Close margin (<5 mm)	8 (2.1)	15 (9.8)	
Negative margin (≥5 mm)	196 (50.5)	60 (39.2)	
Unknown	181 (46.6)	76 (49.7)	
Radiotherapy			<0.001
No	381 (98.2)	103 (67.3)	
Yes	3 (0.8)	49 (32.0)	
Unknown	4 (1.0)	1 (0.7)	

Data are presented as the median (interquartile range) or number (%).

Eligibility was based on clinical nodal status (cN0), whereas Table 2 shows postoperative pathological nodal status.

Abbreviations: BCS, breast-conserving surgery; HER2, human epidermal growth factor receptor 2;

ALNS, axillary lymph node sampling; SLNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection.

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