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SPECIAL ARTICLE

2020 Annual Report of National Clinical Database-Breast Cancer Registry: 10-year mortality of elderly breast cancer patients in Japan

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Abstract

The Japanese Breast Cancer Society initiated the breast cancer registry in 1975, which transitioned to the National Clinical Database-Breast Cancer Registry in 2012. This annual report presents data from 2020 and analyzes the ten-year mortality rates for those aged 65 and older. We analyzed data from 93,784 breast cancer (BC) cases registered in 2020 and assessed 10-year mortality rates for 36,279 elderly patients diagnosed between 2008 and 2012. In 2020, 99.4% of BC cases were females with a median age of 61. Most (65%) were diagnosed at early stages (Stage 0 or I). Breast-conserving surgery rates varied with stages: 58.5% at cStage I, 30.8% at cStage II, and 13.1% at cStage III. Sentinel lymph node biopsy was done in 73.6% of cases, followed by radiotherapy in 70% of those post-conserving surgery and chemotherapy in 21.1% post-surgery. Pathology showed that 63.4% had tumors under 2.0 cm, 11.7% had pTis tumors, and 77.3% had no axillary lymph node metastasis. ER positivity was seen in 75.1%, HER2 in 14.3%, and 30% had a Ki67 positivity rate above 30%. Across all stages and subtypes, there was a trend where the 10-year mortality rates increased for individuals older than 65 years. In Stage I, many deaths were not directly linked to BC and, for those with HER2-type and triple-negative BC, breast cancer-related deaths increased with age. Within Stage II, patients older than 70 years with luminal-type BC often experienced deaths not directly linked to BC, whereas patients below 80 years with HER2-type and triple-negative BC, likely had breast cancer-related deaths. In Stage III, breast cancer-related deaths were more common, particularly in HER2 and triple-negative BC. Our prognostic analysis underscores distinct mortality patterns by stage, subtype, and age in elderly BC patients. It highlights the importance of personalized treatment strategies, considering subtype-specific aggressiveness, age-related factors, and comorbidities.

Keywords Japanese Breast Cancer Society · Breast cancer registry · National clinical database · Annual report · Elderly patient · Mortality · Subtype

Preface

The Japanese Breast Cancer Society (JBCS) initiated a breast cancer registry in 1975. In 2004, this registry transitioned to a web-based system in collaboration with the non-profit organization Japan Clinical Research Support Unit and the Public Health Research Foundation, Tokyo, Japan. In 2012, the National Clinical Database (NCD) took over the management of this registry. Further details of this system have been outlined in a prior publication [1]. Facilities across Japan participating in the NCD register patients diagnosed with new-onset breast cancer (BC). Since the inception of its current platform, the National Clinical Database-Breast Cancer Registry (NCD-BCR), in 2012, the registry has documented 945,398 BC cases through 2019 [2, 3].

Utilizing NCD-BCR data, institutions can obtain certification for surgical specialty training programs, and surgeons can either acquire or renew their professional licenses. The data has also been the basis for numerous retrospective observational studies [4–17]. Together, the JBCS and NCD Office aim to improve quality of medical care by relaying quality indicator data to BC treatment providers.

Japan has the most aged population in the world. In 2020, the Japanese Ministry of Health, Labour and Welfare reported that life expectancy was 24.8 years for 65-year-old women and 16.1 years for 75-year-old women. Therefore,

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it is important to evaluate the prognosis for elderly patients with BC in Japan when determining the most appropriate treatment approach.

This annual NCD-BCR report presents an overview of 93,784 BC cases registered in 2020 from 1364 institutes. Additionally, we provide an analysis of 10-year mortality rates for 36,279 elderly patients, over 65 years of age, who underwent surgery for Stage I-III BC between 2008 and 2012.

Demographics and patients' characteristics

Of 93,784 BC cases, 93,193 (99.4%) were female. The median age at cancer diagnosis was 61 years with an interquartile range from 49 to 72 years. Moreover, 44% (41,149 patients) were aged over 65 (Table 1). The distribution of surgical procedures across various regions in Japan for female patients is as follows: 4.4% in Hokkaido, 6.4% in Tohoku, 35.0% in Kanto, 15.8% in Chubu, 5.7% in Chugoku, 3.1% in Shikoku, and 11.6% in Kyushu/Okinawa. Synchronous bilateral BC was observed in 6262 cases (6.7%), and a family history of BC was noted in 16,052 cases (17.2%). Regarding clinical Stage, 57.5% (53,531) of the female patients were diagnosed with early-stage BC of Stage 0 or I.

Pathology

The pathological assessment of surgical specimens for 89,783 patients with BC regardless of preoperative therapy revealed that 10,480 (11.7%) were finally diagnosed as pTis. The most frequent range of invasive tumor size was from 1.1 to 2.0 cm (26,899 patients, 30.0%). Of the 81,549 patients who received surgery on axillary lymph nodes, 77.3% had no axillary lymph node metastasis (pN0), while 6.1% (4952 patients) had metastasis in more than four axillary nodes. Of the 89,853 patients who received breast surgery, 75.1% were ER (estrogen receptor) positive (more than 10% positive cells), 62.1% were PgR (progesterone receptor) positive, and 14.3% were HER2 (Human Epidermal Growth Factor Receptor 2) positive. Out of the 75,370 cases where Ki67 was measured after the breast surgery, 24.8% (22,316 patients) exhibited a Ki67 positivity rate of more than 30%.

Breast cancer treatment

The types of surgeries categorized by cStage are presented in Table 2. Out of the 92,649 patients who underwent surgery, 39,875 (43.0%) had a partial mastectomy. The rates of breast-conserving surgery were 58.5% for cStage I, 30.8% for cStage II, and 13.1% for cStage III. A total

Table 1 Characteristics of breast cancer patients registered in 2020

	N=93,784	%
Sex		
Female	93,193	99.4
Male	591	0.6
Female	*N* = 93,193	
Geographical distribution		
Hokkaido	4129	4.7
Tohoku	5971	6.4
Kanto	32,613	35
Chubu	14,696	15.8
Kinki	16,820	18
Chugoku	5330	5.7
Shikoku	2845	3.1
Kyushu	10,782	11.6
Others	7	0
Age (years)		
Median	61	
IQR	49–72	
Unilateral	82,863	88.9
Bilateral		
Synchronous	6262	6.7
Metachronous	4068	4.4
Family history		
Absence	71,845	77.1
Presence	16,052	17.2
Unknown	5296	5.7
Menstruation		
Premenopausal	28,200	30.3
Postmenopausal	62,467	67
Unknown	2525	2.7
Clinical T status		
Tis	13,759	14.8
T0	412	0.4
T1	42,968	46.1
T2	27,548	29.6
T3	2778	3
T4	4469	4.8
Unknown	1259	1.4
Clinical N status		
N0	76,117	81.7
N1	11,961	12.8
N2	1968	2.1
N3	1900	2
Unknown	1247	1.3
Clinical M status		
M0	89,853	96.4
M1	1686	1.8
Unknown	1654	1.8
Clinical stage		
0	13,683	14.7
I	39,848	42.8

Table 1 (continued)

	N=93,784	%
IIA	22,037	23.6
IIB	7314	7.8
IIIA	2188	2.3
IIIB	3072	3.3
IIIC	1431	1.5
IV	1686	1.8
Unknown	1934	2.1

TNM classifications were identified using the UICC staging system

of 68,156 patients (73.6%) underwent a sentinel lymph node biopsy (SLNB), and among them, 7164 (7.7%) subsequently had axillary node dissection. Among 48,040 patients without distant metastasis who received mastectomy, a total of 5563 (11.6%) patients underwent breast reconstruction procedures (Table 3).

The number of patients without distant metastasis who underwent postoperative radiotherapy is outlined in Table 4. Among the 39,216 patients who had breast-conserving surgery, 27,457 (70.0%) received whole breast irradiation, while 2080 (5.3%) were treated with radiotherapy to both the whole breast and regional lymph nodes. Of the 48,411 patients who had a mastectomy, 4808 (9.9%) received radiotherapy to the chest wall and regional lymph nodes, and 588 (1.2%) received radiotherapy only to the chest wall.

The types of systemic therapies administered either before or after surgery to patients without distant metastasis are detailed in Table 5. Of the 89,853 patients who underwent surgery, 10,773 (12.0%) were given neoadjuvant chemotherapy. Post-surgery, 18,971 patients (21.1%) received chemotherapy, and 56,365 (62.7%) were treated with endocrine therapy.

Table 3 Procedure of reconstructive surgery among patients without distant metastasis

Type of reconstructive surgery	*N* of patients	%
None	42,474	88.4
Tissue Expander	3372	7.0
Implant	350	0.7
Autologous	1534	3.2
Others	307	0.6
Unknown	3	0.0
Total number of mastectomy[a]	48,040	

[a] Mastectomy includes nipple sparing, skin sparing mastectomy

Table 4 Radiotherapy after breast surgery for patients without distant metastasis

	N of patients
Breast conserving surgery[a]	39,143
Mastectomy[b]	48,335
Whole breast only	27,457
Chest wall only	588
Regional lymph nodes only	207
Whole breast + regional lymph nodes	2080
Chest wall + regional lymph nodes	4808
Other	788
Total number of patients who received radiotherapy	35,928

[a]Breast conserving surgery includes breast segmentectomy

[b]Mastectomy includes nipple sparing, skin sparing mastectomy and modified radical mastectomy

Ten-year mortality of elderly patients after surgery for breast cancer

In addition to presenting the characteristics of breast cancer

Table 2 Surgical procedure according to cStage

Type of Surgery	Number of patients (%)						
	Stage 0	Stage I	Stage II	Stage III	Stage IV	Unknown	Total
No surgery	22 (0.2)	95 (0.2)	81 (0.3)	27 (0.4)	5 (0.4)	14 (0.7)	244 (0.3)
Breast segmentectomy	76 (0.6)	22 (0.1)	4 (0)	0 (0)	0 (0)	46 (2.4)	148 (0.2)
Partial mastectomy	5888 (43.1)	23,243 (58.4)	9039 (30.8)	871 (13.1)	171 (14.1)	663 (34.3)	39,875 (43)
Mastectomy	6296 (46.1)	14,276 (35.8)	18,285 (62.3)	5242 (78.6)	874 (71.9)	637 (33)	45,610 (49.2)
Nipple sparing mastectomy	571 (4.2)	840 (2.1)	601 (2)	59 (0.9)	17 (1.4)	70 (3.6)	2158 (2.3)
Skin sparing mastectomy	581 (4.2)	661 (1.7)	555 (1.9)	73 (1.1)	12 (1)	39 (2)	1921 (2.1)
Modified radical mastectomy or above	5 (0)	19 (0)	90 (0.3)	181 (2.7)	38 (3.1)	11 (0.6)	344 (0.4)
Others	17 (0.1)	36 (0.1)	26 (0.1)	7 (0.1)	5 (0.4)	25 (1.3)	116 (0.1)
Unknown	2 (0)	3 (0)	4 (0)	0 (0)	0 (0)	5 (0.3)	14 (0)
Missing	214 (1.6)	632 (1.6)	644 (2.2)	213 (3.2)	94 (7.7)	422 (21.8)	2219 (2.4)
Total number of patients	13,672	39,827	29,329	6673	1216	1932	92,649

Table 5 Types of systemic treatment in the pre- or post-operative therapies for patients without metastasis

$N = 89,853$	Preoperative therapy		Postoperative therapy	
	n	%	*n*	%
Endocrine therapy				
AIs	2374	2.6	33,964	37.8
SERMs	897	1.0	17,572	19.6
AIs or SERMs + LHRHa	181	0.2	3896	4.3
Others	298	0.3	933	1.0
Chemotherapy				
Anthracyclines	9169	10.2	9352	10.4
Taxanes	9588	10.7	9896	11.0
TC	259	0.3	4321	4.8
Capecitabine	29	0.0	1307	1.5
S-1	44	0.0	446	0.5
Carboplatin	97	0.1	95	0.1
Others	464	0.5	1273	1.4
Molecular targeted therapy				
Trastuzumab	4051	4.5	8592	9.6
Pertuzumab	3373	3.8	4648	5.2
T-DM1	12	0.0	420	0.5
Bevacizumab	183	0.2	65	0.1
Others	2	0.0	5	0.0

AI Aromatase inhibitors, *SERM* selective estrogen receptor modulator, *LHRHa* luteinizing hormone releasing hormone agonists, *T-DM1* trastuzumab emtansine

patients registered in 2020, we conducted an analysis of the ten-year mortality rates for elderly BC patients diagnosed between 2008 and 2012. This analysis focused on patients with available clinical data, including age, ER, PgR, and HER2 status (Supplement figure). We utilized cStage information for patients who underwent neoadjuvant therapy and pStage information for those who did not. The BC subtypes were categorized as follows: luminal-type (ER or PgR positive with over 10% cell positivity), HER2-type (HER2 positive with any ER/PgR status), and triple-negative (ER and PgR negative with HER2 negative status). Patients with synchronous or metachronous bilateral BC were excluded from the analysis.

In Fig. 1 and supplementary tables, we present the ten-year mortality rates of elderly BC patients stratified by Stage, subtype, and age. In all stages and subtypes, 10-year mortality rates increased with age. For Stage I BC, it is noteworthy that the incidence of deaths due to non-breast cancer-related causes surpassed that of breast cancer-related deaths among individuals aged 65 and older, regardless of subtype. In HER2-type and triple-negative BC, there was a progressive increase in the likelihood of death due to BC as age advanced. In Stage II BC, patients aged 70 years or older with luminal-type BC were likely to die from causes other than BC. In contrast, patients under 80 years old with HER2-type and triple-negative BC tended to have a higher rate of death from BC compared to other causes. In Stage III, the risk of breast cancer-related mortality was notably elevated, surpassing the risk of death from other causes especially for HER2 and triple-negative BC in most age groups.

Our study reveals distinct mortality patterns by stage and subtype in elderly breast cancer patients and underscores the need for personalized treatment strategies that consider subtype-specific aggressiveness and age-related health factors. As elderly populations continue to grow, healthcare systems must adapt to meet the evolving needs of elderly breast cancer patients, aiming for optimal outcomes and quality of life.

Postscript

The detailed data regarding the treatment for BC, available within the Japanese Breast Cancer Registry, is a result of voluntary contributions by healthcare professionals, including physicians, across Japan. We sincerely acknowledge and appreciate their dedication in inputting this information. It is through their collective efforts that we can conduct data analysis, publish research papers, and ultimately make a more significant impact on the lives of BC patients.

We anticipate that the annual report derived from this registry will provide valuable support to physicians and scientists in comprehending the evolving trends in BC characteristics and treatment modalities in Japan.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s12282-023-01532-8.

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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 offer the original clinical data.

Declarations

Conflict of interest YS have received honorariums from Pfizer, Astra Zeneca, Daiichi Sankyo, Eisai, Eli Lily, Chugai Chugai Pharmaceu-

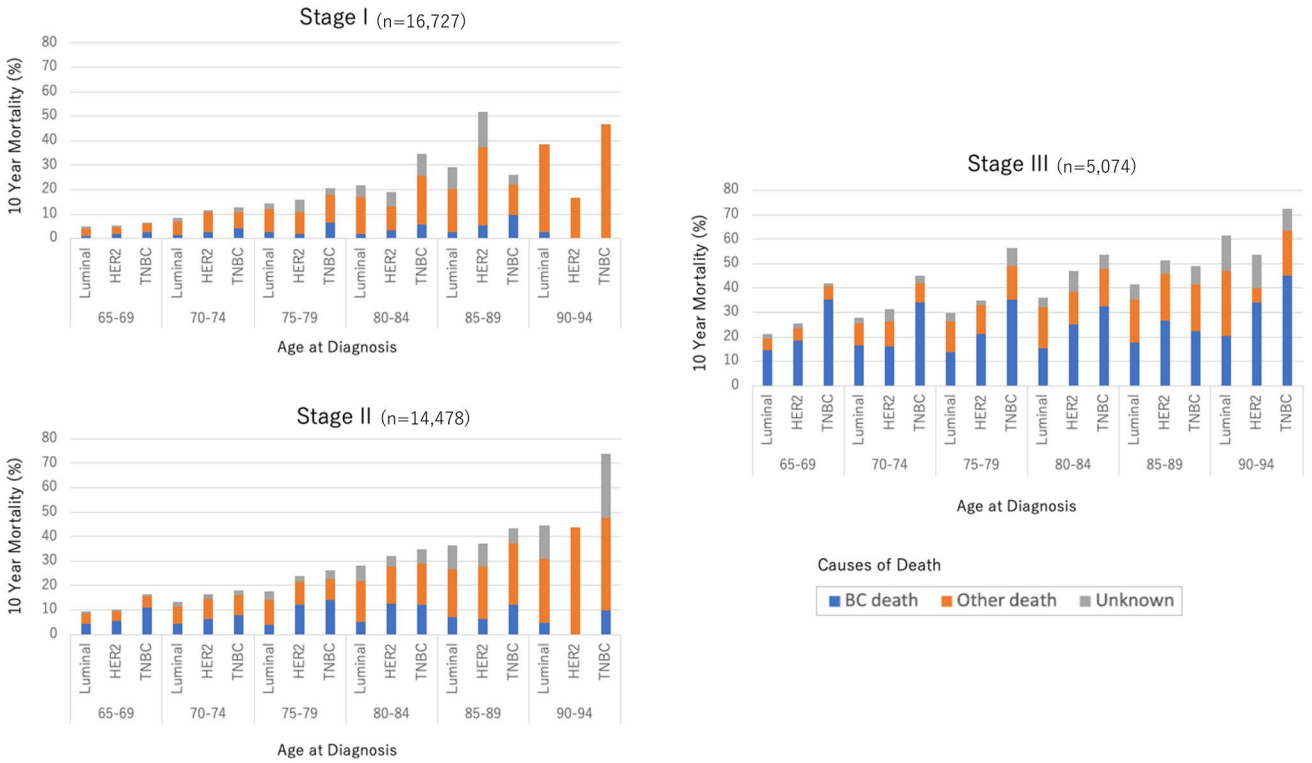

Fig. 1 Ten-year mortality among elderly patients who received a surgery for breast cancer (BC) diagnosed between 2008 and 2012

tical Ltd, MSD, and Nihon Kayaku. HK have received honorariums from Chugai Pharmaceutical Ltd and consultation fee from EPS corporation. HK and NK are affiliated to HQA, a social collaborative department supported by National CLinlical Database, Johnson & Johnson KK, Nipro corporation and Intuitive Surgical Sarl. NN have received honorariums from Chugai, Eli Lilly, MSD, Daiichi Sankyo, AstraZeneca, and Pfizer. MM have received honorariums from Chugai, AstraZeneca, Eli Lilly, Pfizer, MSD, Taiho, Daiichi Sankyo and Eisai. TK have received grants from Pfizer Co. Ltd, Kanzawa Medical Research Foundation and Japan Kampo Medicines Manufacturers Association. TI have received grants from Pfizer. MN have received honorariums from AstraZeneca, Eli Lilly, Pfizer, Novartis, Chugai, Taiho, Daiichi Sankyo, Eisai, Kyowa-Kirin, MSD, Myriad genetics, and Denka. NH have received grants from MSD, Chugai, and Konica Minolta Japan and honorariums from Eli Lilly, Astrazeneca, taiho, Eizai, ExactScience, Daiichi-Sankyo, Novartis, Pfizer, and Chugai. MY have received consulting fees from Eli Lilly and Chugai and honorariums from Agilent technologies, Chugai, Ono Yakuhin, MSD and Daiichi Sankyo. CW have received a honorarium from Chugai. MT have received research grants from Chugai, Takeda, Pfizer, Taiho, JBCRG assoc., KBCRN assoc., Eisai, Eli-Lilly and companies, Daiichi-Sankyo, AstraZeneca, Astellas, Shimadzu, Yakult, Nippon Kayaku, AFI technology, Luxonus, Shionogi, GL Science, and Sanwa Shurui. MT have received honorariums from Chugai, Takeda, Pfizer, Kyowa-Kirin, Taiho, Eisai, Daiichi-Sankyo, AstraZeneca, Eli Lilly and companies, MSD, Exact Science, Novartis, Shimadzu, Yakult, Nippon Kayaku, Devicore Medical Japan, and Sysmex. SS have received grants from Taiho, Eisai, Chugai, Takeda, and Daiichi Sankyo and honorariums from Chugai/Roche Astra Zeneca, Eli Lilly, Pfizer, Kyowa Kirin, Daiichi Sankyo and MSD.

Ethical approval This article does not contain any studies with animals performed by any of the authors. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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