Annual report of the Japanese Breast Cancer Society registry for 2016

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Abstract
The Japanese Breast Cancer Society (JBCS) registry began data collection in 1975, and it was integrated into National Clinical Database in 2012. As of 2016, the JBCS registry contains records of 656,896 breast cancer patients from more than 1400 hospitals throughout Japan. In the 2016 registration, the number of institutes involved was 1422, and the total number of patients was 95,870. We herein present the summary of the annual data of the JBCS registry collected in 2016. We analyzed the demographic and clinicopathologic characteristics of registered breast cancer patients from various angles. Especially, we examined the registrations on family history, menstruation, onset age, body mass index according to age, nodal status based on tumor size and subtype, and proportion based on ER, PgR, and HER2 status. This report based on the JBCS registry would support clinical management for breast cancer patients and clinical study in the near future.

Keywords Japanese Breast Cancer Society · Breast Cancer Registry · National Clinical Database · Menstruation · Nodal status
Preface

The Japanese Breast Cancer Society (JBCS) registry began data collection in 1975, and started a new web-based system with the cooperation of the non-profit organization, Japan Clinical Research Support Unit and the Public Health Research Foundation (Tokyo, Japan) in 2004. The registry, starting in 2012, runs on the National Clinical Database (NCD) which is a multidisciplinary registry platform for interventional and cancer registries. The details were described previously [1]. The eligibility for registration is that patients were diagnosed to have a new onset breast cancer at NCD participating facilities throughout Japan. The registration criteria do not require the patient to have undergone a breast surgery. As NCD does not support the linkage of a patient across hospitals, double registration may occur especially for the cases without breast surgery. However, as 97.4% of patients registered in 2016 had breast surgery, there are few cases with double registration. As of 2016, it contains records of 656,896 breast cancer patients from more than 1400 hospitals throughout Japan. Affiliated institutions provide data covering more than 50 demographic and clinicopathologic characteristics of newly diagnosed primary breast cancer patients via a web-based registration system. Follow-up information on 5-, 10-, and 15-year prognosis after the first treatment (preoperative systemic therapy or surgery) is requested. The JBCS registry is directed and governed by the Registration Committee of JBCS. TNM classification is now registered according to the 7th edition of the Union for International Cancer Control staging system [2], and histological classification is registered according to the General Rules for Clinical and Pathological Recording of Breast Cancer [3], which was further transferred to the Classification of Tumors of the Breast and Female Genital Organs [4].

Herein, we present the summary of the annual data of JBCS registry collected in 2016 (Tables 1, 2, 3; Figs. 1, 2, 3, 4, 5, 6, 7). The number of institutes involved in the 2016 registration was 1422, and the total number of patients was 95,870, including 5803 patients with simultaneous bilateral breast cancers. The incidence per year of breast cancer, including ductal carcinoma in situ, was reported to be 107,627 in 2016 by the National Cancer Center and the Ministry of Health, Labor and Welfare [5, 6]. Thus, approximately 84% of newly diagnosed breast cancer patients were included in the JBCS registry in 2016. While the number of patients has increased, the number of institutes has not increased since NCD was started in 2012 (Fig. 1). As a result, the number of registered patients per institute has gradually increased.

| Table 1 | Patients’ characteristics |
|---------|--------------------------|
| All     | N=95,870 %               |
| Gender  |                          |
| Female  | 95,257 99.4              |
| Male    | 613 0.6                  |
| Female  | N=95,257 %               |
| Unilateral | 85,973 90.3         |
| Bilateral |                         |
| Synchronous | 5803 6.1                  |
| Metachronous | 3479 3.7               |
| Family history |                   |
| Absent | 75,073 78.8              |
| Present | 13,197 13.9              |
| Unknown | 6985 7.3                 |
| Menstruation |                     |
| Premenopausal | 31,255 32.8              |
| Postmenopausal | 61,252 64.3           |
| Unknown | 2748 2.9                 |
| Surgery  |                          |
| Present | 91,541 96.1              |
| Absent  | 662 0.7                  |
| Biopsy alone | 3054 3.2                |
| Tumor size |                         |
| Tis     | 13,069 13.7              |
| T0      | 444 0.5                  |
| T1      | 44,405 47.1              |
| T2      | 27,636 29.0              |
| T3      | 2933 3.1                 |
| T4      | 4609 4.8                 |
| Unknown | 1661 1.7                 |
| Nodal status |                     |
| N0      | 77,035 80.9              |
| N1      | 12,700 13.3              |
| N2      | 2009 2.1                 |
| N3      | 1735 1.8                 |
| Unknown | 1778 1.9                 |
| Metastasis |                     |
| M0      | 91,362 95.9              |
| M1      | 1957 2.1                 |
| Unknown | 1938 2.0                 |
| Stage   |                          |
| 0       | 12,986 13.6              |
| I       | 41,490 43.6              |
| IIA     | 22,134 23.2              |
| IIB     | 7655 8.0                 |
| IIIA    | 2200 2.3                 |
| IIIB    | 3098 3.3                 |
| IIIC    | 1229 1.3                 |
| IV      | 1957 2.1                 |
| Unknown | 2508 2.6                 |

TNM classifications were identified using the UICC staging system
The TNM classifications in this Table are from clinical data.
Summary of findings

Among the 95,870 patients, 95,257 were women (99.4%) and the mean ± standard deviation of onset age was 59.7 ± 13.9 years. We show data of patient characteristics on female breast cancer, such as unilateral or bilateral disease, family history, menstruation, operation, tumor size, nodal status, metastasis, and stage in Table 1. There were 13,197 (13.9%) patients with a family history of breast cancer. Family history in NCD means that at least one first- or second-degree relative have a history of breast cancer. Patients with family history of breast cancer based on patient interviews have increased since 2013, perhaps reflecting our growing interest in the family history of hereditary tumors around that time (Fig. 2). This is also supported by the decreasing proportion of those with “unknown” family history status. According to the meta-analysis in United Kingdom, it was reported that at least one first-degree relative had a history of breast cancer in 12.9% of breast cancer patients [7], which is similar to the proportion in this report, but the true reason of the increased proportion of patients with a family history of breast cancer is unclear in this study.

Moreover, we found that 33% of breast cancer patients were premenopausal (Table 1), which is closely related to the distribution of onset age. To view this from another angle, we analyzed data on menstruation by age. As a result, approximately half of Japanese breast cancer patients at age 52 were premenopausal (Fig. 3). The data may aid the clinicians to decide whether to begin aromatase inhibitors for menopausal patients who are not menstruating after chemotherapy or tamoxifen. The distribution of breast cancer patients by age of onset is shown in Fig. 4. The bimodal distribution of onset in late 40 s and late 60 s is unique in Japanese patients and there has been a similar trend for years. We also analyzed the data

Table 2  Comparison of clinical and pathological classifications

|               | n   | %   | pTis | n   | %   | pT1 | n   | %   | pT2 | n   | %   | pT3 | n   | %   | Unknown | n   | %   |
|---------------|-----|-----|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|---------|-----|-----|
| (a) Tumor size|     |     |      |     |     |    |     |     |      |     |     |     |     |     |         |     |     |
| cTis          | 12,618 | 16.4 | 4963 | 39.3 | 3805 | 30.2 | 1356 | 10.7 | 511  | 4.0  | 1983 | 15.7 |
| cT0           | 383  | 0.5 | 66   | 17.2 | 148  | 38.6 | 39   | 10.2 | 4    | 1.0  | 126  | 32.9 |
| cT1           | 40,446 | 52.6 | 1276 | 3.2  | 32,178 | 79.6 | 4181 | 10.3 | 453  | 1.1  | 2358 | 5.8  |
| cT2           | 20,007 | 26.0 | 267  | 1.3  | 5050 | 25.2 | 12,583 | 62.9 | 898  | 4.5  | 1209 | 6.0  |
| cT3           | 1494  | 1.9 | 18   | 1.2  | 111  | 7.4  | 474  | 31.7 | 770  | 51.5 | 121  | 8.1  |
| cT4           | 1563  | 2.0 | 7    | 0.4  | 179  | 11.5 | 799  | 51.1 | 421  | 26.9 | 157  | 10.0 |
| Unknown       | 354  | 0.5 | 19   | 5.4  | 91   | 25.7 | 44   | 12.4 | 33   | 9.3  | 167  | 47.2 |
| Total         | 76,865 | 100.0 | 6616 | 8.6  | 41,562 | 54.1 | 19,476 | 25.3 | 3090 | 4.0  | 6121 | 8.0  |

| Node          | Clinical | Pathological |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|---------------|----------|--------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|               | n   | %   | N+ | n   | %   |     |     |     |     |     |     |     |     |     |     |     |
| (b) Nodal status|     |     |    |     |     |     |     |     |     |     |     |     |     |     |     |     |
| Negative      | 68,872 | 89.6 | 52,126 | 75.7 |
|               | 1–3 | 7235 | 10.5 |
|               | 4–9 | 842  | 1.2  |
|               | 10≤ | 273  | 0.4  |
|               | Unknown | 8396 | 12.2 |
| Positive      | 7730  | 10.1 | 822  | 10.6 |
|               | 1–3 | 3849 | 49.8 |
|               | 4–9 | 1467 | 19.0 |
|               | 10≤  | 915  | 11.8 |
|               | Unknown | 677  | 8.8  |
| Unknown       | 263  | 0.3 | 263  |            |
| Total         | 76,865 | 100.0 | Total | 76,865 |        |

The TNM classification was identified by the UICC staging system

N+ number of involved nodes
on body mass index by age. As shown in Fig. 5, the body mass index of Japanese patients steadily increases after their late 40 s. Proper control of their own body weight is recommended, because obesity is known as one of risk factors for postmenopausal breast cancer.

Our data show the comparison of clinical and pathological classifications on tumor size and nodal status in 76,865 patients without preoperative systemic therapy and M1 disease (Table 2). Pathological T1 classification was similar in the number relative to that in clinical T1
classifications, while only 39.3% of the clinical Tis cases were diagnosed as Tis pathologically (Table 2a), suggesting clinical Tis may be overestimated. Thus, our data revealed that there were not a few differences between clinical and pathological Tis evaluations. Furthermore, of 68,872 clinical node-negative cases, 52,126 (75.5%) was node negative but 12.1% was node-positive pathologically, while of 7730 clinical node-positive cases, 6231 (80.6%) was node positive but 10.6% was node-negative pathologically (Table 2b). From this result, it is necessary to pay close attention to the selection of the surgical procedure.

The frequencies of lymph node metastasis by pathological tumor size and subtype in patients without neoadjuvant chemotherapy (NAC) are shown in Fig. 6. HER2-positive and triple negative breast cancer had high rates of lymph node metastasis compared to ER+/HER2– disease. For example, approximately 15% of pT1c disease had lymph node metastasis, while more than 30% of T2 cases had positive lymph nodes. Treatment should be selected based on such essential information as it when considering NAC or surgery.
Finally, our data show the frequency of subtypes classified based on ER, PgR, and HER2 expression from immunohistochemical staining, which is fundamental data of the population of Japanese breast cancer patients (Fig. 7). There were differences in these biological characteristics between M0 and M1 disease. In M1 cases, there was increased ER negativity, PgR negativity, HER2 positivity, and nuclear grade 3 (Table 3). These factors should be considered first when evaluating biological features of individual breast cancer.

**Postscript**

The data input to JBCS registry has varied over time. This registry also needs to be gradually taking in the opinions of clinicians and balancing it with what has not changed. At the same time when we register new cases, we need to analyze, discuss, publish, and progressively develop JBCS registry. We believe that this annual data report provides significant information to guide daily medical care for breast cancer patients.
**Fig. 5** Body mass index (BMI) according to age

**Fig. 6** Nodal status based on tumor size and subtype

**Fig. 7** Proportion based on ER, PgR, and HER2 status

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**Author contributions** Study concept and design: MK and HJ. Assembly of data: UI and HK. Manuscript writing: MK and HK. Critical revision of the manuscript for important intellectual content: The Registration Committee of the JBCS (HK, HM, MN, TK, YK, KA, NH, SA, NN, EO, KI, KT, MY, YY, SI, and HJ), and UI. Final approval of manuscript: SI and HJ.

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Compliance with ethical standards

Conflicts of interest HK, UI, and HM are affiliated with the department of Healthcare Quality Assessment at the University of Tokyo. The department is a social collaboration department supported by National Clinical Database, Johnson & Johnson K.K., and Nipro corporation. NH and YY have both received honorariums as a speaker or consultant/advisory role from Chugai Pharmaceutical Co. (Tokyo, Japan). The other authors declare that they have no conflict of interest.

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.

Informed consent Informed consent was obtained from all individual participants included in the study.

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References

1. Kurebayashi J, Miyoshi Y, Ishikawa T, Saji S, Sugie T, Suzuki T, et al. Clinicopathological characteristics of breast cancer and trends in the management of breast cancer patients in Japan: based on the Breast Cancer Registry of the Japanese Breast Cancer Society between 2004 and 2011. Breast Cancer. 2015;22:235–44.
2. Sobin LH, Gospodarowicz MK, Wittekind C. TNM classification of malignant tumours. 7th ed. New York: Wiley; 2010. p. 131–141.
3. The Japanese Breast Cancer Society. General rules for clinical and pathological recording of breast cancer. 17th ed. Tokyo: Kanehara Shuppan; 2012.
4. Lakhani SR, Ellis IO, Schnitt SJ, Tan PH, van de Vijver MJ. WHO classification of tumours of the breast. 4th ed. Lyon: IARC Press; 2012.
5. The Center for Cancer Control and Information Services of National Cancer Center. 2019. https://ganjoho.jp/reg_stat/index.html. Accessed 23 Sept 2019.
6. Ministry of Health, Labor and Welfare. 2019. https://www.mhlw.go.jp/content/10900000/000053552.pdf. Accessed 1 Nov 2019.
7. Collaborative Group on Hormonal Factors in Breast Cancer. Familial breast cancer: collaborative reanalysis of individual data from 52 epidemiological studies including 58,209 women with breast cancer and 101,986 women without the disease. Lancet. 2001;27:1389–99.

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