Breast cancer in women: a descriptive analysis of the national cancer database

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Summary. Background and aim of the work: Breast cancer is the most common cancer in women in the United States. National Cancer Database (NCDB) is one of the largest tumor databases of the United States. This study aimed to evaluate the features of breast cancer in women from a large updated database. Methods: We describe and analyze the frequencies and percentages of the clinical and pathological features of women diagnosed with breast cancer registered in NCDB, in a period from 2004 to 2015. Results: A total of 2,423,875 women were diagnosed with breast cancer between 2004 and 2015. The nationally representative analysis demonstrated that the incidence of breast cancer among women increased over the years. Upper-outer quadrant was the most frequent primary tumor site, and the intraductal carcinoma was the most frequent histology. The prevalence of breast cancer increased with age. The most frequent grade at diagnosis was grade II. Broadly, invasive characteristics were noted more frequently in younger patients. Left and right breast were affected with almost the same frequency, with a slight predominance of the left breast. The most frequent surgical treatment was a partial mastectomy. Reconstruction with implant was the most frequent choice. Post-mastectomy radiation therapy was administered in the majority of patients. Conclusions: To the authors’ knowledge, the current study is the largest descriptive analysis to date on the clinical and pathological features of breast cancer in a population-based database. The increase in incidence over the years indicates an important need for etiologic research and innovative approaches to improve breast cancer prevention. (www.actabiomedica.it)

Key words: breast, cancer, breast neoplasms, epidemiology, NCDB, women

Introduction

Breast cancer in the United States is the most common cancer in women after skin cancer, regardless of race or ethnicity (1). The incidence rate for female breast cancer in the United States from 2010 to 2014 was 123.6 per 10000 population, and an estimated of 40920 American females will die from breast cancer in 2018 (2).

Data concerning this type of cancer is submitted to the nationally recognized National Cancer Database (NCDB) every year (3). The NCDB - jointly sponsored by the American College of Surgeons and the American Cancer Society, is a clinical oncology database sourced from hospital registry data that are collected in more than 1500 Commission on Cancer (CoC)-accredited facilities. NCDB data are used to analyze and track patients with malignant neoplastic diseases, their treatments, and outcomes. As a result, the data represent more than 70 percent of newly diagnosed cancer cases nationwide and more than 34 million historical records (3). The purpose of this work
is to update the demographic and clinical data about breast cancer in women, meaningful to the surgeons and the scientific community.

**Methods**

We aimed to analyze data from the NCDB to assess the demographic and clinical characteristics of female breast cancer patients between 2004 and 2015 (3). Demographics and cancer-specific characteristics were calculated using IBM SPSS Statistics for Windows, Version 22.0 software (IBM Corp., Armonk, NY) and reported as frequencies and percentages. We included all female patients with breast cancer reported in the database.

Age of female patients was divided into three groups, as follows: ≤40 years, 40 to 60 years and >60 years. The race was classified into White, Black, Asian, Native American and other races. The mean of the number of days between the date of diagnosis and the most definitive surgical procedure on the primary site was calculated. Tumor size was divided into the following groups: <2 cm, 2-4.9 cm, and ≥5 cm. The tumor location was classified according to the International Classification of Diseases for Oncology, Third Edition which includes: breast upper-outer quadrant (UOQ), breast upper-inner quadrant (UIQ), breast lower-outer quadrant (LOQ), breast lower-inner quadrant (LIQ), breast central portion, breast axillary tail, breast overlapping lesion, and nipple (4). Laterality identified the side of the breast on which the reportable primary tumor originated.

Histology results were named according to the third edition of International Classification of Diseases for Oncology codes (ICD-O-3), reported by registries for cases diagnosed in 2001 and subsequently (4). We regrouped the histology types into the most meaningful types that have a higher percentage of occurrence in the database, as follows: 8343 code into ‘papillary’ type; 8070, 8071, 8072, 8074, 8075, 8076, 8052 codes into ‘squamous’ type; 8453, 8500, 8503, 8507, 8514, 8521 codes into ‘intraductal’ type; 8140, 8147, 8190 codes into ‘adenocarcinoma’ type; 8520 code into ‘lobular’ type; 8522, 8523, 8524, 8560, 8940 codes into ‘mixed’ type; 8530 code into ‘inflammatory’ type; 8540, 8541 and 8543 into ‘Breast Paget’ type; 9020 code into ‘phylloides’ type; other codes were grouped as ‘others’.

The behavior of the breast cancer was reported as benign, borderline, in situ/carcinoma in situ and invasive. The grade was reported as follows: grade I, II, III and IV, where well differentiated (grade I) was the most like normal tissue, and undifferentiated (grade IV) was the least like normal tissue, as stated in diagnosis.

The stage was assigned depending on the pathologic stage group, when it was not reported it was assigned depending on the clinical stage group. The stage was divided into 0, I, II, III and IV, according to American Joint Committee on Cancer (AJCC) 7th edition traditional stage classification. We did not consider patients with not applicable or unknown stage.

The records of the surgical procedure performed in the primary site were divided into no surgery, partial mastectomy, complete mastectomy, and unknown; other kinds of procedures were excluded. The complete mastectomy group included total mastectomy, subcutaneous mastectomy, modified radical mastectomy, radical mastectomy, extended radical mastectomy, bilateral mastectomy for a single tumor involving both breasts and mastectomy NOS (not otherwise specified). Types of reconstruction after complete mastectomy were divided into reconstruction with autologous tissue, with implant and combined (with tissue and implant). We included only the patients that had a reported a type of reconstruction.

Radiation therapy was reported as follows: none (radiation not administered); beam radiation (x-ray, cobalt, linear accelerator, neutron beam, betatron, spray radiation, intraoperative radiation and stereotactic radiosurgery as gamma knife and Proton beam); radioactive implants (brachytherapy, interstitial implants, molds, seeds, needles, or intracavitary applicators of radioactive materials as cesium, radium, radon, and radioactive gold); radioisotopes internal use of radioactive isotopes (iodine131, phosphorus32, strontium 89 and 90) administered orally, intracavitary, or by intravenous injection; combination of beam radiation with radioactive implants or radioisotopes.
Results

A total of 2423875 women were diagnosed with breast cancer between 2004 and 2015 (Table 1). The incidence of this disease among women increased over the years (Figure 1). Mean age was 60.91±13.36 (18-90 years old). 136525 female patients (5.6%) were ≤40 years old, 1065754 (44%) patients were between 40 and 60 years old, and 1221596 (50.4%) patients were >60 years old (Figure 2). The predominant race was white (2022918 patients, 84.3%), followed by black (271401 patients, 11.3%), Asian (6138 patients, 0.2%), Native American (78535 patients, 3.2%) and other (18256 patients, 0.7%). The average number of days between the date of diagnosis and the date on which the most definitive surgical procedure was performed on the primary site was 51. Concerning the size of the tumor, 31574 (1.30%) patients had a <2 cm tumor, 148008 (6.11%) patients had a tumor between 2-4.9 cm, and 2244293 (92.59%) patients had a tumor >=5cm (Table 2).

Within this cohort, the location of the breast cancer (Figure 3) was UOQ for 807728 patients (39.50%), UIQ for 255431 patients (12.49%), LOQ for 170278 patients (8.33%), LIQ for 136025 patients (6.65%), the central portion of the breast for 124531 patients (6.09%), the nipple for 14392 patients (0.7%), axillary tail of breast for 9972 patients (0.49%) and overlapping lesion of breast for 526593 patients (25.75%).

Table 1. Demographic data

| Characteristic                              | n     | %   |
|--------------------------------------------|-------|-----|
| Total females with breast cancer           | 2423875 | 100 |
| Age                                        |       |     |
| <=40 years old                             | 136525 | 5.60% |
| 40-60 years old                            | 1065754 | 44.00% |
| >60 years old                              | 1221596 | 50.40% |
| Race*                                      |       |     |
| White                                      | 2022918 | 84.39% |
| Black                                      | 271401 | 11.32% |
| Asian                                      | 6138 | 0.26% |
| Native American                            | 78535 | 3.28% |
| Other                                      | 18256 | 0.76% |
| Period of diagnosis                        |       |     |
| 2004-2006                                  | 513042 | 21.17% |
| 2007-2009                                  | 588678 | 24.29% |
| 2010-2012                                  | 631994 | 26.07% |
| 2013-2015                                  | 690161 | 28.47% |

*patients with unknown race were excluded
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primary tumor site was left breast in 50.6% of patients and the right breast in 49% of patients.

Histology results were reported (Table 2 and 3, Figure 4) as follows: 1629174 (67.21%) patients had intraductal carcinoma, 235379 (9.71%) patients had lobular carcinoma, 15073 (0.62%) patients had adeno-carcinoma, 8831 (0.36%) patients had papillary carcinoma, 8277 (0.34%) patients had inflammatory carcinoma, 7087 (0.29%) patients had mammary Paget, 3227 (0.13%) patients had phylloides, 937 (0.04%) patients had squamous carcinoma, 293746 (12.12%) patients had a mixed histology between these types, and 222144 (9.16%) patients had another types of tumor on histology.

The behavior of the breast cancers was invasive for 1932688 patients (79.7%) followed by in situ carcinoma in situ for 491187 (20.3%) patients; there was not any benign or borderline tumor included in the database. The grade as stated in the final pathologic diagnosis (Table 2, Figure 5) was I for 461096 patients (19%), II for 920687 patients (38%), III for 719178 patients (29.7%), IV for 20216 patients (0.8%), not determined for 302698 patients (12.5%). With respect to stage, 486856 (20.88%) patients corresponded to Stage 0, 961981 (41.27%) patients to Stage I, 587352 (25.20%) patients to Stage II, 203159 (8.71%) patients to Stage III, 91864 (3.94%) patients to Stage IV.

Overall, 1320210 (54.57%) patients underwent partial mastectomy, whereas 922391 (38.13%) patients underwent complete mastectomy (Table 4, Figure 6).

Table 2. Breast cancer characteristics

| Characteristics of tumor | n     | %   |
|--------------------------|-------|-----|
| **Tumor size**           |       |     |
| <2 cm                    | 31574 | 1.30% |
| 2-4.9 cm                 | 148008| 6.11% |
| >=5 cm                   | 2244293| 92.59%|
| **Primary tumor site**   |       |     |
| Left breast              | 1225286| 50.60% |
| Right breast             | 1188795| 49.00% |
| **Location**             |       |     |
| Nipple                   | 14392 | 0.70% |
| Central portion of the breast | 124531 | 6.09% |
| Upper-inner quadrant     | 255431| 12.49% |
| Lower-inner quadrant     | 136025| 6.65% |
| Upper outer quadrant     | 807728| 39.50% |
| Lower outer quadrant     | 170278| 8.33% |
| Axillary tail of breast  | 9972  | 0.49% |
| Overlapping lesion of breast | 526593| 25.7% |
| **Histology types**      |       |     |
| Papillary carcinoma      | 8831  | 0.36% |
| Squamous carcinoma       | 937   | 0.04% |
| Intraductal carcinoma    | 1629174| 67.21% |
| Adenocarcinoma           | 15073 | 0.62% |
| Lobular carcinoma        | 235379| 9.71% |
| Mixed types              | 293746| 12.12% |
| Inflammatory carcinoma   | 8277  | 0.34% |
| Mammary Paget            | 7087  | 0.29% |
| Phylloides               | 3227  | 0.13% |
| Others                   | 222144| 9.16% |
| **Behavior**             |       |     |
| In situ                  | 491187| 20.30% |
| invasive                 | 1932688| 79.70% |
| **Grade**                |       |     |
| I                        | 461096| 21.70% |
| II                       | 920687| 43.40% |
| III                      | 719178| 33.90% |
| IV                       | 20216 | 0.95% |
| **Stage**                |       |     |
| Stage 0                  | 486856| 20.88% |
| Stage I                  | 961981| 41.27% |
| Stage II                 | 587352| 25.20% |
| Stage III                | 203159| 8.71% |
| Stage IV                 | 91864 | 3.94% |

* 378925 patients with not otherwise specified location of the tumor were excluded
** 302698 patients who did not have information on grade were excluded
*** 92663 patients with unknown stage were excluded
According to the type of reconstruction after complete mastectomy, 93405 (40.02%) patients underwent reconstruction with autologous tissue, 106130 (45.47%) patients underwent reconstruction with implants, and 33861 (14.51%) patients underwent combined reconstruction with tissue and implant (Table 3).

Radiation therapy was not administered in 1140676 patients (47.63%). 1165746 patients (48.67%) underwent beam radiation, 72500 patients (3.03%) radioactive implants, 625 patients (0.03%) radioisotopes and 2462 patients (0.10%) combination of beam radiation with radioactive implants or radioisotopes (Table 3).

Radiation therapy before surgery was administered in 7967 patients (0.33%) and after surgery in 1214097 patients (50.77%). Overall thirty-day mortality was 0.1% (2200 patients), whereas overall ninety-day mortality was 0.3% (7635 patients).

Discussion

The current study is the largest descriptive analysis to date on the clinical and pathological features of breast cancer in a population-based database. Breast cancer occurs more frequently in the UOQ, and we observed an overall prevalence of 39.50% in this study. Previous studies on smaller cohorts of patients observed a prevalence of UOQ tumor location ranging from 36.1% to 62% (Table 7) (5-8, 10-12). The higher frequency of occurrence of breast cancer in the UOQ is generally attributed to the higher amount of tissue in that breast quadrant (13). Nevertheless, the larger amount of breast tissue alone in UOQ cannot completely explain the disproportional occurrence of breast cancer in each quadrant (14). Ellsworth et al. observed a greater genomic instability in outer breast

Table 3. Age distribution depending on histology

| Histology             | Mean age (years) | Std. Deviation | Number of patients |
|-----------------------|------------------|----------------|-------------------|
| Papillary             | 68.11            | 12.757         | 8831              |
| Squamous              | 64.51            | 14.469         | 937               |
| Intraductal           | 60.53            | 13.448         | 1629174           |
| Adenocarcinoma        | 63.44            | 14.064         | 15073             |
| Lobular               | 61.92            | 12.867         | 235379            |
| Mixed                 | 61.13            | 12.931         | 293746            |
| Inflammatory          | 57.84            | 13.929         | 8277              |
| Angiomyosarcoma       | 69.38            | 7.999          | 8                 |
| Paget                 | 63.62            | 14.949         | 7087              |
| Phylloides            | 52.35            | 14.548         | 3227              |
| Others                | 62.04            | 13.436         | 222136            |
| Total                 | 60.91            | 13.366         | 2423875           |
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Darbre observed that the higher occurrence of breast cancer in UOQ could be related to the use of cosmetics applied to the adjacent underarm and upper breast area, that may contain both DNA-damaging chemicals and chemicals which in turn could mimic estrogen action (16).

Our descriptive analysis of breast cancer in the United States showed that the incidence of this disease among women has increased over the years, with exception of a sharp reduction in 2010 (Figure 1). Hou et al. already showed a significant increase in the incidence rates of all breast cancer from 2000 to 2009 (17). We confirmed the same upgoing trend from 2010 to 2015 as well. Furthermore, the prevalence of breast cancer increased with age, which Stapleton et al. also observed while studying the Surveillance, Epidemiology, and End Results (SEER) Program database (18). From our NCDB analysis, 94.4% of patients were diagnosed with breast cancer after 40 years old (44% between 40 and 60 years old and 50.4% after 60 years old). As such, annual mammography is strongly suggested after the age 40, as it is demonstrated to decreases mortality (19).

The most frequent histology type in our study was an intraductal carcinoma, followed by lobular carcinoma, in accordance with the literature data (Table 4) (20, 21). Broadly, invasive characteristics were noted more frequently in younger patients, in accordance with the findings by Escarela et al. from a SEER analysis (21). Presence of tumor cells in lymphatic channels (not lymph nodes) or blood vessels within the primary tumor was noted more frequently in younger patients, as well as a higher grade at diagnosis (Table 5 and 6).
The post-mastectomy reconstruction with implant was the most used reconstructive modality, whereas the reconstruction with autologous tissue and combined were less frequently performed, probably due to the cost and the necessity of suitable instruments such as the microscope (22). Moreover, disadvantages of autogenous tissue-based reconstruction could bring to prefer the reconstruction with implants, including longer anesthesia, more blood loss, a longer hospitalization, risk of necrosis of the flap, and possible issues at the donor site (scars, and abdominal hernias) (23). The risk of complications after breast reconstruction with autologous flap increases with age and BMI (body mass index), in smokers and diabetic patients.

### Table 4. Management. NOS: Not otherwise specified

| Treatment                                           | n    | %    |
|-----------------------------------------------------|------|------|
| **Type of surgery**                                 |      |      |
| None                                                | 171966 | 7.11%|
| Local tumor destruction, NOS                        | 352  | 0.01%|
| Partial mastectomy                                  | 1320210 | 54.57%|
| Subcutaneous mastectomy                             | 18218 | 23.79%|
| Total (simple) mastectomy                           | 575422 | 0.75%|
| Modified radical mastectomy                         | 306483 | 12.67%|
| Radical mastectomy                                  | 11128 | 0.46%|
| Extended radical mastectomy                         | 427  | 0.02%|
| Bilateral mastectomy for a single tumor involving both breasts, as for bilateral inflammatory carcinoma | 288  | 0.01%|
| Mastectomy, NOS                                      | 11140 | 0.46%|
| Surgery, NOS                                         | 3481  | 0.14%|
| **Type of reconstruction**                          |      |      |
| Autologous tissue                                    | 93405 | 40.02%|
| Implant                                             | 106130 | 45.47%|
| Combined (tissue and implant)                       | 33861 | 14.51%|
| **Type of radiation**                               |      |      |
| None (Radiation not administered)                   | 1140676 | 47.63%|
| Beam radiation                                      | 1165746 | 48.67%|
| Radioactive implants                                 | 72500  | 3.03%|
| Radioisotopes                                       | 625   | 0.03%|
| Combination of beam radiation with radioactive implants or radioisotopes | 2462 | 0.10%|
| Radiation therapy NOS                               | 13012 | 0.54%|
| **Radiation sequence with surgery**                 |      |      |
| No radiation therapy and/or surgical procedures     | 1162082 | 48.59%|
| Radiation before surgery                            | 7967  | 0.33%|
| Radiation after surgery                             | 1214097 | 50.77%|
| Radiation before and after surgery                  | 1009  | 0.04%|
| Intraoperative radiation                            | 5017  | 0.21%|

* 4760 patients who did not have information about surgery were excluded
** 28854 patients who did not have information on radiation were excluded
*** 32429 patients who did not have information on radiation sequence were excluded
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Figure 6. Type of surgery

Table 5. Age distribution depending on Grade

| Grade                                | Mean age (years) | Std. Deviation | Number of patients |
|--------------------------------------|------------------|----------------|-------------------|
| Grade I                              | 63.29            | 12.589         | 461096            |
| Grade II                             | 61.80            | 13.238         | 920687            |
| Grade III                            | 58.53            | 13.632         | 719178            |
| Grade IV                             | 58.90            | 13.226         | 20216             |
| Cell type not determined, not stated, not applicable | 60.38            | 13.333         | 302698            |
| Total                                | 60.91            | 13.366         | 2423875           |

Table 6. Presence or absence of tumor cells in lymphatic channels (not lymph nodes) or blood vessels within the primary tumor as noted microscopically by the pathologist. 1101720 patients with missing data were not included

| Lymph-vascular invasion | Mean age (years) | Std. Deviation | Number of patients |
|-------------------------|------------------|----------------|-------------------|
| Lymphvascular invasion is not present | 61.60            | 12.792         | 858226            |
| Lymphvascular invasion is present | 59.24            | 13.947         | 168431            |
| Not applicable          | 61.57            | 12.898         | 6272              |
| Unknown                 | 61.25            | 13.588         | 289226            |
| Total                   | 60.91            | 13.366         | 2423875           |
Post-mastectomy radiation therapy (PMRT) is generally recommended for patients with advanced disease (24). It has been shown to improve control of local disease and overall survival. There is also a reduction in relapse rates for patients with more than three positive lymph nodes. In our cohort, PMRT was administered to 1214097 patients (50.77%).

**Table 7. Percentage of primary breast tumor location in UOQ (upper-outer quadrant) as reported in other studies and in this study**

| Author, year | Location of the study | Total Number of patients included | Database analyzed | Years | UOQ tumor location (%) |
|--------------|-----------------------|----------------------------------|-------------------|-------|-----------------------|
| Hazrah P (5) | India                 | 187                              | Department Of Surgery All India Institute of Medical Sciences | 1994-2005 | 62                    |
| Rummel S (6) | USA                   | 980                              | Clinical Breast Care Project | 2001-2013 | 51.5                  |
| Wu S (7)     | China                 | 1044                             | Sun Yat-Sen Cancer Center | 1999-2007 | 50.2                  |
| Sarp S (8)   | Switzerland           | 1522                             | Geneva Cancer Registry | 1984 - 2002 | 39                    |
| Nunes RD (9) | Brazil                | 2582                             | Population-Based Cancer Registry of Goiânia (RCBPGO) | 1989-2003 | 53.7                  |
| Siotos C (10)| USA                   | 5295                             | Johns Hopkins Sidney Kimmel Comprehensive Cancer Center | 2003-2015 | 36.2                  |
| Sohn VY (11) | USA                   | 26,121                           | The Department of Defense tumor registry encompasses all military facilities from the United States Army, Air Force, and Navy | 1990-2005 | 57                    |
| Eisemann N (12) | Germany              | Not specified                   | Epidemiological cancer register of Schleswig-Holstein | 1999-2009 | 36.1                  |
| Sisti A (this study) | USA              | 2423875                         | National Cancer Database (NCDB) | 2004-15 | 39.50             |

(23). Post-mastectomy radiation therapy (PMRT) is generally recommended for patients with advanced disease (24). It has been shown to improve control of local disease and overall survival. There is also a reduction in relapse rates for patients with more than three positive lymph nodes. In our cohort, PMRT was administered to 1214097 patients (50.77%).

**Conclusion**

This nationally representative analysis of the years 2004-2015 demonstrates that UOQ was the most frequent primary tumor site and the intraductal carcinoma was the most frequent histology. The prevalence of breast cancer increased with age. The most frequent grade at diagnosis was grade II. Left and right breast were affected with almost the same frequency, with a slight predominance of the left breast. Most frequent surgical treatment was a partial mastectomy. Reconstruction with implant was the most frequent choice.

**Ethical approval:** This article does not contain any studies with human participants or animals performed by any of the authors.

**Funding:** This study was supported in part by the Mayo Clinic Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery.

**Conflict of interest:** Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

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Received: 19 April 2019
Accepted: 27 April 2019
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