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Characteristics and treatment of human epidermal growth factor receptor 2 positive breast cancer: 43,485 cases from the National Cancer Database treated in 2010 and 2011

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Abstract

BACKGROUND: Although identification of human epidermal growth factor receptor 2 (Her2) positive breast cancer represents one of the greatest advances over the past 3 decades, it has not been studied extensively on a national level.

METHODS: The National Cancer Database is a joint project of the American Cancer Society and the American College of Surgeons and contains data on about 70% of the cancer cases in the United States. Data on Her2 have been collected since 2010 and was used for this study.

RESULTS: Of 298,937 cases of invasive breast cancer with known Her2 status diagnosed in 2010 and 2011, 43,485 (14.5%) were Her2 positive. Her2 positivity was greatest in Asian/Pacific Islanders and least in non-Hispanic Whites and was markedly more common in younger women. The incidence of Her2 positive tumors ranged from a low of 13.9% in the Mountain West region to a high of 16.0% in the West South Central region ($P < .001$). Compared with Her2 negative tumors, Her2 positive tumors were larger (2.6 vs 2.2 cm, $P < .001$), more likely to have positive nodes (39% vs 31% $P < .001$), have lymphovascular invasion (30% vs 20%, $P < .001$), and be high grade (56% vs 29%, $P < .001$). There were also differences by histology: invasive ductal 16.4%, invasive lobular 5.5%, tubular 2.3%, inflammatory 36%, and Paget's with invasion 59%. When adjusted for age, race, tumor size, and nodal status Her2 positive tumors were much more likely to receive chemotherapy (odds ratio = 5.5, confidence interval = 5.2 to 6.0) and somewhat less likely to undergo breast preservation (odds ratio = .78, confidence interval = .76 to .80).

CONCLUSIONS: Her2 positive tumors have distinct epidemiologic, clinical, and treatment characteristics.

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The human epidermal growth factor receptor 2 (Her2) is a transmembrane tyrosine kinase receptor that is encoded on the long arm of chromosome 17.[1,2] It can form heterodimers with other members of the epidermal growth factor receptor family, and this causes activation of intracellular pathways that promote cellular proliferation, survival, motility, and loss of adhesion. Since the 1980s, it has been recognized that a subpopulation of breast cancers overexpress the Her2 receptor, and these cancers tend to be more aggressive and portend a worse prognosis than other subtypes.[3] Despite their more aggressive nature, however, these tumors do respond to Her2–targeted therapies, including trastuzumab, pertuzumab, and lapatinib. These drugs are now used routinely in the adjuvant, neoadjuvant, and metastatic setting.[4–8] Identification of Her2 and development of specific targeted therapies has been one of the greatest advances in breast cancer therapy over the past 30 years.

The incidence of Her2 positive breast cancer in the United States has been reported to range from 10% to 30%. While there have been many small series which have described rates of Her2 positivity, there is little national data describing the epidemiology of this important subtype. The National Cancer Database (NCDB) began collecting information regarding Her2 status for breast cancer in 2010, and these data have recently become available. The purpose of this study was to characterize the epidemiology of Her2 positive cancers in the United States for 2010 to 2011 and also to describe trends in treatment with regard to surgery and chemotherapy.

Methods

The NCDB is a joint project of the Commission on Cancer of the American College of Surgeons and the American Cancer Society and contains data on about 70% of the cancer cases in the United States. After approval by the NCDB, patient deidentified data were downloaded from the website and analyzed in this study.

Study population

The population used for this study consisted of all patients with stage 1 to 4 invasive breast cancer diagnosed in 2010 and 2011, with known estrogen receptor (ER), progesterone receptor (PR), and Her2 status. Cases were categorized according to the combination of receptors. Hormone receptor positive cases were either ER or PR positive.

Race, histology, and treatment variables

The NCDB classifies histology in many categories, with relatively few cases in each group. To allow a valid analysis, only histologic categories with greater than 200 cases were included and the rest were categorized as "other". Similarly, race included many small groups of different Asian ethnicities, so we categorized all of them as "Asian/Pacific Islander". American Indians were included in the "other" category for this analysis. For determination of surgical treatment, only cases that had definitive surgery, either mastectomy or lumpectomy, were included. The pathologic complete response to chemotherapy variable was available for about 71% of the patients who had neoadjuvant chemotherapy.

Tumor size and stage

Since a significant percentage of patients underwent neoadjuvant chemotherapy, the AJCC clinical T, N, and M stages were used to compare tumor size and nodal status. A separate NCDB variable, number of positive nodes, was used as another outcome variable to compare the Her2 positive and Her 2 negative groups.

Statistical analysis

Statistical analyses were performed with IBM SPSS, version 22. Bivariate comparisons were performed with chi-square tests, and multivariable analysis was performed with binary logistic regression. Statistical tests were 2-sided, and *P*-values less than .05 were considered significant.

Results

The Her2 assays available in the NCDB are shown in Table 1. The results demonstrate consistent findings, with all the assays showing around 14% of the cases to be Her2 positive. For the remainder of the analyses in this study, we chose to use the Her2 value determined by the tumor registrar at each local hospital. The registrars were instructed to use gene amplification assays first, and then use immunochemistry assay for cases where the amplification assay was borderline or not performed. As a result, 89% of all cases in the NCDB were known to be Her2 positive or negative and were used for the remainder of this study.

A total of 298,937 cases of invasive breast cancer diagnosed in 2010 or 2011 with known positive or negative Her2 status were included in the study. Characteristics of the group are shown in Table 2. Overall, 43,485 (14.5%) of breast cancers were Her2 positive. There were significant differences by race and ethnicity. Her2 positivity was greatest in Asian/Pacific Islanders and least in Whites and was also more common in Hispanics compared with non-Hispanics. There were also significant differences by age. The incidence of Her2 positive breast cancer was significantly more common in younger women, ranging from 28% in women under 30 to only 11% in those over 70. There were also geographic differences with respect to the incidence of Her2 positive tumors; the lowest was in the Mountain West region (13.9%), and the highest in the West South Central region (16.0%).

There were interesting patterns with regard to coexisting hormone receptor (HR) positivity and Her2 positivity.