

EDITORIAL

Is Breast Cancer in Asian and Asian American Women a Different Disease?

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In this issue, Lin et al. (1) compared age-specific breast cancer incidence using cancer registry data from several East Asian countries (Hong Kong, Japan, Korea, Taiwan, Singapore, and China [Shanghai]) and the National Cancer Institute's Surveillance, Epidemiology, and End Results Program in the United States. They also compared case distributions of pathological characteristics (estrogen receptor [ER]; progesterone receptor [PR]; human epidermal growth factor 2 [HER2]; subtypes based on ER, PR, and HER2; and grade [specifically grade 3]) between Asia (using data from several large Asian hospitals) and the United States (Surveillance, Epidemiology, and End Results data). They found distinct age-specific incidence and clinicopathological patterns among the Asian populations compared with US data. Specifically, across the Asian countries, contemporary (2011–2014) breast cancer incidence peaked during the ages of 45–49 years and either declined thereafter with age (Japan, Korea) or stabilized with age (all other East Asian countries). This is in stark contrast to the age-specific pattern observed among US non-Hispanic white women, where incidence increases exponentially with age beginning around age 40 years to around age 80 years, with the highest incidence in the 75- to 79-year-old age group, 30 years older than for women in Asia. Examining breast cancer incidence among Asian Americans, specifically for Chinese, Japanese, and Koreans (2), the authors found that age-specific patterns were between those for women in Asia and US non-Hispanic white women, with a slightly later age peak (in the age 60 decade). Comparing the case distributions of ER, PR, HER2, subtypes, and grade III, Asian women also exhibited unique characteristics relative to non-Hispanic white women, specifically higher proportions of ER+ and lower proportions of triple-negative breast cancer at a younger age, but lower proportions of ER+ and higher proportions of HER2+, triple-negative breast cancer, and grade 3 tumors at older ages. Breast cancers diagnosed among women in Asia compared with

those among non-Hispanic white women were also proportionally more likely to be HER2+ than other subtypes, with patterns among Asian American women again between those for women in Asia and US non-Hispanic white women.

These pan-Asian patterns are consistent with previous results from Taiwan based on publications also from Lin et al. (3,4). However, longitudinal analyses of birth cohorts show that age-specific patterns may be more similar between women in East Asian countries and the United States than expected, especially among more recent birth cohorts where age-specific rates of breast cancer exceed those for US non-Hispanic white women, especially for Taiwan, Singapore, and South Korea (5). As breast cancer age patterns among Chinese, Japanese, and Korean Americans appear to fall between those of women in Asia and non-Hispanic whites (1), it would follow that lifestyle factors related to Westernization are strongly suspected to be responsible for these patterns. However, the authors contrasted the breast cancer age-specific patterns with patterns for colorectal cancer, another cancer that is vulnerable to lifestyle changes with Westernization, and concluded, based on the contrasting patterns for breast and colorectal cancer, that Westernization alone is unlikely to explain the breast cancer age-specific patterns. The comparison with colorectal cancer, while an interesting approach, should be interpreted with caution, because colorectal cancer has obviously different risk factors, pathological characteristics, and screening approaches than breast cancer.

The observation of a higher proportion of HER2+ tumors among Asians and Asian Americans than non-Hispanic whites is consistent with previous US studies (6–8), although when considering incidence rates, higher rates of HR+ cancers were observed only for Filipina and Vietnamese women (8). However, whether this reflects differences in underlying disease biology, as proposed by Lin et al. (1), or differences in prevalence of risk

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factors unique to each subtype remains inconclusive and deserves further study. Our work and that of others suggests that the spectrum of inherited pathogenic variants in cancer susceptibility genes is fairly similar among Asians and Asian Americans as among other racial and ethnic groups (9–11). Nevertheless, in a recent study comparing the molecular landscape of breast cancer in a young Korean patient population vs The Cancer Genome Atlas population with more older cases, a number of molecular differences were identified, most of which were driven by the striking age differences between the two cohorts (12). Interestingly, independent of age, tumors in Korean patients had a more active immune microenvironment than The Cancer Genome Atlas cases, as evidenced by higher expression of cytotoxic T-cell markers and the cancer immunotherapy target PD-L1. Further tumor genomic studies are needed to characterize the molecular landscape of breast tumors between Asian and white women and to ascertain whether they may have clinical implications.

Women in Asian countries have historically had lower breast cancer risk than women in the United States or European countries (13). However, breast cancer incidence has been increasing rapidly among women in Asia and in Asian American women (2,5,8), warranting an urgent increased research focus on this disease in these populations. Changes in reproductive patterns, obesity, food intake, and physical activity may underlie some of the temporal and geographic changes in age-specific patterns of breast cancer risk. Cross-national and multi-generational studies may help elucidate the factors responsible for these dynamic incidence and risk patterns and may uncover novel risk factors, as with earlier generations of migrant studies. The rapid shift in risk among Asian women may also be translating into a reversal of risk among Asian American women, with our recent pilot case-control study demonstrating surprisingly higher risk among foreign-born than US-born Asian American women (14). The earlier age at onset among Asians has long been noted among US clinicians, and now empirical data from both the United States and Asia have accumulated to support this observation, which likely reflects higher risk among recent cohorts. Public health outreach is necessary to increase awareness among the general public of Asians and Asian Americans regarding their breast cancer risk (15). Given the earlier age of breast cancer onset, Asians may benefit from starting mammographic screening earlier than age 50 years [the age for starting routine screening in some practice guidelines (16,17)]. Additional research is needed to guide effective management of the unique patterns of breast cancer risk among Asian and Asian American women.

Notes

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