

Comparison of breast cancer incidence, clinicopathologic features, and risk factor prevalence in women aged 20-29 at diagnosis to those aged 30-39

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Women younger than 30 make up only 1% of those diagnosed with breast cancer,¹ but a number of studies have demonstrated that breast cancer in young women has a more aggressive biology and is associated with poorer outcomes than in postmenopausal women.²⁻⁴ This may in part be due to a higher frequency of more aggressive phenotypes,⁵⁻⁷ but young age itself has also been identified as an independent indicator of poor prognosis.⁶

Given this prognosis, risk factors for women under 40 remain a topic of interest in the literature, and those so far identified vary significantly from those for postmenopausal women.⁸ However, there is no standard definition of which ages constitute “young” patients with breast cancer, and studies frequently combine women up to 45 years of age. This practice may be obscuring characteristics inherent to those aged 20-29, since they are intrinsically outnumbered by patients diagnosed at older ages. Thus, unique attributes may be under-recognized in the literature. We hypothesize that women diagnosed at 20-29 will demonstrate unique clinicopathologic features and trends in incidence when compared with the other age groups with which they have been traditionally combined.

Study of this question was Institutional Review Board (IRB)-approved, and all data collection and storage were compliant with the Health Insurance Portability and Accountability Act of 1996. The Surveillance Epidemiology and End Results (SEER) 9 registries of the National Cancer Institute were used to determine breast cancer incidence by race and by year from 1975 to 2014. These incidences were corrected for changes in the general population over the time

periods included. The Oregon Health & Science University (OHSU) electronic medical record (EMR) was then queried to identify all patients with a diagnosis of breast cancer 2005-2017. Inclusion criteria were female sex, age at diagnosis 20-39 years, histologic diagnosis of breast cancer, and receipt of oncologic care at OHSU within the time period examined. All data were extracted from the EMR.

Linear and polynomial regressions were performed to evaluate and compare changes in the rate of breast cancer diagnosis over time using JMP, version 13.0, Cary, NC. Tumor characteristics and clinicopathologic features of individual patients were compared using independent t tests, chi-square analysis, and nonparametric testing using IBM SPSS Statistics for Windows, Version 24.0, Armonk, NY. The level of significance was set at $P < .05$.

The SEER data base revealed 656 598 women diagnosed with breast cancer between 1975 and 2014. Of these, 3823 (0.58%) were aged 20-29 at diagnosis, 10 384 (1.58%) were aged 30-34, and 23 219 (3.53%) were aged 35-39. From 1975 to 2014, the overall incidence of breast cancer in women aged 20-29 at diagnosis was 4.82/100 000 persons. This was significantly lower than in women aged 30-34 (26.23/100 000, $P < .0001$) or 35-39 (61.68/100 000, $P < .0001$). Linear regression revealed a significant increase in the rate of breast cancer diagnosis in women aged 20-29 from 1975 to 2014 ($R = .376$, $P = .010$), but there were no significant changes in those aged 30-34 ($R = .197$, $P = .222$) or 35-39 ($R = .089$, $P = .583$).

Patients who had presented to OHSU with breast cancer diagnosed at 20-39 were identified via query of the EMR. Of the 566

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patients identified, 424 otherwise met criteria for inclusion. The predominant reason for exclusion was failure to have received oncologic care at OHSU within the time period examined. Patients were predominately white (88.4%) and nonhispanic (91.2%) with invasive ductal carcinoma (88.2%). 49.8% had luminal biology; 12.0% were BRCA-positive.

Comparison of tumor characteristics at diagnosis and presentation in patients who were diagnosed at 20-29 with those diagnosed at 30-34 and 35-39 revealed no significant difference in mean tumor size, median anatomic stage, frequency of ductal pathology, BRCA positivity, or association with pregnancy. A significantly higher percentage of tumors in patients diagnosed at 20-29 were detected by palpation of a mass than those 30-34 (96.3% vs 85.8%, $P = .043$) or 35-39 (96.3% vs 85.5%, $P = .032$). Comparison of risk factors revealed a significantly lower median number of pregnancies in those aged 20-29 (0 vs 2 and 0 vs 2, $P = .001$), and mean age at first birth was significantly younger than in those aged 30-34 (22.5 vs 25.1 years, $P = .003$) or 35-39 (22.5 vs 26.8 years, $P < .0001$). There were no significant differences in the percentage of patients with a family history of breast cancer. Examination of lifestyle factors revealed that women aged 30-34 were more likely to use alcohol (47.5% vs 63.8%, $P = .037$). BMI at diagnosis was significantly higher in those patients aged 35-39 (25.4 vs 27.3 kg/m², $P = .017$).

The predominant conclusion of this study is that the rate of breast cancer diagnosis has been increasing in women younger than 30 years of age, while it has remained stable since 1975 in women aged 30-39. This increase was not previously appreciated in the literature when age groups were pooled.

A more detailed single institution retrospective review revealed that women aged 20-29 at diagnosis had had fewer children than those with whom they were compared, which is notable given that multiparity is an established risk factor for premenopausal breast cancer.⁹ In addition, women aged 30-39 had significantly higher alcohol usage. Trends in the changes of these risk factors over time and comparison of outcomes were not able to be analyzed in this study due to limited sample size. Consequently, larger, population-based

studies will be necessary to understand the exact role of these risk factors in breast cancer in women aged 20-29.

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