SIOG 2017 - Abstract Submission

Track 4: Modern diagnostics & therapeutic areas

Diagnostics & genomic tools

O27

GENETIC PROFILE AND CLINICAL CHARACTERISTICS OF OLDER WOMEN WITH BREAST CANCER IN THE CLINICAL CANCER GENOMICS COMMUNITY RESEARCH NETWORK

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Introduction: The role of breast cancer (BC) susceptibility gene mutations is known in younger women with BC, and young age at onset is a recognized criterion in the NCCN guidelines for genetic cancer risk assessment (GCRA). However, the potential role of germline cancer susceptibility mutations in older women with BC is not well studied, in part because they are less likely to undergo GCRA.

Objectives: We aimed to characterize and compare the germline mutation profile of women with a history of BC aged ≥65 years and <65 years at the time of GCRA in the Clinical Cancer Genomics Community Research Network (CCGCRN), a large consortium of over 40 collaborating clinics across the United States and Latin America.

Methods: Genetic testing results from all women with breast cancer (invasive or ductal carcinoma in situ) enrolled in the CCGCRN registry from 1997 to 2016 were included in this analysis. Socio-demographic characteristics, clinical variables and genetic profiles were compared between women aged ≥65 and <65 years at the time of GCRA. Data was analyzed using Fisher's test and x^2 statistics, with a two-sided p value of <0.05 considered significant.

Results: We identified 1,035 women aged ≥65 years and 8,900 women aged <65 years who were diagnosed with BC. 10.4% of women ≥65 (n=108) and 11.6% of their younger counterparts (n=1,033) were found to carry a BC-associated germline mutation (p=0.27). Germline mutations in high-risk genes (e.g. *BRCA*) represented 85% of carriers among women ≥65 years (n=92), and 96% of those <65 (n=987), (p<0.01). *BRCA2* was the most frequently mutated high-risk gene among women ≥ 65 years, representing 41.6% of cases (n=45), followed by *BRCA1* (37%, n=40), *PALB2* (6%, n=6) and *TP53* (<1%, n=1). The most frequently identified mutations in high-risk genes for women <65 were in *BRCA1* (53%, n=547), *BRCA2* (37%, n=386), *PALB2* (3%, n=26) and *TP53* (2%, n=23). Notably, mutations in moderate-risk genes were found in 17% of women ≥65 (n=18) and in 4% of those <65 (n=45) (p<0.01). Among women ≥65 with a mutation in in a moderate-risk gene, the most prevalent was *CHEK2* (14%, n=15), followed by *ATM* (2%, n=2) and *NF1* (<1%, n=1). While *CHEK2* was also the most common mutated moderate-risk gene among women <65 years (3%, n=32), it represented a smaller proportion of cases compared to the older group (3% vs 14%, p< 0.01). ATM (1%, n=14) and NF1 (<1%, n=7) were observed in a similar proportion as the older group.

Among women aged ≥65, mean age at first BC diagnosis was 56.4 years (range 29-84), compared to 40.8 years (range 19-64) in women <65. 25.9% of older women (n=28) had their first BC diagnosed at age ≥65, of which 60.7% (n=17) were associated with *BRCA2* and 21.4% (n=6) with *BRCA1* mutations. *BRCA2* mutations were more frequent among women diagnosed with BC at age ≥65 than in those <65 (p<0.01). Older women with germline mutations were more likely to present with stage 0-II BC (93% vs 77%, p<0.01) and with hormone receptor (HR) positive tumors (68% vs 53%, p=0.04).

Conclusion: Older women were more likely than their younger counterparts to have mutations in moderate-risk genes or in the *BRCA2* high-risk gene, which could explain why older women carrying BC susceptibility mutations presented more frequently with HR-positive tumors. Our results show that older women should not be excluded from GCRA, and clinicians should be aware of the NCCN criteria for their inclusion.

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