Stage IV Breast Cancer Increasing in Incidence and Proportion Over the Last Decade

Dana-Farber study finds metastatic breast cancer incidence increased by 1.2% per year across all age and racial groups and tumor subtypes.

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A new study from Dana-Farber Cancer Institute shows that cases of Stage IV breast cancer, a common but largely difficult to treat disease, are increasing both in incidence and as a proportion of all breast cancer diagnoses. According to the findings, published today in JAMA Network Open, the incidence rate of Stage IV breast cancer has increased significantly, from 9.5 cases per 100,000 women in 2010 to 11.2 cases per 100,000 women in 2021. Stage IV, or de novo metastatic breast cancer, refers to cancer has already spread to distant organs at the time initial diagnosis.

“Early detection of breast cancer is critically important,” said Dr. Jose Leone, medical oncologist at Dana-Farber and senior author of the study. “By understanding population-based outcomes, which this study provides, there is an opportunity to create the most impact to the population.”

Breast cancer incidence rates for all types of the disease have risen 1% annually from 2012 to 2021. Despite these trending increases in the disease, historically Stage IV has a smaller proportion of all breast cancer cases. Leone and colleagues evaluated incidence, proportion, and overall survival in a population-based database from the Surveillance Epidemiology, and End Results (SEER) Program.

The investigators analyzed 761,471 breast cancer diagnoses, 98.8% of which were females, from 2010 to 2021 in the U.S. Median age diagnosis was 63 years. Increases across Stage I-III breast cancers were observed across all tumor subtypes, including HR-positive/HER2-negative, HR-positive/HER2-positive, HR-negative/HER2-positive, and triple-negative disease.

The researchers found that stage IV breast cancer incidence increased by 1.2 percent per year across all age groups, racial groups and tumor subtypes compared to 1 percent per year for all breast cancers. Additionally, the proportions of stage IV disease increased modestly from 5.6 percent in 2010 to 6.0 percent in 2021. For each successive year from 2010 to 2021, overall survival of patients diagnosed with stage IV breast cancer improved moderately across HR-

positive/HER2-negative, HR-negative/ HER2-positive, and HR-positive HER2-positive breast cancer.

Interestingly, while men make up less than 1% of breast cancer diagnoses, the incidence rate in men represented a 3.7% increase per year, higher than women.

"When we think about incidence, we think may think of risk factors such as hormone replacement therapy or factors that apply more specifically for women," Leone said. "But the fact that the increase in incidence is overall in all groups of interest, suggests that the underlying factors may be affecting everyone."

Leone added that the study underscores the importance of determining which factors contribute to these increases and the need to identify of breast cancer before patients present with stage IV disease. While overall survival improved due to greatly improved therapeutics, research is needed to determine factors contributing to increased incidence, potential changes in natural history of breast cancer, disease screening, and incidence and mortality of other conditions.

"This study raises concern because we don't have good answers as to why we are seeing an increase in de novo metastatic breast cancer, regardless of breast cancer subtype." Leone said. "While our medicines for treating metastatic breast cancer have improved dramatically in recent years, earlier-stage breast cancer is often curable, and our study highlights the need to identify the factors driving increasing incidence of advanced disease."

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