Why Has the Incidence of Stage IV Breast Cancer Not Decreased?

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BACKGROUND

Esserman (JAMA 2009) and Bleyer & Welch (NEJM 2012) were first to highlight that since widespread adoption of screening mammography, the incidence of localized breast cancer has increased dramatically while distant disease has not decreased. The explanation for this is unknown.

We recently showed that many breast cancers are small due to favorable biology that promotes indolence rather than early death (Lannin, NEJM 2017). This study explores the concept of Stage IV as a biological entity whose phenotype differs from that of small cancers typically found by screening.

METHODS

Step 1. SEER*Stat 8.3.5 was used to compare population based incidence of localized, regional, and distant breast cancer in SEER during 1973-2015 (Nov. 2017 submission).

Step 2. NCDB was queried for invasive breast cancers found 2010-2015 to determine factors related to de novo Stage IV in a large modern population.

Step 3. Five biological variables found to be related to Stage IV (ER, PR, Her2, Grade, and LVI) were used in developing an index of tumor biology. Subsets of the possible 48 combinations of these variables were formed, and the proportion of Stage IV was determined in each. Three groups emerged based on the proportion of biologically aggressive tumors and <1/4 the proportion of indolent tumors.

Step 4. Proportions of the 3 biological groups were compared across disease stages. Multivariate logistic regression assessed the strength of relationship between aggressive biology and Stage IV when adjusted for important patient’s disease variables.

RESULTS


Distribution of Tumor Biology by Stage

CONCLUSIONS

• Significant differences exist in the distribution of biological variables across breast cancer stages

• Compared with Stage I, Stages III and IV have >4x the proportion of biologically aggressive tumors and <1/4 the proportion of indolent tumors

• These variables are primitive measures of tumor biology, but the distribution patterns would likely apply to more sophisticated measures as well.

• Differences in tumor biology likely account for why Stage IV incidence has not decreased with screening mammography.

OBJECTIVES

• Characterize the biology of Stage IV breast cancer to determine what makes this disease subset unique

• Compare Stage IV tumor biology with the biology of cancers most commonly found on screening mammography.

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