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ASO AUTHOR REFLECTIONS

ASO Author Reflections: Oncotype DX RS Complementing the Prognostic Stage in the Updated AJCC 8th Edition for $T_{1-2}N_1M_0$ ER-Positive HER2-Negative Breast Cancer

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PAST

The breast cancer staging system used to be based on anatomic factors. Then the molecular subtype based on the validation of biologic markers was introduced to describe the prognosis and treatment benefit.[1] The prognostic stage system in the American Joint Committee on Cancer (AJCC) 8th edition for the first time incorporated nearly all the important biologic factors together with anatomic tumor-node-metastasis (TNM) factors. It would be the most accurate predictor of outcome in case of discordance between tumor burden and biology. In this era of precise medicine, clinical and genetic risks should be equally considered. Oncotype DX is the only multigene assay available to improve the classification of the prognostic stage. Cases with $T_{1-2}N_0M_0$ estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative cancer and RS lower than 11 should be categorized as pathologic prognostic stage IA. However, the significance of RS has not yet been fully evaluated for lymph node (LN)-positive cases.[2–4] This study aimed to evaluate the prognostic significance of Oncotype DX RS in $T_{1-2}N_1M_0$ ER-positive HER2-negative breast cancer based on the pathological prognostic stage using the Surveillance, Epidemiology, and End Results (SEER) database.

PRESENT

In this study, 4059 patients were categorized as prognostic stages IA–IIB.[5] The study categorized RS lower than 11 as low risk, 11–25 as intermediate risk, and higher than 25 as high risk. The RS risk groups were positively correlated with the pathological prognostic stages. The RS risk groups in breast cancer-specific survival (BCSS) and overall survival (OS) differed significantly. Moreover, RS risk group was an independent prognostic factor for BCSS and OS together with the pathological prognostic stage. In the subgroup analysis, the survivals were similar across pathological prognostic stages in the RS low-risk group but differed significantly among pathological prognostic stages in the RS intermediate-risk group. Survivals also differed significantly among the RS risk groups in pathological prognostic stage IA. This finding added to increasing evidence that RS results provide independent prognostic significance to complement the prognostic staging system and further suggested that $T_{1-2}N_1M_0$ ER-positive HER2-negative breast cancer with an RS lower than 11 might be expected to be classified as a lower stage.

FUTURE

Although to date, this study was the largest to explore the prognostic significance of Oncotype DX RS in $T_{1-2}N_1M_0$ ER-positive HER2-negative breast cancers, the intrinsic bias in any retrospective study could not be completely avoided. A further prospectively designed study with an even longer follow-up period is warranted to show the differences in survival outcomes between pathological prognostic stages IA and IB. Moreover, as

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chemotherapy use is known to be underreported in the SEER database, further studies also should incorporate treatment data into survival analyses among the RS risk groups. Finally, the SEER database does not collect information on local recurrence or distant metastasis. Further studies should evaluate the prognostic significance of RS for these end points. Generally, ER-positive HER2-negative breast cancer in $T_{1\text{-}2}N_1M_0$ stage is considered to have an intermediate risk of relapse, with much controversy in the aspect of adjuvant treatment. The incorporation of genetic risk assessment into the pathological prognostic stage system could better guide individualized treatment under more accurate prognosis prediction.

DISCLOSURE Authors declare that he has no conflicts of interest.

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