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Recurrence risk of node-negative and ER-positive early-stage breast cancer patients by combining recurrence score, pathologic, and clinical information: A meta-analysis approach.

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Background: The 21-gene Onco*type* DX Recurrence Score (RS) is widely used for assessment of recurrence risk and prediction of chemotherapy benefit in patients with early stage ER-positive breast cancer. Pathologic and clinical factors such as tumor size and grade, and patient age also provide independent prognostic utility and might be combined with the RS to achieve more prognostic power.

Methods: All patients in the NSABP trial B-14 and the ATAC study who had ER-positive tumor specimens with successful Onco*type* DX RS assay were included. B-14 patients were node-negative and were treated with tamoxifen. ATAC patients were node-positive or node-negative, and were treated with tamoxifen or anastrozole. Meta-analysis methods were used to assess the risk of distant recurrence by combining the individual study multivariate risk assessments using RS-pathologic-clinical (RSPC) information. A RSPC risk index was defined a priori as the predicted risk of distant recurrence at 10 years with predetermined cut-offs at 12% and 20% risk.

Results: The meta- analysis included 647 B-14 patients and 1088 ATAC patients. RSPC prognosis combining clinical and pathology information with RS is more powerful than using RS alone (likelihood ratio test p-value < 0.001). The RSPC risk index was shown superior to RS in risk discrimination among node-negative, ER+, tamoxifen-treated patients. Compared with RS risk stratification, fewer patients were classified as intermediate risk by the RSPC index (18% vs 26%; p-value 0.001), and 72% of pts with intermediate RS 18-30 were either up-staged or down-staged. Average risk in the low, intermediate- and high-risk classes were similar between the RSPC and RS classifications.

Conclusions: The RSPC index combining RS with pathology and clinical information with RS supplied more powerful prognosis for early stage breast cancer patients than RS alone. It was estimated that its application would reduce patients with intermediate risk by 30% and enhance personalized treatment decisions in oncology practice.