Use of the OncotypeDX Recurrence Score® (RS) as a continuous prognostic biomarker in hormone receptor (HR) positive HER2neu negative early breast cancer with intermediate risk of recurrence may asses risk of recurrence or death more appropriately

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Background:

The OncotypeDX Recurrence Score® (RS) is a validated multigene assay yielding prognostic and predictive information in patients with hormone receptor (HR) positive HER2neu negative early breast cancer and is part of guideline recommendations in national and international guidelines. The clinical utility of the RS has been prospectively investigated using risk levels of low risk (0-10), intermediate risk (11-25) and high risk (26-100). In patients older than 50 years the risk groups low and intermediate are indicating a low risk of recurrence (justifying omission of adjuvant chemotherapy), whereas an RS of 26-100 indicates high risk. In patients age 50 and younger the granularity is higher with risk levels of low (0-15), low to medium (16-20), intermediate (21-25) and high risk (26-100). However, a continuous interpretation of the score would be helpful in risk assessment and counseling given the fact that recurrence risk is a biological continuum. Here we are presenting an analysis of RS values as a continuous parameter from a real-world population.

Methods:

Patients included in this analysis had HR positive HER2neu negative early breast cancer with 0-3 involved lymph nodes assessed as intermediate risk by institutional guidelines including Ki67 and a complete follow-up. An RS was performed in all tumors with material from the core cut biopsy. Patients with a RS of 26 and higher received neoadjuvant chemotherapy. Disease free survival (DFS) events were defined as local or distant recurrence or death from any cause. Overall survival (OS) events were defined as death from any cause. Associations of Recurrence Score® and DFS or OS events were calculated by Cox Regression. A time-dependent receiver operating characteristic (ROC) analysis at 5 years was performed to assess the discriminative ability of the Oncotype DX Recurrence Score, tumor size, and Ki-67 for disease-free survival. Subsequently, time-dependent area under the curve (AUC) values were estimated over the entire 5-year follow-up period using Cox proportional hazards models to account for censored survival data.

Figure 1: DSF and OS events by Oncotype DX Recurrence

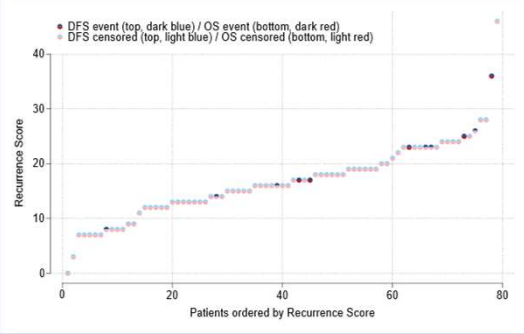


Figure 2: Time−dependent ROC for 5 years DFS

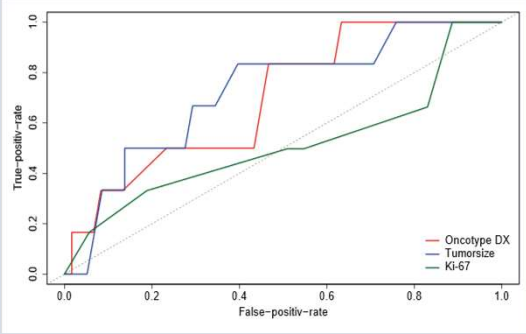
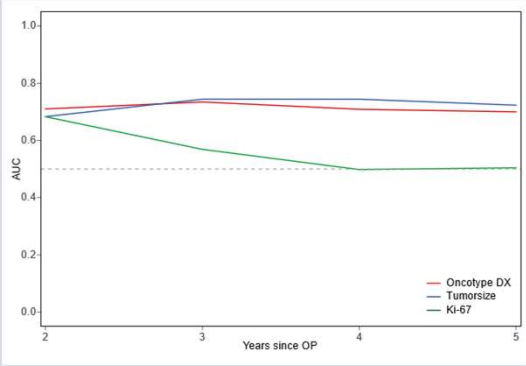


Figure 3: Time−dependent AUC for 5 years DFS



Results:

1 male and 78 female patients were included in this analysis. Median follow-up was 6.9 (0.9-11.0) years. Patient characteristics were as follows: median tumor size 1.4 (0.3-4.5) cm, median age at diagnosis 60.7 (34.7-82.5) years, median Ki67 20 (2-35) %, median RS 16 (0-46). Sixty-two patients (79.5%) were postmenopausal. 2 (2.5%), 74 (93.7%) and 3 (3.8%) patients had grade 1, 2 and 3 disease, respectively. 79 (100%) patients had ER positive, 73 (92.4%) patients had PR positive tumors. 20 patients (25.3%) had node positive (1-3 positive lymph nodes) disease. 9 (11.4%) patients received anthracycline- and taxane- containing neoadjuvant chemotherapy. During follow-up 5 (6.3%) patients experienced a locoregional recurrence and 8 (10.1%) patients a distant recurrence. 5 (6.3%) patients died, in 4 cases (5.1%) from breast cancer. The risk for a DFS event increased by 8.1% by every one-unit (integer) in RS (p=0.022). For OS events, every one-unit increase in RS increased the risk of death by 9.3% (p=0.027).

At 5 years, the time-dependent ROC analysis for disease-free survival showed an AUC of 0.70 for the Oncotype DX Recurrence Score, 0.72 for tumor size, and 0.51 for Ki-67. Over the entire 5-year follow-up period, the time-dependent AUC remained stable above 0.5 for Oncotype DX and tumor size, indicating consistent prognostic performance over time.

Conclusions:

In our population of patients with intermediate risk by traditional risk parameters including Ki67 survival was excellent with 93.7% of patients alive after a median follow-up of 6.9 years. However, within this selected risk group the continuous assessment of the RS performed using material from core cut biopsies indicated an increased risk for a DFS or OS event by every one-unit increase in RS, while the discriminatory performance of the RS for disease-free survival was comparable to tumor size and remained stable over time, supporting its consistent prognostic value across the analyzed cohort.

Our analysis is hypothesis-generating and justifies an approach in a multicenter registry population with greater statistical power allowing multivariate analysis and the assessment of confounding parameters. If our results can be reproduced in a large-scale analysis they could help estimate the risk of an individual patient with more granularity than by use of risk groups alone.

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