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Comparison of risk assessment in primary ER+, HER2- Breast Cancer in a real-world data set: classical pathological parameters vs. 12-gene molecular assay (EndoPredict)

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Background

Risk assessment on a molecular level is becoming more common in modern pathology to determine the recurrence risk for patients diagnosed with estrogen receptor-positive (ER+), human epidermal growth factor receptor 2-negative (HER2-) breast cancer (BC). The gene expression test EndoPredict (EP) was trained and validated to predict a 10-year risk of distant recurrence to support therapy decision regarding endocrine therapy alone or in combination with chemotherapy. The EP test provides the 12-gene molecular score (12-gene MS) and the EPclin score combining the 12-gene MS with tumor size and nodal status. In this project we investigated the correlation of 12-gene MS and EPclin score with classical pathological markers like tumor grading and proliferation.

Methods

Retrospectively, we investigated EP test results in a total of 1652 patients tested in routine clinical practice from 2017 to 2020 at the Institute of Pathology, Charité University Hospital, Berlin. Consecutive cases with valid EP test result and available tumor grading and proliferation (Ki67) status were included in the dataset. 12-gene MS and EPclin were classified as low or high risk based on validated cutoff values at 5 and 3.32867, respectively. Ki67 cut-offs were set according to St. Gallen guidelines at 20% for binary classification (Bustreo et al., 2016) and Federal Joint Committee (G-BA) guidelines, using 10% and 30% for three classes (low, intermediate, high).

Tab.1 Baseline parameters of study cohort

	Mean	95% CI	IQR
12-gene MS	6.66	6.55 -6.78	2.97
EPclin	3.59	3.56- 3.63	1.00
	Category	**Frequency N(%)**	
12-gene MS	low (< 5.0)	410 (24.8)	
	high (≥ 5.0)	1242 (75.2)	
EPclin	low (< 3.3)	626 (37.9)	
	high (≥ 3.3)	1026 (62.1)	
Grading	G1	140 (8.5)	
	G2	1328 (80.4)	
	G3	184 (11.1)	
Ki67	low (< 20%)	1203 (72.8)	
	high (≥ 20%)	449 (27.2)	

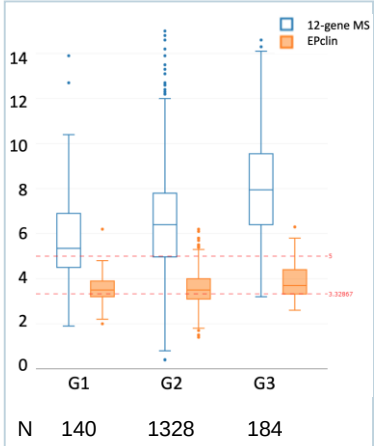

Fig.2 Box-Plots 12-gene MS and EPclin by tumor grading groups. Cut-off for 12-gene MS at 5.0 and for EPclin at 3.3.

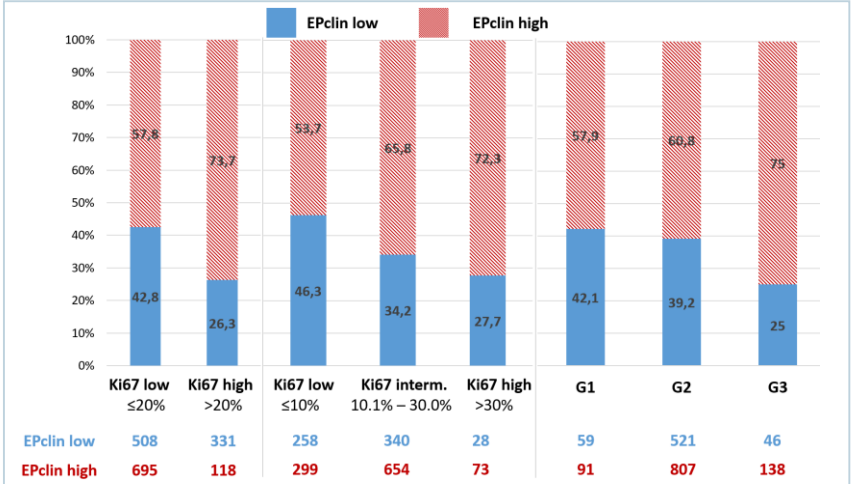

Fig.1 Distribution of EPclin low and high risk according to Ki67 and Grading

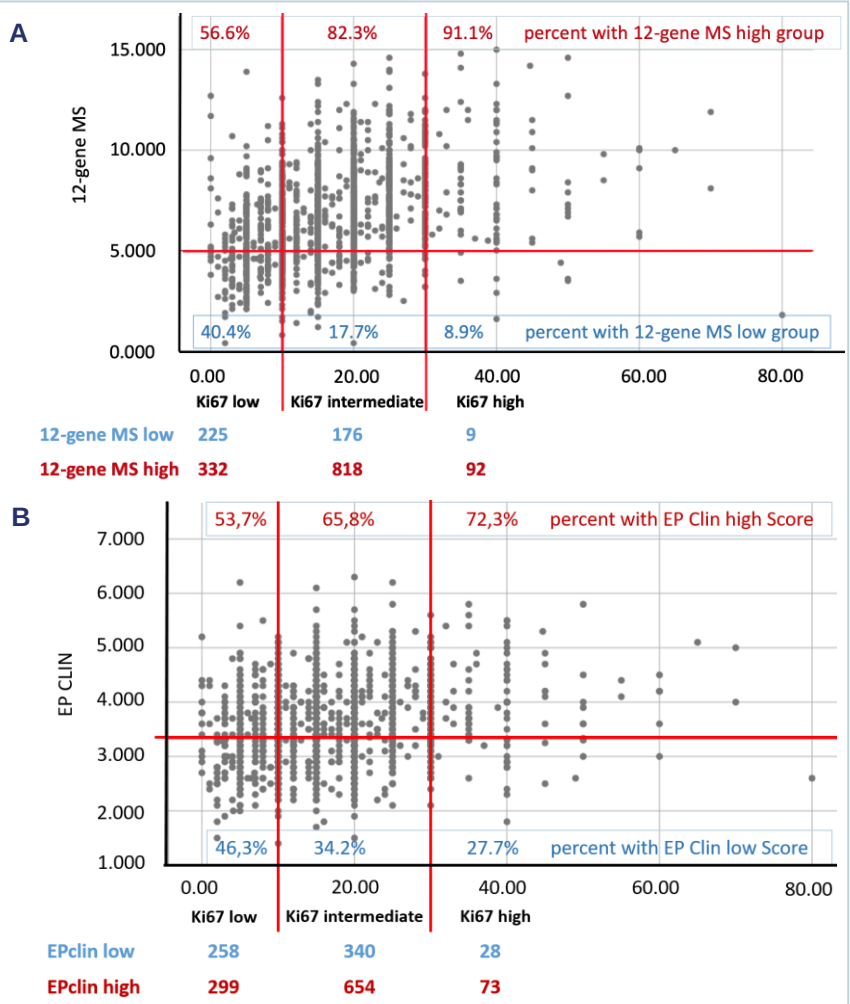

Fig.3 Scatterplot of (A) 12-gene MS and (B) EPclin vs. Ki67 and Ki67 groups. Percent values describe percent of patients in high and low group according to Ki67.

Results

In our dataset with 1652 cases, 1242 (75.2%) cases were detected as 12-gene MS high-risk and 1026 (62.1%) as EPclin high-risk. Mean Ki67 expression was 17.5% (95%CI 16.9 – 17.9). As expected, we found a strong association between risk scores and clinical parameters with p-values ≤ 0.001. In the Ki67 binary low group (N=1203, Ki67≤20%) 695 (57.8%) patients had an EPclin high-risk score. In the Ki67 binary high expression group (>20%) 331 (26.3%) patients had an EPclin low-risk score. Similar results were found using three Ki67 classes. In the Ki67 low (N=557, ≤10%) group 299 (53.7%) patients had EPclin high results and in the Ki67 high (N=101, >30%) group 28 (27.7%) patients were classified as EPclin low (p<0.001). Regarding tumor grading we observed a correlation between poorly differentiated breast cancer (G3) and a higher EPclin risk score. Nevertheless, in Grade 1 tumors (N=140) 57.9% of patients had an EPclin high-risk score (p=0.001). In comparison, in 25% (N=46) of G3 cases EPclin score was low. Similar results were seen using 12-gene MS.

Conclusion

In this study we showed that 12-gene MS and EPclin risks are distributed differently among Ki67 expression groups, especially in Ki67 low (≤10%) and high (>30%) tumors with a substantial proportion of patients with EPclin high-risk results in Ki67 low tumors and vice versa. We are currently collecting longer clinical follow-up information for all patients.

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