HER-2 LOW NON-METASTATIC BREAST CANCER A CLINICO PATHOLOGICAL STUDY

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Introduction

The recently highlighted HER2 low breast cancer (BC) subgroup (IHC 1+ or IHC 2+/ISH negative) has challenged the established binary categorization of BC into HER2 overexpressing tumors and HER2 negative. This raises the question of whether the HER2 low status influences disease phenotype in a manner similar to HER2 overexpression.

Aim of the work

To Identify the prevalence of low HER-2 status among non-metastatic BC patients in comparison to HER-2 negative and HER-2 positive, and to compare treatment outcome of HER-2 low to HER-2 negative non-metastatic BC.

Patients and methods

This retrospective study of 1029 early BC patients diagnosed between 2014 and 2022 in Alexandria university hospitals. Tumors originally reported as HER2 negative were recategorized into HER2 0 and HER2 low based on the results of IHC and FISH. HER2 low and HER2 positive groups were compared to HER2-0 in terms of clinical and pathological features.

Results

192 (18.7%) patients were HER2 positive, 779 (75.7%) were reported as HER2 negative, and were reclassified into 441 (56%) HER2-0, and 338 (43%) HER2 low. 58 (5.6%) patients with undetermined HER2 status were excluded.

HER2 positive were more likely to be associated with negative hormone receptor (HR) status than HER2-0 (32.8% vs. 16.6%; p<0.001). The rate of HER2-low significantly increased as the level of ER expression increased, from 37 of 190 (19.5%) ER-negative to 40 of 143 (28%) ER-low, 94 of 264(35.6%) ER-moderate and 167 of 432(38.7%) ER strong, p=<0.001.

Conversely, negative HR status was less observed in the HER2 low tumors compared to HER2-0 (10.7% vs. 16.6%; p=0.019).

Median age at presentation was significantly lower in HER2 positive compared to HER2-0 (45 years vs. 49 years, p=0.019), while there was no significant difference between HER2 low and HER2-0 (50 years vs. 49 years; p=0.182)

HER2 positive tumors were more likely to be of high grade compared to HER-0 (27.6% vs. 15%; p<0.001), while this difference wasn't observed between HER2 low and HER2-0 (15.7% vs. 15%; p=0.784).

Ki67 level was more likely to be 20 or more in the HER2 positive compared to HER2-0 (87.2% vs. 67%; p=0.011). Conversely, with HER2 low ki67 was less likely to be 20 or more than HER2-0 (45% vs. 67%; p=0.008).

Both HER2 positive and HER2 low were more likely to have a ductal histology compared to HER2-0 (94% vs, 80.4%, p=0.004 and 88.1% vs. 80.4%; p<0.001).

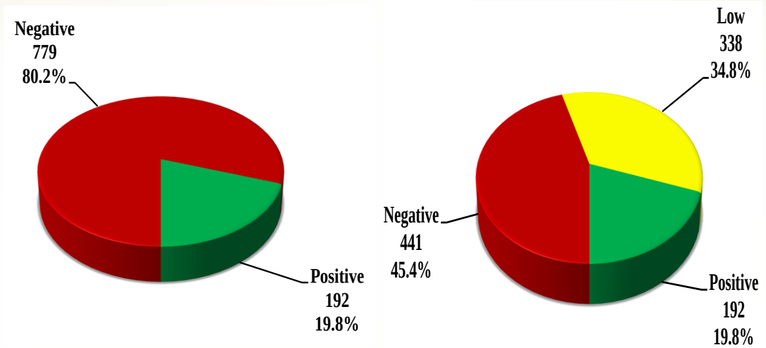

Figure (1) : Distribution of patients based on HER2 Status (n = 971)

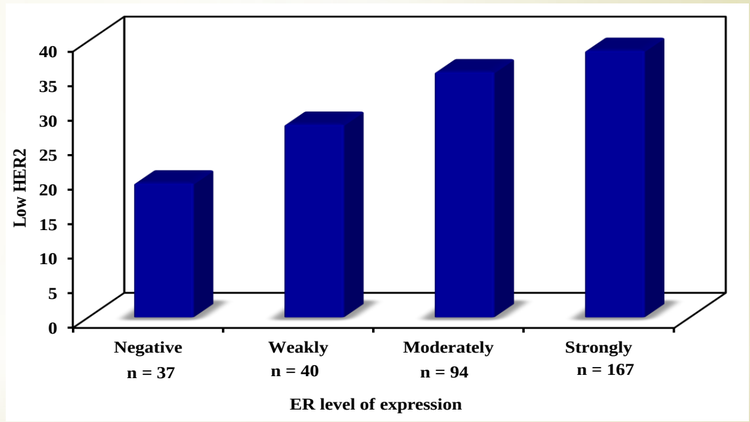

Figure (2) : Relationship between low HER2 and ER level of Expression

Conclusion

The presence of HER2 overexpression appears to impact disease phenotype, a characteristic not observed in the HER2 low group, which challenges the idea of categorizing HER2 low as a distinct subtype from HER2-0.