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Differential expression of the insulin-like growth factor receptor among early breast cancer subtypes.

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Abstract

INTRODUCTION:

We sought to determine the level of protein expression of the critical components of the insulin-like growth factor receptor (IGFR) pathway and to evaluate their prognostic significance across the different early breast cancer subtypes.

PATIENTS AND METHODS:

Archival tumor tissue from 1,021 women with early, node positive breast cancer, who were

prospectively evaluated within two randomized clinical trials, was used to construct tissue microarrays that were stained for hormone receptors (HR), Ki67, HER2, epidermal growth factor receptor (EGFR) and cytokeratins 5/6, to classify tumors into five immunophenotypical subgroups. Immunohistochemical (IHC) expression of IGF1R-alpha and beta subunits, IGF2R and IGF-binding protein 2 (IGFBP2) was assessed using the immunoreactive score (IRS). Repeated internal cross-validation was performed to examine the statistical validity of the cut off points for all biomarkers.

RESULTS:

After a median follow-up time of 105.4 months, overall 370 women (36.2%) had relapsed and 270 (26.4%) had died. Tumors expressing IGF1R-alpha above the median IRS were significantly more frequently HR positive (luminal A+B+HER2), as compared to HER2-enriched and triple negative ones ($p<0.001$ for both comparisons). IGF2R was overexpressed significantly more frequently in HR negative tumors ($p=0.001$) and had an inverse correlation with all other biomarkers. Patients with luminal A and B tumors with high IGF1R-alpha and negative EGFR expression ($N=190$) had significantly higher 4-year survival rates, as compared to the rest (log-rank $p=0.046$), as did patients with luminal A and B tumors with high IGF1R-alpha and low IGF2R expression, as compared to the rest ($N=91$), (log-rank $p=0.035$). After adjustment for significant variables, patients in the latter group had a relative 45% reduction in the risk of death, as compared to the rest ($p=0.035$).

CONCLUSION:

Aberrant expression of components of the IGF1R pathway is associated with better clinical outcomes in women with luminal A and B, node positive, early breast cancer.