Differential expression of senescence tumour markers and its implications on survival outcomes of breast cancer patients

ABSTRACT

Breast cancer is a heterogeneous disease displaying different histopathological characteristics, molecular profiling and clinical behavior. This study describes the expression patterns of senescence markers P53, DEC1 and DCR2 and assesses their significance on patient survival as a single or combined marker with P16 or P14 using breast cancer progression series. One thousand and eighty (1080) patients with primary invasive ductal carcinoma, no special type, were recruited through an 11-year retrospective study period. We constructed tissue microarrays of normal, benign hyperplasia, ductal carcinoma in situ and invasive ductal carcinoma from each patient and performed immunohistochemical staining to study the protein expression. Statistical analysis includes Pearson chi-square, Kaplan-Meier log ran test and Cox proportional hazard regression were undertaken to determine the associations and predict the survival outcomes. P53, DEC1 and DCR2 expression correlated significantly with normal, benign, premalignant and malignant tissues with ($p<0.05$). The expression profile of these genes increases from normal to benign to premalignant and plateaued from premalignant to malignant phenotype. There is a significant association between P53 protein expression and age, grade, staging, lymphovascular invasion, estrogen receptor, progesterone receptor and HER2 whereas DCR2 protein expression significantly correlated with tumour grade, hormone receptors status and HER2 ($p<0.05$ respectively). P53 overexpression correlated with increased risk of relapse ($p = 0.002$) specifically in patients who did not receive hormone therapy ($p = 0.005$) or chemotherapy ($p<0.0001$). The combination of P53+/P16+ is significantly correlated with poor overall and disease-free survival, whereas a combination of P53+/P14+ is associated with worse outcome in disease-free survival ($p<0.05$ respectively). P53 overexpression appears to be a univariate predictor of poor disease-free survival. The expression profiles of DEC1 and DCR2 do not appear to correlate with patient survival outcomes. The combination of P53 with P16, rather P53 expression alone, appears to provide more useful clinical information on patient survival outcomes in breast cancer.