Human Kallikrein Gene 14 (*KLK14*) Expression: An Indicator of Poor Prognosis in Breast Cancer Patients

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The human kallikrein gene 14 (*KLK14)* is a recently identified member of the kallikrein gene family, which harbors several genes aberrantly expressed in various cancers as well as established (Prostate Specific Antigen, PSA, hK3) and potential (hK6, hK10) cancer tumor markers. Similar to other kallikrein genes, *KLK14* was found to be regulated by steroid hormones, particularly androgens and progestins, in breast and ovarian cancer cell lines. Preliminary studies indicate that *KLK14* is differentially expressed in breast, ovarian, prostatic and testicular tumors. The aim of this study was to determine the prognostic significance of *KLK14* expression in breast cancer. We studied *KLK14* expression in 178 histologically confirmed epithelial breast carcinomas by quantitative RT-PCR and correlated expression levels with clinicopathological variables (tumor stage, grade, histologic type etc.) documented at the time of surgery and with outcome [disease-free survival (DFS) and overall survival (OS)] monitored over a median of 76 months. *KLK14* mRNA levels ranged from 0 to 1219 arbitrary units in breast cancer tissues, with a mean ± SE of 136 ± 22. An optimal cutoff value of 40.5 arbitrary units was selected to categorize tumors as *KLK14*-positive or negative. Higher concentrations of *KLK14* mRNA were more frequently found in patients with advanced stage (III) disease ($p = 0.032$). No statistically significant association was found between *KLK14* and the other clinicopathological variables. *KLK14* overexpression was found to be a significant predictor of decreased DFS (hazard ratio of 2.31, $p = 0.001$) and OS (hazard ratio of 2.21, $p = 0.005$). Cox multivariate analysis indicated that *KLK14* was independent prognostic indicator of DFS and OS. *KLK14* is an independent prognostic variable in subgroups of patients with a tumor size ≤ 2 cm, those who are nodal positive, estrogen receptor (ER) positive or progestin receptor positive. We conclude that *KLK14* expression, as assessed by quantitative RT-PCR, is an independent marker of unfavorable prognosis for breast cancer.

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