

PROGNOSTIC VALUE OF PEPSINOGEN C IN BREAST CANCER

Andreas Scorilas, Eleftherios P. Diamandis, Michael A. Levesque, Anastasia Diamandi, M. Javad Koshravi, Maurizia J. Giai, Riccardo Ponzzone, Riccardo Roagna, Piero Sismondi, and Carlos López-Otin. Mount Sinai Hospital, Toronto, Ontario, Canada, University of Toronto, Ontario Canada, University of Turin, Turin, Italy, University of Oviedo, Oviedo, Spain and Diagnostic Systems Laboratories, Canada.

The objective of this study was to evaluate the prognostic value of pepsinogen C (PepC) in breast cancer patients. PepC is an aspartic proteinase involved in the digestion of proteins in the stomach and is also synthesized by a subset of human breast tumors. PepC concentration was measured with a highly sensitive enzyme-linked immunosorbent assay (detection limit 0.2 µg/L, dynamic range up to 10 µg/L, precision 4-12% and mean recovery $103 \pm 2.7\%$). in breast tumour cytosols from 151 patients (median follow-up, 67 months) stratified according to nodal status. First, an optimal cutoff value (1.75 ng/mg of total protein of the extract) was defined by statistical analysis. PepC values were then compared with other established prognostic factors, in terms of disease-free survival (DFS) and overall survival (OS). High PepC status was found more frequently in small ($P=0.003$) and well-differentiated tumors ($P=0.042$) as well as in stage I ($P=0.003$) and node negative patients ($P=0.040$). No significant associations of PepC concentration with age and steroid receptor status were observed. In univariate analysis, negative PepC status proved to be a significant predictor of reduced disease-free ($P=0.0086$) and overall survival ($P=0.025$). Cox multivariate analysis in subgroups of patients as defined by nodal status indicated that PepC status was a strong factor to predict the DFS ($P=0.0039$) and the strongest factor to predict the OS ($P=0.0046$) in node-positive but not in node-negative patients. In conclusion, pepsinogen C may be used as an independent favorable prognostic factor in node-positive breast cancer patients since there is no significant association of PepC with other clinical prognostic factors in this group of patients.