Anticancer Res. 2013 Oct;33(10):4573-84.

The prognostic significance of WNT pathway in surgically-treated colorectal cancer: β-catenin expression predicts for disease-free survival.

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Source

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Abstract

BACKGROUND:

The wingless-type MMTV integration site family of proteins (WNT) pathway is highly involved in colorectal cancer development. The aim of this study was to explore the prognostic significance and clinicopatological correlations of this pathway in a cohort of surgically-treated patients with non-metastatic colorectal cancer in relation to the site of expression of pathway proteins.

MATERIALS AND METHODS:

Immunohistochemical expression of nuclear cyclin D1, membranous E-cadherin and P-cadherin, membranous and nuclear β-catenin in the invasive front (IF), the tumor center (TC), as well as their mean, were assessed in 106 paraffin-embedded tissue samples. Adenomatous Polyposis Coli (APC), Axin-2 (AXIN2), cyclin-D1 (CCND1), Matrix Metalloproteinase-7 (MMP7), Secreted Frizzled Related Protein (SFRP) 1, 2 and 4 and WNT5A were evaluated by RT PCR.

RESULTS:

Membranous β-catenin expression was statistically reduced in the IF. Cyclin-D1 was reduced in tumors arising closer to the rectum. Reduced nuclear expression of cyclin-D1 in the IF was associated with lymphatic, venous and perineural invasion. Loss of membranous β-catenin in the TC was more common among N2 tumors. Higher SFRP4 mRNA was associated with advanced T stage. In univariate analysis, membranous expression of β-catenin in TC and IF, and their mean, was associated with longer disease-free survival (DFS). In multivariate analysis, tumor stage and mean β-catenin expression were prognostic for longer DFS (hazard ratio=0.33; p=0.01). β-Catenin expression in the IF remained significant when the mean expression was not included in the multivariate analysis (hazard ratio=0.41; p=0.028).

CONCLUSION:

Mean membranous expression of β-catenin, as well as that in the IF, is prognostic for longer DFS in patients with non metastatic colorectal cancer.