

Prognostic and predictive factors in colorectal cancer

Akademisk avhandling

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Avhandling baseras på följande delarbeten:

- I Kristoffer Derwinger, Göran Carlsson, Bengt Gustavsson
Stage migration in colorectal cancer related to improved lymph node assessment
European Journal of Surgical Oncology 33 (2007) 849-853
- II Kristoffer Derwinger, Göran Carlsson, Bengt Gustavsson
A study of lymph node ratio as a prognostic marker in colon cancer
European Journal of Surgical Oncology 34 (2008) 771-775
- III Kristoffer Derwinger, Yvonne Wettergren, Elisabeth Odin, Göran Carlsson,
Bengt Gustavsson
A study of the MTHFR gene polymorphism C677T in colorectal cancer
Accepted Clinical Colorectal Cancer, in press
- IV Irina Corin, Kristoffer Derwinger, Lisa Larsson, Jörgen Bergström, Bengt
Gustavsson
A study of the expression of Cyclin E and its isoforms in tumour and adjacent
mucosa, correlated to patient outcome in early colon cancer
Submitted British Journal of Cancer



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Abstract

Aim: The aim of the thesis was to study prognostic and predictive factors in patients treated for colorectal cancer (CRC).

Method: In paper I, a retrospective comparison was made between the patients treated in 1999 (n=180) with those treated in 2004 (n=175). During the period, a multidisciplinary team conference and an improved cooperation with the pathologists had been initiated. The focus of interest was the lymph node assessment, its' development and how this affected clinical staging and treatment. In paper II, the lymph node diagnostics were studied in patients with stage III colon cancer 1999-2003 (n=265). Prognostic markers were evaluated along with the use of the lymph node ratio as a prognostic indicator to differentiate the risk assessment within the stage group. In paper III, single nucleotide pair (SNP) gene analyses was made for the metylenetetrahydrofolate reductase (MTHFR) gene polymorphism C677T in patients treated for colorectal cancer 1999-2006 (n=544). The functional polymorphisms were then correlated to pathology, stage, outcome and side effects of chemotherapy. Comparisons of genotype prevalence were made against a cohort of 299 blood donors as well as the pathology data of the other 1256 patients treated during this period. In paper IV, the presence of cyclin E in both tumour and mucosa was studied in 114 patients with stage I/II colon cancer treated 2003-2007. The expression was analyzed in both tumour and adjacent mucosa and the results were correlated to pathology, staging and prognosis.

Results: In paper I, an improved lymph node assessment was shown to lead to stage migration and thus an increase of patients with stage III disease. A highly variable outcome in stage II associated to an inadequate assessment was also found. In paper II, stage III disease was found to have heterogeneous survival prognosis and the lymph node ratio was a significant marker for the outcome ($p < 0.001$). In paper III, no correlations between polymorphism genotype and the risk of cancer or cancer stage were found. There was a significant correlation to the risk of suffering side-effects ($p < 0,05$) and to the outcome in stage III colon cancer ($p < 0,003$). In paper IV, cyclin E was found to be expressed in both full length form and shorter isoform in both tumour and adjacent mucosa. A high total expression of cyclin E correlated significantly to the risk of tumour recurrence ($p < 0,0063$).

Conclusion: The lymph node assessment is a key factor in CRC pathology and of importance for both clinics and research. Additional prognostic information can be gained in stage III colon cancer by use of the lymph node ratio. The function of the folic acid metabolism can affect the risks associated with 5-fluorouracil treatment and also the outcome in stage III colon cancer. Cyclin E is expressed in both tumour and mucosa and could be an independent prognostic factor in stage I/II colon cancer.

Key words: Colorectal cancer, TNM, staging, lymph nodes, metastasis, MTHFR, cyclin E