Experimental and population-based studies on colorectal cancer

Thymidine phosphorylase as a potential biomarker

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av
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Avhandlingen baseras på följande delarbeten:

I. Elinor Bexe Lindskog, Yvonne Wettergren , Elisabeth Odin , Bengt Gustavsson, Kristoffer Derwinger
Thymidine phosphorylase gene expression in stage III colorectal cancer
Clin Med Insights Oncol. 2012; 6: 347-353

II. Kristoffer Derwinger, Elinor Bexe Lindskog, Erik Palmqvist, Yvonne Wettergren
Changes in thymidine phosphorylase gene expression related to treatment of rectal cancer
Anticancer Res. 2013; 33(6): 2447-51

III. Elinor Bexe Lindskog, Kristoffer Derwinger, Bengt Gustavsson, Peter Falk, Yvonne Wettergren
Thymidine phosphorylase expression is associated with time to progression in patients with metastatic colorectal cancer
BMC Clin Pathol. 2014; 14: 25

IV. Elinor Bexe Lindskog, Katrín Ásta Gunnarsdóttir, Kristoffer Derwinger, Yvonne Wettergren, Bengt Glimelius, Karl Kodeda
A population-based cohort study on adherence to practice guidelines for adjuvant chemotherapy in colorectal cancer
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Experimental and population-based studies on colorectal cancer
Thymidine phosphorylase as a potential biomarker

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Background: Colorectal cancer (CRC) is one of the most common malignancies, and the only reliable treatment option for cure is surgery.

Method: Quantitative real-time polymerase chain reaction was used to analyze the gene expression of the enzyme thymidine phosphorylase (TP), which was related to prognostic factors (paper I, n=254), evaluated as a predictive factor (paper III, n=125), and assessed by change of treatment (paper II, n=28). Data from the Swedish Colorectal Cancer Registry were retrieved and analyzed in order to assess adherence to present clinical guidelines (n=34,000).

Results: In stage III CRC, TP analyzed in tumor tissue correlated with lymph node staging, with higher expression levels relating to a greater number of positive nodes and a worse N-stage. Higher TP expression was also associated with a worse histological tumor grade. Rectal cancer exhibited significantly higher TP expression in mucosa and tumor tissue compared to colon cancer. There was a significant increase of TP gene expression when comparing rectal cancer biopsies before and after radiotherapy. In addition, a decrease in TP levels was noted after chemotherapy. In patients with metastatic CRC, time to progression was significantly longer in patients with high TP expression, but there was no correlation to tumor response rate or palliative survival.
The factors associated with adherence to guideline treatment in colon cancer stage III patients were lower age, less comorbidity, worse N-stage, and presence of a multidisciplinary team conference. One-third of the patients started their adjuvant chemotherapy more than eight weeks after surgery.

Conclusion: TP may be useful in prognostic and predictive situations. TP is affected by radiotherapy, which might be used in clinical settings. However, there are conflicting results, and TP and the methods of analyzing TP need to be evaluated further in larger studies. The adherence to guideline treatment in colon cancer stage III is acceptable in younger and healthier patients. In addition, there is scope for shortening the waiting time until the start of chemotherapy.

Keywords: colorectal neoplasms, thymidine phosphorylase, chemotherapy, adjuvant, biological markers, prognosis, practice guidelines, radiotherapy

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