Tumor M2-PK Stool Test: A screening tool for colorectal cancer

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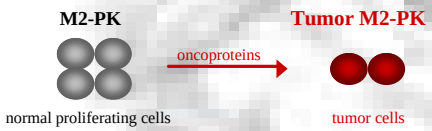
Introduction

Colorectal Cancer (CRC) is the fourth most common cause of tumor-related death worldwide. In Europe, almost 217,000 patients are newly diagnosed each year with CRC, and about 111,000 people die from CRC. As a non-invasive test the screening of stool samples for occult blood has been established. This method is helpful, but could give only a hint of events related to colorectal cancer in about 30% of cases [1]). The search for an appropriate screening marker is an important element in the framework of an improved prognosis of colorectal neoplasia.
Proliferating cells, especially tumor cells, express a special isoenzyme of pyruvate kinase, termed M2-PK which can occur in a tetrameric form with a high affinity to its substrate phosphoenolpyruvate (PEP) and in a dimeric form with a low PEP affinity (http://www.metabolic-database.com). In tumor cells the dimeric form is usually predominant and is therefore termed *Tumor M2-PK*.



Determinations of *Tumor M2-PK* in EDTA-plasma samples of patients with gastrointestinal tumors revealed an upregulation of Tumor M2-PK in oesophageal, gastric, colonic and rectal carcinomas [2, 3, 4].

Recently it could be shown that Tumor M2-PK can be quantified in feces of patients with colorectal tumors [5].

Material and Methods

The present study includes 276 patients that underwent complete colonoscopy after the determination of Tumor M2-PK in stool. Stool samples of patients with colorectal cancer and patients without pathological findings were tested. Histology was obtained from the routine biopsies and/or from surgery. Tumor M2-PK in stool extracts was determined immunologically with a new quantitative sandwich-type enzyme immunoassay (ScheBo® • Tumor M2-PK™) which is based on two monoclonal antibodies (ScheBo® • Biotech AG, Germany).

Groups	n	Mean [U/ml]	Median [U/ml]	Range [U/ml]
Colorectal cancer	116	53.5 ± 9.7	23.8	0.11 – 800.0
Colon Cancer	70	65.3 ± 15.3	31.5	0.11 – 800.0
Rectal Cancer	46	35.6 ± 7.1	13.2	0.48 – 215.0
Controls	160	3.2 ± 0.4	1.5	0.11 – 34.3

Table 1: Fecal Tumor M2-PK levels in patients with colorectal cancer and controls

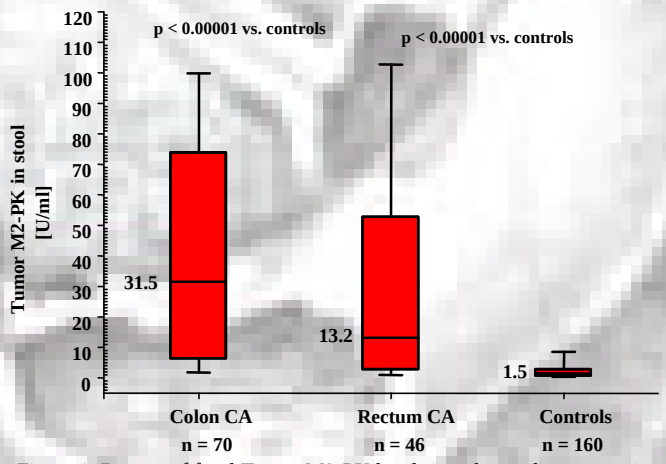


Figure 1: Ranges of fecal Tumor M2-PK levels in colorectal cancer patients and controls

Results

Data from 160 controls and 116 patients with colorectal cancer and have been evaluated to date (Figure 1 and Table 1). There is a highly significant difference ($p < 0.00001$) between tumor patients and controls. At a cut off point of 4 U/ml, the sensitivity was calculated to be 84% for colon cancer and 74% for rectal cancer and the specifity as 81%. The intra-assay variance was evaluated by 18-fold determination of five samples (5 – 66 U/ml), giving an average coefficient of variance (CV) of 7.9% (3.5 - 13.6%). The inter-assay variance was calculated with five samples 4 - 73 U/ml, tested on ten different days. The mean CV was 7.3 % (3.8 - 12.6%).
Fecal Tumor M2-PK levels are correlated with tumor size and inversely correlated with tumor differentiation (data not shown).
In comparison to a variety of indirect tests that detect blood in stool with a sensitivity less than 30% Tumor M2-PK has a much higher sensitivity, when a single spot stool sample is analyzed. The test directly detects a tumor-specific enzyme that is released by the tumor itself. Tumor M2-PK has the potential as a screening tool for the early detection of colorectal cancer.

Conclusions

The fecal levels of Tumor M2-PK are significantly higher in patients with colorectal cancer than in the healthy control group ($p < 0.00001$) and suggest that Tumor M2-PK levels are correlated with tumor size and histology. Overall specificity is 81 % and sensitivity is 80%.
The present study shows that the determination of Tumor M2-PK in the stool is a valuable tool for the detection of colorectal cancer in individuals without prior endoscopic evidence of colorectal neoplasms.

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