Pyruvate kinase M2 (Tumor M2-PK) as a screening tool for colorectal cancer (CRC). A review.

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Introduction: Colonoscopy is currently supposed to be the best screening tool for colorectal cancer. However, the acceptance of this method is very poor, although it has been included in screening programs in the German health system since 2002. Therefore, evaluation of additional screening tools seems of great interest. Recently, testing for fecal occult blood (FOBT), genetic alterations or alterations in tumor metabolism (e.g. Tumor M2-PK) is under investigation.

Methods: The use of M2-PK measurement in the feces has been reported in 6 studies (original papers and abstracts) until today. The data of these studies were analysed and critically reviewed.

Results: The overall sensitivity of M2-PK was 77.9% concerning CRC. Specificity ranged from 74.3% (endoscopic controls) to 83.3% (general population). Overall results are given in table 1; study details are shown in table 2. The lower specificity in endoscopic controls may be due to the fact that these patients had a clinical indication for colonoscopy and therefore diseases of the upper GI tract seemed not to be unlikely. Overall sensitivity for adenomas was 45.9%, increasing to 61.1% for adenomas larger than 1 cm. A high percentage of positive results (90.4%) was also observed in patients with chronic inflammatory bowel disease.

Table 1: Results of present studies concerning the use of M2-PK in feces for CRC screening

<table>
<thead>
<tr>
<th>Author</th>
<th>Type of Study</th>
<th>Included Patients</th>
<th>Mean Age</th>
<th>Study Population</th>
<th>Reason for Colonoscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hardt PD et al., 2003 [7]</td>
<td>Uncolorectal, transanal study</td>
<td>79 (82.5)</td>
<td>62.8 years</td>
<td>CRC, IBD, adenoma, 47 healthy controls</td>
<td>Indication for colonoscopy for different reasons</td>
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<tr>
<td>Haug U et al., 2004 [9]</td>
<td>Endoscopy, prospective study</td>
<td>48 (90.0%)</td>
<td>50 years</td>
<td>CRC, IBD, adenoma</td>
<td>Indication for colonoscopy for different reasons</td>
</tr>
<tr>
<td>Voller T et al., 2004 [11]</td>
<td>Multicenter, prospective study</td>
<td>3/5 (75.6%)</td>
<td>50 years</td>
<td>CRC, IBD, adenoma</td>
<td>Indication for colonoscopy for different reasons</td>
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Conclusions: According to the results of this meta-analysis the M2-PK-Test appears to be superior for CRC screening as compared to FOBT and genetic testing. Sensitivity for FOBT is reported to be 40% for CRC [1,2] and <20% for adenomas [2]. Specificity for FOBT is reported to be 20-98% [3]. However, false-positive results are seen in up to 80% of symptomatic patients [4]. One major reason for the limitations of FOBT is that many carcinomas do not bleed at all or bleed only intermittently [5,6].

Testing for multi-target genetic alterations seems to be promising with a reported sensitivity of 63-100% [4]. Yet, the limitations of this screening tool are its high costs and the very limited handling and shipping time of the feces.

Colonoscopy is supposed to be the gold standard of CRC screening. However, a procedure that is not accepted by the screening population can hardly be successful. Concerning handling, effectiveness and costs M2-PK seems to be a good possibility for large scale screening of colorectal carcinoma. It might even be used to detect larger adenomas. Elevated M2-PK in patients with acute and/or chronic inflammatory bowel diseases are probably due to proliferation of epithelial cells and leukocytes in the inflammatory area. Since IBD patients are subject to endoscopic surveillance anyway, they are not part of the population to be included in general CRC screening programs. Therefore, M2-PK elevation in IBD patients is not a limitation for the use of this marker in general population screening.

According to the presented data, M2-PK testing in the feces should be recommended for general population screening because of its superior performance.

References:

Table 2: Study design of the currently available studies concerning the use of M2-PK in feces as a screening tool for CRC.

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<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Hardt PD et al., 2004 [8]</td>
<td>Multicentric retrospective study</td>
<td>204 (p&lt;0.05)</td>
<td>54 years</td>
<td>CRC, IBD, adenoma</td>
<td>Indication for colonoscopy for different reasons</td>
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<tr>
<td>Naumann M et al., 2005 [9]</td>
<td>Multicentric, prospective study</td>
<td>232 (90.4)</td>
<td>60-75 years</td>
<td>CRC, IBD, adenoma</td>
<td>Indication for colonoscopy for different reasons</td>
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