

LETTERS TO THE EDITOR

Fecal tumor M2 pyruvate kinase is not a specific biomarker for colorectal cancer screening

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Table 1 Comparison of published studies using Fecal M2-PK assay (cut-off value 4 U/mL) for CRC screening (adapted from Shastri *et al*^[2])

Authors	Study design	Patient No. (M/F)	Average age (yr)	Sensitivity (%)		Specificity (%)	
				CRC	Polyp	CRC	Polyp
#Hardt ^[4]	Single centre, retrospective	78 (58/29)	68.2	69	50	-	-
Hardt ^[5]	Multicenter, retrospective	204 (NA)	NA	73	-	78	-
Naumann ^[6]	Multicenter, prospective	232 (129/112)	NA	85	37	65	-
Vogel ^[7]	Multicenter, prospective	138 (61/77)	58	77	48	72	-
Shastri ^[2]	Multicenter, prospective	317 (152/165)	56	81	26	71	71
Tonus ^[1]	Single centre, retrospective	96 (54/42)	66	78	-	93	-

Colonoscopy was not done to compare the results of M2-PK. CRC: colorectal cancer; M: male; F: female; NA: not available.

TO THE EDITOR

We read with great interest and a bit of surprise the article by Tonus *et al*^[1]. We would share herein our comments about it. The specificity of the fecal tumor M2 pyruvate kinase (M2-PK) reported by Tonus *et al*^[1] for diagnosing colorectal cancer (CRC) is 93%. This is considerably higher than in any of the previously published studies. In our work^[2], the maximum specificity of fecal M2-PK is 78% (Table 1). There is a vast difference of 15% between the previous studies and the current study of Tonus *et al*^[1], which is difficult to explain. We are skeptical about such a high specificity reported by the authors^[1]. Is their observation an 'outlier' as compared to the available studies till now? Although few reports in the abstract form have shown that M2-PK has performance characteristics with specificities exceeding 90%, none of them have ever been published. Most of these studies reported in abstracts form involve a small number of patients and are retrospective.

There are some questions about the study design of this paper^[1]: (1) The total number of patients included in the study was significantly small (96 patients) with the control group (42 patients), in fact it is smaller than the patients having CRC. (2) The diagnosis of CRC was known before performing the screening tests, has this biased the results of fecal M2-PK tests? (3) Calculation of the receiver operating curve (ROC) using the individual values of fecal M2-PK could have helped determine whether the cut-off value of fecal M2-PK used is appropriate.

The main shortcoming of M2-PK is that it is rather an indicator of inflammation than cancer per se. It is positive in patients with different colorectal diseases irrespective of their etiology (whether CRC, IBD, diarrhea, diverticulitis, pouchitis *etc*) as demonstrated by Herzig group in a study of patients with ileal pouch-anal anastomosis (IPAA)^[3]. In our study, it is also positive in about 88% of patients with inflammatory bowel disease (Crohn's disease and ulcerative colitis)^[2].

As has been discussed previously, Fecal M2-PK is a weak screening biomarker for CRC with a low specificity and can not be recommended for application^[2]. The low specificity of the test could lead to a high rate of false positive results triggering the need for colonoscopy in all these subjects. This could prove hazardous for the society due to the costs, risks and the manpower utilization associated with all these unwanted and unindicated colonoscopies.

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