EVALUATION OF QUANTITATIVE DETECTION OF FECAL HUMAN HAEMOGLOBIN FOR COLORECTAL CANCER SCREENING

Kocna P., Vaníčková Z., Kovářová J., Krechler T., Kohout P., Beneš Z., Granátová J.

Institute of Clinical Biochemistry and Laboratory Diagnostics, 4th Internal Department - 1st Medical Faculty of Charles University & General Faculty Hospital, 2nd Department of Medicine, Department of Clinical Chemistry; Faculty Thomayer Hospital; Prague, Czech Republic

ABSTRACT

Introduction: Colorectal cancer (CR-CA) screening in the Czech Republic has been done for thirty years using guajac Haemoccult test. Quantitative immunochemical fecal occult blood test (qi-FOBT) appears to be far the best in the world at present. This study evaluates this qi-FOBT for screening in the Czech Republic.

Patients and methods: 813 consecutive patients indicated to colonoscopy were enrolled to this study. Immunochemical quantitative tests were run using OC- SENSORμ analyser (EIKEN, Japan). Values of qi-FOBT (ng/ml) were calculated as mean of two samples, and optimal cut-off value was evaluated in the range 75 - 150 ng/ml.

Results: Values of qi-FOBT (mean ± SD) were 45.4 ± 70.9 in the control group, 73.9 ± 106.2 for small polyps <10 mm, 776.5 ± 721.1 for advanced polyps >10 mm and 782.5 ± 387.5 for CR-CA cases. With cut-off value 75 ng/ml was the sensitivity 75 %, specificity 84 %, accuracy 82 %, positive predictive value 50.5 % and negative predictive value 95.5 % to detect advanced polyps and tumors compared to control group.

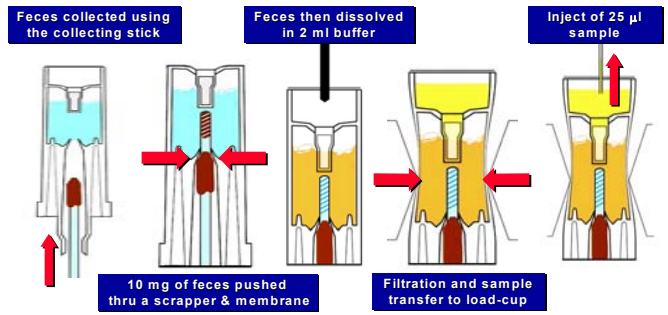
Conclusions: Quantitative aspect of immunochemical detection of haemoglobin in the stool clearly offers new dimension for non-invasive laboratory screening of colorectal cancer. This multicenter study of 813 patients evaluated by colonoscopy will now be used as analytically defined background for CR-CA screening population study in the Czech Republic.

OC-SENZORμ - ANALYSER

- Fully automated FOB analyzer
- Latex agglutination immuno-turbidimetry
- One step rate assay
- Throughput 80 samples / hour
- Disposal acrylic 5 mm cuvette
- Thermostatic 37 °C block heater
- Reagent storage 25 °C block heater
- Light source L.E.D. - 660 nm
- Light detector - silicon photo diode
- Memory capacity 999 test results
- Built-in thermal printer + RS-232C
- Built-in barcode reader

OC-SENSOR SAMPLING CASETTE

OC-Sensor sampling devices were optimized to semi-quantitative fecal quantity (10 mg ± 10%), stabilizing extraction, filtration of heterogenous fecal solution and injection of 25 μl to measuring cuvette.



METHODS

813 patients (410 men, 413 women, mean age 57.4 years) were included to this study. 22 patients were exluded (menses and hematuria during stool sampling) total colonoscopy was performed on 682 patients (83.88%) partial colonoscopy, with double-contrast barium enema or CT colography, was performed in 109 patients (13.37%).

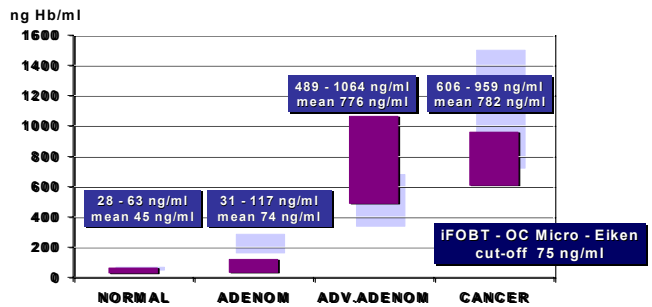
Group	Finding	Count	%	Mean	95%CI
1	Normal	189	23.19	26.43	14.63 - 38.23
1h	Hemorrhoids	226	27.73	61.26	30.60 - 91.90
1+1h	Normal incl. hemor.	415	45.40	45.40	27.84 - 62.94
2	Polyp ? 9mm	170	20.86	73.90	30.78 - 117.01
3	Polyp ? 10mm	43	5.28	776.51	488.63 - 1064
4	Carcinoma	31	3.80	782.48	605.76 - 959.19
5	Inflammation	73	8.96	523.32	384.10 - 662.52

RESULTS

Group	Finding	Mean	First	Highest
1	Normal	47.58	45.39	75.19
2	Polyp ? 9mm	69.07	73.90	108.23
3	Polyp ? 10mm	788.26	776.51	896.53
4	Carcinoma	773.08	782.48	947.23
V2	neoplasia/dysplasia	15.97	15.96	21.91
V3	neoplasia/dysplasia	167.57	152.15	370.77
V4	neoplasia/dysplasia	600.60	668.57	722.85
V5	neoplasia/dysplasia	708.74	708.8	877.63
5	Inflammation	577.20	523.32	766.14

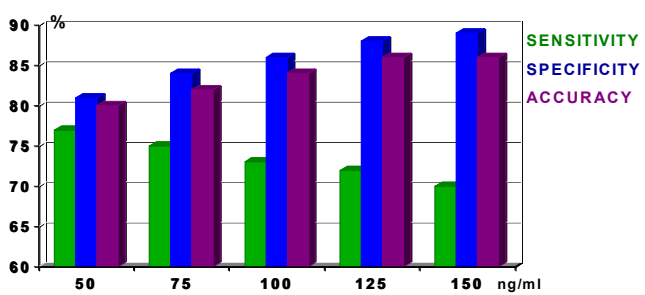
Schlemper RJ et all. Gut 2000, 47: 251: The Vienna classification of gastrointestinal epithelial neoplasia
V1 Negative for neoplasia/dysplasia V2 Indefinite for neoplasia/dysplasia
V3 Non-invasive low grade neoplasia - low grade adenoma/dysplasia
V4 Non-invasive high grade neoplasia: 4-1 High grade adenoma/dysplasia, 4.2 Non-invasive carcinoma (carcinoma in situ), 4.3 Suspicion of invasive carcinoma
V5 Invasive neoplasia: 5.1 Intramucosal carcinoma, 5.2 Submucosal carcinoma or beyond

STUDY IN THE CZECH REPUBLIC



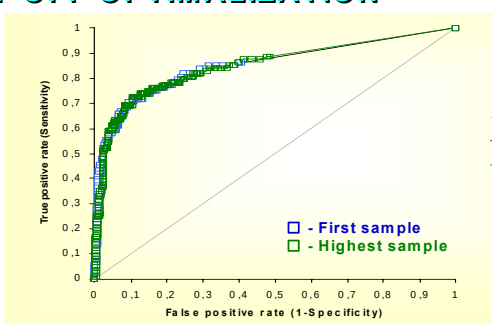
Results of this study - 2008 in the Czech Republic are compared with results published by *Levi Z. et all.* *Ann Intern Med. 2007;146:244-255: A Quantitative Immunochemical Fecal Occult Blood Test for Colorectal Neoplasia*

CUT-OFF OPTIMALIZATION



Parameters of qI-FOBT for Clinically Significant Neoplasms for different fecal hemoglobin thresholds for the higher of the two tests. Specificity, sensitivity and accuracy for range 50 - 75 -100 - 125 and 150 ng/ml Hb.

CUT-OFF OPTIMALIZATION



ROC analysis of group 1 - control group against group of clinically significant neoplasms for both the first and the higher of the two tests

CONCLUSIONS

- **Quantitative aspect of immunochemical detection of haemoglobin in the stool clearly offers new dimension for non-invasive laboratory screening of colorectal cancer.**
- **This multicenter study of 813 patients evaluated by colonoscopy was used to optimize screening parameters using OC-Sensor tests.**
- **Sensitivity, specificity and accuracy of the first test, the mean of the two tests, and the higher of the two tests, relative to the cut-off values of 50,75,100,125,150 ng/mL of hemoglobin in the stool in the group having clinically significant neoplasms and in the group having confirmed colorectal carcinoma were statistically evaluated.**
- **The optimal cut-off for population screening in the Czech Republic was found to be 75 ng/ml and the number of tests required was found to be one.**
- **We calculated the sensitivity 75 %, specificity 84 % and accuracy 82 % for cut-off value 75 ng/ml.**

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