

# A COMPARISON OF THE IMMUNOCHEMICAL FECAL OCCULT BLOOD TEST, TOTAL COLONOSCOPY AND FLEXIBLE SIGMOIDOSCOPY FOR DETECTION OF ADVANCED NEOPLASIA

Iovănescu Dana<sup>1</sup>, Carmen Neamtu<sup>1\*</sup>, Miuțescu Eftimie<sup>1</sup>, Miutescu Bogdan Petru<sup>1</sup>, Burlea Amelia, Ciprian Duta<sup>3</sup>, Bogdan Totolici<sup>1</sup>

<sup>1</sup>„Vasile Goldiș” Western University of Arad – Faculty of Medicine, Pharmacy and Dental Medicine, Arad, Romania

<sup>2</sup>Department of Pathology, County Hospital Arad, Romania

<sup>3</sup>„Victor Babes” University of Medicine and Pharmacy Timisoara, Second Surgical Clinic, Timisoara, Romania

**ABSTRACT.** Colorectal cancer is a major health issue in the European Union but the disease is particularly suitable for screening. Screening for colorectal cancer using fecal occult blood testing, flexible sigmoidoscopy, or colonoscopy is recommended. The aim of this study was to compare the effectiveness of colonoscopy, flexible sigmoidoscopy and fecal immunochemical tests in detecting advanced neoplastic lesions. A number of 45 patients, 21 males and 24 females, were investigated using colonoscopy, flexible sigmoidoscopy and fecal immunochemical tests. Colonoscopy found 9 patients with advanced neoplasia: 6 with cancer and 3 with advanced adenomas. Fecal immunochemical test were positive in 4 cases of advanced neoplasia and flexible sigmoidoscopy revealed 3 cases. Colonoscopy is the mainstay in colorectal cancer screening but fecal immunochemical tests and flexible sigmoidoscopy can also play a role, because compared with no screening, any of the common screening strategies will reduce mortality.

**KEY WORDS.** screening, colorectal carcinoma, advanced neoplasia, adenoma, colonoscopy, sigmoidoscopy, fecal immunochemical tests

## INTRODUCTION

Colorectal cancer is a major health issue in the European Union where it represents the second most common fatal malignancy after lung cancer (Ferlay J et al., 2008).

However many of these deaths could be avoided through systematic early detection of colorectal lesions, before they become symptomatic. The disease begins as a benign adenomatous polyp, which develops into an advanced adenoma with high-grade dysplasia and then progresses to an invasive cancer (Kinzler KW et al., 2002; Markowitz SD et al., 2009). The average duration of the development of an adenoma to colorectal cancer is estimated to take at least 10 years. The prolonged natural history of this cancer affords time to detect and eliminate early neoplastic lesions before they reach an advanced stage (Bresalier RS et al., 2010) and make the disease particularly suitable for screening.

The Council of the European Union recommended in 2003 implementation of population-based screening programmes using evidence based tests for colorectal cancer (Quirke P et al., 2012). U.S. Preventive Services Task Force recommends screening for colorectal cancer using high-sensitivity fecal occult blood testing, flexible sigmoidoscopy with interval fecal occult blood testing, or colonoscopy (U.S. Preventive Services Task Force 2008; Pignone M et al., 2002). Colonoscopy is considered to be the gold standard against which the sensitivity of other colorectal cancer screening tests is compared. A successful screening programme should be adapted to suit healthcare system. When deciding which test to use several factors should be considered: staff (doctors, nurses, and laboratory staff), availability of endoscopy units.

## AIM

The aim of this study was to compare the effectiveness of colonoscopy, flexible sigmoidoscopy and fecal immunochemical tests in detecting advanced neoplastic lesions, in order to assess the possibility of implementing a screening programme in Romania.

## MATERIALS AND METHODS

This is a retrospective study. The patients referred to the outpatient clinic in the County Hospital Arad who performed immunochemical test, flexible sigmoidoscopy and colonoscopy between January 2012 and December 2014 were assessed. We used the rapid immunochemical test HEM-CECK 1 (VedaLab, France) in this study. The patients were instructed how to collect the stool sample by scraping the probe attached to the cap of a sampling bottle over a broad area of the stool surface. The sample is placed in the sampling bottle and is collected at the laboratory in the first 24 hours. The test contains antibody raised against human globin and has no reaction with animal hemoglobin or foodstuff (fruits or vegetables) that contains compounds with peroxidase activity. Because there is no dietary interference the test does not require dietary restrictions. Colonoscopy is the mainstay of the examination of the colon but it is not perfect – it is invasive, uncomfortable, requires bowel preparation and harms may arise from the preparation the patient undergoes to have the procedure, the sedation used during the procedure, and the procedure itself an invasive procedure, with a small but not insignificant risk of major complication perforation, post excision haemorrhage. In Romania there are insufficient capacity of endoscopy units, so flexible sigmoidoscopy can be an alternative. Only the left-sided colon can be inspected but the procedure is less time consuming, no sedation is needed and bowel preparation is simpler but if during the examination a polyp is detected, a colonoscopy is needed.

Colonoscopy and flexible sigmoidoscopy were performed after prior informed consent.

Before colonoscopy all patients were given written instructions containing diet recommendations (a low-residue diet for all of the day before colonoscopy) and the colonic cleansing protocol. A split-dose bowel cleansing regimen of 4l Polyethylene glycol-electrolyte lavage solution was used. Propofol deep sedation was used at colonoscopy. Before sigmoidoscopy we used a bowel preparation consisting of a single enema self-administered at home or at the endoscopy unit.

If polyps were detected at colonoscopy they were endoscopically removed and those

recovered were retrieved for histological examination. If a colon cancer was detected, biopsies were taken. The exclusion criteria were rectal bleeding, incomplete colonoscopies, missing of the histology report (no material retrieved, or patient refusing biopsy, no biopsy taken).

The following data were registered for each patient: age, gender, the result of the fecal immunochemical test, the sigmoidoscopy and colonoscopy report with polyp number, size, location (right-sided or left sided, right-sided colon location was defined between the splenic flexure and the cecum) histologic type, the degree of dysplasia. Advanced neoplastic lesions were defined as cancer or adenomas that are larger as 10 mm, have villous architecture or manifest high-grade dysplasia.

Statistical analysis was performed.

## RESULTS AND DISCUSSIONS

A number of 45 patients, 21 males and 24 females, were investigated using colonoscopy, flexible sigmoidoscopy and fecal immunochemical tests. The mean age was 63.22 years (44 – 77 years).

In 28 patients, 13 males and 15 females, no significant lesions were found at colonoscopy and sigmoidoscopy. The mean age was 65.57 (52 – 77 years). The fecal immunotest was negative in 24 patients but in 4 cases we found false positive results.

Cancer was found in 6 (13.3%) patients (1 male and 5 females), the mean age was 61.5 years (53 - 67 years) (**Fig.1**). In 3 patients the location of the lesion was right-sided, in 2 patients the location was left sided and one of the patients was detected with synchronous cancers located both in the right and in the left colon. Three patients also were detected with polyps – in two patient they were small low risk adenomatous polyps located in the opposite part of the colon compared with the tumor, but in one case an advanced polyp (20 mm in size, exhibiting a tubulovillous histology and high grade dysplasia) was detected.

Only 4 of the 6 patients detected with cancer had a positive immunochemical test (**Fig.2**), 2 of the patients were missed (the patient with synchronous neoplasm and another patient with a left sided lesion). Flexible sigmoidoscopy, as expected, was not able to detect the right sided lesions. Sigmoidoscopy revealed 2 patients with cancer and in another patient it revealed a polyp-finding that would be indication for additional colonoscopy. Combining immunochemical test with flexible sigmoidoscopy would detect all the 6 cancer patients.

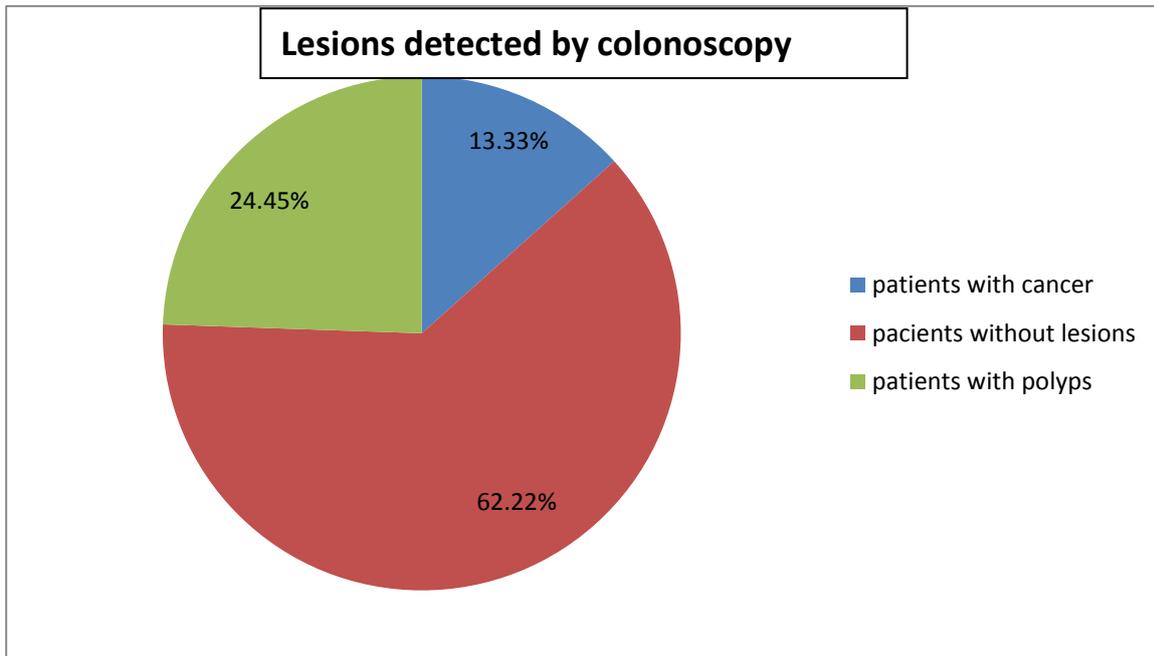


Fig 1: The results of colonoscopy

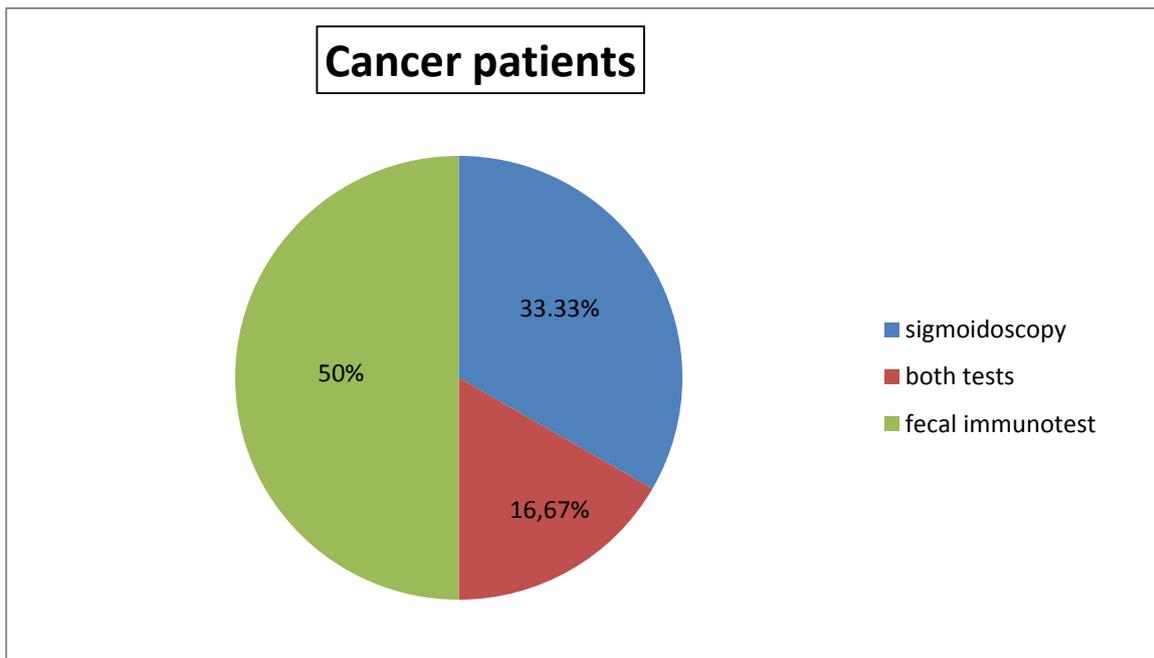


Fig 2: Cancer detected by sigmoidoscopy and fecal immunochemical test

In other 11 patients, 7 males and 4 females, with a mean age of 58.18 years (44.73 years) colonoscopy detected polyps. A number of 32 polyps were found, two patients were found harbouring only one polyp, and the others were detected with more than one polyp. Four patients were found only with hyperplastic lesions, 3 patients had only adenomas and 4 patients presents both type of lesions. A number of 12 hyperplastic polyps were found – they were small lesions usually less than 5 mm (only one was between 5 and 9 mm), and they were equally right and left sided. In two patients with adenomas we also found associated one sessile-serrated polyp. We found 8 patients with a total number of 18 adenomas (2.25 adenomas per patient): 10 left sided and 8 right sided. They were usually small lesions only 2 were greater than 10mm, one had a tubulovillous pattern and 3 were found to harbour high grade dysplasia (**Table I**). Three polyps met the advanced neoplasia criteria and only one's size was less than 10mm.

Table I: Adenomatous polyp's features

Adenoma size	Total number	Right sided adenomas	Left sided adenomas	Villous histology	High grade dysplasia
<5mm	14	4	8	0	0
5-9mm.	2	1	1	1	1
≥10mm	2	1	1	0	2

The result of the fecal immunochemical test was positive in only two of the patients detected with adenomas (one patient presented 5 small adenomas), it was negative in all patients with only hyperplastic polyps, but the result was negative in all the patients with advanced polyps.

Flexible sigmoidoscopy found polyps only in 6 patients (from the 11 patients with polyps). Patients with right sided polyps were missed but also 2 patients with small (< 5 mm) left sided polyps were omitted. Only one of 3 patients with advanced adenomas was found at sigmoidoscopy. Sigmoidoscopy detected also 2 of the 3 patients harbouring only hyperplastic polyps. Combining immunochemical test with flexible sigmoidoscopy would found 7 of 11 patients (one of the patients

found with polyps at sigmoidoscopy had a positive immunochemical test).

Using colonoscopy we have found 9 patients with advanced neoplasia: 6 with cancer and 3 with advanced adenomas. One of our patients underwent a post excision haemorrhage which was controlled by placing endoscopic hemoclips.

Fecal immunochemical test were positive in 4 of the 6 cancer patients but in none of the patients with advanced adenomas. Flexible sigmoidoscopy revealed three advanced neoplasia, two cancers and one advanced adenoma (**Fig.3**). Sigmoidoscopy omitted some small left sided lesions, probably due to the poor bowel preparation.

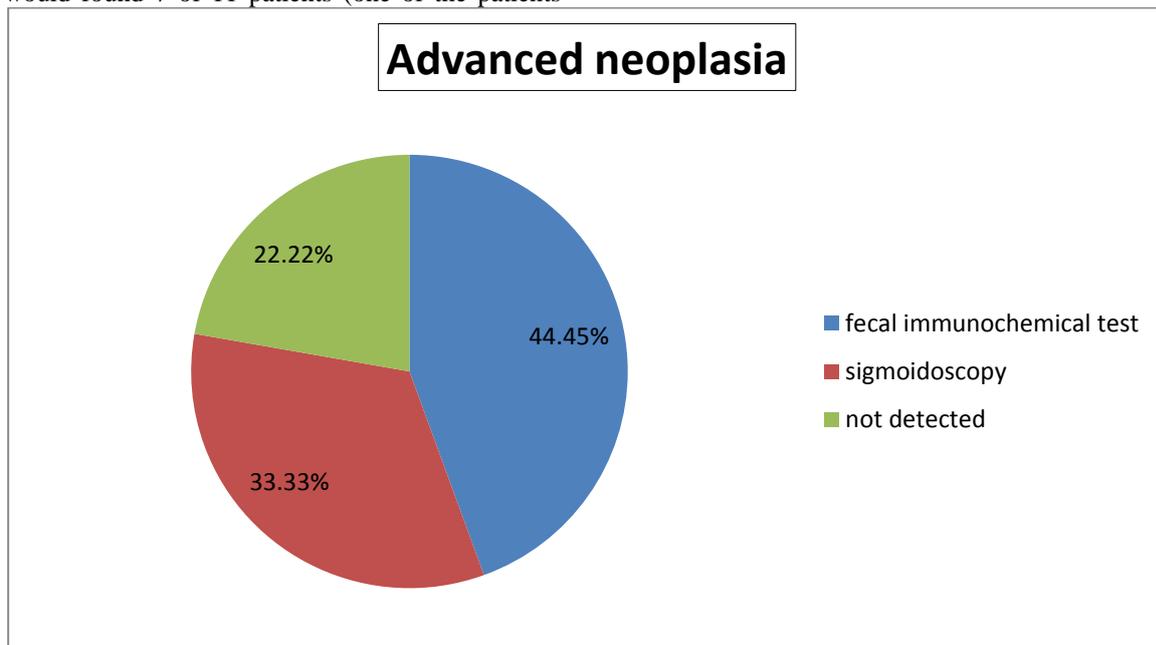


Fig 3: Advanced neoplasia detected by immunochemical test and sigmoidoscopy

Hence, immunofecal test missed 5 of the patients with advanced neoplasia (but only two with cancer) and sigmoidoscopy omitted 6 patients (4 with cancer). Combining immunochemical test with flexible sigmoidoscopy would detect 7 patients with advanced neoplasia (all the cancer patients and one of the advanced adenoma patients). The results of immunofecal test were false positive in 4 patients where no lesion where found.

The importance of performing colonoscopy which is the best method to detect colorectal lesions is obvious. High quality and safe colonoscopy is dependent on cecal intubation, careful and complete visualisation of the mucosa with longer withdrawal times, with the adequacy of pre-procedure bowel cleansing. In order to run a successful screening programme in Romania many endoscopy units must be developed, well trained health care professionals must be available and

many coordinated resources are needed. When a colorectal screening is implemented one must bear in mind the adverse effects of colonoscopy related to the sedation, to the procedure itself and to the excision of the detected lesions.

Immunochemical tests proved themselves as cheap, harmless procedures which reduce cancer mortality if used as an annual screening tool (Popescu A et al., 2009; Miutescu B et al., 2013; Miutescu B et al., 2013). They show a greater relative sensitivity than guaiac fecal occult blood tests. False positive test results can lead to anxiety and unnecessary follow up colonoscopies. The immunochemical tests have false negative results but usually the skipped lesions are advanced polyp and not cancers. Repeating the test annually will offer the possibility that the missed lesion could be found in the next year, and the prolonged natural history afford time to detect this lesion before it reach an incurable stage.

There are some evidence that flexible sigmoidoscopy screening reduces colorectal carcinoma incidence and mortality. Sigmoidoscopy is cheaper, less time consuming, do not need sedation, and bowel preparation is simpler but the major disadvantage is that only the left side of the colorectum can be inspected. Finding a polyp, during the sigmoidoscopy, results in an indication for a follow-up colonoscopy.

Combining sigmoidoscopy screening with interval fecal occult blood test can also be an option. Compared with no screening any of the common screening strategies will reduce mortality from colorectal cancer. Because the different options for colorectal cancer screening tests are variably acceptable to patients eliciting patient preferences is considered an important step in improving adherence.

## CONCLUSIONS

Colonoscopy is the mainstay in colorectal cancer screening. It can prevent colorectal carcinoma by the detection and removal of precancerous lesions and it is used widely for the diagnostic evaluation of other positive screening tests. Fecal immunochemical tests and flexible sigmoidoscopy can also play a role in colorectal cancer screening. Compared with no screening any of the common screening strategies will reduce mortality from colorectal cancer. Because the different options for colorectal cancer screening tests are variably acceptable to patients, eliciting personal preferences is considered an important step in improving adherence.

## AUTHOR CONTRIBUTION

All authors have contributed equally to the present work.

## REFERENCES

- Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer* 2010; 127: 2893-2917
- Kinzler KW, Vogelstein B. Colorectal tumors. In: Vogelstein B, Kinzler KW, eds. *The genetic basis of human cancer*. 2nd ed. New York: McGraw-Hill, 2002:583-612.
- Markowitz SD, Bertagnolli MM. Molecular Origins of Cancer Molecular Basis of Colorectal Cancer *N Engl J Med* 2009;361:2449-60
- Bresalier RS, *Colorectal Cancer in Sleisenger and Fordtran's Gastrointestinal and Liver Disease Pathophysiology/Diagnosis/Management Ninth Edition 2010 Elsevier p 2191-2238* Feldman M, Friedman LS, Brandt LJ, MD
- Quirke P, Risio M, Lambert R, von Karsa L, Vieth M. European guidelines for quality assurance in colorectal cancer screening and diagnosis. First Edition--Quality assurance in pathology in colorectal cancer screening and diagnosis. *Endoscopy*, 2012; 44(3):SE 4-16, 105-114, 116-130.
- U.S. Preventive Services Task Force Screening for Colorectal Cancer: U.S. Preventive Services Task Force Recommendation Statement *Ann Intern Med*. 2008;149:627-637.
- Pignone M, Saha S, Hoerger T, Mandelblatt J. Cost-Effectiveness Analyses of Colorectal Cancer Screening: A Systematic Review for the US Preventive Services Task Force. *Ann Intern Med*, 2002; 137:96-104.
- Popescu A, Sporea I: Screeningul cancerului de colon între ideal și posibilități. Editura Mirton, Timișoara, 2009; 9-20, 45-103
- Miutescu B, Sporea I, Popescu A, Bota S, Iovănescu D, Burlea A, Mos L, Miutescu E . Results of faecal immunochemical test for colorectal cancers creening, in average risk population, in a cohort of 1389 subjects, *Clujul Medical* 2013 Vol. 86 - no. 2
- Miutescu B, Sporea I, Popescu A, Bota S, Iovănescu D, Miutescu E . Adherence to a colorectal cancer screening using the faecal immunochemical test *Studia Universitatis "Vasile Goldiș"*, Seria Științele Vieții Vol. 23, issue 2, 2013, pp. 111-114

## \*Correspondence

Carmen Neamtu  
 Str. Gradinarilor Nr.43  
 Arad, Romania  
 Mobile: 0723225793  
 Mail: carmen.neamtu@gmail.com