

EARLY ENDOSCOPIC PHOTODYNAMIC DIAGNOSIS OF COLONIC LESIONS

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EARLY ENDOSCOPIC PHOTODYNAMIC DIAGNOSIS OF COLONIC LESIONS. (Abstract) **Aim:** The aim of the study is to improve the quality of early endoscopic verification of aplastic changes of the colonic mucosa by use of the photodynamic diagnosis method. **Material and methods:** The study is based on 2,817 video colonoscopies; biopates were taken in 1,206 cases, representing 43% of the total number of endoscopic examinations. In 72 patients (44 males and 28 female) with neoplasia of the colon videocolonoscopy examination using the photodynamic diagnostics method was performed. **Results:** The results of endoscopic examination using the method of photodynamic diagnosis of 72 patients (44 male and 28 female) with neoplasia of the colon are presented. The method of photodynamic diagnostics is based on the differences of the autofluorescence spectra, which is characteristic for the unchanged mucous membrane of the colon ($\lambda_{\max}=535-565$ nm) and induced by the photosensitizer of fluorescence of morphologically atypical cells ($\lambda_{\max}=595-640$ nm). **Conclusions:** The use of photodynamic diagnostics allowed to increase the accuracy, sensitivity and specificity of neoplastic processes of the colonic mucosa verification to 97.1%, 94.9% and 94.2%, accordingly, and the frequency of coincidence of endoscopic and pathohistological diagnoses 95.2%. **Keywords:** COLON, CANCER, NEOPLASM, DIAGNOSIS, ENDOSCOPY.

About 600,000 new cases of colorectal cancer are registered worldwide annually. In the general structure of all malignancies, the colorectal cancer possesses the fourth place in terms of morbidity and mortality with the average incidence (standardized indicator) of 13.0 cases per 100,000 population. Moreover, 44.5% of patients are diagnosed in advanced disease stages. Morphologically, the diagnosis was confirmed in 81.7%, with positive histologic findings in 78.5% of patients. About 20-35% of patients die of colorectal cancer

during less than one year (1). The issue of colorectal lesions diagnostics in the early stages of disease remains relevant in modern coloproctology, considering the incidence of colorectal cancer, the presence of complications in treated patients and mortality rates among patients with this pathology (2-4), though screening techniques significantly improved the situation. Endoscopic verification of the pathological process is the “gold standard” in the diagnosis of pre-malignant diseases and malignant neoplasms of the colon (5-7). Only a visual

assessment of pathological changes of the intestinal mucosa in the early stages, even by an experienced endoscopic specialist can't be considered sufficiently informative considering the minimal or unclear macroscopic changes in the structure of pathologically affected epithelium (8). On the other hand, endoscopic sampling of biopsy material from pathologically affected mucosa just under visual control has similar disadvantages, especially with spread mucosal processes (9). This is because, quite often, neoplastic cells have a small and multifocal mosaic type of localization within the pathologic area of the mucosa detected by endoscopist (9).

Mentioned above stimulates clinicians and researchers to find possible ways and techniques that make it possible to increase the recognition value of endoscopic diagnostics of precancerous diseases and malignant neoplasms of the colon in the early stages of development of the pathological process (2). Use of new physical approaches like laser-confocal endoscopy or chromoendoscopic techniques opens new horizons in colorectal diagnostics (10). Among them, use of fluorescent media for colorectal endoscopies is one of the promising.

The aim of the study is to improve the quality of early endoscopic verification of aplastic changes of the colonic mucosa by the use of the photodynamic diagnostics method.

MATERIAL AND METHODS

In total, 2817 video colonoscopies were performed during 2016-2019. Bioplates were taken in 1,206 cases, representing 43% of the total number of endoscopic examinations. In 72 patients (44 males and

28 female) with neoplasia of the colon videocolonoscopy examination using the photodynamic diagnostics method was performed. The mean age of the patients was 59.3 ± 10.2 years. According to The Paris endoscopic classification of superficial neoplastic lesions: esophagus, stomach and colon (11), 11 patients (15%) had a 0-Is type of neoplasia, 18 (25%) had 0-Ip, in 16 patients (22%) – 0-Isp. Non-polypoid neoplasms of type 0-IIa took place in 6 patients (8%), 0-IIb – in 2 (3%). LST-G (0-IIa+Is) neoplasms were diagnosed in 2 patients (3%), LST-NG (0-IIa) in 3 (4%). Type I polypoid cancers were found in 14 patients (20%).

The method of photodynamic diagnostics (FDD) is based on the differences of the autofluorescence spectra, which are characteristic for the unaltered colonic mucosa ($\lambda_{\max}=535-565$ nm) (fig. 1) and the induced fluorescence of morphologically atypical cells with photosensitizer ($\lambda_{\max}=595-640$ nm) (fig. 2).

For the photodynamic diagnostics we used the fluorescence diagnostics system SFD.M16-1S.2 manufactured by the Ukrainian National Technical University and the photosensitizer medium hypericin.

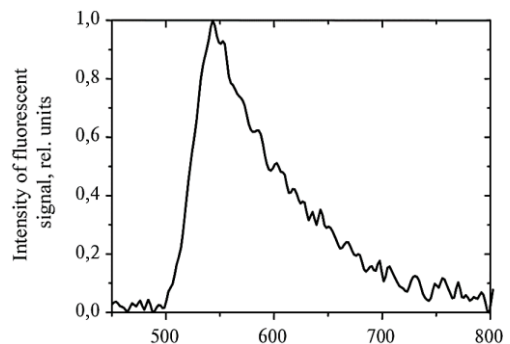


Fig. 1. Diagram of the fluorescence spectrum of the normal colonic mucosa.

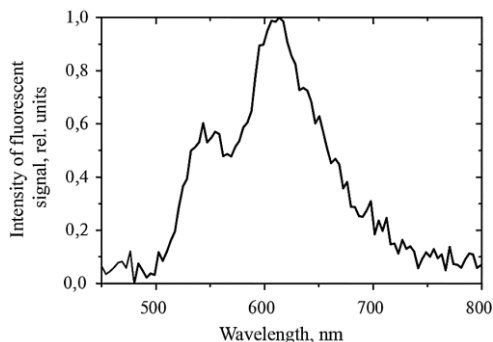


Fig. 2. Diagram of the fluorescence spectrum of the morphologically atypical cells.

The advantages of use of the photosensitizing medium are as follows:

- Oral administration of photosensitizer.
- Colonoscopy within 8-12 hours after the administration of the drug.
- The biological half-life of the drug is about 24 hours.
- The absence of the need for “shadow exposure” of the patient (staying in a darkened room) in the period after receiving a photosensitizer, that allows performing of examination in an outpatient conditions.

The advantages of use of fluorescent diagnostics system SFD.M16-1S.2 are:

- Optical radiation supply, excitation of fluorescence and collection of fluorescent signal through standard optical fibers that are compatible with the instrumental channel of serial endoscopes.
- The registration period of the fluorescence spectrum from the study area does not exceed 1-2 seconds, that does not fundamentally affect the total duration of traditional endoscopic examination.

Endoscopic examination was performed within 8-12 hours after patients receive two capsules of 8 mg hypericin. Its pharmaco-

logical action is based on the photosensitizing properties of hypericin, which selectively accumulate only in the dysplastic, metaplastic and tumor cells of the gastrointestinal mucosa and are retained in them during 4-12 hours after ingestion of the drug (2). During the video colonoscopy, the nature of the suspected pathologically affected mucosal area was visually assessed. From areas that had photosensitizer-induced fluorescence characteristics for morphologically affected cells biopsy material was taken.

For comparison, three groups of patients, comparative by age and nature of pathological changes of the colonic mucosa, whose biopsy material was collected only on the basis of visual assessment of the nature of pathological changes (28 patients), using the method of chromoendoscopy with indigo-carmin solution (23 patients), and for assessment of neoplastic changes` nature in the colonic mucosa by narrow band imaging (NBI) video colonoscopy 32 patients were involved into the study.

In all cases, the final verification of neoplastic changes in the biopsy material of the colonic mucosa was performed by certified pathologist. Evaluation of the results of the study was made by comparing the data of the visual and morphological nature of pathological changes, namely the presence of dysplasia of different severity, metaplasia or malignant cells in biopsy material, obtained in the researched and control groups of patients, and calculation of statistical indicators, as sensitivity, specificity and accuracy of appropriate diagnostic methods.

RESULTS

The nature of pathology presented in patients of comparison groups is shown in first table. Analyzing the findings, it should

be noted, that endoscopic diagnostic techniques based on the use of a chromoendoscopy or NBI mode colonoscopy have a fundamental disadvantage of dependence of

the result, as with conventional endoscopy, on the experience and professionalism of the physician performing the endoscopic examination.

TABLE I
The nature of neoplastic changes of the colonic mucosa in studied patients

Type of neoplasia	Colonoscopy, standard	Colonoscopy with chromoendoscopy	Colonoscopy in NBI mode	Colonoscopy with FDD	Total
0-Is	3 (11%)	3 (13%)	3 (9%)	11 (15%)	20 (13%)
0-Ip	5 (18%)	2 (9%)	6 (19%)	18 (25%)	31 (20%)
0-Isp	7 (25%)	4 (17%)	5 (16%)	16 (22%)	32 (21%)
0-IIa	2 (7%)	2 (9%)	4 (13%)	6 (8%)	14 (9%)
0-IIb	2 (7%)	2 (9%)	2 (6%)	2 (3%)	8 (5%)
LST-G	2 (7%)	1 (4%)	2 (6%)	2 (3%)	7 (4%)
LST-NG	0 (0%)	1 (4%)	1 (3%)	3 (4%)	5 (3%)
Cancer I	7 (25%)	8 (35%)	9 (28%)	14 (20%)	38 (25%)
Total	28 (100%)	23 (100%)	32 (100%)	72 (100%)	155 (100%)

In contrast, the method of photodynamic diagnostics enables real-time differentiation of the unchanged and pathologically affected areas of the gastrointestinal mucosa more objectively, and, accordingly, to detect neoplastic processes on the early stages reliably and in time, with the decision of further treatment. In this case, the

degree of dysplastic changes of tumor has a direct dependence on the intensity of the fluorescent signal from the pathological area, which may be an additional factor in verifying the focus with the maximal pathological changes in the mucosa.

The statistics obtained during the study is shown in second table.

TABLE II
Comparative characteristics of methods for early diagnostics of aplastic processes in colon

Variable	Colonoscopy, standard	Colonoscopy with chromoendoscopy	Colonoscopy in NBI mode	Colonoscopy with FDD
Accuracy	71.4%	87.5%	93.7%	97.1%
Sensitivity	72.1%	89.7%	90.6%	94.9%
Specificity	65.7%	81.3%	83.7%	94.2%
Frequency of endoscopic and histological data congruence	68.5%	83.4%	87.3%	95.2%

DISCUSSION

Early diagnosis of colonic lesion is an important, though difficult issue (2, 3). This study shows benefits of the endoscopic photodynamic diagnostics of colonic lesions. While this method shows multiple benefits compared to standard endoscopy of confocal endomicroscopy (9), several short comes and limitations were revealed, similar to previously published papers (5, 10). Among the disadvantages of the photodynamic diagnostics method revealed during the study are the possibilities of influencing the quality of the fluorescence signal of the blood in the lumen of the intestine and the influence on the intensity and quality of the signal at a distance from the mucosa at which the fiber is located. The latter should be not more than within a few millimeters.

The technique of photodynamic diagnostics made it possible, during endoscopic examination in real time, to collect biopsy

material precisely from focuses in which dysplastic, metaplastic or malignant cells are localized, even in the mosaic location within the pathological focus of the colonic mucosa for the further pathohistological examination of biopsies. The results indicate that photodynamic diagnostics can be considered as a highly informative screening method for early verification of neoplastic changes of the colonic mucosa.

CONCLUSIONS

The use of proposed photodynamic diagnostics allows to increase the accuracy, sensitivity and specificity of verification of neoplastic processes of the colonic mucosa to 97.1%, 94.9% and 94.2%, respectively. Photodynamic diagnostics is a modern, highly informative screening method of early endoscopic detection of aplastic colonic processes with the frequency of coincidence of endoscopic and pathohistological diagnoses 95.2%.

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NEWS

PEOPLE WITH PRE-EXISTING MENTAL HEALTH DISORDERS DURING THE COVID-19 PANDEMIC

Because of their life circumstances, people with pre-existing mental health disorders might have a higher risk of SARS-CoV-2 infection than those without mental health disorders. Risk factors for infection with SARS-CoV-2 and a severe course of COVID-19 include severe mental illness, alcohol or drug misuse, and homelessness, all of which are associated with other risk factors such as comorbid physical conditions. People with mental disorders are at increased risk of infections in general (and thereby potentially at increased risk of COVID-19) and are more likely to develop severe organ dysfunction and to die in ICUs than people without mental disorders. SARS-CoV-2 might also cause dysregulation of the stress system, which could contribute to the development or exacerbation of psychiatric disorders. Elderly people are at especially high risk of severe COVID-19 illness and mental-health-related consequences because they might already have some cognitive decline. Institutions can become epicenters for infection. Physical distancing can be challenging in these contexts, either because the nature of patients' conditions makes it difficult to manage (e.g., people with learning disabilities) or because of overcrowding (e.g., prisons). Increased death rates in assisted living facilities have been reported worldwide, especially among older people and people with learning disabilities. People with pre-existing mental health disorders have reported increased symptoms and poorer access to services and supports since the onset of the COVID-19 pandemic. Early discharge from psychiatric units and disruption of face-to-face psychiatric care have become common, the negative consequences of which could include relapse, suicidal behavior, lack of access to medical care, and social isolation. Quarantine and lockdown might particularly affect people with pre-existing mental health problems: increased symptoms of anxiety and depression, and high rates of post-traumatic stress disorder and insomnia have been reported (Moreno C, Wykes T, Galderisi S, *et al.* How Mental Health Care should change as a Consequence of the COVID-19 pandemic. *The Lancet Psychiatry* 2020; 7(9): P813-824).