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CLINICAL GUIDELINES
Polyp of the colon and rectum (K62.1, K63.5, D37.4, D12.0, D12.1, D12.2, D12.3, D12.4, D12.5, D12.6, D12.7, D12.8), adults, children (PROJECT)

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LIST OF ABBREVIATIONS

IBD — inflammatory bowel diseases
CEV — colon endoscopy videocapsular
HB — hot biopsy
HP — hot polypectomy
BEN — benign epithelial neoplasm
GIT — gastrointestinal tract
CRC — colorectal cancer
MRI — magnetic resonance imaging
CG — clinical guidelines
CR — colon and rectum
SEN — superficial epithelial neoplasm
RCT — randomized clinical trial
RRS — rectoromanoscopy, proctoscopy
APS — adenomatous polypous syndrome
LE — level of evidence
US — ultrasound
CR — category of recommendations
CP — cold polypectomy
ADR — adenomadetection rate
ESD — endoscopic submucosal dissection
EMR — endoscopic mucosal resection

TERMS AND DEFINITIONS

Cold forceps/loop biopsy is the mechanical (without the use of electric current) removal of a fragment of biological tissue with biopsy forceps or a polypectomy loop.

Hot forceps/loop biopsy is the removal of a fragment of biological tissue with biopsy forceps or a polypectomy loop using electric current.

Neoplasm (synonyms: neoplasia; tumor) is a clone of cells that differ from other tissues by autonomous growth and somatic mutations [1].

Intraepithelial neoplasia is a type of noninvasive epithelial tumor, the term that replaced and defined the terms adenoma and dysplasia in the agreed Vienna Classification of epithelial neoplasia of the digestive tract [2].

Polyp (in the broadest sense) is a collective term that is firmly embedded in everyday professional speech, as a short, convenient term for practical use, which refers to almost any intraluminal neoplasm. The collective term 'polyp' is mainly used to refer to benign epithelial neoplasms, but it is also used to refer to formations of a different origin (inflammatory, hamartomic, subepithelial/submucosal), mainly in situations where the true nature and origin of the formation is unclear/unknown for the time being. This dualism of definition is reflected in the coding of the disease according to the International Statistical Classification of Diseases.

In particular, in ICD-10 it is encoded both in class II — 'Neoplasms' and in class XI — 'Diseases of the digestive system'. After a seminar in Paris in 2002 distinguished non-polypoid — flat (type *0-II*) and ulcerated (type *0-III*) superficial epithelial neoplasms into a separate category, it became obvious that it is advisable to distinguish the term 'polyp' in its broad (described above) and narrow meaning.

Polyp (in the narrow sense), as a synonym for SEN (type *0-I*) rising above the surface of the intestinal wall, is a term denoting an epithelial neoplasm in which the height exceeds half the diameter (criterion for miniature formations), or protruding into the lumen of the organ by more than 2.5 millimeters (diameter of cups of closed biopsy forceps), associated with a pedicleor a wide base on the intestinal wall.

Malignant polyp is a polypoid epithelial neoplasm with a proven presence of cancer cells in the structure.

Unlike the term 'polypoid cancer', the term 'malignated polyp' emphasizes the specialist's confidence that he/she is dealing with a malignant tumor, the precursor of which was a benign polyp, part of which still retains a benign structure.

Early cancer is a cancerous tumor limited to the mucous or submucosal layer without regional or distant metastases.

Subepithelial formation is a collective term, mainly endoscopic, characterizing both a tumor and a non–tumor focal volumetric lesion of the large intestine, emanating from any layer of the organ wall, except the epithelium. The term 'subepithelial formation/tumor' is gradually being replaced by the term 'submucosal formation/tumor', more accurately reflecting the morphology of the lesions, since some of them, for example, leiomyomas emanating from the muscle plate of the mucous layer or neuroendocrine tumors emanating from deep sections of the glands of the mucous layer, strictly speaking, are intramucosal, although they look when endoscopically examined as 'submucosal'.

Cold polypectomy is the mechanical (without the use of electric current) removal of an epithelial neoplasm with polypectomy loop or biopsy forceps.

Hot polypectomy is the removal of an epithelial neoplasm with polypectomy loop or biopsy forceps using electric current.

Endoscopic submucosal dissectionis a type of intraluminal endoscopic resection of a neoplasm, in which the process of dissection of the mucous layer and submucosal layer is performed through an endoscope with specially designed electrosurgical endo-knives under direct visual control.

Endoscopic mucosal resection is a term used to denote excision through an endoscope (usually with a polypectomy loop) within the unchanged tissues of a fragment of the mucous layer with a neoplasm located in this fragment. The term, in its classical version, is used to refer to the removal of non-polypoid SEN through an endoscope with the preliminary introduction of liquid substances into the submucosal layer.

Epithelial neoplasm is a benign or malignant neoplasm originating from the epithelium of the mucous layer of an organ.

Superficial epithelial neoplasm (SEN)is an epithelial neoplasm which is spreading within the limits of the mucosal or submucosal layers, that is, between two internal layers, superficial to the lumen of the gastrointestinal tract.

Polypoid (towering) SEN (type 0-I) is an epithelial neoplasm whose height exceeds half of its diameter (the criterion for miniature formations), or protruding into the lumen of the organ by more than 2.5 millimeters (the diameter of the cups of closed biopsy forceps), connected to the intestinal wall by a pedicle or a wide base.

Non-polypoid SEN — epithelial neoplasm, whose height does not exceed half of its diameter, or does not protrude into the lumen of the organ by more than 2.5 millimeters (the diameter of the cups of closed biopsy forceps). These include flat (type 0-II) and ulcerated (type 0-III) neoplasia.

1. BRIEF INFORMATION ON THE DISEASE OR CONDITION (GROUP OF DISEASES OR CONDITIONS)

1.1 Definition of a disease or condition (group of diseases or conditions)

Since K63.5 colorectal polyp and K62.1 rectal polyp denotes not only benign epithelial neoplasms, but also inflammatory, hamartomic and subepithelial formations, these clinical guidelines have been developed for the diagnosis and treatment of benign epithelial neoplasms (BEN) of the colon and rectum (C-and-R), which make up a significant part of the subclass diseases combined in the ICD-10 with a single D12 code, namely D12.0 — D12.8, as well as D37.4. These CG do not consider BEN of the anus and anal canal (code D12.9), hereditary polypous syndromes, as well as non-epithelial neoplasms, as they have pronounced specificity in diagnosis, treatment, and prevention, and separate studies are devoted to them.

BEN of C-and-R, which include all types of serrated neoplasms, including hyperplastic polyps, sessile serrated polyps with or without dysplasia, traditional serrated adenomas, as well as adenomatous epithelial neoplasia, are included in the group of 'superficial' epithelial neoplasms (SEN) [1–5]. At an authoritative global seminar in Paris in 2002, the above-described formations were classified as tumors, the depth of which is limited by the mucous layer or submucosal base, that is, two inner layers, superficial in relation to the intestinal lumen. It is important to emphasize that early colorectal cancers (CRC) were included in the SEN CR group. This decision was made unanimously, since the differential diagnosis between BEN and early CRC in the context of colonoscopy is a difficult task. Tactical and methodological approaches in the treatment of both conditions overlap in many ways, due to the fact that the majority of SEN CR, including a significant proportion of early CRC, can be radically removed using methods of intraluminal endoscopic surgery. Experts note that successful and definitive confirmation of these diseases is possible only after receiving the results of a pathomorphological examination of the removed tumor. Thus, the choice of treatment method has a significant role in improving the outcomes and quality of life of patients [3].

1.2 Etiology and pathogenesis of a disease or condition (groups of diseases or conditions)

A combination of exogenous and endogenous factors is at the heart of the development of SEN CR. To date, the role of external influences, including environment impact, low motor activity, and dietary patterns, national diets, and the nutritional composition of food consumed (foods high in fat, protein, and low in fiber), smoking, and regular alcohol intake in the development of SEN CR has been proven.

Endogenous factors:

– **Age**. A large number of studies demonstrate that the prevalence of colorectal adenomas predictably increases by 10–15% in people aged 50 to 75 years [6–8]. Benign neoplasms of the colon and rectum in children are more common in the first decade of life, with the peak incidence occurring at the age of two to five years [9, 10];

– **Gender.** In men, the detection rate of adenomatous neoplasms of the large intestine during screening colonoscopy is 1.77 times higher than in women [8]. In addition, large epithelial formations of the large intestine (> 9 mm) are 50% more common in the male population than in the female population [11]. In the structure of male morbidity, CRC is 10.9%, and mortality is 9%. In women, morbidity and mortality are the same — 9.5% each [12];

– **Genetics.** There is a correlation between SEN and family history [13,14]. Patients who have a first-degree relative with confirmed CRC have an increased risk of developing polyps in the large intestine, as well as a higher risk of 'developed' adenomas [15,16]. The CRC detection rate increases by 1.76 times in patients who have a first-line relative with a CRC, even after the age of 80 [17]. Hereditary genetic pathogenic variants are the main etiological factor in the formation of SEN in familial adenomatous polyposis of the large intestine (mutation in the *APC* gene) and *MutYH*-associated polyposis (mutations in the *MutYH* gene) [18]. Compared to adults, CRC in children is extremely rare. Hereditary cancer predisposition syndromes (ICSS) are a group of diseases in which

patients are predisposed to a wide range of tumors as a result of pathogenic mutations in germ line genes, which are an important cause of CRC in children [19];

– **Inflammatory bowel diseases (IBD).** Patients with IBD (ulcerative colitis — UC and Crohn's disease — CD) with lesions of at least 30% of the large intestine are at a higher risk of CRC than in the general population [20].

The pathogenesis of the formation of superficial epithelial neoplasms of the large intestine has not been fully investigated. However, today the main ways of carcinogenesis of colorectal cancer are known. The traditional model includes sequential chromosomal instability, which covers 70–90% of cases, accompanied by progression from adenoma to carcinoma. At the same time, the serrated neoplasia pathway, which accounts for approximately 10% of cases, is often associated with mutations in the *BRAF* and *KRAS* oncogenes, while mutations in the *APC* gene are much less common [21–27]. In addition, about 8% of all CRC cases are associated with hereditary and familial forms of the disease, such as familial adenomatous polyposis of the large intestine and Lynch's syndrome. Finally, about 2% of cases develop against the background of prolonged inflammation of the mucous layer in inflammatory bowel diseases, which is called colitis-associated CRC [28–33].

1.3 Epidemiology of a disease or condition (groups of diseases or conditions)

The prevalence of epithelial neoplasms of the large intestine ranges from 20% at the age of 45 to more than 50–60% by the age of 85 [34–39].

The prevalence of large intestine polyps in children and adolescents ranges from 0.08% to 6% [40,41]. According to the results of screening colonoscopies, it was determined that polyps are detected in 20–53% of people aged 50 years and older, among which up to 9.7% are 'developed' tumors, defined as adenomas measuring ⩾ 10 mm or having a villous structure or a high degree of epithelial dysplasia [42–47]. According to a meta-analysis of publications including information on the results of colonoscopy performed in persons aged ⩾ 50 years, polyps were detected in 24% of cases, and the prevalence of 'advanced' adenoma is about 4.5% [48]. It should be noted that the incidence of adenomas is higher among men and increases with age [48,49].

1.4 Specific coding features of a disease or condition (group of diseases or conditions) according to the International Statistical Classification of Diseases and Health-Related Problems

ICD-10 Class and Codes

K62.1 Polyp of the rectum
K63.5 Polyp of the large intestine
D37.4 Neoplasm of an unidentified or unknown nature of the oral cavity and digestive organs
D12 Benign neoplasm of the colon, rectum, anus and anal canal
D12.0 of the cecum
D12.1 of the vermiform appendix
D12.2 the ascending colon
D12.3 the transverse colon
D12.4 the descending colon
D12.5 the sigmoid colon
D12.6 an unspecified part of the colon
D12.7 the rectosigmoid connection
D12.8 the rectum

1.5 Classification of a disease or condition (groups of diseases or conditions)

Depending on the size, SEN CR are divided into [50–52]:

– Miniature (tiny; minute; diminutive): up to and including 5 mm;
– Small: 6–9 mm;
– Medium (medium-sized; intermediate): 10–19 mm;
– Large: 20–39 mm;
– Giant: 40 mm or more.

*Adenomas measuring 10 mm or more and/or adenomas that contain at least 20–25% of the villous component and/or high grade (severe) intraepithelial dysplasia are classified as 'advanced adenomas' [53].

According to Borrmann's modified macroscopic classification of epithelial tumors, proposed by him back in 1926 to describe the appearance and growth pattern of common malignant tumors (types 1–4), superficial epithelial neoplasms belong to type zero. The term 'type 0' was used to distinguish 'superficial' polypoid and non-polypoid epithelial tumors (both benign and malignant) from common ones [3,54].

The Paris Endoscopic Classification of Superficial Epithelial Neoplasms of the Large Intestine in 2002 serves for a more detailed and accurate macroscopic assessment of SEN. It is used to characterize both benign epithelial tumors and their precursors, as well as malignant tumors classified as type 0 during endoscopic examination. Thus, in accordance with the appearance and nature of growth, SENsare conventionally distinguished as follows: towering (polypoid) ones — subtype 0-I, flat (non-polypoid and non-ulcerated) ones — subtype 0-II, ulcerated (ulcerative, loosened) ones — subtype 0-III [3,55].

MACROSCOPIC ENDOSCOPIC CLASSIFICATION OF SUPERFICIAL EPITHELIAL NEOPLASMS (SEN) OF THE DIGESTIVE TRACT (TYPE 0)

Towering (polypoid) type	***0-I***	
SEN (polyp) on apedicle		***0-Ip***
SEN ((polyp) on a wide base		***0-Is***
Flat type	***0-II***	
SEN flat — elevated		***0-II a***
SEN absolutely flat		***0-IIb***
SEN flat — deepened		***0-IIc***
Ulcerated (ulcerative; loosened) type	***0-III***	

In addition, there are mixed forms of SEN that carry signs of two types, for example: deep-elevated (*0-IIc + IIa*); elevated-deep (*0-IIa + IIc*).

Lateral growth (spreading/creeping) tumors (LST — Laterally Spreading Tumor) are a type of large intestine tumors with a special growth pattern creeping along the intestinal mucosa, which allows them to reach a gigantic size without a significant increase in height. The initial/minimum diameter of the LST, which allows them to be classified as creeping tumors, is 10 millimeters.

Laterally growing tumors are divided into LST-G (Granular) and LST-NG (NonGranular — smooth), and each of them is further divided into subtypes. LST-G is subdivided into homogeneous (LST-G-H) and nodular mixed (LST-G-NM) subtypes; LST-NG is subdivided into flat-elevated (LST-NG-FE) and pseudodepressed (LST-NG-PD) subtypes [4,55,56].

The NICE International Endoscopic Classification (NBI International Colorectal Endoscopic) of epithelial neoplasms of the large intestine, 2009, is based on an assessment of the color, microvascular architectonics and surface pattern of epithelial neoplasms of the large intestine when they are examined in a narrow light spectrum (NBI — Narrow Band Imaging) without magnification [57,58]. According to the NICE classification, epithelial neoplasms of the large intestine are classified into 3 types, according to the prognosis of their pathomorphological structure: type 1 — hyperplastic and serrated polyps on a wide base; type 2 — all adenomas, both with mild and severe dysplasia, as well as cancer with minimal depth of invasion into the submucosa; type 3 — cancer with deep invasion [59].

In 2018, a group of Japanese experts introduced a fourth category, dividing type 2 into two subgroups: 2A, which includes mild dysplasia, and 2B, severe dysplasia or early cancer [60].

Universal endoscopic classification of large intestine tumors in narrow-spectral mode with magnification: JNET classification of the Japanese NBI expert group.

According to the JNET classification, epithelial neoplasms of the large intestine are divided into 4 types, according to the prognosis of their pathomorphological structure:

type 1 — hyperplastic polyps/serrated formations on a wide base; type 2A — low grade intramucosal neoplasia; type 2B — high grade intramucosal neoplasia / cancer with superficial invasion into the submucosal layer; type 3 — cancer with deep invasion [61,62].

The WASP classification (Workgroup Serrated Polyps AndPolyposis) [63] was created for the

differential diagnosis of serrated neoplasms on a wide base from hyperplastic polyps and from classical adenomas according to endoscopic criteria. At the first stage of differential diagnosis, the NICE classification is used to distinguish SEN type 1 (serrated /hyperplastic) from type 2 (adenomatous). At the second stage, these neoplasms are assessed for the presence or absence of endoscopic signs characteristic of serrated lesions. These include:

1) Cloud-shaped surface;
2) Blurry boundary;
3) Irregular shape;
4) 'Black dots/specks' inside the crypts (pits of type II-O according to T.Kimura).

Based on the combination of endoscopic features, a conclusion is drawn about the proposed morphological structure of the formation [64–66].

The classification of the dimpled pattern (microrelief) of the mucous layer and epithelial neoplasms of the large intestine according to S. Kudo, 1994, is used in high-resolution endoscopy with chromocolonoscopy and magnification. There are seven main types of dimple pattern and several additional ones. Types of dimple pattern I and II are characteristic of non-cancerous changes in the large intestine.

In type III and IV, the probability of submucosal invasion reaches 4%, and in type V — 41%. Types IIIL, IIIS, IV, Vi, and VN suggest the presence of neoplasia with a progression from low to high risk of malignancy, where type IIIS may correspond to high–grade neoplasia and cancer; Vi — high-grade neoplasia and cancer limited to the mucous layer and superficial parts of the submucosa; type VN — adenocarcinoma with deep invasion. The risk of malignancy increases in the following sequence: IIIL < IIIS < IV [67].

The World Health Organization (WHO) classification of colon and rectal tumors includes the morphological codes of the International Classification of Oncological Diseases, third edition, second revision (ICD-O-3.2). Tumors are encoded according to their pathomorphological characteristics: /0 — benign tumor; /1 — unidentified, borderline, or indeterminate nature of the tumor; /2 — 'insitu' cancer and grade III intraepithelial neoplasia; /3 — malignant tumors, primary focus [68].

Benign epithelial tumors and their precursors	
Low grade serrated dysplasia	8213/0*
High grade serrated dysplasia	8213/2*
Hyperplastic polyp, microvesicular type	
Hyperplastic polyp, goblet-shaped	
Adenomatous polyp with low grade dysplasia	8210/0*
Adenomatous polyp with high grade dysplasia	8210/2*
Low grade tubular adenoma	8211/0*
High grade tubular adenoma	8211/2*
Low grade villous adenoma	8261/0*
High grade villous adenoma	8261/2*
Low grade tubulo-villous adenoma	8263/0*
High grade tubulo-villous adenoma	8263/2*
Advanced adenoma	
Low grade glandular intraepithelial neoplasia	8148/0
High grade glandular intraepithelial neoplasia	8148/2

** The codes marked with an asterisk were approved by the IARC/WHO Committee for ICD-O at its meeting in April 2019.*

The agreed international Vienna Pathomorphological Classification of epithelial neoplasia of the large intestine was first published in 2000 [69]. The latest revision of the Vienna Classification, which includes recommendations on therapeutic tactics, was published as a draft in 2002 [70] and was recommended for widespread use and (partially) adopted in the latest WHO classification of tumors of the digestive tract in 2019 [2].

VIENNA CLASSIFICATION OF EPITHELIAL NEOPLASIA OF THE DIGESTIVE TRACT; CURRENT VERSION; APPROVED IN 2002 [70]

Category	Subcategories and Diagnosis	Therapeutic tactics
1	**Absence of neoplasia (Neoplasia/**dysplasia **was not detected).** This category includes normal, reactive, regenerative, hyperplastic, atrophic, and metaplastic epithelium).	**Follow-up is at the discretion of the doctor,** depending on the clinical indications.

Category	Subcategories and Diagnosis	Therapeutic tactics
2	**Uncertainty about neoplasia/** dysplasia. It is diagnosed in cases where it is unclear whether there are regenerative or neoplastic changes. The diagnosisis complicated by inflammation and artificial changes.	**Follow-up** and repeated biopsy are necessary, as the nature of the process remains unknown.
3	**Low grade mucosal neoplasia. Low grade adenoma. Low grade dysplasia (mild dysplasia).**	**Endoscopic resection or follow-up*.**
4	**High grade neoplasia of the mucous layer. 4.1 High grade adenoma/ dysplasia. 4.2 Non-invasive cancer (cancer 'insitu').** Non-invasive means the proven absence of invasion (germination) into the own plate of the mucous layer (beyond the basement membrane). **4.3 Suspected invasive cancer.** It is difficult to determine whether there is an invasion into the own plate of the mucous layer or not. **4.4 Intra mucosal cancer.** Intramucosal means that there is invasion (germination) into the own plate of the mucous layer (beyond the basement membrane) or into the muscular plate of the mucous layer.	**Endoscopic or surgical local resection*.**
5	**Invasion of cancer into the submucosa.**	**Surgical resection*.**

Pathomorphological staging of malignant large intestine polyps according to Haggitt, R.C. 1985 [71] distinguishes 5 levels of invasion for polypoid malignant epithelial neoplasms on the pedicle (*Ip* type) [71,72]:

Level 0 — absence of invasion beyond the muscularis mucosae;

Level 1 — invasion through its own muscularis mucosae into the submucosal layer, limited by the head of the polyp;

Level 2 — invasion of the submucosal layer, reaching the neck of the polyp;

Level 3 — invasion of the submucosal layer, spreading to the polyp pedicle at any level up to the base;

Level 4 is invasion into the submucosal layer of the intestinal wall below the base of the polyp pedicle, regardless of the depth of this invasion.

For polypoid malignant epithelial neoplasms on a wide base (*Is* type) according to Haggitt, R.C., only 2 levels of cancer invasion are distinguished: zero and fourth. Thus, according to modern concepts, invasion level 1–3 according to Haggitt, R.C. corresponds to T1sm1, and level 4 can correspond to both superficial (T1sm1) and deeper invasion (T1sm2) into the submucosa. Haggitt's classification was widely used before the Paris Seminar in 2002 and is still used to stage the depth of invasion in malignant polyps on the pedicle (*type 0-Ip* tumors), but to evaluate polypoid tumors on a wide base (*type 0-Is*), it is inappropriate.

Universal pathomorphological staging of the depth of invasion into the submucosal layer of early large intestine cancer (T1) on a wide base, dividing the submucosal base into 3 sublayers of equal thickness according to S.Kudo, 1984 [73] or according to R.Kikuchi, 1995 [74], can be carried out only in pathoanatomic samples containing the entire submucosal layer and at least a part of the own muscular layer of the large intestine, that is, in samples obtained during transabdominal resection of the intestinal segment, or during full-layer endoscopic resection. It is impossible to reliably use these classifications to fully assess the depth of tumor invasion into the submucosal layer after endoscopic resection of the tumor, including using the submucosal dissection method. That is why, in 2002 [3], a universal system for assessing the depth of invasion into the submucosal layer in absolute terms (microns) was adopted for the removed specimens obtained by resection of SEN through an endoscope. The depth of invasion into the submucosal layer is conditionally divided into two levels: superficial (sm1) and deep (sm2); the border between them is at a depth of 1000 μ (microns). It is this assessment system that is now most widely used in clinical practice and in scientific research.

The auxiliary classification in the TNM system — R classification is a classification designed to

assess the completeness of tumor removal. It reflects the effectiveness of the intervention, influences the choice of further treatment tactics, and serves as a significant prognostic factor [75].
The following R categories are distinguished:
RX — It is impossible to assess the presence of a residual tumor
R0 — There is no residual tumor
R1 is a microscopic residual tumor
R2 is a macroscopic residual tumor [76].

1.6 Clinical picture of a disease or condition (groups of diseases or conditions)

In most cases, superficial epithelial neoplasms of the colon and rectum have been asymptomatic for a long time and screening methods are the only way to detect them. When the large size of SEN in the large intestine is reached, nonspecific clinical symptoms may appear, such as constipation or diarrhea, including mucus discharge, blood in the stool, cramps and abdominal pain with a high level of variability. According to some scientific publications, the detection rate of colorectal polyps according to colonoscopy in asymptomatic patients ranges from 18.2% to 46% [77,78,83]. In a research paper by Xiaohua Long et al., diarrhea accounts for 54.2% of all symptoms [78]. n numerous studies on rectal bleeding, the authors emphasize that hematochezia, in particular, is a symptom of progressive large intestine adenoma. This clinical manifestation, characterized by the release of fresh blood from the rectum, may indicate pronounced vascularization and an increased tendency to bleeding, characteristic of large adenomas or malignant neoplasms [79–81].

2. DIAGNOSIS OF A DISEASE OR CONDITION (GROUP OF DISEASES OR CONDITIONS), MEDICAL INDICATIONS AND CONTRAINDICATIONS TO THE USE OF DIAGNOSTIC METHODS

The criterion for diagnosis is the detection of colon and/or rectal SEN according to endoscopy or an alternative instrumental method of large intestine examination (computed tomographic colonoscopy, ultrasound, MRI).

2.1 Complaints and medical history

• It is **recommended** to carefully collect and evaluate the patient's complaints and medical history, including using questionnaires, in order to identify risk factors for the development of large intestine neoplasms and formulate indications for further follow-up [82, 86–89].
For adults, the category of recommendation — B (the level of evidence — 3).
For children, the category of recommendation — C (the level of evidence — 5).
Comment: *According to the results of a meta-analysis of data from population screening studies, among patients who underwent colonoscopy, using questionnaires as methods of stratification to identify relatives with large intestine neoplasms in the family history, the rate of adenomas (ADR) during colonoscopy was 33.3% [85].*
At the same time, in the framework of pilot screening studies with a positive rapid examination of feces for latent blood by immunochromatographic method, the detection rate of adenomas during colonoscopy was 54.1%, and with a high level of risk according to the survey data — 67.3% [86,89].
In children, the most common clinical manifestations are hematochezia and rectal bleeding [87].
There are often complaints of prolapse of polypoid formations through the anus, with episodes of polyp pinching and self-amputation and subsequent bleeding [88].

2.2 Physical examination

• Patients with SEN are **recommended** to undergo a thorough physical examination, including digital rectal examination to exclude concomitant pathology of the anal canal and diagnosis of bulky neoplasms in the abdominal cavity [90–93].
For adults, the category of recommendation — C (the level of evidence — 5).
For children, the category of recommendation — B (the level of evidence — 2).
Comment: *Palpation of the abdomen and digital rectal examination suggest the presence of neoplasms*

of the colon and rectum [90, 91]. However, reliable diagnosis requires the administration of instrumental diagnostic methods such as colonoscopy, ultrasound of the abdominal cavity (complex), transrectal ultrasound of the rectum, computed tomography of the small intestine with contrast [92,93].

2.3 Laboratory diagnostic tests

• It is **recommended** to perform a general (clinical) blood test and a biochemical general therapeutic blood test, an indicative test of the hemostasis system in order to select a drug to prepare the large intestine for diagnostic and surgery and to assess the risks of intra- and postoperative bleeding [88,94–97].

For adults, the category of recommendation — C (the level of evidence — 4).

For children ,the category of recommendation — C (the level of evidence — 4).

Comment: *Risk factors such as male gender (RR = 1.64), hypertension (RR = 1.54), taking antithrombotic drugs (RR = 4.04), SEN size greater than 10 mm (RR = 3.83), SEN localization in the right parts (RR = 2.48) and the use of mucosectomy to remove tumors (RR = 2.99) are risk factors for postoperative bleeding [96,97]. Thus, in patients taking antithrombotic therapy for a long time, it is necessary to monitor the hemostasis, timely discontinuation of antithrombotic drugs, or prescribe bridge therapy before endoscopic removal of the SEN [89].*

2.4 Instrumental diagnostic tests

• Colonoscopy is **recommended** in all cases of a positive rapid examination of feces for latent blood by immunochromatographic method, with a high risk of detecting polyps and cancer according to a questionnaire, or in the case of a previously identified neoplasm of the large intestine in order to determine treatment tactics [86,89,98–116].

The category of recommendation — C (the level of evidence — 5).

Comment: *Colonoscopy is indicated [98] for:*

– *persons with a family history of hereditary polyposis and colorectal cancer [99,100];*
– *patients with familial adenomatous polyposis, Peitz-Jaegers' syndrome, juvenile polypous syndrome and serrated polypous syndrome [101–106];*
– *patients with previously diagnosed epithelial neoplasms of the large intestine [107];*
– *patients with inflammatory bowel diseases [107–109];*
– *patients who have undergone radiation and chemotherapeutic treatments for diseases of the large intestine or neigh boring organs [110,111].*

• Performing a planned colonoscopy for the diagnosis of epithelial benign neoplasms of the colon and rectum is **not recommended** in all cases when the risk of conducting the study exceeds its diagnostic value, and the results of the study do not affect the choice of tactics and method of treatment of the patient at the time of colonoscopy and making this decision [98].

The category of recommendation — C (the level of evidence — 5).

Comment: *Absolute contraindications to planned colonoscopy are: acute phase of cerebrovascular accident; acute phase of myocardial infarction; severe degrees of cardiovascular, pulmonary and mixed insufficiency (decompensation stage), which are observed in coronary heart disease, heart defects, massive pulmonary embolism; cardiac arrhythmias (especially in unstable conditions), such as: paroxysmal bradyarrhythmia, atrial fibrillation or atrial fibrillation paroxysms, group ventricular extrasystoles in the form of bigeminia or trigeminia, severe degrees of transverse heart block; exfoliating aortic or cardiac aneurysm.*

Absolute contraindications to planned colonoscopy are also: super-severe (fulminant) forms of inflammatory bowel diseases (ulcerative colitis, Crohn's disease, ischemic colitis, radiation colitis); acute inflammatory infiltrates of the abdominal cavity (including acute diverticulitis); suspected abdominal abscess, peritonitis. Relative contraindications to colonoscopy are: acute inflammatory diseases of the anorectal zone (anal fissure, hemorrhoids in the acute stage, thrombosis of hemorrhoids, paraproctitis); early postoperative period (surgeries

on the organs of the abdominal cavity and pelvis); pronounced hepatosplenomegaly; severe ascites; hydrothorax, hydropericardium; severe disorders of the blood coagulation system; hemorrhagic vasculitis; pregnancy (especially in the second or third trimester).

• Prior to the start of endoscopic intervention, it is **recommended** to obtain the informed voluntary consent of the patient to conduct research and treatment in order to confirm that the patient has received complete and understandable information about the medical intervention, including goals, methods, risks and alternatives, and voluntarily agrees to it [117].

The category of recommendation — C (the level of evidence — 5).

Comment: *The positive aspects of screening/diagnostic testing and endoscopic surgery, as well as the risks associated with it, should be explained to each patient in an understandable way. Before obtaining informed voluntary consent (IVC) by the attending physician or other medical professional, the patient or his legal representative is provided with complete information in an accessible form about the goals, methods of medical care, possible types of medical interventions, and the consequences of these medical interventions, including about the likelihood of complications, as well as the expected results of medical care. The IVC is issued in the form of an official document, signed by the patient or his legal representative.*

• It is **recommended** to ensure that the patient is adequately prepared for colonoscopy using a special low-fiber diet and medications certified for colonoscopy preparation. Some patients also need correction of the general status and disorders caused by comorbidities [118–135].

For adults — the category of recommendation — B (the level of evidence — 1).

For children — the category of recommendations — B (the level of evidence — 2).

Comment: *High-quality patient's bowel cleansing provides the opportunity for intubation of the cecum, a detailed examination of the mucous layer of all parts of the large intestine and the detection of pathological changes, including neoplasms. In conditions of unsatisfactory preparation, the detection of neoplasms is difficult or impossible [126].*

• To ensure the effectiveness of diagnostic and therapeutic measures during colonoscopy, as well as to minimize complications, it is **recommended** to evaluate the quality of the patient's preparation for colonoscopy according to the Boston scale and reflect the degree of bowel preparation in the protocol/conclusion of the endoscopy [136–140].

The category of recommendation — C (the level of evidence — 4).

Comment: *The Boston scale is a repeatedly validated, convenient in daily work, and the most widely used in the world [137–140]. Its use ensures the standardization of recording the quality of preparation and examination of the large intestine during colonoscopy. According to the Boston scale, the quality of large intestine cleansing for colonoscopy can be considered adequate with a score of 6 or more points, provided that the score of each of the 3 assessed segments is at least 2 points [139,140].*

• When performing colonoscopy, it is **recommended** to use carbon dioxide (CO_2) to expand the intestinal lumen [141,142].

The category of recommendation — B (the level of evidence — 1).

Comment: *Carbon dioxide does not support combustion and is absorbed from the intestinal lumen into the blood 13 times faster than oxygen and 160 times faster than nitrogen. In this regard, its use in endoscopic procedures prevents explosions, uncontrolled emphysema and pain associated with the performed manipulation [142].*

• It is **recommended** to remove the colonoscope from the cecum to the anus for at least 6 minutes for a qualitative examination of the large intestine [136,143–148].

The category of recommendation — B (the level of evidence — 2).

Comment: *There is a correlation between the rate of adenoma detection (ADR) and the time of colonoscope extraction from the cecum dome to the anus. The detection rate of adenomas (9.4%-32.7%) depends on the time of endoscope extraction (which*

varies from 3.1 to 16.8 minutes). With an extraction time of more than 6 minutes, the ADR is statistically significantly higher than with a faster large intestine examination (28.3% vs. 11.8%, p < 0.001) [144,145]. The optimal time for removing a colonoscope by an experienced specialist, without taking into account the performance of clarifying visual diagnostics and biopsy, should be at least 10 minutes; the minimum allowed time is at least 6 minutes [148].

- To identify pathological changes, it is **recommended** to perform a detailed examination of the terminal ileum and the entire large intestine as the colonoscope is removed [147–149].

The category of recommendation — C (the level of evidence — 5).

Comment: *A detailed examination of the intestinal mucosa is performed during the removal of the colonoscope from the ileum/cecum to the anal canal [149].*

In the event that residual intestinal contents are detected in the intestinal lumen, it is strongly recommended to clean the surface of all examined areas of the mucous layer by injecting fluid through the instrumental canal of the endoscope or, if available, through a separate irrigation canal of the endoscope using a pump. With a significant amount of foamy contents, it is advisable to use a defoamer solution (ATC group: A03AX — other drugs for functional gastrointestinal disorders) [150–152].

- For colonoscopy and detection of epithelial benign neoplasms of the large intestine, it is **recommended** to use high-resolution video endoscopes for multimodal examination and image quality improvement [153–168].

The category of recommendation — B (the level of evidence — 2).

Comment: *In a study by Buchner, A.M. et al., the ADR value during large intestine examination using high-resolution equipment increased from 24.3% to 28.8% (p = 0.012) compared with standard colonoscopy, while the ADR of adenomas with a size of less than 5 mm increased from 16.9% to 19.9% (p = 0.024) [153]. In two retrospective cohort studies [154,157], the ADR values in similar groups increased by 8.2% (p = 0.02) and 12.6% (p = 0.007), respectively, during high-resolution colonoscopy compared with the standard one.*

A number of studies have demonstrated that the use of narrow-band imaging (NBI) technology does not lead to an increase in the ADR value; however, it allows detecting a significantly larger number of flat-type adenomas and adenomas localized in the right colon [156–158].

The effectiveness of narrow-band colonoscopy (NBI) in the differential diagnosis of SEN, determination of its margins, and targeted biopsy has been demonstrated in a number of studies [159,160]. The use of the NBI mode during colonoscopy makes it possible to perform differential diagnosis of SEN according to the NICE and JNET international classifications (in the NBI + magnification × 70 mode) [61,161–163].

A study by Yoshida, N. and co-authors has shown that digital contrast technology — LCI (linked color imaging) improves the detection of colorectal neoplasms compared to white light mode [164].

Suzuki, S. et al. published the results of a large multicenter randomized trial, wherein it was shown that LCI improves the detection rate of adenomas compared to white light mode (58.7% vs. 46.7%; P < 0.01) [165]. The other studies have demonstrated that the use of BLI (blue laser imaging) mode, compared with white light mode examination, can improve the detection of colorectal polyps, especially in relation to their location, size and morphology. The NICE and JNET classifications can be applied when using BLI for endoscopic differential diagnosis of adenomas and hyperplastic polyps [166,167].

In a large cohort study involving 1,936 patients, a higher level of ADR value was shown when using i-SCAN technology, compared with standard colonoscopy in white light mode [168]. However, in the other studies, there was no improvement in the detection rate of adenomas. Currently, the role of i-SCAN in improving the detection rate of adenomas has not yet been definitively proven, and larger prospective studies are required.

- To increase the detection rate of adenomas, it is **recommended** to additionally use software (artificial intelligence) during colonoscopy, which has demonstrated a reproducible level of accuracy in

the automated detection of epithelial benign neoplasms of the large intestine [169–173].

The category of recommendation — B (the level of evidence — 1).

Comment: *In a systematic review, an analysis of 6 randomized controlled trials was conducted to compare ADR during colonoscopy with and without the use of the CADe system (2,480 people in the CADe group, 2,482 — in the control group) [169]. The results of the meta-analysis showed a statistically significant increase in the adenomadetection rate in the case of using computer systems for automatic detection of polyps and an increase in the time of removal of the colonoscope. Another systematic review with a meta-analysis of seven randomized clinical trials (2,595 colonoscopies using CADe systems, 2,622 standard colonoscopies) showed an 80% increase in the average number of detected small adenomas per patient using automatic computer detection tools, compared with standard colonoscopy [170]. However, the studies included in the review were mainly conducted in one country (China); the level of endoscopists who performed colonoscopies was also not indicated. A meta-analysis of six randomized controlled trials (4,996 cases) showed a higher detection rate of adenomas and polyps during colonoscopy using artificial intelligence for flat adenomas and serrated formations on a wide base, although for polyps on the pedicle, 'standard' colonoscopy showed a better result [171]. A large multicenter randomized controlled trial (3,059 patients, 1,519 in the CADe colonoscopy group, 1,540 in the standard colonoscopy control group) showed an increase in the rate of detected adenomas, by both endoscopists with more than 5,000 colonoscopies and less experienced endoscopists [172]. Similar results were obtained in the research of domestic developments [173].*

• It is **recommended** to perform a forceps biopsy of a malignant large intestine tumor in patients aged over 18 years with the collection of at least 6 targeted biopsies from the most suspicious areas of the neoplasm in terms of malignancy in order to determine the histological type of the tumor, the grade of its differentiation and to determine the optimal treatment tactics [174,175].

The category of recommendation — C (the level of evidence — 4).

Comment: *In the study by Gado, A. et al., including 37 cases of CRC, it was shown that the sampling of 6 tumor fragments, compared with a smaller number, allows a statistically significant increase in the rate of histological confirmation of cancer from 61% to 92% ($p < 0.02$). The greatest prognostic accuracy is achieved when performing a targeted biopsy of the central part of the tumor (96.1%) [175].*

• To reduce the risk of colorectal cancer when a superficial epithelial neoplasm of the large intestine is found without signs of deep invasion, its removal with referral for histological examination is **recommended** [167,176–179].

The category of recommendation — C (the level of evidence — 4).

Comment: *SEN in the large intestine suspected of malignancy require a thorough endoscopic assessment, with adequate cleansing and examination of the entire neoplasm using a high-resolution video endoscope with virtual chromoscopy and magnification function, to identify areas of invasive growth for evaluation of the SEN according to S. Kudo's classification. In case of type V pits and the absence of obvious signs of deep invasion, it is proposed to remove the SEN in a single block and stage it according to the morphology. The data of the preoperative biopsy of the superficial epithelial formation of the large intestine do not allow us to reliably exclude the presence of adenocarcinoma micro-focuses in it. Studies on biopsy of malignant colorectal neoplasms have shown that the rate of false negative results can reach 18.5–86% [167]. According to Sung, H.Y., in 39.8% of cases, there were discrepancies in morphological diagnoses after forceps biopsy and resection of large intestine polyps (996 polyps in 813 patients were included in the study) [176]. Khalin, K.D. et al. report that the focus of adenocarcinoma in the superficial epithelial formation of the large intestine during preoperative biopsy was detected only in 16.6% of cases [177]. In a study by Hah, Y., forceps biopsy and resection techniques were compared. The*

factors reducing the diagnostic accuracy of the biopsy were the size of neoplasms > 3 cm, the presence of depression, and the macroscopic type of granular mixed LST. The rate of the morphological diagnosis discrepancy was 57.5% [178]. In the event that, due to any medical, organizational, administrative, legal or other circumstances, removal of the SEN is postponed to the stage of repeated colonoscopy, it is recommended to indicate in the conclusion of the primary colonoscopy protocol that a morphological examination of the neoplasm will be performed after its removal during repeated recommended/planned colonoscopy [182].

If it is impossible to remove the SEN in a single block due to insufficient equipment and/or experience of an endoscopist, the patient should be referred to an expert center [181–183].

If the SEN is subject to endoscopic removal, a biopsy should not be performed, since there is a risk of fibrosis in the submucosal layer, which significantly complicates endoscopic resection of the neoplasm. The incidence of fibrosis after biopsy reaches 77% [182]. The period of development of submucosal fibrosis is 3 weeks after the biopsy, and therefore, in the case of a biopsy, it is advisable to decide on further treatment tactics during this period [183].

• To reduce the risk of contamination and dispersion of tumor cells, it is **recommended** that forceps and loops used for biopsy or removal of potentially malignant tumors in patients aged over 18 years should not be reused during the current intervention, and tumor fragments should be collected at the end of the study [184].

The category of recommendation — C (the level of evidence — 4).

Comment: *Despite the low probability of iatrogenic transfer of tumor cells by the instruments used, it is not possible to completely eliminate the risk of metachronous CRC in this way, and therefore it is necessary to observe the safe (from an oncological point of view) order and sequence of application of transcanal instruments during endoscopic interventions [184].*

• It is **recommended** to consider morphological examination of completely removed superficial epithelial neoplasms as a method of final differential diagnosis of epithelial benign and early malignant neoplasms of the colon and rectum [1,3,70,180].

The category of recommendation — C (the level of evidence — 5).

Comment: *It is not a trivial task to make a reliable differential diagnosis between BEN and early CRC based on the results of an endoscopic examination and even on the results of a forceps biopsy.*

That is why it is recommended to remove both a benign tumor (BEN) and a neoplasm with suspected malignancy (but without signs of deep invasion) in a single block, which allows for a full-fledged morphological examination of the entire neoplasm and, accordingly, a final differential diagnosis [1,180].

• It is **recommended** to extract all epithelial neoplasms of the large intestine removed by endoscopic polypectomy, mucosal resection or submucosal dissection and send the removed specimen to verify the histology and assess the radicality of removal [185–192].

The category of recommendation — B (the level of evidence — 1).

Comment: *According to a meta-analysis by Mason, S.E. et al. [185], existing methods of endoscopic examination and analysis of neoplasms are not able to ensure the safe use of the 'resect and discard' strategy for neoplasms proximal to the rectosigmoid part; all removed neoplasms should be directed to a morphology. For a precise assessment of the horizontal and vertical planes of resection, it is recommended to fix the formations on a dense waterproof base [186–190]. The immediate fixation of the surgical material immediately after removal makes it possible to preserve the shape, size and orientation of the neoplasm and avoid twisting of the macrospecimen during fixation in formalin [186,191]. In addition, excessive stretching of the specimen should be avoided to prevent distortion and damage to the layers [186,192]. Circular tumors removed en bloc can be placed on a cylindrical object of suitable diameter (syringe, etc.) for better fixation.*

• When endoscopically removing superficial epithelial neoplasms of the large intestine

without submucosal invasion, adult patients are **recommended** to consider their removal radical at the negative edges of resection (vertical — Rv — and horizontal — Rh) in order to determine adequate follow-up periods in the future [193–195].

The category of recommendation — C (the level of evidence — 4).

Comment: *Endoscopic removal of superficial epithelial neoplasms is considered radical when removing tumors within healthy tissues (R0). A meta-analysis showed that the risk factors for local recurrence are large size, resection of neoplasms in fragments, as well as the presence of a residual tumor at the edges of resection (Rv1 or Rh1) [195]. If it is impossible to reliably assess the resection line (resection by fragments, pronounced coagulation damage to the edges during electro-excision) (Rx), it is recommended to classify this category of patients as those with an existing risk of neoplasm recurrence and shorten the follow-up interval for them [195,196].*

2.5 Other diagnostic tests

- RRS and sigmoidoscopy are **not recommended** as an independent screening method for large intestine SEN.

RRS and sigmoidoscopy are proposed to be used for a detailed examination of the anal canal area, the disconnected rectum [197–200].

The category of recommendation — C (the level of evidence — 5).

Comment: *An obvious disadvantage of RRS and sigmoidoscopy is the lack of the ability to examine a significant section of the large intestine, which makes their use as an independent method of screening/diagnosis of large intestine SEN less and less significant. This is also due to the growing understanding of the role of the serrated pathway of carcinogenesis, mainly in the right half of the intestine. Indeed, while the specificity of RRS and sigmoidoscopy for the diagnosis of neoplasms of the left half of the intestine is very high (98–100%), their sensitivity to the entire large intestine is unacceptably low and ranges from 35% to 70% for sigmoidoscopy and 10–20% for RRS [199,200].*

- For diagnostic purposes, large intestine (colon) endoscopy videocapsular (CEV) is **recommended** to be used as a complementary or independent/alternative method of endoscopic examination in patients with contraindications to performing flexible colonoscopy, or with incomplete flexible colonoscopy, or in patients who refuse to undergo flexible colonoscopy [201–207].

For adults — the category of recommendation — B (the level of evidence — 2).

For children — the category of recommendation — C (the level of evidence — 5).

Comment: *In 75–100% of patients using CEV, colon sections that were not reached during colonoscopy were visualized [201–204], while mucosal changes were detected in 24–100% of cases. In a study by Spada et al., computed tomography colonoscopy and CEV were compared in patients with incomplete colonoscopy [205]. With CEV, polyps ⩾ 6 mm were detected in 24.5% of patients (95% CI 16.6–34.4%), with computed tomography colonoscopy in 12.2% (95% CI 6.8–20.8%), with a relative sensitivity of 2.0 (95% CI 1.34–2.98), indicating a higher sensitivity of CEV for the diagnosis of formations ⩾ 6 mm. An analysis of the diagnosis of larger epithelial formations showed that with CEV, formations with a diameter of ⩾ 10 mm were detected in 5.1% of patients (95% CI 1.9–12.1%), with computed tomography colonoscopy in 3.1% of patients (95% CI 0.8–9.3%), with a relative sensitivity of 1.67 (95% CI 0.69–4,00).*

The sensitivity of CEV for the detection of polyps > 9 mm ranges from 87% to 92.8%, and the specificity is about 92% [206,207].

- For screening/diagnosis of large intestine SEN, it is **recommended** to use computed tomography colonoscopy as an independent/alternative method in patients with contraindications to colonoscopy, or in patients who refuse to undergo it or with incomplete colonoscopy [205,208–212].

For adults — the category of recommendation — B (the level of evidence — 2).

For children — the category of recommendation — C (the level of evidence — 5).

Comment: *The accuracy of computed tomographic colonoscopy in the diagnosis of colorectal cancer*

and large/widespread epithelial neoplasms is similar to optical colonoscopy in both symptomatic and asymptomatic patients, and significantly exceeds the diagnostic accuracy of irrigoscopy [205,209,211]. In a multicenter study involving 1,177 patients, the sensitivity and specificity of computed tomographic colonoscopy for detecting large intestine neoplasms > 9 mm in size reached more than 90% [208], but this method is significantly inferior to colonoscopy and colon endoscopy videocapsular in detecting flat SEN less than 10 mm in size. A serious obstacle to the use of computed tomography colonoscopy in the screening of high-risk patients is the increasing radiation burden on the patient during repeated examinations [210,211].

• In order to diagnose and detect neoplasms of the large intestine, it is **recommended** to use double-contrast barium enema in patients when it is impossible to examine all segments of the large intestine endoscopically or to use computed tomographic colonoscopy [213–215].

For adults — the category of recommendation — C (the level of evidence — 4).

For children — the category of recommendation — C (the level of evidence — 5).

Comment: *Barium enema with double contrast allows to examine the entire large intestine, with the help of which it is possible to identify up to 50% of large SENs [213].*

• Large intestine endosonography (Endo-Ultrasound) and magnetic resonance imaging (MRI) of the large intestine are **not recommended** to be used in regular clinical practice as an independent method of characterizing benign epithelial neoplasms of the large intestine in patients aged over 18 years [216–221].

The category of recommendation — B (the level of evidence — 1).

Comment: *A multicenter randomized controlled trial comparing magnification chromendoscopy and endo-ultrasound in the staging of early colorectal cancer did not reveal the advantages of endo-ultrasound, and the overall accuracy was 78% for both methods [216]. In four meta-analyses comparing the results of endo-ultrasound, CT, and MRI in assessing the T and N status of primary rectal tumors potentially subject to endoscopic removal, no significant differences were found between these methods [217–220]. The accuracy of both endo-ultrasound and MRI in distinguishing the T1 stage from the T2 stage was significantly limited, while there was a high risk of 'overestimating' the stage of the tumor process. In cases where the results of tumor T-staging differ between optical chromoendoscopy and endo-ultrasound/MRI, the results of visual assessment during endoscopic examination are suggested to be considered a priority [221].*

Endo-Ultrasound and/or MRI can help in assessing the invasion of rectal SEN into the submucosal base if, during visual assessment of the neoplasm, there is a suspicion of its germination into the submucosal layer.

The latest generation of ultrasound endoscopic equipment makes it possible to accurately determine the thickness of the anaplastic tissue, confirm or exclude tumor germination into the submucosal and muscular layers of the intestinal wall [221].

3. TREATMENT, INCLUDING DRUG AND NON-DRUG THERAPY, DIET THERAPY, PAIN RELIEF, MEDICAL INDICATIONS AND CONTRAINDICATIONS TO THE USE OF TREATMENT METHODS

Conservative patient management

• Conservative management, namely follow-up, without removal of epithelial benign neoplasms, is **recommended** for patients with miniature (1–5 mm) hyperplastic rectal polyps, usually multiple, provided that the hyperplastic nature of these polyps is determined with a high degree of reliability according to endoscopic examination using magnification in combination with virtual chromendoscopy [179,222–224].

The category of recommendation — C (the level of evidence — 4).

Comment: *Hyperplastic polyps have an extremely low potential for malignancy (less than 0.6%) [196]. The vast majority of miniature (⩽ 5 mm) rectal polyps are hyperplastic polyps [222,223].*

Endoscopic treatment of patients

• Endoscopic removal of all superficial epithelial neoplasms (SEN) of the large intestine without endoscopic signs of deep invasion is **recommended** [179,224–227].

The category of recommendation — C (the level of evidence — 4).

Comment: *The role of adenomas and serrated formations in carcinogenesis, as well as the effectiveness of their removal in interrupting the sequence of large intestine cancer development, has been proven in numerous studies [225–228].*

Epithelial neoplasms of the large intestine < 10 mm

• It is **recommended** to use the technique of 'cold' forceps biopsy (CFB) to remove epithelial benign neoplasms of the large intestine with a size of ⩽ 2 mm [229–235].

For adults — the category of recommendation — A (the level of evidence — 1).

For children — the category of recommendation — C (the level of evidence — 5).

Comment: *CFB allows complete removal of epithelial neoplasm of the large intestine with a size of ⩽ 2 mm in 95.5–100% of cases [230–232,235]. According to randomized trials, CFB is not inferior to 'cold' loop polypectomy in terms of the rate of complete resection and surpasses it in terms of the rate of removal of distant formations [233,234].*

• It is **not recommended** to use the technique of 'hot' biopsy (HB) to remove epithelial neoplasms of the large intestine, regardless of their size [179,235–237].

For adults — the category of recommendation — B (the level of evidence — 2).

For children — the category of recommendation — C (the level of evidence — 5).

Comment: *In randomized trials, HB was significantly inferior to 'cold' polypectomy in terms of the rate of removal within healthy tissues and led to more pronounced thermal damage to the biopsy material [236–238]. Removal of epithelial neoplasms of the large intestine ⩽ 5 mm by the HB technique leads to the detection of residual neoplasm tissue in 10–17% of cases [239,240].*

• It is **recommended** to use the technique of 'cold' polypectomy (CP) as the main method of removing flat (*type II)* and wide-based polypoid (*Is type*) epithelial neoplasms of the large intestine with a size of < 10 mm [241–243].

For adults — the category of recommendation — B (the level of evidence — 1).

For children — the category of recommendation — C (the level of evidence — 5).

Comment: *According to two meta-analyses, which included 2,481 patients, 4,535 formations, and 1,665 patients, 3,195 formations, comparing the results of 'hot' polypectomy (HP) and 'cold' polypectomy (CP), there was no significant difference in the rate of removal of tumors < 10 mm in size within healthy tissues.*

The time of the procedure, according to the both meta-analyses, was significantly higher in HP [241,242]. A randomized trial comparing CP and HP in patients undergoing antithrombotic therapy showed a significantly lower risk of delayed bleeding in the 'cold' polypectomy group [244].

• In case of suspected severe dysplasia or early carcinoma in an epithelial neoplasm of the large intestine with a size of < 10 mm, its removal using endoscopic resection of the large intestine mucosa in patients over 18 years of age (EMR) is **recommended** [245,246].

The category of recommendation — C (the level of evidence — 4).

Comment: *CP leads to a more superficial removal of epithelial neoplasms of the large intestine, compared with HP: the rate of the presence of a mucosal muscle plate in the specimen did not differ in the HP and CP groups; however, the tissues of the submucosal layer were more often detected in the specimens after 'hot' polypectomy [247]. According to a retrospective study comparing the morphological results of CP and EMR, the depth of resection in the histological specimen (from the level of the mucosal muscle plate) in the CP and EMR groups was 76 and 338 microns, respectively (p < 0.001) [248]. The rate of removal of neoplasms with positive or non-morphologically assessed vertical resection edges was more often observed in the CP group than in the EMR group, 6% and 1%, respectively (p < 0.05) [248].*

Epithelial neoplasms of the large intestine 10–19 mm in size

• It is **recommended** to remove flat (*type II*) and wide-based (*Is type*) epithelial neoplasms of the large intestine with a size of 10–19 mm using endoscopic resection of the large intestine mucosa (EMR) either 'hot' (HP) or 'cold' polypectomy (CP) [243,249,250].

For adults — the category of recommendation — B (the level of evidence — 2).

For children — the category of recommendation — C (the level of evidence — 4).

Comment: *EMR and HP have a similar rate of complete resection when removing epithelial neoplasms up to 14 mm in size [239,250]. Submucosal injection of the solution reduces the risk of deep thermal damage to the intestinal wall.*

• It is **recommended** to perform endoscopic resection of the large intestine mucosa (EMR) when removing epithelial neoplasms of the large intestine in a single block or within healthy tissues with the minimum possible number of its fragments [250–252].

The category of recommendation — C (the level of evidence — 4).

Comment: *Endoscopic removal of epithelial neoplasms of the large intestine in fragments is an independent risk factor for local recurrence [251], the rate of which significantly increased when the formation was removed in 3 or more fragments [252]. The time of recurrence was minimal (3.8 ± 1.9 months) when the tumor was removed in 5 or more fragments [251].*

• It is **recommended** to use both saline sodium chloride solution** and more viscous solutions for submucosal injection during endoscopic resection of the mucous layer [243,250,252,253].

The category of recommendation — B (the level of evidence — 1).

Comment: *According to the meta-analysis data, the use of more viscous solutions during EMR increases the likelihood of single-block removal and reduces the risk of incomplete tumor removal without affecting the complications rate [253].*

• It is **not recommended** to perform routine preventive clipping of a mucosal defect in order to prevent delayed bleeding after endoscopic removal of epithelial neoplasms of the large intestine in adult patients [254,255].

The category of recommendation — B (the level of evidence — 1).

Comment: *Prophylactic clipping of a mucosal defect in order to prevent delayed bleeding did not demonstrate advantages, both in the general group and in neoplasms > 20 mm in size [254,255]. Prophylactic clipping leads to an increase in the duration of the intervention [256].*

Epithelial neoplasms of the large intestine > 20 mm in size

• It is **recommended** to choose a technique for the removal of a flat or polypoid on a wide base epithelial neoplasm of the large intestine measuring ⩾ 20 mm, depending on a preliminary endoscopic assessment of its morphological structure in patients aged over 18 years [257,258].

The category of recommendation — B (the level of evidence — 2).

Comment: *Compared with EMR, ESD is associated with a higher rate of complete resection, as well as with less involvement of the lateral edges of resection and recurrence, and has an advantage in histological assessment of the specimen [258].*

• It is **recommended** to perform endoscopic removal of a flat or wide-based epithelial neoplasm of the colon measuring ⩾ 20 mm with a high/significant risk of having a malignant tumor focus in a single block.

The method of choice is dissection in the submucosal layer or hybrid dissection in the submucosal layer in patients aged over 18 years [259,260].

The category of recommendation — B (the level of evidence — 2).

• It is **recommended** to perform endoscopic removal of a flat or wide-based epithelial formation of the colon measuring ⩾ 20 mm without endoscopic signs of deep invasion by endoscopic resection of the mucous layerwith one or more fragments, or dissection in the submucosal layer, depending on the experience of the medical institution in patients aged over 18 years [261–263].

The category of recommendation — B (the level of evidence — 2).

Comment: *When neoplasms ⩾ 20 mm in size are removed after EMR with fragments, the rate of local recurrence is 20% [264]. ESD increases the likelihood of complete removal of the formation compared to EMR and reduces the risk of local recurrence; however, these advantages are achieved due to a greater risk of perforation and increased duration of intervention. The potential need for surgery for ESD complications is greater than for EMR complications [262,265,266].*

According to one of the largest studies on EMR, the risk of local recurrence after EMR in fragments is 16% and 4% 4 and 16 months after the intervention, respectively, with a recurrence size of ⩽ 5 mm in 71.7% of cases, and its endoscopic treatment successful in 93.1% of cases [263]. Risk factors for the development of local recurrence after EMR in fragments were the size of the neoplasm > 40 mm, massive bleeding during the intervention, and the presence of severe dysplasia/HGD [267].

• If a medical organization does not have sufficient experience in removing 'complex' epithelial neoplasms of the large intestine through an endoscope (> 40 mm in size, occupying more than 2/3 of the circumference of the intestine, recurrent, without' lifting'), it is **recommended** to refer an adult patient to an expert-level institution [268–270].

The category of recommendation — C (the level of evidence — 4).

Comment: *EMR or ESD in the removal of complex epithelial neoplasms of the large intestine, performed in specialized centers, are effective and fairly safe procedures [268,270].*

• The use of transanal endoscopic microsurgery (TEM) is **recommended** as an alternative method of local removal of large and giant epithelial rectal neoplasms in patients aged over 18 years [271,272].

The category of recommendation — B (the level of evidence — 1).

Comment: *The duration of ESD was significantly higher than that of TEM, but the rate of complications, recurrences, and removal of large epithelial formations and early rectal cancer as a single block did not differ. The postoperative hospital stay was 1.6 times longer after TEM [273].*

• It is **recommended** (if possible and necessary equipment is available) to mark large intestine neoplasms with an endoscopic BLACK EYE marker in patients aged over 18 years, suspected of early cancer, as well as other neoplasms with the expected difficulty of detecting them during surgery and/or repeated endoscopic examination [273].

The category of recommendation — B (the level of evidence — 2).

Comment: *The endoscopic marking with the BLACK EYE in the localities of suspected malignancy, as well as early cancer, helps to identify the site of resection during a control colonoscopy or during surgery.*

*It is preferable to mark more than one, usually 2–3 marks, on different intestinal walls distal to the neoplasm and document in detail the injection (material, volume, position relative to the neoplasm) in the examination protocol. It has been shown that the administration of the BLACK EYE after a preliminary submucosal injection of saline sodium chloride solution** is safe [273].*

Epithelial neoplasms on pedicle in the large intestine

• It is **recommended** to use the technique of hot polypectomy (HP) to remove epithelial neoplasms of the large intestine on the pedicle (*type 0-Ip*), as well as the use of mechanical hemostasis (using a single-use ligature device or clip applicator) in order to prevent immediate and delayed bleeding when removing type *0-Ip* polyps with a head size ⩾ 20 mm and/or pedicle size ⩾ 10 mm in diameter [179,224,243,250,274,275].

The category of recommendation — B (the level of evidence is 1).

Comment: *The main method of removing polyps on the pedicle is HP. The main type of complications in the removal of such tumors is delayed bleeding. Such methods of mechanical hemostasis as endoscopic ligation or clipping reduce the risk of*

bleeding after removal of epithelial neoplasms on the pedicle [276,277]. The greatest effect of bleeding prevention has been demonstrated in cases of neoplasms on the pedicle > 20 mm in size [278].

4. MEDICAL REHABILITATION AND SPA TREATMENT, MEDICAL INDICATIONS AND CONTRAINDICATIONS TO THE USE OF MEDICAL REHABILITATION METHODS, INCLUDING THOSE BASED ON THE USE OF NATURAL HEALING FACTORS

There are no specific rehabilitation measures for patients with benign neoplasms of the colon and rectum. Medical rehabilitation measures after endoscopic surgery are aimed, as after any surgery, at the fastest possible recovery in the postoperative period. However, they are different for patients after ESD, EMR, and 'cold' loop polypectomy and imply limited exercise and dietary restrictions for 7–14 days.

5. PREVENTION AND FOLLOW-UP, MEDICAL INDICATIONS AND CONTRAINDICATIONS TO THE USE OF PREVENTIVE METHODS

Prevention of BEN and reduction of the risk of CRC implies a multifaceted approach that covers lifestyle, correction of bad habits and screening studies. The methods of prevention of BEN and CRC are divided into two categories: primary preventive methods aimed at identifying and correcting risk factors, and secondary preventive methods involving diagnosis (screening) and removal of epithelial neoplasms of the large intestine.

The primary prevention of BEN and CRC includes the need to follow a certain lifestyle, as well as the exclusion of risk factors for the development of BEN and CRC.

There is a correlation between reducing the risk of developing BEN, CRC, and human eating behavior aimed at increasing the consumption of vegetables and fruit, whole grains, eliminating large amounts of red and processed meat, high-fat foods, and limiting alcohol consumption [279–281].

Secondary prevention of BEN and CRC (screening) includes the diagnosis and removal of large intestine BEN, which reduces the risk of developing CRC [282].

- Rapid examination of feces for latent blood by immunochromatographic method is **recommended** for persons aged 40 years and over 18 years [21,86,281,283].

The category of recommendation — B (the level of evidence — 1).

Comment: *The advantages of stool analysis for latent blood include: non-invasiveness, sensitivity to cancer and adenomas is 79% and 30%, respectively, and low cost [283,284].*

- In persons aged over 18 years with a positive rapid stool test for latent blood by the immunochromatographic method, it is **recommended** to use screening colonoscopy with the detection and removal of all BENs [285].

The category of recommendation — C (the level of evidence — 5).

Comment: *Primary screening colonoscopy should be performed upon reaching the age of 40 (Order of the Ministry of Health of the Russian Federation dated 04/27/2021 N 404n (as amended on 02/01/2022) "On approval of the Procedure for preventive medical examination and medical examination of certain groups of the adult population") [48]. In patients with first-line relatives with CRC, screening colonoscopy should be performed at the age of 10 years younger than the age of the blood relative at the time of CRC diagnosis [286].*

The follow-up period for patients who underwent endoscopic electrosurgical removal of epithelial neoplasms of the large intestine is determined by the morphological characteristics of these neoplasms, as well as the method of their removal [287].

- It is **recommended** to use criteria of low and high risk of CRC development in people aged over 40 years when choosing the interval for repeated colonoscopy after removal of aBEN [288–291].

The category of recommendation — C (the level of evidence — 4).

Comment: *Patients at low risk of developing CRC: 1–4 adenomas < 10 mm with low grade dysplasia with/without villous components, or with any serrated polyp less than 10 mm without dysplasia) are recommended to have a repeat colonoscopy after 3 years [288,289].*

A follow-up colonoscopy after 1–2 years is recommended for patients at high risk of CRC: adenomas ⩾ 10 mm or with high-grade dysplasia, the number of adenomas ⩾ 5, serrated polyps ⩾ 10 mm, as well as serrated polyps of any size with dysplasia [289].

If no polyps requiring follow-up are found during the first follow-up colonoscopy, a repeat colonoscopy will be performed after 3 years. If polyps corresponding to a high risk of CRC are detected at the first control colonoscopy, the next endoscopic examination is performed after 1–2 years [289,291].

INTERVALS BETWEEN REPEATED COLONOSCOPIES [288–295]

Indicators	Colonoscopy after tumor removal after	Repeated colonoscopy after	Follow-up after
Fragmentary adenoma resection	3-6 months	1 year	3 years
Criteria for high-risk CRC	1-2 years	3 years	According to risk criteria
Criteria for low-risk CRC	3 years	According to risk criteria	According to risk criteria

• It is **recommended** to take into account the method of polypectomy when choosing the timing of repeated colonoscopy after removal of BEN [292–295].

The category of recommendation — B (the level of evidence — 2).

Comment: *In the case of fragmentary resection of a polyp larger than 20 mm, endoscopic examination should be performed after 3–6 months, followed by a follow-up colonoscopy after 1 year.*

This is due to the fact that fragmentary removal of BEN is associated with a significant risk of tumor recurrence and the development of interval-dependent CRC [292–295].

6. ORGANIZATION OF MEDICAL CARE

Medical care for patients with benign neoplasms of the large intestine, with the exception of medical care within the framework of clinical testing, in accordance with Federal Law No. 323-FL dated 11/21/2011 "On the Basics of Public Health protection in the Russian Federation" (with amendments and additions), is organized and provided:

1) In accordance with the regulations on the organization of medical care by type of medical care, which is approved by the Ministry of Health of the Russian Federation;
2) In accordance with Order of the Ministry of Health of the Russian Federation dated 12/06/2017 N 974n "On approval of the Rules for endoscopic examinations", Order of the Ministry of Health of the Russian Federation dated 04/02/2010 N 206n "On approval of the Procedure for providing medical care to the population with diseases of the large intestine, anal canal and perineum of the coloproctological profile", Order of the Ministry of Health of the Russian Federation dated 11/15/2012 N 922n "On approval of the Procedure for providing medical care to the adult population in the field of "surgery", by Order of the Ministry of Health of the Russian Federation dated 02/19/2021 N 116n "On approval of the Procedure for providing medical care to the adult population with oncological diseases", by Order of the Ministry of Health of the Russian Federation dated 06/09/2020 N 560n "On approval of the Rules for X-ray examinations", by Order of the Ministry of Health of the Russian Federation dated 06/08/2020 N 557n "On approval of the Rules for ultrasound examinations", by Order of the Ministry of Health of the Russian Federation dated 05/18/2021 N 464n "On approval of the Rules for conducting laboratory tests";

3) Based on current clinical guidelines;
4) Taking into account the standards of medical care approved by the Russian Ministry of Health.

During a diagnostic colonoscopy, a total SEN biopsy of up to 10 mm in size can be performed using a cold total loop or forceps biopsy.

The recommended number of neoplasms subject to total biopsy should not exceed 5 [296].

The rate of complications during total biopsy by cold polypectomy [297] in outpatient settings is: 0.07% — perforation, 0.14% — bleeding, 0.07% — submucosal hematoma [299], which is comparable to complications during diagnostic colonoscopy without additional interventions.

It is recommended that all the material obtained during endoscopic biopsy or endoscopic removal of neoplasms and sent for lifetime morphological diagnosis be placed in a vial with a sufficient amount (at least 20 times the volume of the specimen) of 10% solution of neutral (buffered) formalin for a period of no more than 24–48 hours (Order of the Ministry of Health of the Russian Federation dated March 24, 2016 No. 179n "On the Rules for conducting pathological examinations").

Treatment of patients with benign neoplasms of the large intestine is carried out as planned in the endoscopic department of a medical organization as part of the provision of primary specialized medical care in a day hospital in the profiles of coloproctology, oncology, surgery, as well as in the provision of specialized medical care in these profiles in a day or 24-hour hospital.

The indication for hospitalization in a medical organization for the provision of primary specialized medical care in a day hospital is the presence of a superficial epithelial neoplasm (SEN)Is and / or type II with a size of less than 10 mm, in the amount of up to 10 pieces, the absence of recurrent benign neoplasms and signs of invasion into the submucosa in patients with anesthetic risk of I or II degree on the ASA scale. Also, the provision of specialized medical care in a day hospital or a short-stay hospital is indicated if: the size of polyps on the pedicle (Ip), i.e. the diameter of the pedicle is less than 10 mm, the size of its head is less than 20 mm, the size of SEN Is and / or II type is less than 20 mm, the absence of recurrent benign neoplasms and signs of invasion into the submucosa, the number of formations is up to 10, the degree of anesthetic risk on the ASA scale is I or II.

Indications for hospitalization in a medical organization for the provision of specialized medical care in a 24-hour hospital are: polyps on the pedicle (Ip) with a diameter of more than 10 mm, the head of the polyp with a size of more than 20 mm, as well as SEN Is and/or type II and laterally creeping tumors with a size of more than 20 mm. Hospitalization is also indicated in the presence of more than 10 neoplasms to be removed, suspected superficial invasion or recurrent neoplasm, as well as in patients with polyps of any size and anesthetic risk on the ASAIII scale and higher. A high risk of complications — bleeding, perforation, are also indications for referral to a 24-hour hospital. When the patient is in a 24-hour hospital, there are no restrictions on the methods of endoscopic removal of SEN.

7. ADDITIONAL INFORMATION (INCLUDING FACTORS AFFECTING THE OUTCOME OF THE DISEASE OR CONDITION)

• Possible adverse events and complications during colonoscopy and removal of BEN of large intestine.

Possible adverse events and complications are one of the most important factors influencing the outcome of diagnosis and treatment/removal of superficial epithelial neoplasms of the large intestine. For their registration and classification by severity, it is proposed to use the new integrated classification "AGREE" [299]. It is suggested that all adverse events that occur should be recorded both at the stage of preparation for colonoscopy (even if the planned colonoscopy was not performed), and during its implementation and for at least 30 days after it. When several adverse events occur during/after a colonoscopy that are clearly

ORGANIZATION OF MEDICAL CARE FOR PATIENTS WITH EPITHELIAL NEOPLASMS

Indicators	Indications for various types of medical care			
	Primary specialized medical and sanitary care (outpatient)	**Primary specialized medical and sanitary care (day hospital)**	**Specialized medical care (day hospital), short-stay hospital**	**Specialized medical care (24-hour hospital)**
SEN size and type	Is and/or type II less than 10 mm	Is and/or type II less than 10 mm	Polyps on the pedicle with a diameter of less than 10 mm (Ip); polyp head less than 20 mm (Ip); SEN Is and/or type II less than 20 mm	Polyps on the pedicle (Ip) more than 10 mm; polyp head more than 20 mm; SEN Is and/or type II, LST more than 20 mm
Number of neoplasms	Up to 5 pieces	Up to 10 pieces	Up to 10 pieces	Not regulated
Recurrent neoplasms and invasion	Unacceptable	Unacceptable	Unacceptable	Suspected surface invasion or recurrent neoplasm
Removal method for SEN	Cold total loop or forceps biopsy	Cold polypectomy, hot polypectomy	Cold and hot polypectomy. Endoscopic resection of the mucous layer	Without restrictions
Anaesthetic risk (ASA)	I or II	I or II	I or II	I, II, III and higher
Additional indications	-	-	-	Having a high risk of bleeding or perforation of the large intestine
Equipping a medical organization	Endoscopic office or endoscopic department	Availability of a license to provide primary health care in a day hospital in anesthesiology and intensive care	Availability of a license to provide primary health care in a day hospital or a short-stay hospital in anesthesiology and intensive care	Availability of a license to provide specialized medical care in inpatient settings in anesthesiology and intensive care.

related to each other, it is necessary to classify only the most serious adverse events [300].

Diagnostic errors (for example, incorrect interpretation of the results of chromocolonoscopy or endo-ultrasound) are not included in the "AGREE" classification of adverse events/complications in gastrointestinal endoscopy and are considered separately.

• **Bleeding during colonoscopy for BEN removal.**

Bleeding is the most common complication in the removal of SEN of the large intestine, observed in 0.3% — 6.1% of patients. Most postoperative bleeding develops in the first 7 days, but it can develop up to 14 days after surgery [301]. Intestinal bleeding, including severe bleeding, can develop after a biopsy, as well as as a result of 'rough' endoscope manipulations during a diagnostic colonoscopy [302]. The risk of bleeding depends on the patient's condition, the size and histological type of the lesion, its location in the intestine, and the method of removal.

• Risk factors for bleeding related to the patient's condition are: the presence of cardiovascular diseases, in particular hypertension; disorders of the blood coagulation system, including as a result of taking nonsteroidal anti-inflammatory and anti-rheumatic drugs (NSAIDs), platelet aggregation inhibitors(ATCcodeB01 antithrombotic agents, except heparin) and antithrombotics.

• Risk factors related to the nature of the neoplasm are: the size of the formation is more than 10 mm; the diameter of the pedicle is more than 5 mm; localization in the right parts of the large intestine; malignancy and the presence of inflammatory changes.

• Risk factors related to the nature of surgical endoscopic intervention include: endoscopic electrosurgical removal of large intestine neoplasms, especially EMR and ESD; the use of only cutting (risk factor for immediate bleeding) or exclusively coagulating (risk factor for delayed bleeding) current; visible crossed vessel in the wound bottom; pronounced coagulation damage in the wound bottom; hematoma and visible muscle fibers in the wound bottom. When formations up to 10 mm are removed by cold loop resection, intraoperative bleeding occurs with a rate of up to 5.7%, and the risk of delayed bleeding is 0–0.5%.

When performing EMR of formations over 20 mm, the risk of bleeding is 5% — 7%. When large (up to 40 mm) adenomas are removed, the risk of bleeding increases to 8.9% of cases, and when giant (more than 40 mm) adenomas are removed, it increases to 18.4% [303–308].

• **Emergency colonoscopy is the main method of instrumental diagnosis, stopping and preventing recurrence of bleeding.**

Endoscopic stop of bleeding can be performed using hemostatic forceps in the soft coagulation mode and/or by mechanical hemostasis using a device for applying single-use ligatures to the stump of the polyp pedicle or clip applicators. Thermal hemostasis should be performed with great caution due to the risk of delayed perforation, especially in the right large intestine.

As an alternative method of hemostasis, it is possible to use irrigating hemostatic agents, powders (Hemoblock, EndoClot, etc.).

In case of ineffectiveness of endoscopic hemostasis, urgent surgery is necessary.

• **Damage to the large intestine wall during colonoscopy.**

Damage to the large intestine wall can occur during diagnostic colonoscopy, biopsy, and is unavoidable during removal of the large intestine SEN. The degree and depth of damage range from a superficial defect of the mucous layer to organ perforation and, when performing tumor resection, are ranked in accordance with the Sydney Classification of damage to the large intestine wall during endoscopic resection [310].

The distinguished defect types are as follows:

• 'Type 0' defect. The usual post-resection wound. The mucous layerwith the neoplasm is completely excised, the submucosal layer is partially resected. Obliquely directed intersecting fibers of the connective tissue of the submucosal layer are visible (dull blue if a colored solution has been introduced); intact vessels of the submucosal layer may be visible. There is no risk of delayed perforation. Tactics: you can complete this resection without clipping.

• 'Type I' defect. The mucosa and submucosa are completely resected. The muscle layer is visible, but it is not mechanically damaged. The risk of delayed perforation is minimal. Tactics: it is possible to complete this resection; clipping is at the discretion of the doctor.

The authors of the classification performed wound clipping in 31.6% of patients.

• 'Type II' defect. Local loss of the boundary between the submucosa and the muscle layer (usually due to fibrosis), suspicious of damage to the muscle layer, or making it impossible to assess damage to the muscle layer. The risk of delayed perforation is 1.7%. Tactics: preventive clipping.

• 'Type III' defect. The muscle layer is damaged (partially resected).

A target symptom in a post-resection wound (defect target sign = DTS) or in a macro-specimen (specimen target sign = STS). Tactics: wound clipping to prevent delayed perforation; hospitalization; a short course of antibacterial therapy using broad-spectrum antibiotics; observation in a 24-hour hospital.

• 'Type IV' defect. Obvious/ clearly defined hole with a white coagulation ring around it; no visible contamination with intestinal contents. Full-layer resection with a hole; the wound is clean (not contaminated with intestinal contents). Tactics: immediate clipping; hospitalization; antibacterial prophylaxis or therapy in consultation with a clinical pharmacologist; observation in a 24-hour hospital.

• 'Type V' defect. Explicit/clearly defined hole with a white coagulation ring around it, with visible contamination by intestinal contents. Full-layer resection with a perforation hole. Tactics: emergency hospitalization, taking decision on surgery.

• The clinical picture in the postoperative period depends on the depth and degree of damage to the large intestine wall, as well as the timeliness of the diagnosis of complications and the therapeutic measures taken. Along with non-specific and non-dangerous manifestations of 'postoperative discomfort', characteristic manifestations are also distinguished, which are isolated into separate nosological units.

• Postcoagulation syndrome (PCS) occurs in 4.8% to 14.2% of cases and, as the name suggests, is associated with thermal trauma to the muscular and serous lining of the large intestine without perforation. Typical manifestations of PCS syndrome are: local pain, soreness on palpation and symptoms of irritation of the peritoneum in the projection of the intervention; fever and chills; increased levels of leukocytes and C-reactive protein. An X-ray scan of the abdominal organs or CT scan of the abdominal organs show no signs of perforation. NSAIDs (ATC M01A Nonsteroidal anti-inflammatory and antirheumatic drugs) are prescribed to relieve pain and general inflammatory response, and broad-spectrum antibiotics (ATC J01 Antibacterial drugs of systemic action) are prescribed in consultation with a clinical pharmacologist. The patient is under observation to rule out delayed perforation. Most patients recover without complications, but in some cases the described clinical picture may be a harbinger of delayed perforation [313–316].

• Perforation of the large intestine (type IV or V defect according to the Sydney Classification) can develop directly during endoscopic intervention (intraoperative) and in the postoperative period (delayed perforation). It is important to recognize an intraoperative perforation immediately during the intervention. In the absence of contamination of the wound and abdominal cavity (type IV defect), it is recommended to clip the through defect (ideally after complete removal of the neoplasm), hospitalize the patient, or prolong its duration, conduct antibacterial prophylaxis or therapy in consultation with a clinical pharmacologist and follow-up in a 24-hour hospital. If endoscopic suturing is not possible, surgery is recommended.

• If the wound and abdominal cavity are contaminated with intestinal contents (type V defect), it is recommended that the situation be discussed by a consultation with a coloproctologist or a surgeon. If it is acceptable, the following steps should be done: clipping of the through defect, hospitalizing the patient, or extending its duration, carrying out antibacterial prophylaxis or therapy in consultation with a clinical pharmacologist. If endoscopic suturing is not possible, surgery is recommended. If the condition worsens, signs of peritonitis appear, a significant amount of fluid is in the abdominal cavity, or if endoscopic resection is incomplete, surgical treatment is indicated.

• Delayed perforation is a perforation of the large intestine wall that is diagnosed/develops after a certain period of time after performing EMR/ESD. Missed intraoperative perforation is often diagnosed in the immediate postoperative period by the presence of free gas in the abdominal cavity with an X-ray of the abdominal organs, or preferably with CT of the abdominal organs, which is more sensitive as a diagnostic method. The 'true' delayed perforation caused by deep/transmural damage to the intestinal wall during the surgery (for example, type III defect according to the Sydney Classification) develops at a later date. The rate of delayed perforations reaches 1.0–1.9% after EMR and 0.1–0.4% after ESD. In most cases, delayed perforation is confirmed within 14 hours after resection; in a third of cases, after 24 hours. Delayed perforation is diagnosed based on the characteristic clinic of perforation of a hollow organ into the abdominal cavity/retroperitoneal tissue (signs of intoxication and inflammatory reaction, pain and soreness on palpation of the abdomen, peritoneal symptoms). The volume and method of emergency surgery are determined

depending on the location of the perforation and the nature of the complications.

• Fulminant necrotizing fasciitis (Fournier's syndrome) is rare, but the mortality rate reaches 20–40%. The cause of the syndrome is perforation of the lower ampullary rectum. When the pelvic fiber is infected, the infectious and inflammatory process can spread to the tissues of the perineum, anterior abdominal wall, causing multiple muscle necrosis and inflammation of the surrounding fascia, which can quickly lead to the development of sepsis and DIC syndrome. Perforation of the extraperitoneal part of the rectum can be diagnosed as mediastinal emphysema, subcutaneous emphysema, or perirectal abscess. It is necessary to immediately begin treatment with broad-spectrum antibiotics (ATC J01 Antibacterial drugs of systemic action) and perform surgery.

• Large intestine stenosis in the area of endoscopic intervention refers to late complications, it is rare, as a rule, after circular resection / dissection of large formations, in particular, the rectum. The method of choice in the treatment of this complication is endoscopic balloon dilation of large intestine stenosis [315,316].

• Risk factors that increase the likelihood of adverse events / complications during endoscopic surgery, including the risk of postcoagulation syndrome and perforation of the intestinal wall, are: inadequate preparation of the patient and intestine for intervention; fibrosis of the submucosal layer; the size of the neoplasm (the most complex are giant SEN, more than 40 mm), localization of the formation (dome of the cecum, hepatic and splenic bends); the type of formation and the nature of its growth; localization in the projection of large vessels; technical unpreparedness and technical difficulty of removing the SEN; little experience of an operating endoscopist; long duration of surgery.

• One of the leading risk factors is fibrosis of the submucosal layer, the causes of which are: inflammation; desmoplastic tissue reaction in response to tumor growth; tumor mass effect (usually with a neoplasm size of ⩾ 40 mm); laterally creeping tumors of the non-granular type with LST-NG-PD depression; localization of SEN in caecum; tumor growth through the fold; previously performed biopsy; 'trial' injections into the submucosa; incomplete removal with delayed re-intervention, etc. According to severity, fibrosis of the submucosal layer is divided into 3 degrees: F0 fibrosis is absent — the submucosal layer is transparent; F1 — moderate fibrosis — a white spider-like structure in the transparent submucosal layer; F2 — severe fibrosis — a white muscle-like structure without a transparent submucosal layer [317].

• **Infectious complications during colonoscopy.** The infectious complications associated with colonoscopy include transient bacteremia, which is caused by the entry of normal intestinal flora into the bloodstream. The rate of bacteremia during colonoscopy reaches 4% (from 0% to 25%). However, clinical manifestations of infection (up to reported cases of infectious endocarditis) are extremely rare, and in most cases, do not require antibiotic prophylaxis. Possible infectious complications of colonoscopy also include the development of pararectal abscesses, acute appendicitis and acute diverticulitis. According to the literature, acute diverticulitis is most common among them, the incidence of which within 30 days from the moment of colonoscopy can reach 0.84 (0.50–1.33) per 1,000 colonoscopies. The risk of complications increases in patients aged over 70 years, as well as in the presence of diverticular disease and the physical status of patients II-III according to ASA [318,319].

• **Cardiorespiratory complications during colonoscopy.** The incidence of cardiorespiratory complications varies widely from 0.06% to 19.1%, and in the group of patients aged over 80 years, it reaches 28.9% [318,320]. The most serious complications in this group are angina pectoris, acute myocardial infarction, transient ischemic attack (TIA), and stroke, usually caused by concomitant diseases [318,320,322,323]. TIA is most common, and the incidence of TIA within 30 days of colonoscopy can reach 16.8 (16.1–17.6) per 10,000 colonoscopies [318,321].

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