



# The Method of "Cold" Snaring Mucosa Resection with Preliminary Hydro-Preparation for the Removal of Colorectal Epithelial Neoplasms Through an Endoscope

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**Aim:** to analyze the safety and effectiveness of the method of cold snaring resection with preliminary hydropreparation when removing superficially colorectal epithelial neoplasms with a diameter of 5 to 25 mm.

**Material and methods.** The number of complications and disease recurrence after endoscopic excisions by "cold" snaring resection with preliminary hydropreparation of superficially neoplasms with a diameter of 5 to 25 mm was assessed.

**Results.** Neoplasms were removed in a single block in 89/122 (72.95 %) cases. Neoplasms with a diameter of 5 to 9 mm were excisions in a single block in 100 % of cases, with a diameter of 9 to 14 mm in 28/30 (93.33 %) cases, with a diameter of 15 to 19 mm in 12/38 (31.57 %) cases. According to the results of a lifetime pathoanatomic examination of the removed material, serrated dysplasia (serrated dysplasia, low grade) was detected in 76 cases; micro vesicular hyperplastic polyps (Hyperplastic polyp, micro vesicular type MVHP) were established in 9 cases; hyperplastic polyps containing goblet cells (Hyperplastic polyp, goblet cell GCHP) were in 5 cases; tubular adenoma with dysplasia (Tubular adenoma, low grade) was in 32 cases. Delayed bleeding and perforation of the intestinal wall, both at the time of resection, and in the delayed period was not observed. No local recurrence was detected in the groups of patients with neoplasms diameters of 5–9 and 10–14 mm. One case of local recurrence was detected in a group of patients with a neoplasms diameter from 15 to 19 mm (1/38 = 2.63 %) and one case in a group with a neoplasms diameter of 20–25 mm (1/5 = 20 %).

**Conclusions.** Cold endoscopic snaring resection of colorectal epithelial neoplasms with preliminary hydropreparation in the submucosa is a safe and effective method of excisions superficially epithelial neoplasms of the colon with a diameter of 5 to 19 mm.

**Key words:** colorectal epithelial neoplasm, cold snaring mucosal resection, serrated dysplasia

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## Метод «холодной» петлевой резекции с предварительной гидропрепаровкой при удалении эпителиальных новообразований толстой кишки через эндоскоп

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**Цель исследования:** провести анализ безопасности и эффективности применения метода «холодной» петлевой резекции с предварительной гидропрепаровкой при удалении плоских эпителиальных новообразований толстой кишки диаметром от 5 до 25 мм.

**Материал и методы.** Была выполнена оценка количества осложнений и рецидивов новообразований после эндоскопического удаления 122 эпителиальных новообразований толстой кишки у 98 пациентов методом «холодной» петлевой резекции с предварительной гидропрепаровкой плоских новообразований диаметром от 5 до 25 мм.

**Результаты.** Единым блоком новообразования были удалены в 89/122 (72,95 %) случаев. Новообразования диаметром от 5 до 9 мм удалялись единым блоком в 100 % случаев, диаметром от 9 до 14 мм — в 28/30 (93,33 %) случаев, диаметром от 15 до 19 мм — в 12/38 (31,57 %) случаев. По результатам прижизненного патолого-анатомического исследования удаленного материала, согласно 5-му изданию Международной гистологической классификации опухолей пищеварительной системы (ВОЗ, 2019 г.), в 76 случаях была выявлена зубчатая дисплазия легкой степени (serrated dysplasia, low grade); в 9 случаях установлены микровезикулярные гиперпластические полипы (Hyperplastic polyp, microvesicular type MVHP); в 5 случаях — гиперпластические полипы, содержащие бокаловидные клетки (Hyperplastic polyp, goblet cell); в 32 случаях — тубулярная аденома с легкой дисплазией (Tubular adenoma, low grade). Отсроченного кровотечения и перфорации стенки кишки как в момент выполнения резекции, так и в отсроченный период не наблюдалось. В группах пациентов с диаметром новообразований 5–9 и 10–14 мм местного рецидива выявлено не было. Один случай местного рецидива был выявлен в группе пациентов с диаметром новообразований от 15 до 19 мм (1/38, что составило 2,63 %) и один случай в группе с диаметром новообразований 20–25 мм (1/5, что составило 20 %).

**Выводы.** «Холодная» эндоскопическая петлевая резекция эпителиальных новообразований толстой кишки с предварительной гидропрепаровкой в подслизистом слое является безопасным и эффективным методом удаления плоских эпителиальных новообразований толстой кишки диаметром от 5 до 19 мм.

**Ключевые слова:** эпителиальные новообразования толстой кишки, «холодная» резекция слизистой оболочки, зубчатая дисплазия

**Конфликт интересов:** авторы заявляют об отсутствии конфликта интересов.

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## Introduction

The accumulation of clinical experience and the continuous development of the technical capabilities of endoscopic equipment allow successful removal of colorectal epithelial neoplasms of various sizes, localization and degree of dysplasia by minimally invasive endoscopic methods. The choice of the removal method depends on many factors: the type and size of the neoplasm, its morphological analysis, operator's experience, technical support. Much attention is currently being paid to determining the optimal methods for excisions epithelial neoplasms, especially in outpatient casual practice.

Cold polypectomy is currently the most common endoscopic technique for the excisions epithelial superficially neoplasms of the colon and neoplasms on a wide base between from 3 to 9 mm in size. Due to the ease of use, relatively low cost and low rate of delayed complications it has been widely used in practice in recent years. It is included in the guidelines of the European Endoscopic Society (ESGE) and the American Endoscopic Society (ASGE) [1, 2]. The 2013 Draft recommendations of the Russian Endoscopic Society for Physicians-Endoscopists also recommended the method of cold polypectomy as a method of choice when removing miniature (3–5 mm) and small (6–9 mm) serrated dysplasia of the colon and adenomas with lower dysplasia. It is recommended to remove such masses directly during primary (screening) or diagnostic colonoscopy without prior forceps biopsy [4–7].

Endoscopic mucosal resection is recommended for excision colorectal epithelial neoplasm larger than 10 mm in diameter. When severe dysplasia or stage 0–I colorectal cancer (Tis–T1sm1-sm2N0M0) is suspected or present, endoscopic resection with submucosal dissection in a single block is recommended to remove the neoplasm [3, 8, 9]. These excision techniques are used when the patient is admitted to hospital. Negative aspects of electric current application at removal of colorectal neoplasms using electrosurgical techniques limit the use of such techniques in outpatient practice. In particular, a number of researchers report that there is a risk of delayed bleeding in 0.3–6.1 % of cases due to thermal damage to the vessels of the submucosal layer of the colon. There are reports in the literature on the risk of another serious complication and delayed perforation of the intestinal wall due to electrothermal trauma. For example, some authors have reported delayed perforations in 0.3–1 % of cases after of coagulation during removal of colorectal neoplasms [10–13].

The only alternative to electrosurgical excision of epithelial neoplasms of the colon is the method of cold excision using a polypectomy loop in mechanical resection mode without electric current. A reduction in the number of delayed perforations and especially delayed bleeding has been reported: 0 % for cold loop excision epithelial neoplasms versus 0.3–6.1 % after classical electrosurgical excision [11, 12].

However, cold polypectomy is the method of choice for epithelial neoplasms up to 10 mm and is

not recommended for neoplasms with a larger diameter. In addition, cold polypectomy also has disadvantages. For example, some authors reported cases of perforation of the intestinal wall during cold polypectomy, due to entrapment of deep layers and shearing of the tissue trapped in the loop [11]. There is also a potential for nonradical removal due to unclear edge control of the seized superficially epithelial neoplasm [14, 15]. The explanation for this is that when a superficially epithelial neoplasm, even if relatively small, is localized in a bend or fold of the intestinal wall, it is often technically difficult to position and controllably capture the required amount of tissue into a loop. Currently, the most controversial issue is the choice of the optimal method for recurrence colorectal epithelial neoplasms with a diameter of 10 mm or more, especially in outpatient practice.

In recent years, publications have appeared on performing cold snaring resection [16–18] of the mucosa in superficially colorectal epithelial neoplasms and neoplasms on a broad base with preliminary hydropreparation in the submucosa layer [9, 18–20]. This technique, as described by the authors, combines the advantages of classical endoscopic mucosal resection and cold polypectomy.

**The purpose** of this retrospective study was to evaluate the use of cold endoscopic snaring resection with the preliminary injection of physiological saline into the submucosa for colorectal epithelial neoplasms of diameter of 5 to 25 mm in routine outpatient practice. Emphasis was placed on analyzing the safety of the technique and completeness of the removal of superficially neoplasms with a diameter of 10 to 19 mm.

## Materials and methods

During the period from January 2020 to July 2021, the removal of colorectal superficially neoplasms by cold endoscopic snaring resection with preliminary hydropreparation was performed in 98 patients at the medical center “RN – Modern Technologies”: 65 (66.32 %) women and 33 (33.67 %) men aged 22 to 89 years; average age was  $61.5 \pm 1.2$  years (Table 1). Informed consent was obtained from all patients to perform the manipulation. Multiple growth of neoplasms was observed in 18/98 (17 %) patients; the maximum number of neoplasms removed in one patient was 9. A total of 122 epithelial neoplasms were removed: 49/122 (40.16 %) small (from 5 to 9 mm), 68/122 (55.73 %) medium-sized (from 10 to 19 mm), 5/122 (4.09 %) large neoplasms with a diameter of 20 to 25 mm. The size of the neoplasms was determined by comparison with the size of the opened branches of the forceps. We divided the group of patients with neoplasms from 10 to 19 mm into group 2A, which included patients with a neoplasm size of 10–14 mm, their number was 30/122 (24.59 %) and group 2B – 38/122 (31.14 %) with a neoplasm size

of 15 to 19 mm. The average size of the neoplasms was  $14.5 \pm 1.4$  mm.

We assessed the number of resections in a single block. The initial assessment was made endoscopically when examining the defect after removal of the neoplasm in white light and during examination using the NBI mode. The completeness of neoplasm removal was also assessed by morphological evaluation of the edges of the histological material (R0/R1). The presence and number of complications in the follow-up groups and the rate of neoplasms recurrence were evaluated. Patients with pedicular neoplasms and with areas of depression in superficially neoplasms were not included in the study. Patients with severe dysplasia or adenocarcinoma during endoscopic optical evaluation were also excluded. Endoscopic optical evaluation was performed according to the visual criteria of the (NBI International Colorectal Endoscopic classification, 2011), WASP (Workgroup serrated polypS and Polyposis classification, 2016), JNET (Japanese NBI Expert Team, 2011). Morphological evaluation was performed according to the International Histological Classification of Tumors of the Colon and Rectum (WHO 2019, 5th edition). The basic characteristics of patients and the characteristics of neoplasms are presented in Table 1.

All examinations were performed on an EVIS EXERA-III video system and an Olympus CF-HQ 190L colonoscope (Japan) with narrow-band imaging (NBI), Digital Zoom and Dual Focus mode using a high-resolution monitor G2 HB RADIANCE. The high-resolution optical systems made it possible to perform an endoscopic assessment of the morphology of neoplasms without performing a forceps biopsy and to remove it without conducting a preliminary pathological examination. We were able to exclude patients with high-grade dysplasia and adenocarcinomas, which was confirmed by histological evaluation.

A peristaltic pump “Olympus” (Japan) of the AFU-100 series was used for targeted washing of the intestine, the area of neoplasms and post-resection wound defect. Injection into submucosa layer was performed with single-use injectors “Olympus” and “EndoStars”. Mechanical loop resection of neoplasms was performed using “Olympus” loops of crescent and oval shapes of 10, 15 and 20 mm. Both mono- and polyfilament loops were used. Cold endoscopic resection was performed as follows. From 3.0 to 10.0 ml of saline solution was injected into the submucosal layer under the neoplasm. We used a physiological solution without additional dyes. Next, we captured of the visible neoplasms tissue with the surrounding the normal mucosa with a polypectomy loop and cut off by tightening the loop without using of electrocoagulation. The removed material was extracted by aspiration into a trap (for neoplasm diameter smaller than 10 mm) or by loop trapping (for diameter larger than 10 mm) with simultaneous extraction of a colonoscope. The material was fixed

Table 1. Main characteristics of patients

Average age, years:	64.6 ± 11.01
Women	65 (66.32 %)
Men	33 (33.67 %)
Average size of neoplasms, mm	14.5 ± 1.4
Number of neoplasms in one patient:	
1 neoplasm	24 (19.67 %)
1–3 neoplasms	92 (75.40 %)
of 3 or more neoplasms	6 (4.91 %)
Maximum number of neoplasms	9
Localization of polyps:	
The right parts of the colon	79 (64.75 %)
The left parts of the colon	40 (32.78 %)
Rectum	3 (2.45 %)
Size of polyps:	
Group 1 (5–9 mm)	49/122 (40.16 %)
Group 2 A (10–14 mm)	30/122 (24.59 %)
Group 2 B (15–19 mm)	38/122 (31.14 %)
Group 3 (20–25 mm)	5/122 (4.09 %)
By type of structure:	
0 – type IIa according to the Paris Classification	59/122 (48.36 %)
0–Is type according to the Paris classification	21/122 (17.22 %)
LST-G-H (granular, homogeneous type)	32/122 (26.22 %)
LST-NG-FE (non-granular, elevated type)	10/122 (8.20 %)
Morphological optical endoscopic assessment (assessment according to NICE, WASP, JNET classifications):	
Hyperplastic type	98/122 (80.33 %)
of Colon Adenoma	24/122 (19.67 %)

in a 10 % formalin buffered solution and sent for pathomorphological examination with a mandatory assessment of the vertical and lateral margins of resection in the preparation.

## Results

After injecting physiological saline into the submucosa, there was an improvement in visualization of the edges of the epithelial neoplasm due to the difference in thickness and change in tissues color in the growth area of the epithelial neoplasm compared to normal epithelium (Fig. 1).

This allowed the loop to be positioned more accurately, capture the neoplasm and remove it radically.

The neoplasms were excision in 89 out of 122 cases (72.95 %) in a single block, whereas the neoplasms of the 1st group (from 5 to 9 mm) were 100 % removed in a single block. The presence of a “safety cushion” in the submucosa and convenient positioning of the loop made it possible to capture neoplasms from 9 to 14 mm in diameter together with the adjacent mucosa without their fragmentation in 28 cases out of 30 (93.33 %) (Fig. 2), which favorably influenced the morphological assessment of the radicality of the performed resection.

Epithelial neoplasms larger than 15 mm in diameter were in most cases removed in stages of 2-3 seizures. In group 2B, only 12 of 38 (31.57 %) neoplasms were resected in a single block. In the group

of patients with neoplasms larger than 19 mm, single-block resection was not performed.

After resection of the neoplasm, all patients underwent obligatory endoscopic evaluation of the margins of the defect in order to detect residual neoplasm tissue. The edges of the defect were examined in white light and in NBI and dual focus modes. In Group 1 and Group 2A, no residual neoplasm tissue was detected at the margin of the defect. Residual neoplasm tissue at the margin of post-resection mucosal defect were detected in 8 cases out of 38 (21.05 %) in Group 2B (with neoplasm diameter from 15 to 19 mm). In the group with neoplasms from 20 to 25 mm, residual tissue was detected in 2 cases out of 5 (40 %). All cases with residual tissue at the resection margin were observed after removal of the neoplasm in portions (groups 2B and 3) and these were identified by resection with a cold loop (4 of 10 patients) or removal of the neoplasm with biopsy forceps (6 of 10 patients) with a repeat visual assessment of the resection margin.

Immediately after removal of each mass, a slight inflow of blood from the capillaries was noted in the form of blood accumulation in the wound area. The bottom of the defect was washed with water to visually assess the presence of residual neoplasm tissue and sites of possible damage to the intestinal muscle layer. After washing with distilled room temperature water the blood flow usually stopped on its own. Bleeding from the submucosal layer vessels at



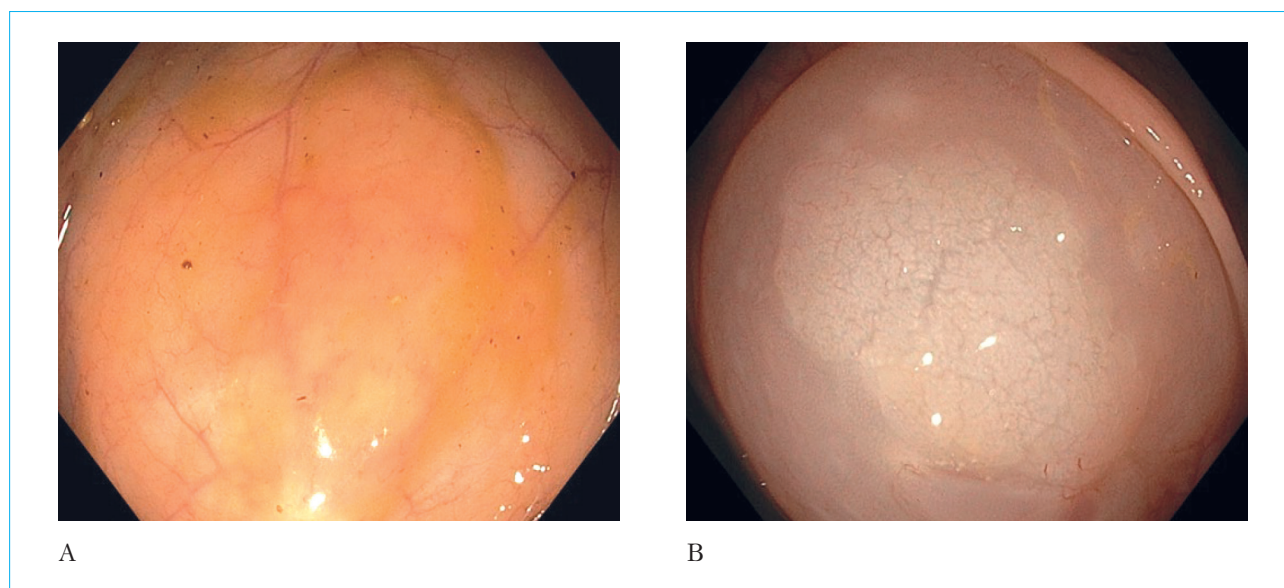


Fig. 1. Epithelial neoplasm of the colon: A examination in white light, the boundaries of the neoplasm are not clearly defined; B examination in white light, after performing submucosal injection, visualization of the boundaries is clear

the moment of neoplasm removal which did not stop after washing with water occurred in 3 cases out of 122 (2,45 %). Bleeding occurred in two cases in patients with neoplasms larger than 20 mm and in one case with a size of 16 mm. Endoscopic clipping 12 (Olympus, HC-610-090L) was successfully used for hemostasis. No hospitalisation was required. No cases of delayed bleeding were observed.

No intestinal wall perforation was observed, either at the time of resection or in the delayed period. By creating a hydrocushion in the submucosa layer under the epithelial neoplasm and distancing the deep layers of the intestinal wall, the risk of the loop capturing the muscular layer of the intestine was minimal, virtually eliminating the possibility of perforation of the wall.

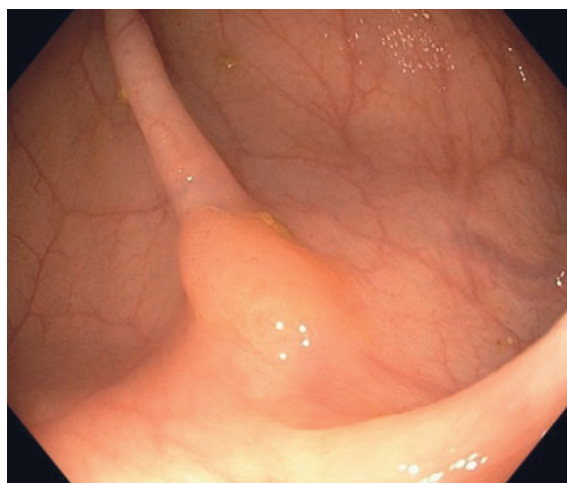
Serrated dysplasia (low grade) was detected in removed material in 76 cases; hyperplastic polyp, microvesicular type (MVHP) was in 14 cases; hyperplastic polyp, goblet cell (GCHP) was in 9 cases; tubular adenoma with mild dysplasia (tubular adenoma, low grade) was in 23 cases.

A control colonoscopy was performed in all patients after 6 months. A case in which the focus of an epithelial neoplasm was visually determined in the area of the scar was taken as a recurrence of the neoplasm. The examination was performed in white light, NBI and double focus mode. No local recurrence was detected in the groups of patients with neoplasm diameters of 5–9 and 10–14 mm. In most cases, scarring of the colon mucosa after performing a “cold” loop resection could not be determined with precise accuracy. One case of neoplasm recurrence was detected in a group of patients with a neoplasm diameter from 15 to 19 mm (1/38, which

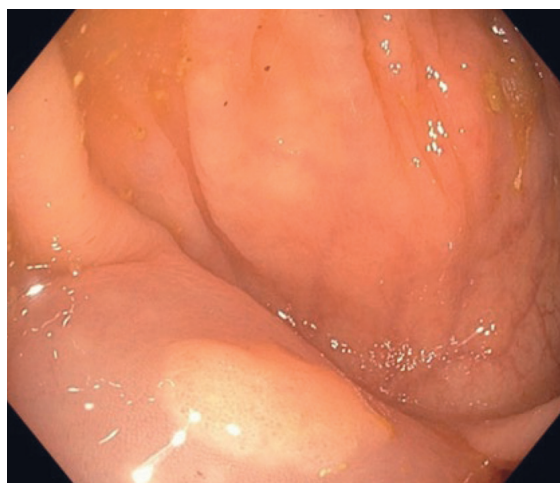
was 2.63 %), one case in a group with a neoplasm diameter of 20–25 mm (1/5, which was 20 %). Both cases of relapse were detected during a follow-up examination after 6 months. The size of the recurrent neoplasm was 3 and 7 mm in diameter, according to visual morphological assessment, the type of neoplasm could be classified in both cases as dentate dysplasia, which corresponded to the previous morphological conclusion. In case of a recurrence of the neoplasm, the method of traditional resection with preliminary hydro-preparation using electrocoagulation was applied.

## Discussion

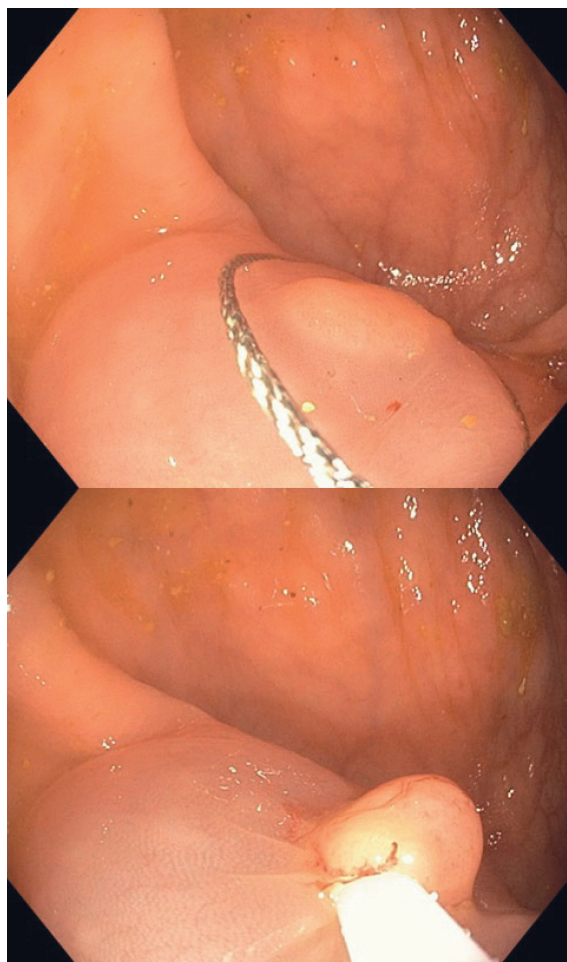
We have not encountered descriptions of the use of cold mucosal resection in squamous epithelial neoplasms with prior hydropreparation in the Russian literature. However, studies using the described technique have been reported in the foreign literature. X. Yuan et al. [9] reviewed 36 studies involving more than 3,200 endoscopic resections for squamous epithelial polyps of the colon, evaluating the incidence of R0 resections and the incidence of single-block resections. Secondary outcomes were safety and recurrence rate. Overall, mucosal resection techniques with elevation of the resected site were found to be effective with an R0 resection rate of 90 % (95 % confidence interval (CI) 0.81–0.94) and a single-block resection rate of 85 % (95 % CI 0.79–0.91). With regard to safety, pooled data showed that hot resection (UEMR and EMR) had a higher risk of bleeding than cold resection [3 % (95 % CI 0.01–0.05,  $I^2 = 68$  %) versus 0 % (95 % CI 0–0.01,  $I^2 = 0$  %)].



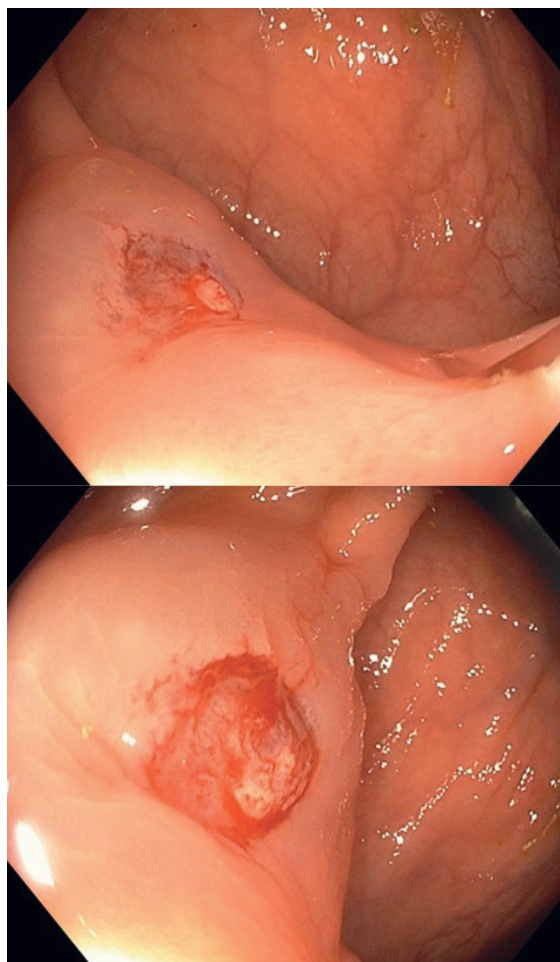
A



B



C



D

Fig. 2. Endoscopic excision of superficially colon epithelial neoplasm: A a flat epithelial neoplasm is located on the fold of the intestine; B submucosal injection was performed saline solution — the boundaries of the neoplasm are more clearly defined, the size of the neoplasm is determined, a safe layer for mucosal resection is created; C the neoplasm is cut off by a loop without the use of electroexcision; D inspection of the edges of the defect after resection

*Table 2.* The nature of the removal of neoplasms, depending on their size

Specifications	Group 1 5–9 mm	Group 2A 10–14 mm	Group 2B 15–19 mm	Group 3 20–25 mm
Number of neoplasms	49	30	38	5
Resection is performed as a single unit	49 (100 %)	28 (93.33 %)	12 (31.57 %)	0
The resection was performed in parts	0	2 (6.66 %)	26 (68.42 %)	5 (100 %)
a fragment of neo-tissue at the edges of the defect	0	0	8 (21.05 %)	2 (40 %)

*Table 3.* Results of lifetime pathoanatomic examination of removed neoplasms

Specifications	Group 1 5–9 mm	Group 2A 10–14 mm	Group 2B 15–19 mm	Group 3 20–25 mm
Number of patients	49	30	38	5
Serrated dysplasia, low grade	30	18	24	4
Hyperplastic polyp, microvesicular type	7	3	3	1
Hyperplastic polyp, goblet cell	3	3	3	0
Tubular adenoma, low grade	9	6	8	0
Recurrent neoplasms	0	0	1 (2.63 %)	2 (40 %)
Bleeding during endoscopic	0	0	1 (2.36 %)	2 (40 %)

N.J. Tutticci et al. [19] evaluated the safety and efficacy of cold endoscopic mucosal resection for dentate dysplasia  $\geq 10$  mm with prior submucosal injection of succinate methylene blue stained gelatin in 163 cases. Only scalloped lesions were included in the study, most of them localized to the right colon, the size in the subgroups ranged from 10 mm to 30 mm. Marginal biopsies were positive in 2 (1.2 %) cases. Residual dentate dysplasia after 5 months was detected in only 1 case. No delayed bleeding was observed. It was concluded that the cold resection method was safe and effective in the removal of large dentate lesions of the right colon.

Using the technique of cold resection of the colon mucosa with prior hydropreparation, we concluded that the use of the method in the removal of squamous epithelial neoplasms with a diameter of 5 to 15 mm is safe and radical. After hydropreparation, a neoplasm up to 9 mm is captured in one block in 100 % of cases, and from 10 to 15 mm in 93,33 % of cases, which in its turn is reflected in the radicality of neoplasm removal (R0 in group 1 and 2A in 100 % of cases). Only one-third of cases (12/38 = 31.57 %) in Group 2B were resected in a single block and the majority of cases (26/38 = 68.42 %) were resected in a piecemeal fashion. The recurrence rate in the group with neoplasms from 15 to 19 mm was, however, 2.63 % (1 of 38 patients), which may

indicate a high success rate. Bleeding occurred in Group 2B in one case, which also indicates that the technique is safe and can be used in an outpatient setting. In group 3 (patients with neoplasms of more than 20 mm) 5 neoplasms were removed, with two bleedings and two neoplasm recurrences, which is 40 %. The high rate of complications and recurrent neoplasms casts doubt on the feasibility of the method for removing neoplasms of this size.

## Conclusion

Cold endoscopic loop resection of epithelial neoplasms of the colon with prior hydropreparation in the submucosa is a safe and effective method of removing flat epithelial neoplasms of the colon from 5 to 19 mm. The method requires careful assessment of the dimple pattern at the diagnostic stage, excluding patients with signs of severe dysplasia and malignization in the neoplasm. The method allows to position the loop more precisely in cases of inconvenient location of the neoplasm in the bend or fold of the large intestine, to control clearly the volume of the intestinal wall tissue by depth and the visible edge of the neoplasm, thereby reducing the risk of possible perforation of the intestinal wall and the risk of neoplasm recurrence. The risk of delayed complications is minimal.



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