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Endoscopic treatment of patients with adenomas of the major papilla of the duodenum in familial adenomatous polyposis

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ABSTRACT *AIM: to evaluate the feasibility of endoscopic techniques in the treatment of patients with adenomas of the major duodenal papilla in familial adenomatous polyposis.*

PATIENTS AND METHODS: from January 2020 to January 2025, thirteen patients with adenomas of the major duodenal papilla (MDP) suffering from familial adenomatous polyposis (FAP) underwent endoscopic procedures. In seven cases, the adenomas of the major duodenal papilla had exclusively extrapapillary components without involvement of the ducts. Four patients presented with type IV adenomas, while two cases were classified as type III according to the endoscopic classification of benign neoplasms of the MDP. In six instances, there was noted extension of the adenoma to the common bile duct (CBD), and in three cases, the adenoma extended to the walls of the main pancreatic duct (MPD). The study examined the main aspects of MDP neoplasms, including their growth patterns and extent of spread. Additionally, the advantages of endoscopic techniques for removing these neoplasms were discussed, along with intraoperative and postoperative complications arising from the interventions.

RESULTS: in all cases, endoscopic removal of adenomas of the MDP was successfully performed. It should be noted that in 7 out of 13 cases (53.8%), when neoplasms of types I and III were present, the adenomas were removed en bloc, while in 6 out of 13 cases (46.2%), fragmentary removal was performed for adenomas of types II and IV. However, complications arose in 3 out of 13 cases (23.1%) after the intervention: two patients developed moderate post-procedural pancreatitis, and one patient experienced bleeding that required endoscopic hemostasis. In 2 out of 13 cases (15.4%), residual adenoma tissue was detected, necessitating repeat endoluminal intervention. It is noteworthy that the complications (bleeding) and recurrences were managed with repeat endoscopic procedures without the need for high-trauma surgical operations.

CONCLUSION: the study demonstrated the feasibility of endoscopic procedures for the treatment of patients with adenomas of the MDP against the background of FAP.

KEYWORDS: *adenoma of the major duodenal papilla, endoscopic surgery, familial adenomatous polyposis, pancreatitis, adverse events*

CONFLICT OF INTEREST: *the authors declare no conflict of interest*

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INTRODUCTION

Epithelial neoplasms of the major papilla of the duodenum (MDP) are rare. However, the presence of familial adenomatous polyposis (FAP) significantly increases the risk of developing epithelial neoplasms of MDP [1,2]. FAP is an inherited disease with an autosomal dominant type of inheritance caused by a mutation of the *APC* gene (adenomatous polyposis coli). As a result, the development of, in particular, tubular and tubulevillous adenomas of the gastrointestinal tract with a high risk of malignancy is characteristic [3,4]. According to the world literature, adenomas of the MDP and duodenum, as a rule, form 10–15 years after the initial detection of large intestine adenomas with a rate of occurrence from 30% to 92% of cases [14].

Given the high risk of malignancy, all MDP adenomas must be removed. When choosing a treatment

method, it is necessary to take into account the presence or absence of FAP in the anamnesis. According to a number of studies, in the presence of FAP, the risk of malignant transformation of MDP adenoma increases significantly. In this regard, the importance of the endoscopic approach to adenoma removal is reduced, since this method of treatment does not eliminate the risk of malignancy of other tumors of the duodenum [5,6]. Therefore, when diagnosing, it is extremely important to evaluate not only the adenoma of the MDP, but also all other neoplasms of the duodenum, since the risk of malignancy exists in all formations.

Comprehensive diagnosis of epithelial neoplasms of the duodenum in the presence of FAP includes both radiation methods (CT and MRI) and endoscopic examinations (duodenoscopy and endosonography). This approach allows not only to assess the nature of the tumor, but also significantly influences the choice of the optimal treatment method, as well as predicting the outcome of the disease [2,7,8]. Over a period of more than 20 years, we have accumulated a unique experience in treating patients with MDP tumors, which is currently the largest in the world. Based on this experience, we formulated for the first time the principles of a unified endoscopic description of MDP neoplasms and developed classification typing [2,7,14]. It is worth emphasizing that the development of classification typing of neoplasms has made it possible to significantly advance in the treatment of patients with massive adenomatous growths, as well as with MDP tumors on the background of FAP and extensive intraductal tumor spread, using minimally invasive endoscopic technologies.

AIM

The main objective of our study was to assess the feasibility of using endoscopic techniques in the treatment of patients with MDP adenomas on the background of FAP.

PATIENTS AND METHODS

The study is single-centered and retrospective. In the period from January 2020 to January 2025, in the surgical endoscopic department of the Vishnevsky National Research Medical Center of Surgery of the Ministry of Health of Russia, endoscopic surgeries were performed in thirteen patients with MDP adenomas suffering from FAP. All the patients had previously undergone surgery for large intestine cancer. In particular, colectomy with ileorectal anastomosis was performed in 9 patients, subtotal resection of the colon and rectum was performed in 3 patients with reduction of the colon to the anal canal zone with the formation of a colorectal anastomosis, and colectomy was performed in 1 patient in combination with extirpation of the rectum and subsequent ileostomy.

Before the surgery, all the patients with familial adenomatous polyposis, in addition to abdominal CT and MRI, underwent duodenoscopy and endosonography, during which the condition of the MDP, as well as the largest non-ampullary duodenal tumors, was assessed. During the diagnosis, the nature of the growth and the grade of spread of the neoplasm were assessed both on the intestinal walls and on the ducts according to the endoscopic classification of neoplasms of the MDP (Table 1).

Type I (Extra-Papillary): tumor with extra-papillary growth. Neoplasm of this type is localized within the MDP, with no signs of extention to the duodenum and terminal parts of the CBD and MPD.

Type II (Extra-Papillary + Duodenum): a tumor with extra-papillary growth and spread along the walls of the duodenum. Depending on the direction of growth of the tumor component laterally spreading to the walls of the duodenum, 4 subtypes are distinguished:

SP (Supra-Papillary) — spreading in the proximal direction from the MDP,

IP (Infra-Papillary) — spreading distally from the MDP,

LPR (Latero-Papillary Right) — latero-papillary spreading to the right of the MDP,

Table 1. *Distribution of neoplasms of the papilla of Vater according to growth characteristics and spread to the walls of the duodenum and terminal parts of the ducts*

Type	Characteristics of the neoplasm
I type (EP)	extra-papillary tumor growth without extention to the walls of the duodenum
II type (EP + D)	extra-papillary tumor growth with extention to the walls of the duodenum
SP	supra-papillary extention proximally to the MDP
IP	infra-papillary extention distally from the MDP
LPR	latero-papillary extention to the right of the MDP
LPL	latero-papillary extention to the left of the MDP
PD	the spread of adenoma to the walls of the para- or peripapillary diverticulum
MI	invasion by neoplasm of the muscular wall of the duodenum
III type (ID)	Intraductal tumor growth
CBD	the tumor spreads to the terminal part of the CBD
MPD	the tumor spreads to the terminal part of the MPD
IA	intra-ampullary tumor
CBD + MPD	the tumor spreads to the terminal parts of the CBD and MPD
IV type (EP + ID)	the tumor with mixed extra-papillary and intraductal growth

LPL (Latero-Papillary Left) — latero-papillary spreading to the left of the MDP. There are also 2 additional subtypes of type II: *PD (Peri/Parapapillary Diverticulum)* — when the adenoma spreads to the walls of the para- or peripapillary diverticulum,

and *MI (Muscle Invasion)* — when the neoplasm invades the muscular layer of the duodenum wall.

Type III (Intra-Ductal): a tumor with intraductal spread. Depending on the nature of ductal structures involved in the tumor process, type III neoplasms are divided into 4 subtypes:

CBD (Common Bile Duct) — the tumor spreads to the terminal part of the CBD, *MPD (Main Pancreatic Duct)* — the spread of the tumor to the terminal part of the MPD, *IA (Intra-ampullary)* — the tumor is represented exclusively by the intra-ampullary component, subtype *CBD + MPD* — the tumor spreads simultaneously to the terminal parts of the both ducts.

Type IV (Extra-Papillary + Intra-Ductal): tumors with mixed extra-papillary and intraductal growth.

Neoplasms of this type generally represent combinations of *types I and III*, or *types II and III*.

Statistical Analysis

The statistical analysis was carried out using the StatTech v. 4.8.3 program (developed by Stattech LLC, Russia). Quantitative indicators were evaluated for compliance with the normal distribution using Shapiro-Wilk's test. Quantitative indicators, the sample distribution of which corresponded to the normal, were described using arithmetic means (M) and standard deviations (SD). The 95% coincidence interval (95% CI) was indicated as a measure of representativeness for the mean values. In the absence of a normal distribution, quantitative data were described using the median (Me), lower and upper quartiles (Q1–Q3). Categorical data were described with absolute values and percentages. 95% coincidence intervals for percentages were calculated using Klopper-Pearson's test.

RESULTS

The study included 13 patients with MDP adenomas on the background of FAP, including 7/13 (53.8%) men and 6/13 (46.2%) women. The mean age of the patients was 33.54 ± 6.69 years. MDP neoplasms in 5/13 (38.5%) patients were represented by type I adenomas (Fig. 1). Type II adenomas were detected in 2/13 (15.4%) patients (Fig. 2). Type IV adenomas were detected in 4/13 (30.8%) patients: three of them had a combination of types II and III, while one patient had a combination of types I and III (Fig. 3). In 2/13 (15.4%) cases, MDP adenomas were represented by type III neoplasms (Fig. 4). In addition, in 6/13 cases, the

Table 2. *Distribution of patients according to the endoscopic classification of MDP neoplasms (Starkov, Yu.G. et al., 2022)*

Parameter		M ± SD		95% CI
Age, years (M ± SD)		33.54 ± 6.69		29.50–37.58
Gender, n (%) Male Female		7 (53.8%) 6 (46.2%)		25.1–80.8 19.2–74.9
The size of the extra-papillary part of the adenoma, mm (M ± SD)		20.27 ± 4.36		17.34–23.20
The length of the CBD, mm (M ± SD)		13.50 ± 3.02		10.33–16.67
The length of theMPD, mm (M ± SD)		4.00 ± 1.00		1.52–6.48
Classification typing		**Number of patients**	**%**	**95% CI**
I type		5	38.5	13.9–68.4
II type		2	15.4	1.9–45.4
III type		2	15.4	1.9–45.4
IV type	I + III	1	7.7	0.2–36.0
	II + III	3	23.1	5.0–53.8

involvement of the CBD with an average length of 13.50 ± 3.02 mm was noted, and in 3/13 cases, the adenoma spread to the walls of the MPD with an average length of 4.00 ± 1.00 mm (Table 2).

In 5/13 (38.5%) cases, when patients had type I MDP adenomas, the neoplasms were removed by MDP resection. In 2/13 (15.4%) cases, with the spread of adenoma to the intestinal wall (type II), resection of the MDP was supplemented by resection of the duodenal mucosa. Papillectomy was performed in 2/13 (15.4%) patients with type III adenomas, while the intraductal component of the adenoma was removed using loop excision or intraductal radiofrequency ablation (RFA). In type IV MDP adenomas, papillectomy was supplemented with resection of the duodenal mucosa in 3/13 (23.1%) patients, and dissection in the submucosal layer in 1/13 (7.7%) case. In 2 patients, the intraductal part of the adenoma was subjected to loop excision, while in the other 2 patients, intraductal RFA was performed. Pancreatic duct stenting to prevent pancreatitis was successfully performed in 11/13 (84.6%) cases, while CBD stenting to prevent cicatricial stricture was performed in 6/13 (46.2%) cases.

Figure 1. *Duodenoscopy: the adenoma of the MDP without signs of spreading to the intestinal walls, the adenoma of the duodenum is visualized lateropapillarly to the left of the MDP*

In 7/13 (53.8%) cases, the MDP adenoma was removed in a single block, while 6/13 (46.2%) patients with large neoplasms underwent fragment-by-fragment removal. It is worth noting that 2/13 (15.4%) patients had intraoperative bleeding in the area of the postresection lesion after the removal of large adenomas. However, in the both cases, endoscopic hemostasis was successfully performed without the need for additional procedures.

Postoperative complications were noted in 3/13 (23.1%) patients. Two of them developed symptoms of postmanipulatory pancreatitis, which were successfully treated with conservative therapy. In one case, after removal of a large MDP adenoma, bleeding from the vessel of the submucosal layer in the area of the postresection lesion occurred in the early postoperative period, which required endoscopic hemostasis.

During dynamic follow–up in the postoperative period, in the period from 3 to 6 months with a median of 5.5 (5.25–5.7) after endoscopic

removal of the MDP adenoma, 2/13 (15.4%) patients had residual fragments of adenoma in the area of the mouth of the MPD and the lumen of the CBD. In this regard, those patients underwent repeated intraluminal interventions, which provided a good disease-free result. With further follow-up of patients for a period of 1 to 5 years, there were no signs of recurrence of adenomatous growths, which confirms the radical removal of MDP neoplasms.

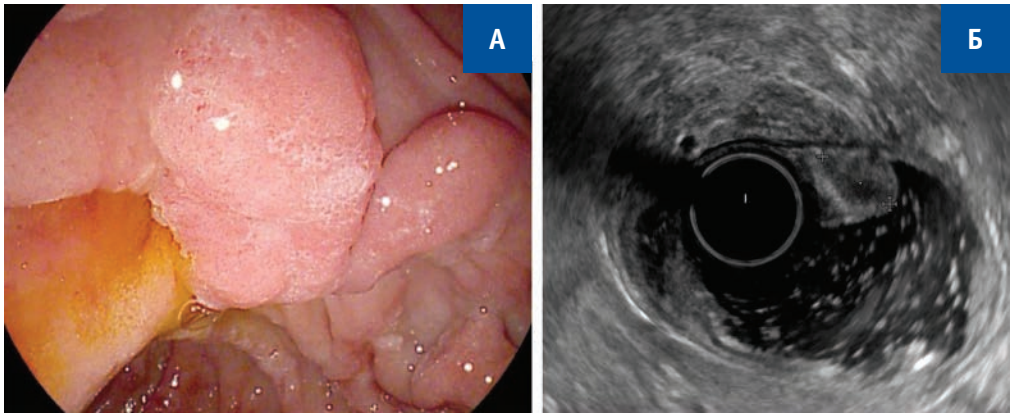

Figure 2. *А — duodenoscopy: MDP adenoma with infrapapillary spread to the intestinal wall; Б — endosonography: no signs of adenoma spreading to the terminal sections of the ducts*

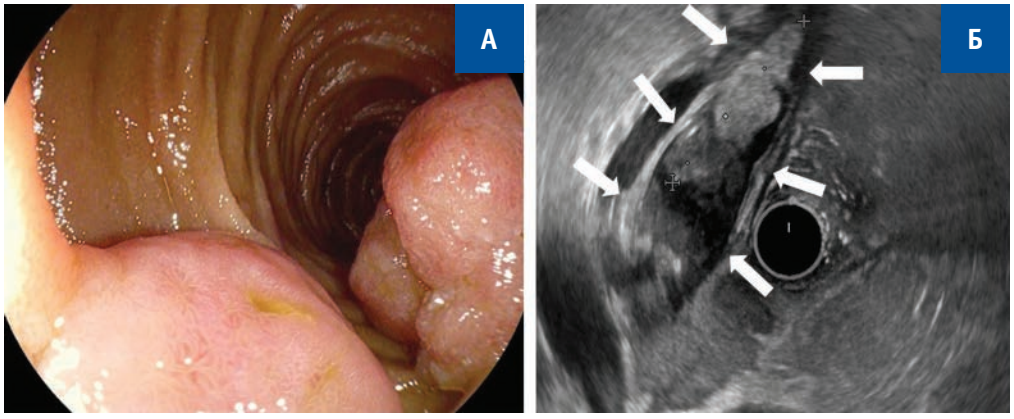

Figure 3. *А — duodenoscopy: MDP adenoma with suprapapillary extension to the intestinal wall, a large duodenal adenoma is also visualized distal from MDP; Б — endosonography: an extended intraductal component of the adenoma in the lumen of the CBD (arrows)*

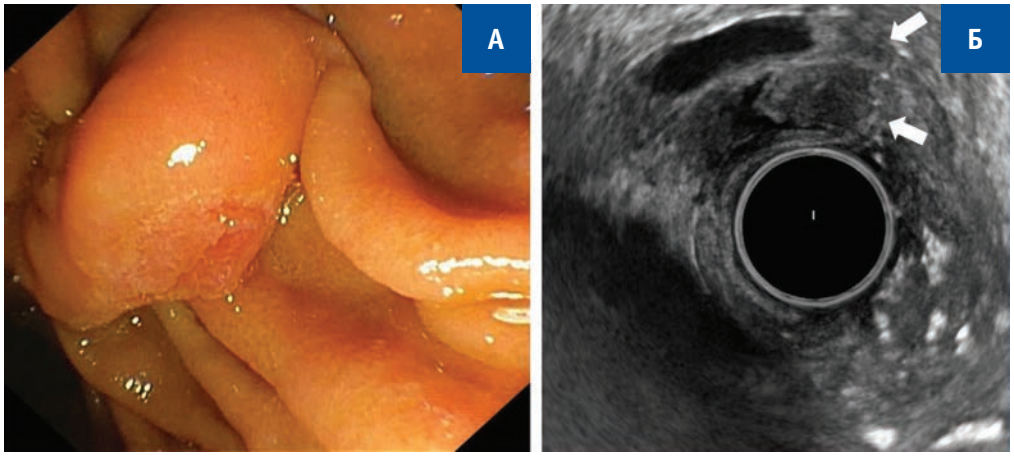

Figure 4. *А — duodenoscopy: MDP adenoma is exclusively intraductal in nature without the presence of an extrapapillary component; Б — endosonography: intraductal adenoma spreading to the walls of the MPD and CBD simultaneously (arrows)*

Table 3. *The results of endoscopic treatment of patients with MDP adenomas in FAP*

Results		Number of patients	%	95% CI
Resection method	MDP resection	5	38.5	13.9–68.4
	MDP resection with resection of the duodenal mucosa	2	15.4	1.9–45.4
	Papillectomy	2	15.4	1.9–45.4
	Papillectomy with resection of the duodenal mucosa	3	23.1	5.0–53.8
	Papillectomy with dissection in the submucosal layer	1	7.7	0.2–36.0
The nature of the resection	*en bloc*	7	53.8	25.1–80.8
	Fragmented	6	46.2	19.2–74.9
MPD stenting		11	84.6	54.6–98.1
CBD stenting		6	46.2	19.2–74.9
Intraoperative complications		2	15.4	1.9–45.4
Postoperative complications		3	23.1	5.0–53.8
Residual adenomas		2	15.4	1.9–45.4
Histologyresult	High grade	3	23.1	5.0–53.8
	Low grade	10	76.9	46.2–95.0

It should also be noted that during the examination 3 years later, in one case, after endoscopic removal of the MDP adenoma, an epithelial neoplasm was detected in the area of the bulbo-duodenal junction with endoscopic signs of malignancy. According to the biopsy data, adenocarcinoma of the duodenum was confirmed, which required duodenectomy with preservation of the peripapillary flap to form a choledochopancreatoyunoanastomosis.

In all cases, the results of histological examination of the removed tumor confirmed the adenomatous nature of the neoplasms. In 10/13 (76.9%) patients, the tumor had a low grade of dysplasia, while the remaining 3/13 (23.1%) patients had a high grade of dysplasia. The structure of the performed endoscopic surgeries, as well as intra- and postoperative complications and the results of morphological examination are presented in Table 3 (Table 3).

DISCUSSION

Familial adenomatous polyposis is found mainly in young patients and is a rare disease with an average incidence of 1 patient per 10,000 people per year. In most cases, FAP leads to the development of colorectal cancer. However, the main cause of death in familial adenomatous polyposis is cancer of the duodenum or MDP [9].

According to a number of authors, periodic screening studies, including duodenoscopy and, if necessary, endosonography with an assessment of all epithelial neoplasms of the duodenum, including MDP, are recommended to prevent duodenal cancer development.

The incidence of screening studies is mainly determined by Spigelman A.D.'s classification, which provides a detailed assessment of the severity of duodenal polyposis [10,11].

It should be noted that in the presence of FAP, the risk of malignancy of MDP adenoma is significantly higher than in the absence of FAP. Due to the high risk of degeneration of the adenoma into a malignant tumor, all MDP adenomas require removal. However, after removal of the MDP adenoma, the possibility of malignancy of the other duodenal neoplasms remains, which requires a comprehensive diagnosis of all duodenal neoplasms, due to the fact that the risk of malignancy is present in all neoplasms [5,6].

Prior to the widespread introduction of endoscopic surgery, trans-duodenal papillectomy and pancreatoduodenal resection were the only methods of surgical treatment of patients with MDP adenomas. However, these surgeries are associated with a high risk of death (up to 10%), as well as a high incidence of complications (up to 45%). In recent years, endoscopic surgeries have increasingly been considered as an alternative to traditional

surgical procedures [13]. The introduction of the endoscopic classification of benign neoplasms of the MDP made it possible to clearly define the criteria for selecting patients for intraluminal surgeries [7,13].

Thus, Ramai D. et al. in 2021, published a large multicentered study, including 99 patients with familial adenomatous polyposis and MDP adenomas. In turn, the authors of the study note the lack of clear criteria for the selection of patients for endoscopic surgeries. In this regard, there is a high recurrence rate, which exceeds 26%, and postoperative complications are over 28% [12].

CONCLUSION

Thus, in our study, in the treatment of patients with adenomatous growths of the duodenal papilla in familial adenomatous polyposis, the choice of optimal intraluminal endoscopic surgery was carried out individually, depending on the type of MDP adenoma and the condition of non-ampullary adenomatous growths, due to a clear understanding of the nature of growth and the degree of spread of MDP neoplasms. Minimally invasive endoscopic surgeries have made it possible to achieve a safe and effective result, avoiding highly traumatic surgeries.

AUTHORS CONTRIBUTION

Concept and design of the study: *Yury G. Starkov*
Collection and processing of the material: *Ayubkhan I. Vagapov*
Statistical processing: *Ayubkhan I. Vagapov, Rodion D. Zamolodchikov, Seda V. Dzhantukhanova*
Writing of the text: *Ayubkhan I. Vagapov*
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