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Surgery for familial adenomatous polyposis

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ABSTRACT

AIM: to analyze the results of surgery for familial adenomatous polyposis (FAP).

PATIENTS AND METHODS: the case series study included 20 patients with FAP, 85% of procedures with anastomosis and 15% with a permanent ileostomy. Laparoscopic approach was used in 35%.

RESULTS: the mean time of operation time was 243 minutes, the mean intraoperative blood loss was 244 ml, and the mean hospital stay was 17.2. Three (15.0%) patients developed postoperative complications. Laparoscopic procedures were advantageous in terms of intraoperative blood loss and faster recovery. The first polyps were detected in the rectal stump within 6–8 months after surgery, desmoid tumors within 24.3 months. Most patients had an acceptable quality of life with an mean number of stools per day 11.1.

CONCLUSIONS: FAP is a complex problem of modern medicine requiring the teamwork of various medical specialists. Minimally invasive interventions for FAP have advantages over open procedures.

KEYWORDS: familial adenomatous polyposis, examination, surgical treatment, polyposis, desmoid tumors

CONFLICT OF INTEREST: the authors declare no conflict of interest

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INTRODUCTION

Familial adenomatous polyposis (FAP) is a genetic autosomal dominant type disease, occurring in 1 out of 6,800–29,000 people and characterized by multiple colorectal adenomas with progressive growth and mandatory malignancy [1,2]. In most patients, colorectal adenomas develop in the second decade of lifetime, and colorectal cancer develops in the third or fourth decade [3]. Recently, the only treatment method for FAP is preventive surgery on the colon and rectum. Surgery for FAP include: proctocolectomy with J-pouch, colectomy with ileorectal anastomosis and proctocolectomy with permanent ileostomy [4]. Colectomy with ileorectal anastomosis is associated with better functional results and quality of life. However, the remaining rectum requires lifetime control due to the risk of polyposis progression and the development of rectal cancer [5]. When choosing a surgical

method for FAP, the age of the patient, the severity of rectal adenomatosis, genetic mutations and, of course, the choice of the patient him/herself are taken into account [6].

AIM

to analyze the results of surgery for familial adenomatous polyposis (FAP).

PATIENTS AND METHODS

Twenty patients with FAP were included in the retrospective study (November, 2015 — October, 2021). There were 11 men (55.0%), 9 women (45.0%). The patients were aged 42.2 (21–74) years. The BMI was 24.7 kg/m². The clinical characteristics of the patients are presented in Table 1. All the patients were checked-up including colonoscopy with multiple adenoma

Table 1. *Clinical features of patients with FAP*

Indicator	FCAP (<i>n</i> = 20) M; Me (Q1; Q3); <i>n</i> (%)
Age, years	42.2; 39 (32.5; 49.5)
BMI	24.7; 26.2 (22.1; 26.8)
Gender: Females Males	9 (45%) 11 (55%)
Family history	13 (65%)
Hereditary mutations	20 (100%)
Classical form of FAP	20 (100%)
Colorectal cancer	12 (60%)

Table 2. *Types of operations in patients with FAP*

Indicator	Open, <i>n</i> (%)	LS, <i>n</i> (%)	Total, <i>n</i> (%)	<i>p</i>
Colectomy with rectal resection, J-pouch, preventive ileostomy	1 (7.7%)	7 (100%)	8 (40%)	< 0.001
Colectomy with rectal resection, small intestine rectal anastomosis, preventive ileostomy	7 (53.7%)	0 (0.0%)	7 (35.0%)	0.044
Proctocolectomy with J-pouch, preventive ileostomy	2 (15.4%)	0 (0.0%)	2 (10.0%)	0.52
Proctocolectomy with permanent ileostomy	3 (23.1)	0 (0.0%)	3 (15.0%)	0.47
Total	13 (100%)	7 (100%)	20 (100%)	

Note: the exact bilateral Fisher test

biopsy (Fig. 1), proctoscopy, genetics, gastro-duodenoscopy, X-ray.

To perform a molecular genetic test, genomic DNA was isolated from peripheral blood leukocytes according to a standard technique. The concentration of the obtained DNA specimens was measured on a Qbit 2.0 fluorimeter (Invitrogen, USA) using a set of QuantiTMMdsDNA. 15 coding exons of the *APC* gene with adjacent parts of introns (50–100 nucleotide pairs) were amplified by polymerase chain reaction using 23 pairs of primers. Further, the obtained DNA fragments were sequenced along two complementary chains using the ABI PRISM 3500 device (8 capillaries; Applied Biosystems).

**Figure 1.** *Endoscopic picture of FAP*

Table 3. Characteristics of procedure and the postoperative period in FCAP

Indicators	Laparoscopic (n = 7)		Open (n = 13)		p
	M N (%)	Me (Q1;Q3)	M N (%)	Me (Q1;Q3)	
Operation time, min.	307	310 (310; 315)	208	160 (160; 260)	0.045*
Intraoperative bloodloss, ml	207	200 (200;200)	264	250 (200; 300)	0.057*
The appearance of intestinal peristalsis, day	1,6 1.6	2 (1; 2)	2.5	3 (2; 3)	0.013*
Recovery of motor activity, day	1.6	2 (1; 2)	3.5	3 (3; 4)	0.0007*
Postoperative complications	2 (28.6%) n = 7		1 (7.7%) n = 13		0.27**
Postoperative hospital stay	20.1	17 (13; 24)	15.6	16 (15; 17)	0.66*

Note: * significance of differences between open and laparoscopic surgeries, Mann-Whitney test; ** significance of the differences between open and laparoscopic surgeries, the exact bilateral Fisher test

All the patients had a classical form of FAP with the presence of specific complaints. Complaints of general weakness were in 8 (40%) patients, admixture of blood and mucus in the feces — 7 (35.0%) patients, abdominal pain — in 7 (35.0%) patients, frequent liquid stools — in 6 (30.0%) patients, constipation — in 5 (25.0%) patients, discomfort in the rectum — in 3 (15.0%) patients, weight loss — in 3 (15.0%) patients. Thirteen (65.0%) patients had a family history. Hereditary mutations were found in all patients. Histologically, 13 (65.0%) patients showed tubular intestinal adenomas, 7 (35%) patients had tubulo-villous adenomas, 5 (25.0%) had low-grade epithelial dysplasia, 3 (15.0%) had low- and high-grade intraepithelial neoplasia.

Colorectal cancer was revealed in 12 (60.0%) patients: primary multiple tumors were found in 5 (41.7%) patients, rectal cancer — in 5 (41.7%), colon cancer — in 2 (16.6%) patients. One patient with rectal cancer had distant liver metastases.

The average age of the patients with FAP without colorectal cancer was 33.3 years, the average age of the patients who developed colorectal

cancer on the background of FAP was 48.2 years ($p = 0.003$).

The time from diagnosis to surgical treatment was 3.9 months. All the patients underwent curative surgery (Table 2): 17 (85.0%) procedures with anastomosis and 3 (15.0%) with permanent ileostomy. Seven (35.0%) procedures were performed laparoscopically. Two patients underwent curative surgery after previous colon resections.

The stages of operations for FAP were standard. The J-pouch, the and the removed specimen are shown in Figures 2–4.

**Figure 2.** J-pouch

The operation time, intraoperative blood loss, postoperative complications, and postoperative hospital stay were assessed.

After surgery, patients were under the control of a gastroenterologist to ensure adequate digestion and defecation by conservative treatment. The follow-up included endoscopy of the rectum and J-pouch, imaging of the abdominal cavity. Functional results of surgery were evaluated by the GIFO scale [7].

Statistical data processing was carried out using the STATISTICA 12.0 statistical package. Quantitative indicators are represented by the mean (M), median (Me) and quartile values Q1 and Q3 in the format M, Me (Q1; Q3). The numerical values of the two groups were compared using the nonparametric Mann-Whitney test.



Figure 3. Pouch-anal anastomosis



Figure 4. Removed specimen in FAP

Categorical data were presented in the form of absolute and relative incidence (%). Comparison of feature incidence was carried out using the exact bilateral Fisher test, the threshold level of significance of p was assumed to be 0.05. The patients' survival rate was assessed using the Kaplan-Meier test.

RESULTS

The results showed that the mean operation time for FAP was 243 minutes, the mean intraoperative blood loss was 244 ml, and the mean hospital stay was 17.2 days. There were no intraoperative complications.

Postoperative complications developed in 3 (15.0%) patients. In the early postoperative period, complications were detected in 2 (10.0%) patients only after laparoscopic colectomy with rectal resection, the formation of J-pouch and preventive ileostomy: one patient developed a pouch leakage on the 5th day after surgery. Another patient developed a pouch leakage on the 4th day. Both complications required re-operation: relaparoscopy, peritoneal washout and additional peritoneal drainage.

In the late postoperative period, complications developed in 1 (5.0%) patient after colectomy with rectal resection, J-pouch and preventive ileostomy: on the 65th day after surgery rectovaginal fistula developed, transanal fistulectomy was performed.

A comparative analysis showed (Table 3) that laparoscopic procedures have advantages relative to intraoperative blood loss (1.3 times less, $p = 0.057$), intestinal motility (by 1.9 days faster, $p = 0.0007$). The advantage of laparoscopic approach was also the cosmetic effect due to the absence of large incisions of the anterior abdominal wall. Open procedures were faster (1.5 times, $p = 0.047$).

The preventive ileostomy takedown was performed in all cases. In the patients without postoperative complications, ileostomy closure was performed after 3 months; in the patients with postoperative complications, ileostomy closure was performed after 14 months. No

Table 4. Functional results of colectomy with rectal resection and J-pouch 1 year after ileostomy closure ($n = 8$)

Indicator	M, Me (Q1; Q3); n (%)
Scale GIFO, M, Me (Q1; Q3)	70.3 70 (65; 77)
Daily stool incidence, M, Me (Q1; Q3)	11.1 9 (6.5; 14)
Incidence of daytime stool, M, Me (Q1; Q3)	8.1 7 (4; 10)
Incidence of night stool, M, Me (Q1; Q3)	3.03 (1; 5)
Laundry contamination, n (%)	4 (50%)
Daytime, n (%)	4 (50%)
Night time, n (%)	4 (50%)
Episodes of intestinal discomfort, n (%)	7 (87.5%)
Taking antidiarrheal medications, n (%)	4 (50%)
Gas incontinence, n (%)	7 (87.5%)
Ability to distinguish gases/feces, n (%)	7 (87.5%)
Perianal skin irritation, n (%)	6 (75%)
Stool consistency:	
Liquid, n (%)	3 (37.5%)
Mixed, n (%)	5 (62.5%)
Dense, n (%)	0%
Dietary restrictions, n (%)	6 (75%)

postoperative complications were noted after ileostomy takedown.

The functional results of colectomy with rectal resection, J-pouch in 8 patients 1 year after the closure of the ileostomy are presented in Table 4.

As can be seen from the table, most patients have an acceptable quality of life with stool on average 11.1 times a day, gas incontinence, the ability to distinguish gases/feces, and a mixed stool. At the same time, most patients reported dirty under wear, episodes of abdominal discomfort and irritation of the perianal skin. Also, most patients are forced to limit their diet, half of the patients take antidiarrheal medications.

After preventive colorectal surgery, eight patients returned to work within 8 to 12 months after treatment; the remaining patients were

not employed before the surgery, but returned to their former lives.

During follow-up after surgery, the first polyps of the rectal stump were detected within 6–8 months after surgery in 5 (33.3%) of 15 patients; in 4 (80.0%) of these patients, a stapler iliac-rectal/anal anastomosis was performed. All the patients underwent endoscopic removal of revealed new polyps. Gastroduodenal polyps were detected within 10 to 14 months after surgery in 2 (10.0%) patients (their endoscopic removal was also performed); ileum polyps were not detected in our patients during the follow-up.

Desmoid tumors of the abdomen or abdominal wall were detected on average in 24.3 months after surgery in 3 (15.0%) patients, all of which developed after laparoscopic procedures (42.9%). All the patients with desmoid tumors

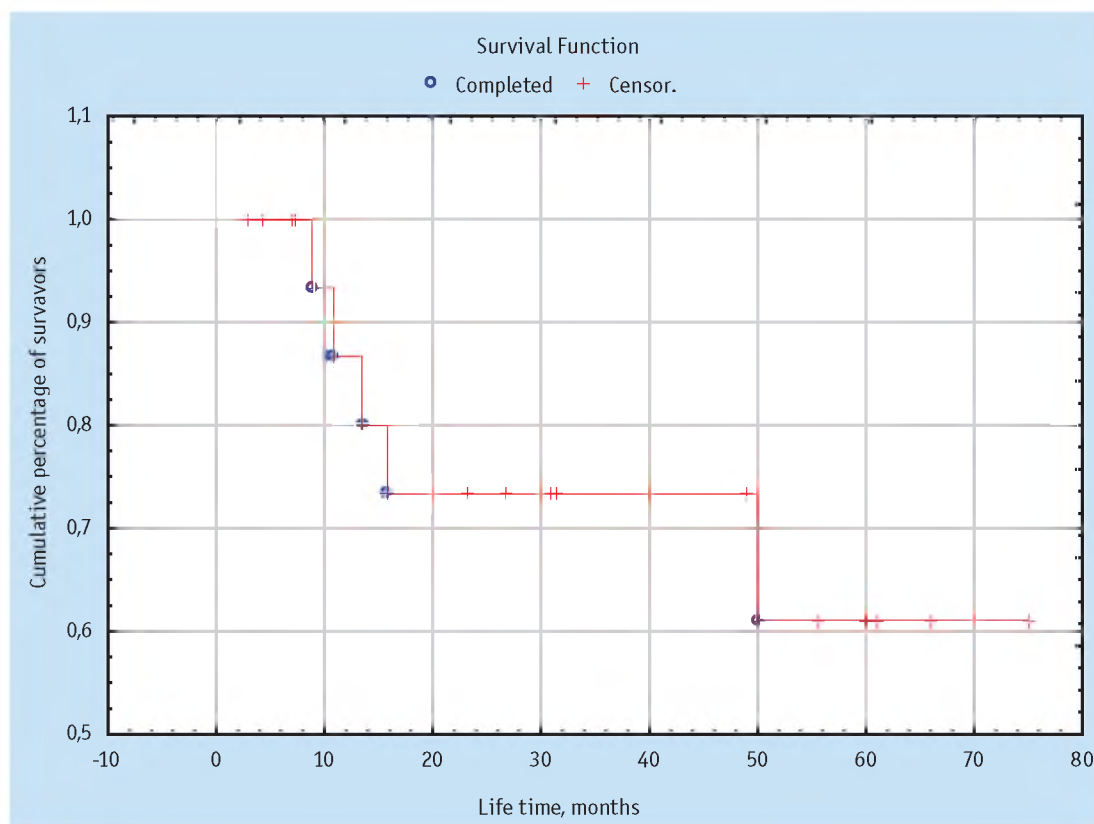


Figure 5. Survival of patients with FAP, months (75% survival -14.2 months)

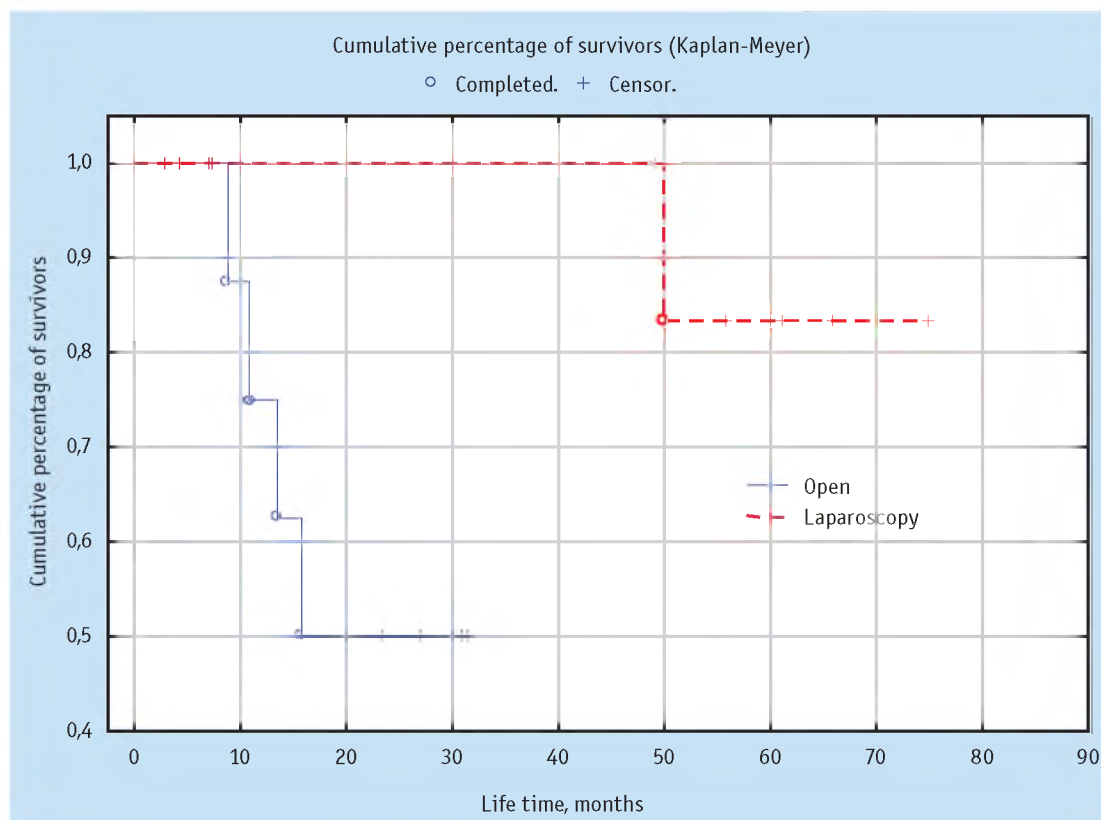


Figure 6. Survival of patients with FAP after open and laparoscopic surgeries

Note: significance of differences between survival $p = 0.045$, Log-rank criterion

were operated on. In two of these patients, abdominal desmoid tumors originated from the mesentery root of the small intestine with involvement of the main vessels and the inability to remove them. Then the patients received conservative treatment. One patient had a desmoid tumor located in the abdominal wall; after its removal, surgery was performed twice with an interval of six months for newly identified desmoid tumors of the abdominal wall.

During the follow-up, 5 (25.0%) patients died, of whom 4 (20.0%) patients died due to the colorectal cancer progression, 1 (5.0%) patient died due to an aggressive abdominal desmoid tumor (Fig. 5).

The analysis showed significant better survival of patients with minimally invasive access (Fig. 6).

DISCUSSION

According to the literature, the average age of patients with FAP during surgery was 28–33.5 years [4,8,9] with a gender ratio (male / female) of 0.93. On average, 60% of patients had a family history of FAP. Colorectal cancer was detected in 31–60% of patients with an average age of 34.6 years [8,10].

The data obtained in the study are generally consistent with the literature data: the gender ratio (male/female) was also about one — 1.2. Family history was observed in 65% of patients. 60% of patients with FCAP were diagnosed with colorectal cancer at an average age of 48.2 years. The differences relate to the average age of patients at the time of surgical treatment: our patients were older, with an average age of 42.2 years. Apparently, this is due to the peculiarities of the diagnosis of FAP in different countries, in particular, the presence or absence of registers of patients with FAP, as well as current clinical guidelines for the treatment of FAP [11,12].

We performed 75% of colectomies with rectal resection and 25% of proctocolectomies. When choosing surgery for FAP, we took into account the choice of the patient. Currently, there is no 'gold' standard of surgery in FAP, since many

factors influence the choice of surgery. In some studies, the main surgery for FAP was colectomy with rectal resection [13], in others — proctocolectomy [8].

There are studies indicating that colectomy with rectal resection has a risk of rectal cancer of 13% with a mortality rate of 7%. Therefore, it can be a first-choice surgery only with weakened variants of FAP [13]. Proponents of performing proctocolectomy in FAP also appeal to the data that almost a third of patients with colectomy and rectal resection will have rectal incontinence and the need for secondary proctectomy within 20 years after surgery and more than half — after 30 years. Approximately 10% will develop rectal cancer after 20 years and 20% after 30 years of follow-up, resulting in a cumulative mortality of 8% over 20 years [13]. In this study, the overall incidence of postoperative complications was 15%; all of them required re-operations. These data are consistent with other studies in which the incidence of postoperative complications was from 5.3% to 26.2%, with the incidence of re-operations up to 14.3% [14,15,16].

A comparison of laparoscopic and open procedures for FAP revealed the following advantages of minimally invasive access: less intraoperative blood loss (by 1.3 times), rapid recovery of intestinal motility (by 0.9 days) and motor activity (by 1.9 days). However, at the same time, operation time was longer (1.5 times).

Campos, F, et al. [10] compared the results of 38 laparoscopic and 25 open procedures for FAP and found that the duration of laparoscopic procedure was longer than open (374 min. vs. 281 minutes, $p = 0.003$). The incidence of early postoperative complications (28% vs. 28.9%), the postoperative hospital stay (10.9 vs. 8.9 days) and re-operation rate (28% vs. 21%) in the groups of patients did not differ statistically. However, the greater number of late postoperative complications (16% vs. 2.6%; $p < 0.001$) and the incidence of late re-operations (16% vs. 5.2%; $p < 0.05$) were higher after open surgeries.

In general, laparoscopic procedures for FAP are becoming a standard surgery in many institutions [4].

To date, the functional results of surgery for FAP are one of the main factors for decision making in choosing one or another approach. Studies show that the functional results of colectomy with rectal resection are significantly better than proctocolectomy in terms of stool incidence during the day and at night, underwear soil, gas and stool incontinence, stool consistency and the need for antidiarrheal drugs [11]. The study confirmed the data on good functional results of colectomy with rectal resection, since most patients had an acceptable quality of life with a stool on average 11.1 times a day; employed patients were able to return to work. According to the literature, endoscopic control of the pouch and the remaining part of the rectal mucosa after surgery should be carried out for life due to the risk of developing adenomas and their further malignancy. Thus, in the study by Zahid, A. et al. [17] adenomas were found in 12 (44.0%) of 27 patients with an average time till the formation of the first polyp — 88 months. An interesting fact is that in this study, none of the five patients who underwent manual ileo-anal anastomosis developed adenomas at follow-up, compared with 12 (55.0%) of 22 patients with stapler anastomosis ($p = 0.047$).

In the study, the first adenomas of the rectal stump were detected earlier — within 6–8 months after surgery in 5 (33.3%) of 15 patients; in 4 (80.0%) of these patients, a stapler ileo-rectal/anal anastomosis was formed. Adenomas of the small intestine J-pouch were not detected.

Another problem that arises in the treatment of FAP is the occurrence of aggressive desmoid tumors.

Literature data indicate that the overall risk of desmoid tumors during life in patients with FAP reaches 21% [18]. In most patients, desmoid tumors develop after surgery, so surgical trauma is considered a potential risk factor for their development through the activation of an abnormal wound healing process caused by somatic *APC* mutations. Other risk factors for the development of desmoid tumors include family history, female gender and location of mutation in the *APC* gene. However, until the end, the cause

of desmoid tumors after surgery for FAP has not been established at the moment.

As for the risk of developing desmoid tumors depending on surgical access, the literature data are ambiguous: some studies do not find a difference in the incidence of desmoid tumors with laparoscopic and open access, other studies report a lower incidence of desmoid tumors after laparoscopic surgery (4% vs. 16.3%) [9]. In the patients included in our study, desmoid tumors developed in 15% of cases during follow-up; all of them were observed after laparoscopic surgery.

The literature data unanimously indicate that the main causes of death of patients with FCAP are colorectal cancer and aggressive desmoid tumor. In our study, 20% of patients died from the progression of colorectal cancer, 5% of patients died from an aggressive desmoid tumor, which is consistent with other studies. Thus, in the study by Sahakitrungruang, C, et al. [16] out of 29 patients, 7 (24.1%) patients died from colorectal cancer and 2 (6.9%) from desmoid tumor.

CONCLUSION

Despite the rarity of the disease, FAP is a complex problem of modern medicine, including the MDT of different specialties: gastroenterologists, geneticists, endoscopists, radiologists, surgeons, oncologists, and others. Diagnostic problems with determining the type of FAP and examining relatives are intertwined with traumatic surgery that changes the patient's quality of life and requires diet and drug support, but does not always guarantee the absence of progression of polyposis with the development of cancer, as well as aggressive desmoid tumors. Minimally invasive surgeries in FCAP have advantages over open surgeries and can become standard surgeries.

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