

# Laparoscopic surgical treatment for ulcerative colitis

Ph.D. Thesis

JÁNOS TAJTI M.D.

Supervisor: György Lázár M.D., Ph.D., D.Sc.



Department of Surgery

Faculty of Medicine

University of Szeged

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## CONTENTS

LIST OF PAPERS.....	4
LIST OF ABBREVIATIONS .....	6
1. INTRODUCTION.....	7
2. AIMS .....	8
3. PATIENTS AND METHODS .....	8
3.1. Patients.....	8
3.2. Surgery.....	9
3.2.1. Laparoscopic technique.....	9
3.2.2. Conventional technique.....	10
3.3. Short-, mid- and long-term follow-up .....	10
3.3.1. Comparison of preoperative data .....	10
3.3.2. Comparison of operative/intraoperative data.....	10
3.3.3. Comparison of postoperative data.....	10
3.4. Quality of life.....	11
3.4.1. Questionnaires.....	11
3.5. Statistics.....	12
4. RESULTS.....	13
4.1. Comparison of the conventional and the minimally invasive surgical method in treatment for UC, short and mid-term result (Study I) .....	13
4.1.1. Preoperative results .....	13
4.1.2. Surgical Procedures .....	13
4.1.3. Postoperative results .....	15
4.1.4. Mid-term follow-up results .....	15
4.2. Comparison of the conventional and the minimally invasive surgical method in treatment for UC, long-term results (Study II) .....	18
4.2.1. Preoperative results .....	18
4.2.2. Surgical Procedures .....	19
4.2.3. Postoperative results .....	20
4.2.4. Long term follow-up results.....	20
4.3. Evaluate quality of life after surgery for UC by investigating the connection between gastroenterological and psychological conditions, daily activities (Study III.) .....	21
4.3.1. Patients.....	21
4.3.2. Representation of illnesses.....	22
4.3.3. Psychological consequences of having a stoma.....	22

4.3.4. Results for emotional state and mood .....	22
4.3.5. Comparing laparoscopy and open surgery.....	23
4.3.6. Complications .....	24
4.3.7. Headache.....	25
5. DISCUSSION .....	26
6. CONCLUSION .....	30
7. ACKNOWLEDGEMENTS .....	32
REFERENCES .....	33

## LIST OF PAPERS

**This doctoral thesis is based on the following publications:**

- I. **Tajti J Jr**, Simonka Z, Paszt A, Abraham S, Farkas K, Szepes Z, Molnar T, Nagy F, Lazar G. Role of laparoscopic surgery in the treatment of ulcerative colitis; short- and mid-term results. *Scand J Gastroenterol.* 2015; 50: 406-412. *IF: 2.199*
- II. **Tajti J Jr**, Simonka Zs, Paszt A, Ábrahám Sz, Farkas K, Szepes Z, Molnár T, Nagy F, Lázár Gy. [Minimally invasive surgical treatment of ulcerative colitis – long-term results] [Article in Hungarian] *Orv Hetil.* 2015; 156(39): 1585-1592. *IF: 0.291*
- III. **Tajti J Jr.**, Látos M, Farkas K, Ábrahám S, Simonka Z, Paszt A, Molnár T, Lázár G. Effect of Laparoscopic Surgery on Quality of Life in Ulcerative Colitis. *J Laparoendosc Adv Surg Tech A.* 2018; 28(7):833-838. *IF (2017): 1.257*
- IV. **Tajti Jr. J**, Látos M, Ábrahám Sz, Simonka Zs, Paszt A, Lázár Gy. [Tension-Type Headache In Ulcerative Colitis]. [Article in Hungarian] *Ideggyogy Sz* 2017; 70(11–12):389–393. *IF (2016): 0.322*

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- I. Simonka Zs, Paszt A, Ábrahám Sz, Pieler J, **Tajti J**, Tiszlavicz L, Németh I, Izbéki F, Rosztóczy A, Wittmann T, Rárosi F, Lázár Gy. The effects of laparoscopic Nissen fundoplication on Barrett's esophagus: Long-term results. *Scand J Gastroenterol.* 2012; 47: 13–21. *IF: 2.156*
- II. **Tajti J Jr**, Pieler J, Simonka Z, Paszt A, Lázár G. [Treatment of pregnancy-associated breast cancer]. [Article in Hungarian] *Magy Seb.* 2014; 67(4): 268-70.
- III. Simonka Z, Paszt A, Géczi T, Ábrahám S, Tóth I, Horváth Z, Pieler J, **Tajti J**, Varga A, Tiszlavicz L, Németh I, Izbéki F, Rosztóczy A, Wittmann T, Lázár G. [Comparison of surgical patients with gastroesophageal reflux disease and Barrett's esophagus] [Article in Hungarian] *Magy Seb.* 2014; 67(5): 287-296.

IV. Farkas K, Saródi Z, Bálint A, Földesi I, Tiszlavicz L, Szűcs M, Nyári T, **Tajti J**, Nagy F, Szepes Z, Bor R, Annaházi A, Róka R, Molnár T. The diagnostic value of a new fecal marker, matrix metalloprotease-9, in different types of inflammatory bowel diseases. *J Crohns Colitis*. 2015; 9(3): 231-7. *IF: 6.585*

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**LIST OF ABBREVIATIONS**

ASA	Anesthesiologists Physical Status
BIPQ	Brief Illness Perception Questionnaire
BMI	Body Mass Index
CRP	C-Reactive Protein
GIQLI	Gastrointestinal Quality of Life Index
Hgb	Hemoglobin
Htc	Hematocrit
ICU	Intensive Care Unit
IBD	Inflammatory Bowel Diseases
IPAA	Ileal Pouch–Anal Anastomosis
MRSA	Methicillin-resistant <i>Staphylococcus aureus</i>
SIBDQ	Short Inflammatory Bowel Disease Questionnaire
UC	Ulcerative Colitis
WBC	White Blood Cell

## 1. INTRODUCTION

Ulcerative colitis (UC) is a chronic inflammatory disease affecting the whole large intestine. The epidemiological data reveal that the incidence of UC is constantly rising, primarily as a consequence of the spreading of the “western” lifestyle and urbanization<sup>[1]</sup>. The incidence of inflammatory bowel diseases (IBD) is 11.3/100,000 in Eastern Europe, 14.0/100,000 in Western Europe, and it is estimated to be 24/100,000 in Hungary<sup>[2]</sup>. In 2010, the IBD registry of five Hungarian centres included 1390 patients, 539 of whom had UC, but since the estimated prevalence of IBD in Hungary is 25,000, these data relate only to the more severe cases<sup>[3]</sup>. The two varieties of IBD are UC and Crohn's disease. Crohn's disease affects the entire gastrointestinal tract, while UC affects the colon and rectum. The exact pathogenesis of IBD is still unknown, but environmental, genetic and immunological impacts and interactions are postulated<sup>[1, 4]</sup>. UC is characterized by inflammation and ulcers of the colon and rectum, and destruction of the intestinal wall, which appear firstly in the recto-sigmoid colon. Thanks to the broad-spectrum medical and biological therapy, the disease can generally be controlled for a long time with conservative treatment, but unresponsive cases with frequent relapses and complicated cases require surgical intervention. An estimated 25-45% of patients with UC need surgery at some time<sup>[1, 5, 6]</sup>. The purpose of the surgical intervention is to remove the affected bowel segment, which can be achieved with either the conventional, open or the laparoscopic technique. The first minimally invasive colon resection, a right hemicolectomy was performed by *Moise Jacobs* in 1990<sup>[7]</sup>. Currently, the generally accepted procedure, which has become the gold standard for the surgical treatment of UC, is total proctocolectomy with the creation of an ileal pouch-anal anastomosis (IPAA)<sup>[8, 9]</sup>. This procedure was first performed with a laparoscopic approach by *Peters* in 1992<sup>[10]</sup>. A number of studies have shown that laparoscopic surgery has numerous advantages, such as less postoperative pain, shorter hospital stay, less time required for recovery of the bowel function, and better cosmetic results<sup>[11]</sup>. The importance of surgical treatment is supported by studies that show that patients treated with conservative methods experienced a worse long-term quality of life compared to those receiving surgical treatment<sup>[12, 13]</sup>. As a result, it can be concluded that surgery provides successful treatment for UC in the long term and it is therefore important to inform the patients about it. Rather limited experience is available, however, as regards the long-term results of laparoscopic surgery. Limited data are available on quality of life in patients with UC undergoing surgery as well. Laparoscopic technique for the surgical

intervention of UC was initiated in the Department of Surgery, University of Szeged in 2005, since then our working group gained the greatest experience in this field in Hungary.

## **2. AIMS**

- (i) Compare the short- and mid-term follow-up results on patients treated for UC with the conventional and the minimally invasive surgical method (Study I.).
- (ii) Compare the long-term follow-up results on patients treated for UC with the conventional and the minimally invasive surgical method (Study II.).
- (iii) Evaluate quality of life after surgery for UC by investigating the connection between gastroenterological and psychological conditions, daily activities (Study III.).

## **3. PATIENTS AND METHODS**

### **3.1. Patients**

Patients who had undergone operation for UC between 1 January 2005 and 1 March 2016 were involved in our investigation.

**Study I.** The first follow-up period - from 1 January 2005 to 31 May 2013, mean follow-up of 38 (1-92) months - was defined as short- and mid-term follow-up, with a total of 45 patients (n=27 women, n=18 men). The mean age of the patients was  $42.29 \pm 14.37$  years in the laparoscopy group and  $38.91 \pm 12.58$  years in the open surgery group.

**Study II.** The second period - from 1 January 2005 to 31 December 2014, mean follow-up of 47.84 (3-111) months - was defined as long-term follow-up, with 56 patients (n=31 women, n=25 men). The mean age of the patients was  $45.09 \pm 14.49$  years in the laparoscopy group and  $38.26 \pm 12.68$  years in the open surgery group.

**Study III.** At the third period between 1 January 2005 and 1 March 2016, surgery was performed for UC in a total of 75 patients. The mean duration of the follow-up was 46 (1-124) months. Our examinations were performed in 58 cases (n=29 women, n=29 men). The mean age of the patients was  $46.98 \pm 13.38$  years in the laparoscopy group and  $45.47 \pm 12.59$  years in the open surgery group.

### **3.2. Surgery**

Strategy for the surgical treatment of UC is determined by the general status of the patients and the type of the surgical indication.

The indication for emergency surgery was the presence of a severe, toxic condition, which was accompanied by bleeding, perforation or severe malnutrition. In case of emergency surgical indication or patients with weak general status three-stage surgical strategy (*i.* total colectomy, mucous fistula and end ileostomy, *ii.* J-pouch creation and ileostomy, *iii.* ileostomy closure) was needed.

The elective interventions were performed because of a condition that could not be controlled with conservative treatment. In an elective case patients with good general status were undergone a two-stage surgical procedure (*i.* proctocolectomy, IPAA and ileostomy, *ii.* closure of ileostomy).

During our practice one-stage surgical procedures (rectum extirpation, proctocolectomy with end ileostomy, colectomy with ileorectostomy, total colectomy with ileostomy) were also performed, because of sphincter disorder.

Conversion from laparoscopy to open surgery was required, because of massive adhesions or because of the risk of bowel injury and perforation. These cases were excluded from the subsequent analyses.

All surgical procedures were carried out in general anaesthesia combined with epidural analgesia. During the procedures we used metronidazole and 2nd generation cephalosporin for antibiotic prophylaxis, while during emergency operations therapy was completed with 3rd generation cephalosporin or imipenem/cilastatin in cases of severe septic-toxic condition or peritonitis.

#### **3.2.1. Laparoscopic technique**

The laparoscopically assisted proctocolectomy + IPAA and the total colectomy + mucous fistula were performed with the use of 6 or 7 ports, depending on the auxiliary incision. The resection of the colon, and the creation of the anastomosis and the mucous fistula were performed from the cosmetically favourable Pfannenstiel incision. The J-pouch was created from the terminal ileum with a straight stapler(s), and a double stapler technique was used for the ileoanal anastomosis. The staple line was protected with a loop ileostomy in every case.

The pouch created as the second surgical step was also achieved from the Pfannenstiel incision.

### **3.2.2. Conventional technique**

In the cases involving the conventional method, a midline laparotomy was performed to explore the abdominal cavity, in the lower recess of which the mucous fistula was created; the pouch and the ileoanal anastomosis were created in the same way as during the laparoscopic interventions.

## **3.3. Short-, mid- and long-term follow-up**

### **3.3.1. Comparison of preoperative data**

During the preoperative period general status of UC patients was examined, namely gender, Body Mass Index (BMI), Anesthesiologists physical status (ASA) class, age, inflammatory parameters, blood count, albumin level, number of stools daily. The time from the onset of UC to surgery, the use of biological therapy was described.

### **3.3.2. Comparison of operative/intraoperative data**

Distribution and duration of the different types of surgical interventions were examined.

### **3.3.3. Comparison of postoperative data**

The length of hospital stay, the number of days spent in the intensive care unit (ICU), the time to the recovery of the bowel function, and the need for transfusion were examined. Postoperative complications were classified as early (within 30 days) or late (after 30 days) with regard to their onset after primary surgery. Complications requiring and not requiring reoperation were investigated. From the aspect of the cosmetic result, the patients graded their satisfaction on a five-item scale (not at all satisfied – slightly satisfied– moderately satisfied – rather satisfied – very satisfied). The preoperative and postoperative general status of the patients were graded on a scale from 1 to 10, where 1 was the best, and 10 was the worst general status. Postoperative number of stools daily and body weight were registered and compared.

### **3.4. Quality of life**

Quality of life was examined with questionnaires considering gastroenterological and psychological conditions, daily activities and headache. Results were analyzed in the laparoscopic group and in patients undergoing open surgery, in patient with or without a stoma, in case of acute and elective interventions, and regarding early and late complications.

#### **3.4.1. Questionnaires**

##### **3.4.1.1. Testing gastroenterological conditions**

###### *3.4.1.1.1. Functional Scoring System*

The functional scoring system is a questionnaire consisting of twelve questions on patients' bowel movements (number of bowel movements during the day and at night, urgency and perianal soreness), incontinence (during the day and at night and use of protective pads), diet, drug therapy and potential social disadvantages<sup>[14]</sup>.

###### *3.4.1.1.2. Gastrointestinal Quality of Life Index (GIQLI)*

The GIQLI studies gastroenterological condition (abdominal pain, epigastric fullness, bloating, flatulence, eructation, increased bowel movements, urgency, diarrhoea, constipation, nausea, blood in the stool, heartburn and bowel incontinence), alimentation (appetite, eating speed and swallowing a bite), physical condition, daily activities, social activities and psychological condition for two weeks before completing the questionnaire<sup>[15]</sup>.

###### *3.4.1.1.3. Short Inflammatory Bowel Disease Questionnaire (SIBDQ)*

The SIBDQ studies gastrointestinal symptoms and their effect on social and physical well-being for two weeks before completing the questionnaire based on ten questions<sup>[16]</sup>.

##### **3.4.1.2. Considering psychological status**

###### *3.4.1.2.1. Spielberger's State-Trait Anxiety Questionnaire and the Beck Depression Inventory*

Spielberger's State-Trait Anxiety Questionnaire and the Beck Depression Inventory were used to measure the level of anxiety and mood<sup>[17, 18]</sup>.

#### *3.4.1.2.2. Brief Illness Perception Questionnaire (BIPQ)*

Illness perceptions and attitude towards healing were studied using the BIPQ, consisting of eight subscales (consequences, timeline, personal control, treatment control, identity, concern, coherence and emotional representation) [19].

#### 3.4.1.3. Examining headache

##### *3.4.1.3.1. Headache Questionnaire*

The nature of the headache was evaluated with the 16-question Headache Questionnaire. It contains questions about frequency of headaches, laterality, localization, nature, severity, duration, accompanying symptoms, patients' opinions on the headache, therapy employed, efficacy of therapy and the effect of the headache on everyday life, based on the criteria of the International Classification of Headache Disorders, 3<sup>rd</sup> edition (beta version) [20].

## **3.5. Statistics**

Patients were examined retrospectively, and statistical analysis was performed with the SPSS program (IBM SPSS Statistics, Version 20.0 2014, Chicago, IL, USA). Pearson and Spearman correlations were used to determine relationships between variables. The independent samples t-test, Mann–Whitney test, ANOVA and Chi-square test were used to compare the groups. Values were considered to be statistically significant if  $P$  was lower than 0.05.

## 4. RESULTS

### 4.1. Comparison of the conventional and the minimally invasive surgical method in treatment for UC, short- and mid-term result (Study I.)

#### 4.1.1. Preoperative results

There was no significant difference in the time from the onset of UC to surgery between the laparoscopic group (8.71 years) and the open surgery group (8.63 years). In the preoperative period, 16 patients (35.55%) received biological therapy, with infliximab. The preoperative laboratory test results, revealed a significant difference between the two groups only in CRP (**Table 1**).

	Age (years)	ASA	BMI	WBC (G/L)	CRP (mg/L)	Hgb (g/L)	Htc (L/L)	Albumin (g/L)
Laparoscopy	41.29	2.19	24.03	8.33	16.79	105.43	33.81	37.79
Open surgery	38.91	2.14	22.88	9.06	47.66	109.13	33.96	33.01
	<i>P=0.818</i>	<i>P=0.490</i>	<i>P=0.529</i>		<i>*P=0.028</i>	<i>P=0.471</i>	<i>P=0.920</i>	<i>P=0.108</i>

**Table 1.** Mean age, American Society of Anesthesiologists physical status (ASA) class, Body Mass Index (BMI) and preoperative laboratory data in the laparoscopic and open surgery groups. \* $P \leq 0.05$

WBC: White Blood Cell; CRP: C-Reactive Protein; Hgb: Hemoglobin; Htc: Hematocrit

On the other hand, the preoperative laboratory data for the patients who participated in emergency surgery indicated an increased inflammatory response. The hematocrit levels (31.31 vs. 35.31 L/L,  $P=0.007$ ) and albumin levels (28.93 vs. 39.67 g/L,  $P<0.001$ ) were significantly lower in the emergency group than in the elective group.

Before the surgical interventions, the mean number of stools daily was 10.78 and 9.64, respectively, in the two groups. The last colonoscopy report before surgery indicated 30 cases (66.67%) of pancolitis, 5 cases (11.11%) of left-sided involvement and 10 cases (22.22%) of distal involvement.

#### 4.1.2. Surgical Procedures

Sixteen (35.5%) of the surgical interventions were emergency procedures, while 29 (64.5%) were elective interventions. The laparoscopic technique was used in 23 (51.1%) and the conventional method in 22 (48.9%) cases. Total proctocolectomy with the creation of a J-

pouch and protective loop ileostomy was carried out laparoscopically in 13 cases and with the open technique in 5 cases. Total colectomy with mucous fistula and end ileostomy was performed using the minimally invasive technique in 8 cases and the conventional method in 13 cases. Conversion from laparoscopy to open surgery was required in 3 cases (3/26, 11.53%), because of massive adhesions during elective surgery (1 case) or because of the risk of bowel injury and perforation during emergency surgery (2 cases). These cases were excluded from the subsequent analyses. The distribution of the various surgical procedure is presented in **Table 2**.

		Laparoscopy (n=23)	Open surgery (n=22)
Two-stage surgery	i. Proctocolectomy, J-pouch, ileostomy	13 (56.5%)	5 (23%)
	ii. Ileostomy closure	11	4
Three-stage surgery	i. Total colectomy, mucous fistula, end ileostomy	8 (34.8%)	13 (59%)
	ii. J-pouch creation, ileostomy	6	12
One-stage surgery	iii. Ileostomy closure	5	11
	Rectum extirpation	2 (8.7%)	0
	Proctocolectomy, end ileostomy	0	2 (9%)
	Colectomy, ileorectostomy	0	1 (4.5%)
Total colectomy, ileostomy		0	1 (4.5%)

**Table 2.** Distribution of surgery

From the aspect of the duration of surgery, the open method was found to be significantly shorter than the laparoscopic intervention (**Table 3**).

	Laparoscopy	Open surgery	
Proctocolectomy, J-pouch, ileostomy	245.42	185	*P=0.040
Total colectomy, mucous fistula, end ileostomy	187	151.67	*P=0.012

**Table 3.** Distribution of duration of surgery (minutes) \*P ≤ 0.05

#### 4.1.3. Postoperative results

There was no death in the perioperative period in either group. There was no significant difference between immediate postoperative results (**Table 4**).

	Laparoscopy (n=23)	Open surgery (n=22)	
Hospital stay (days)	11.50	11.63	P=0.914
Time to recovery of bowel function (days)	1.44	1.55	P=0.656
Time spent in the ICU (days)	2.50	2.09	P=0.437
Need for blood transfusion (units)	2.05	3.13	P=0.57

**Table 4.** Immediate postoperative results in the laparoscopic and open surgery groups

There was no difference (P=0.945) between the laparoscopic group and the open surgery group in the rate of early complications requiring or not requiring reoperation, which are listed in **Table 5**.

	Laparoscopy (n=23)	Open surgery (n=22)	
<b>Requiring reoperation</b>	<ul style="list-style-type: none"> <li>• Ileus (2)</li> <li>• Abdominal wall disruption in the area of the mucous fistula (1)</li> <li>• Stoma repair (1)</li> </ul>	<ul style="list-style-type: none"> <li>• Ileus (3)</li> <li>• Septic condition (1)</li> </ul>	
Total	17.4% (4/23)	18% (4/22)	P=0.945
<b>Not requiring reoperation</b>	<ul style="list-style-type: none"> <li>• Subileus (3)</li> </ul>	<ul style="list-style-type: none"> <li>• Subileus (1)</li> <li>• Anal bleeding (1)</li> <li>• Dehydration (1)</li> <li>• Hydrothorax (1)</li> <li>• Urination problems (1)</li> </ul>	
Total	13% (3/23)	22% (5/22)	P=0.396

**Table 5.** Early postoperative complications (within 30 days) during the short- and mid-term follow up

#### 4.1.4. Mid-term follow-up results

During the follow-up period, wound infection was detected in 8 patients (34.8% of the cases) in the laparoscopic group, and in 7 patients (31.8% of the cases) in the open surgery group;

from this respect, there was no significant difference between the groups ( $P=0.833$ ). Methicillin-resistant *Staphylococcus aureus* (MRSA) infection was confirmed in 2 patients and 1 patient, respectively. During the mean follow-up of 36 months, significantly fewer complications, involving intestinal obstruction, septic condition, anastomotic stenosis, anal bleeding and pouch-vaginal fistula formation, occurred in the laparoscopic group (**Table 6**).

	Laparoscopy (n=23)	Open surgery (n=22)	
<b>Septic condition</b>	0	<ul style="list-style-type: none"> <li>• Severe pouchitis (1)</li> <li>• Perianal abscess (4)</li> <li>• Lesser pelvic abscess (1)</li> </ul>	
Total	0% (0/23)	27% (6/22)	** $P=0.007$
<b>Intestinal obstruction</b>			
– requiring surgical intervention	<ul style="list-style-type: none"> <li>• Ileus (1)</li> </ul>	<ul style="list-style-type: none"> <li>• Ileus (4)</li> </ul>	
– not requiring surgical intervention	<ul style="list-style-type: none"> <li>• Subileus (1)</li> </ul>	<ul style="list-style-type: none"> <li>• Subileus (6)</li> </ul>	
Total	8.7% (2/23)	45% (10/22)	** $P=0.005$
<b>Postoperative hernia</b>	<ul style="list-style-type: none"> <li>• In the ileostomy scar (2)</li> </ul>	<ul style="list-style-type: none"> <li>• In the midline laparotomy scar (4)</li> </ul>	
Total	8.7% (2/23)	18% (4/22)	$P=0.349$
<b>Other</b>	<ul style="list-style-type: none"> <li>• Anastomotic stenosis (1)</li> </ul>	<ul style="list-style-type: none"> <li>• Anastomotic stenosis (5)</li> <li>• Anal bleeding (2)</li> <li>• Severe sphincter damage (1)</li> <li>• Pouch-vaginal fistula (2)</li> <li>• Dehydration (1)</li> </ul>	
Total	4.3% (1/23)	50% (11/22)	*** $P=0.001$

**Table 6.** Late postoperative complications (after 30 days) during the short- and mid-term follow up. \*\* $P \leq 0.01$ , \*\*\* $P \leq 0.001$

In the laparoscopic group, surgery was performed because of ileus in 1 case, and 1 case of subileus resolved after medical therapy. Abdominal wall reconstruction was carried out electively in 2 cases because of a hernia in the scar of the previous ileostomy. Endoscopic dilatation was performed in 1 case of anastomotic stenosis.

In the conventional surgery group, surgery was performed because of ileus as a late complication in 4 cases. Four perianal abscesses were explored, 3 of which were treated by Seton drainage. Perianal exploration was needed in 1 case because of an abscess in the lesser pelvis. In 1 patient, excision of the pouch was required because of severe pouchitis and a

perianal abscess. Rectum extirpation was necessary in 2 patients because of an impaired sphincter function and anal bleeding. The abdominal wall was reconstructed in 4 cases because of postoperative hernia. Two anastomotic stenoses were dilated surgically, while endoscopic dilatation was performed in 3 patients. Six cases of subileus, 1 case of anal bleeding and 1 case of dehydration were resolved through conservative treatment.

During the course of the follow-up, there were significantly fewer urgent admissions to a medical unit in the laparoscopic group (1 vs. 6,  $P=0.034$ ).

The clinical symptoms and endoscopic findings confirmed 15 cases of pouchitis, affecting 41% of the patients with a pouch (6 in the laparoscopic group and 9 in the open surgery group). The inflammation of the pouch was accompanied by cuffitis in 10 cases.

Of the 16 patients treated with infliximab, 4 developed an early postoperative complication.

A significant improvement in the general status (scale from 1 to 10) was measured in both groups after the surgery, but there was no significant difference between the two groups. The postoperative mean number of stools daily at the last medical check-up during the follow-up was the same in the two groups. The preoperative and current body weights indicated an increase in both groups, which was significant in the open surgery patient population (**Table 7**).

		Preoperative	Current	
General status	Laparoscopy (n=23)	8.88±1.5	2.38±2.03	*** $P<0.0001$
	Open surgery (n=22)	8.8±1.74	2.6±2.03	*** $P=0.001$
Number of stools daily	Laparoscopy (n=23)	10.78±5.80	7.83±3.28	$P=0.061$
	Open surgery (n=22)	9.64±5.38	7.81±3.31	$P=0.238$
Body weight	Laparoscopy (n=23)	67.61±16.19	70.83±18.31	$P=0.554$
	Open surgery (n=22)	63.24±16.15	73.68±12.73	* $P=0.030$

**Table 7.** Pre- and postoperative general status, number of stools daily and body weight in the laparoscopic and open surgery groups. \* $P \leq 0.05$ , \*\*\* $P \leq 0.001$

The mean length of the midline laparotomy incision in the open surgery group was  $13.9 \pm 7$  cm, and the mean length of the Pfannenstiel incision in the laparoscopic group was  $10.5 \pm 3.5$  cm. From the aspect of the cosmetic result, the patients graded their satisfaction on a five-item scale, which demonstrated that those who had undergone open surgery were on average “rather satisfied”, while the laparoscopic patients were on average “very satisfied”.

## **4.2. Comparison of the conventional and the minimally invasive surgical method in treatment for UC, long-term results (Study II.)**

### **4.2.1. Preoperative results**

No difference was found between the two groups in the preoperative data. The preoperative laboratory test results (WBC count, CRP, Hgb, Htc and albumin) revealed a significant difference between the two groups in WBC count and CRP (**Table 8**).

	Laparoscopy (n=33)	Open surgery (n=23)	
Age (years)	45.09	38.26	<i>P</i> =0.074
ASA	2.27	2.05	<i>P</i> =0.125
BMI	22.76	22.59	<i>P</i> =0.906
Time (years) from the onset of UC to surgery	9.05	8.26	
WBC (G/L)	8.5	10.42	* <i>P</i> =0.032
CRP (mg/L)	23.29	51.51	* <i>P</i> =0.031
Albumin (g/L)	37.8	33.46	<i>P</i> =0.096
Hgb (g/L)	109.72	109.52	<i>P</i> =0.969
Htc (L/L)	34.27	33.95	<i>P</i> =0.828

**Table 8.** Mean age, American Society of Anesthesiologists physical status (ASA) class, Body Mass Index (BMI) and preoperative laboratory data in the laparoscopic and open surgery groups. \**P*≤0.05

WBC: White Blood Cell; CRP: C-Reactive Protein; Hgb: Hemoglobin; Htc: Hematocrit

The preoperative laboratory data for the patients who participated in emergency surgery indicated an increased inflammatory response. In the preoperative period, 23 patients (41.07%) received biological therapy with infliximab.

As concerns the extraintestinal manifestations of the disease, eye abnormalities were found in 5 cases (10.7%), skin disorders in 7 patients (12.5%), and bone and joint complaints in 18 patients (32.14%). The possibility of primary sclerosing cholangitis arose in 3 patients (5.3%), there were 7 cases (12.5%) of prior deep vein thrombosis, a history of tumour disease (in the kidney or the oral cavity) and tuberculosis were present in 2-2 cases (3.57-3.57%). There are no current smokers among these patients; prior smoking was confirmed in 8 cases, and there was a history of appendectomy in 2 case.

#### 4.2.2. Surgical Procedures

The laparoscopic technique was used in 33 (58.9%) and the conventional method in 23 (41.1%) cases. Twenty (35.7%) of the surgical interventions were emergency procedures, while 36 (64.3%) were elective interventions. The indication for emergency surgery was the presence of a severe, toxic condition, which was accompanied by bleeding in 4 cases, perforation and ileus in 1-1 cases, and severe malnutrition in 2 patients, whereas elective interventions were performed because of a condition that could not be controlled with conservative treatment.

The distribution and characteristics of the various surgical procedures are presented in **Table 9**.

		Laparoscopy (n=33)	Open surgery (n=23)	
Two-stage surgery	<i>i. Proctocolectomy, J-pouch, ileostomy</i>	<b>21 (63.6%)</b>	<b>5 (21.7%)</b>	
	Duration of surgery (minutes)	221	185	<i>P</i> =0.187
	<i>ii. Ileostomy closure</i>	<b>17</b>	<b>5</b>	
	Time from first surgery (months)	3.8	4.4	
Three-stage surgery	<i>i. Total colectomy, mucous fistula, end ileostomy</i>	<b>9 (27.2%)</b>	<b>14 (60.8%)</b>	
	Duration of surgery (minutes)	186.88	151.54	* <i>P</i> =0,006
	<i>ii. J-pouch creation, ileostomy</i>	<b>6</b>	<b>13</b>	
	Time from first surgery (months)	5	5.15	
	<i>iii. Ileostomy closure</i>	<b>6</b>	<b>12</b>	
	Time from first surgery (months)	7.83	9.25	
One-stage surgery	<b>Rectum extirpation</b>	<b>3 (9%)</b>	0	
	<b>Proctocolectomy, end ileostomy</b>	0	<b>2 (8.6%)</b>	
	<b>Colectomy, ileorectal anastomosis</b>	0	<b>1 (4.3%)</b>	
	<b>Total colectomy, ileostomy</b>	0	<b>1 (4.3%)</b>	

**Table 9.** Distribution and characteristics of surgical procedures \**P* ≤ 0.05

Following a histological diagnosis of Crohn's disease, the mucous fistula was converted to ileorectostomy in 2 case in the laparoscopic group.

#### 4.2.3. Postoperative results

There was no significant difference between the groups in the length of hospital stay, the time to the recovery of the bowel function, the number of days spent in the ICU, or the need for transfusion. There was no death in the perioperative period in either group.

#### 4.2.4. Long-term follow-up results

During the long-term follow up there were no significant differences between the two groups regarding early postoperative complications. Of the 23 patients treated with infliximab, 6 developed an early postoperative complication. During the mean follow-up of 47 months, significantly fewer late complications occurred in the laparoscopic group (**Table 10**).

	Laparoscopy (n=33)		Open surgery (n=23)	
	Complication	Therapy	Complication	Therapy
<b>Septic condition</b>	Lesser pelvic abscess (1)	Radiological intervention	Lesser pelvic abscess (1)	Perianal exploration
	Perianal abscess (1)	Seton drainage	Perianal abscess (9)	Seton drainage
	Abdominal wall abscess (1)	Conservative treatment	Severe pouchitis (1)	Pouch excision
Total	9% (3/33)		47.8% (11/23)	***P=0.001
<b>Intestinal obstruction</b>	Ileus (1)	Reoperation	Ileus (5)	Reoperation
	Subileus (7)	Conservative treatment	Subileus (9)	Conservative treatment
Total	24.2% (8/33)		60% (14/23)	**P=0.006
<b>Postoperative hernia</b>	In the ileostomy scar (3)	Abdominal wall reconstruction	In midline laparotomy scar (4)	Abdominal wall reconstruction
Total	9% (3/33)		17.3% (4/23)	P=0.355
<b>Other</b>	Anastomotic stenosis (1)	Endoscopic dilatation	Anastomotic stenosis (6)	Surgical and endoscopic dilatation
	Vascular failure of terminal ileum (1)	Resection of ileum	Anal bleeding (3)	Rectum extirpation (1)
			Severe sphincter damage (1)	Rectum extirpation
			Pouch-vaginal fistula (2)	-
			Dehydration (2)	Conservative treatment
Total	6% (2/33)		60% (14/23)	*P=0.01

**Table 10.** Late postoperative complications and treatment (after 30 days) during the long-term follow up. \*P ≤ 0.05, \*\*P ≤ 0.01, \*\*\*P ≤ 0.001

During the follow-up, 2 patients died, as a result of an oral cavity tumour or a cardiorespiratory insufficiency; the causes of death were not related to the UC. During the course of the follow-up, there were 9 and 12 urgent admissions to a medical unit because of need for transfusion and abdominal pain.

The clinical symptoms and endoscopic findings confirmed 17 cases of pouchitis (7 in the laparoscopic group and 10 in the open surgery group), affecting 40% of the patients with a pouch. The inflammation of the pouch was accompanied by cuffitis in 10 cases. During the follow-up period, wound infection was detected in 8 patients in the laparoscopic group (5 in the wound line, 1 on the perineum, 1 at the site of the drain, and 1 at the site of re-suture on the abdominal wall), and in 7 patients in the open surgery group (4 in the wound line, 1 at the site of the closed ileostomy, 1 at the site of the drain, and 1 at the site of the mucous fistula). MRSA infection was confirmed in 2 patients in the laparoscopic group and 1 patient in the open surgery group. Changes in the general condition, the body weight, the number of stools daily, and the cosmetic results after the surgical interventions were also assessed.

A significant improvement in the general status (scale from 1 to 10) ( $P=0.000$  and  $P=0.000$ ) was measured in both groups after the surgery. The preoperative and current body weights indicated an increase in both groups, which was significant ( $P=0.033$ ) in the open surgery patient population. There was a decreasing tendency of the postoperative mean number of stools daily in the two patient groups. From the aspect of the cosmetic result, those patients who had undergone open surgery were on average “rather satisfied”, while the laparoscopic patients were on average “very satisfied” on a five-item scale.

#### **4.3. Evaluate quality of life after surgery for UC by investigating the connection between gastroenterological and psychological conditions, daily activities (Study III.).**

##### **4.3.1. Patients**

41 patients had undergone laparoscopic surgery, and 17 patients had had open surgeries. Thirty-nine cases were elective interventions, while 19 were emergency surgery. No significant difference was found in the case of the BMI (24.85 vs. 26.82) or the ASA score (2.25 vs. 2.13). There was an average 8.2 years from diagnosing the disease to surgery. In the laparoscopic group, 25 proctocolectomies with IPAA and ileostomy were performed, 13 patients had a total colectomy with end ileostomy and mucous fistula, and 3 rectum

extirpations were carried out. In the open group, a pouch was created in 4 cases, 9 patients had a total colectomy with mucous fistula, and 4 other colon resections were performed. 17 patients had a stoma during the study. In order to homogenize the groups, 6 patients, who were operated dissimilarly from the standard surgical technique ( $n=3$  rectum extirpation,  $n=3$  other colon resection) were excluded during the comparison of laparoscopic and open surgery groups, and during the analysis of complications.

#### **4.3.2. Representation of illnesses**

92.3% of the patients enrolled in the study considered a psychological factor (psychological causes, family or work stress) to be in the background of their disease. 42.3% of the patients pointed to genetic factors, 46.2% of them mentioned environmental hazards (such as inappropriate diet), and 1 patient noted the Chernobyl nuclear disaster as the cause of the disease. Patients viewing genetic factors as being in the background of the disease reached significantly higher scores on the BIPQ (44.14 vs. 35.73;  $P=0.022$ ), so they are more threatened by their disease and know less about the nature of it (coherence subscale: 2.14 vs. 1.10;  $P=0.013$ ).

#### **4.3.3. Psychological consequences of having a stoma**

There were differences in personal control between patients with a stoma ( $n=17$ ) and patients without a stoma ( $n=41$ ) (6.12 vs. 4.12;  $P=0.045$ ). Patients with a stoma felt they had less control over their disease. No difference was found between the two groups during gastroenterological follow-up examinations.

#### **4.3.4. Results for emotional state and mood**

There was a significant connection between depression and the functional scoring system ( $P=0.002$ ;  $r=0.419$ ), the GIQLI ( $P<0.001$ ;  $r=-0.867$ ), the SIBDQ ( $P<0.001$ ;  $r=-0.795$ ) and the BIPQ ( $P<0.001$ ;  $r=0.751$ ), as well as the consequences, personal and treatment control, identity, concern and emotional representation subscales ( $P<0.05$  in all cases). State anxiety significantly correlated with the total score for the GIQLI ( $P<0.001$ ,  $r=-0.624$ ), the SIBDQ ( $P<0.001$ ,  $r=-0.579$ ) and the BIPQ ( $P<0.001$ ,  $r=0.615$ ), as well as with the consequences, personal and treatment control, identity, concern and emotional representation subscales ( $P<0.05$  in all cases). There was a significant connection between trait anxiety and the functional scoring system ( $P=0.012$ ;  $r=0.344$ ), the GIQLI ( $P<0.001$ ;  $r=-0.682$ ), the SIBDQ ( $P<0.001$ ;  $r=-0.684$ ) and the BIPQ ( $P<0.001$ ;  $r=0.608$ ), as well as the consequences, personal

and treatment control, identity, concern and emotional representation subscales ( $P<0.001$ ) (**Table 11**).

Variables	GIQLI
<b>Psychological variables</b>	
Beck Depression Inventory	-0.87**
Spielberger's State Anxiety Scale	-0.62**
Spielberger's Trait Anxiety Scale	-0.69**
Brief Illness Perception Questionnaire	-0.84**
Consequences	-0.89**
Timeline	-0.07 <sup>(NS)</sup>
Personal control	-0.37**
Treatment control	-0.39**
Identity	-0.73**
Concern	-0.71**
Coherence	-0.01 <sup>(NS)</sup>
Emotional representation	-0.78**
<b>Clinical variables</b>	
Functional scoring system	-0.55**
Short Inflammatory Bowel Disease Questionnaire	0.89**

**Table 11.** Pearson's or Spearman's correlation between clinical and psychological variables and Gastrointestinal Quality of Life Index (GIQLI)

\*\* $P \leq 0.01$ ; NS: non significant

#### 4.3.5. Comparing laparoscopy and open surgery

Trait anxiety was significantly lower in patients having undergone laparoscopic surgery ( $n=38$ ) compared with patients who had had open surgery ( $n=14$ ) ( $P=0.018$ ) (average value of trait anxiety in patients with open surgery was 48.71,  $SD=10.91$ ; this value was 40.22,  $SD=9.82$  in the laparoscopic group). Both patient groups had  $>5$  stools in the daytime and  $>1$  at night per week, with no significant difference observed between the groups. No difference was noted between the two surgical methods based on the total score on the gastroenterological questionnaires, although the following statistical differences were found

when evaluating each questionnaire item individually. Incontinence was registered during the day and at night in both patient groups (**Table 12**).

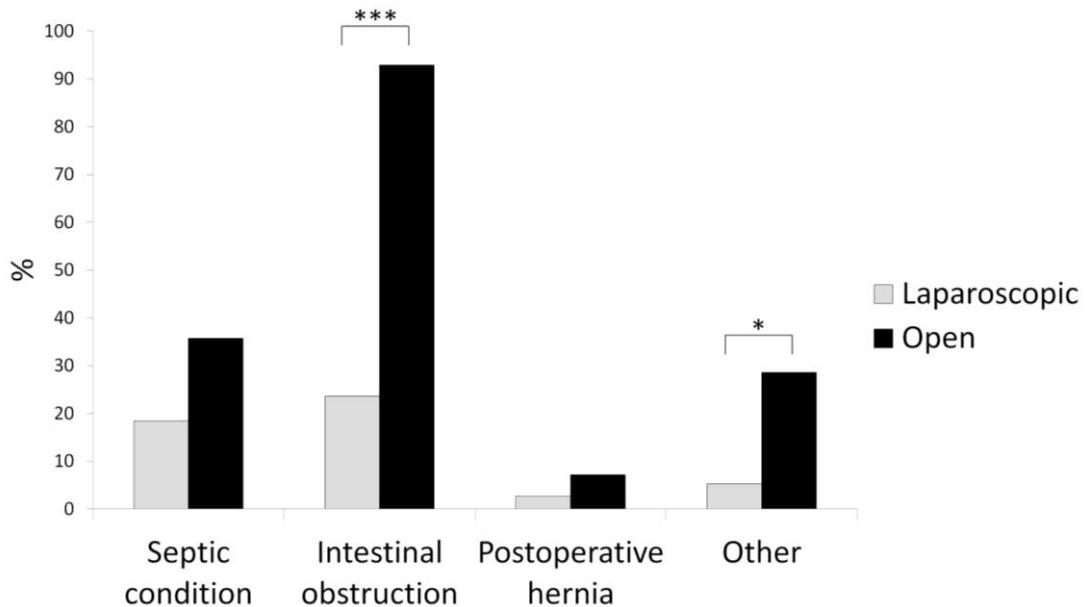
	Laparoscopy (n=28) n(%)	Open surgery (n=11) n(%)
Urgency (Inability to defer evacuation $\geq$ 30 minutes)	14 (50)	6 (54.5)
Evacuation difficulties	5 (17.85)	3 (27.3)
Soiling or seepage in daytime	7 (25)	3 (27.3)
Soiling or seepage at night	11 (39.28)	6 (54.5)
Perianal soreness	15 (53.57)	9 (81.8)
Protective pad in daytime	7 (25)	3 (27.3)
Protective pad at night	12 (42.85)	3 (27.3)
Dietary restrictions	21 (75)	5 (45.5)
Medication (continuous or occasional)	14 (50)	10 (90.9)
Social handicap	13 (46.6)	4 (36.4)

**Table 12.** Total values from the functional scoring system (Based on Ref. [14])

The incidence of abdominal pain was significantly less common (1.895 vs. 2.769;  $P=0.024$ ) in the laparoscopic group based on the GIQLI.

#### 4.3.6. Complications

No difference was found between the minimally invasive and conventional methods in cases requiring early reoperation (ileus, stoma correction, bleeding and sepsis) and in cases not requiring reoperation (subileus, bleeding, septic condition, pancreatitis and dehydration). There were significantly more late complications (septic condition, intestinal obstruction, postoperative hernia and "other" complications, such as bleeding, anastomotic stenosis, pouch-vaginal fistula, perforation and disruption of the abdominal wall) in patients who had undergone open surgery ( $P=0.001$ ), of whom the incidence of intestinal obstruction and "other" complications were significantly higher ( $P\leq0.001$ ) (**Figure 1**).



**Figure 1.** Late postoperative complications

Among late complications the incidence of intestinal obstruction and "other" complications were significantly higher in patients who had had open surgery than in patients who had undergone laparoscopic surgery.  $*P \leq 0.05$ ,  $***P \leq 0.001$

Pouchitis was detected in 17 cases (35.41% of patients with a pouch). Cuffitis occurred in 13 (27.08%) cases. The personal control ( $3.43 \pm 2.35$  vs.  $5.57 \pm 3.31$ ;  $P = 0.024$ ) was higher in patients with no late complication.

#### 4.3.7. Headache

As a result, 43 (74.1%) patients had headaches, of whom 27 (62.8%) had primary headache and 16 (37.2%) had the secondary (symptomatic) type. Among the primary headaches (n=27), tension-type headache was the most common, occurring in 19 (70.4%) cases, of which 17 (89.5%) patients experienced episodic tension-type headache and 2 (10.5%) suffered from chronic tension-type headache; in addition, 8 (29.6%) patients had migraine. Headache influenced quality of life and daily activities slightly to moderately in 79.1% (n=34) of the patients. No difference was found regarding headaches in the laparoscopic and open surgery groups and between patients with a stoma and those without a stoma. In the case of patients with headache, the BIPQ score was significantly higher ( $P=0.036$ ).

## 5. DISCUSSION

The epidemiological data reveal that the incidence of UC is constantly rising [1]. The treatment of UC is primarily based on medical/biological therapy. A surgical intervention is considered in the event of the failure of the conservative therapy and the emergence of severe complications of the disease. An estimated 25-45% of patients with UC needs surgery at some time [1, 5, 6]. The use of minimally invasive surgical technique gathers ground widely also in Hungary, which can be applied safely during the therapy of IBD [21-23]. First proctocolectomy with pouch was performed by *Parks et al.* in 1978, which became the gold-standard technique during the surgical treatment of UC, while its laparoscopic implementation was first mentioned in the early '90s [8, 10, 24]. Proctocolectomy and IPAA creation are adequate alternatives in the surgical treatment of UC, and are currently the most frequently chosen types of surgery [8, 25-27]. Rather limited experience is available, however, as regards the short and long-term results of the laparoscopic surgical management of UC. Limited data are available on quality of life in patients with UC undergoing surgery.

In our study, the perioperative results on patients with UC were analyzed retrospectively in order to compare the laparoscopic and open surgical techniques, with a short- and long-term follow-up. The preoperative laboratory test results revealed a significant difference between the two groups in WBC count and CRP. The preoperative laboratory data for the patients who participated in emergency surgery indicated an increased inflammatory response. Extraintestinal manifestations were found in 42 cases. A number of studies have demonstrated that smoking has a protective effect against the development and the relapse of UC [1, 28], and the finding was similar with appendectomy as a protective factor [1, 29]. There were no current smokers in our patient population, but a history of smoking was present in 8 cases, and 2 patients had undergone appendectomy previously. There was no difference between the open surgery and laparoscopic groups as concerns the length of the hospital stay, the number of days spent in the ICU, the blood loss, or the time required for the recovery of the bowel function.

The minimally invasive technique has also gained popularity in the treatment of UC and, similarly to the open technique, can be used safely [23]. Its advantages include a shorter hospital stay, less postoperative pain, a shorter time for recovery of the bowel function and a better cosmetic result, but it has the disadvantage of a longer duration of surgery [11]. A considerable number of the studies published to date have reported on the various advantages of the laparoscopic technique. An Australian study found that laparoscopy is associated with a

shorter hospital stay, a faster recovery of the bowel function, and a better cosmetic result; however, the two surgical techniques have the same morbidity rate due to the proctocolectomy [30]. Laparoscopic completion proctectomy and IPAA creation following laparoscopic colectomy were studied by *Gu et al.*, who reported a low blood loss, rapid recovery of the bowel function, and a short hospital stay [31]. A Dutch study on colectomies performed because of non-toxic colitis concluded that the minimally invasive technique is more advantageous in cases involving wound infection and abdominal abscess [32]. *Koh et al.* demonstrated that the laparoscopic technique was safe in emergency surgery for UC, and yielded better results in cases of ileus and wound infection as compared with open surgery [33]. Similarly advantageous results concerning the hospital stay, the need for blood transfusion, the cosmetic result and wound infection were reported from two US studies on emergency laparoscopic subtotal colectomies [34, 35]. Current data available in a large international database confirm better rates of both morbidity and mortality in the minimally invasive patient group [21]. Our own results indicate that, other than the cosmetic results, laparoscopic surgery has no clear advantage in the perioperative period. However, the duration of surgery differed significantly in the two patient groups: the laparoscopic interventions took longer to complete.

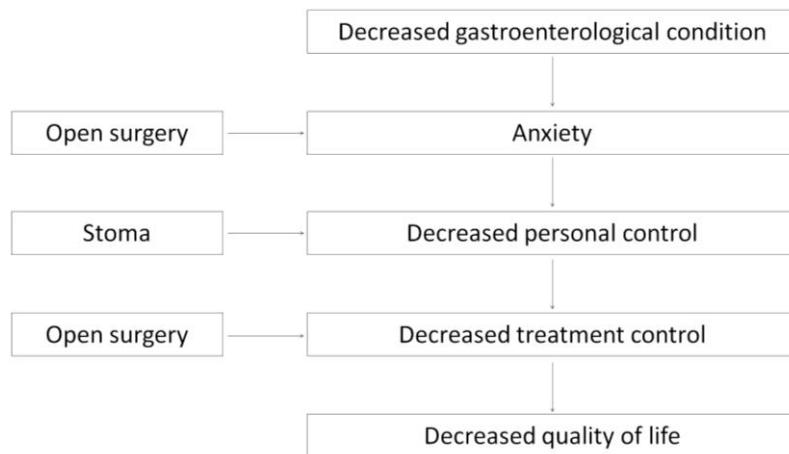
*Fajardo et al.* did not also observe a difference in the rate of morbidity during the short-term follow-up of two-stage laparoscopic and open IPAA surgery [36]. A meta-analysis published in 2010 did not find a difference between the conventional open and the minimally invasive procedure from the aspect of complications such as a lesser pelvic abscess, anastomotic leakage and ileus [37]. Similarly, a recent randomized study likewise confirmed only the cosmetic advantage of the laparoscopic method [38].

Complications were classified as early (within 30 days) or late (after 30 days) with regard to their onset after primary surgery. Our study led to the finding that the minimally invasive method does not have an advantage as concerns the early complications, but it is demonstrably more advantageous in terms of the incidence of late complications. Our study indicated that only 26% of patients who had received infliximab treatment had early postoperative complications and therefore suggests that prior biological therapy is not associated with a higher rate of complications. In several studies, prior biological therapy was considered to have a negative effect on the results of the surgical treatment in UC [39, 40], although this is not supported by other observations [5, 41, 42] or a most recent case-matched study [43]. During the mean follow-up of 47 months, significantly fewer complications,

involving an intestinal obstruction, a septic condition and “other complications” occurred in the laparoscopic group. The obvious explanation for the higher, but not significant rate of hernias in the open surgery group is the more extensive entry opening. The higher rate of ileus and subileus in the open surgery group is probably caused by the higher level of surgical trauma and the adhesions due to the wound surface. *Hull et al.* observed significantly more cases of adhesion after open IPAA surgery, and a similar result was reported by *Indar et al.* [44, 45]. The research by *Bartels et al.* revealed that the incidence of adhesions and postoperative hernias was significantly higher following emergency open colectomies performed because of UC [46].

One of the most common complication in the long term after IPAA surgery performed because of UC is pouchitis [47, 48]. A total of 17 cases of pouchitis were recorded in our study, corresponding to 40% of the patients with a pouch. The exact aetiology of pouchitis is still unknown; no independent risk factor has been recognized. The study by *Kalkan et al.* pointed to the fulminant colitis leading to the surgery and the steroid dependence as the possible causes of pouchitis, whereas *Uchino et al.* were of the opinion that a toxic megacolon and the onset of UC before the age of 26 years may predispose to chronic pouchitis [49, 50]. There was a decreasing tendency of the postoperative mean number of stools daily and an increase in the postoperative body weights in the two patient groups. *Polle et al.* did not detect a difference in the quality of life, the morbidity rate or the functional results following open and laparoscopic proctocolectomies, but confirmed a better cosmetic result among laparoscopic female patients [51]. An Italian study emphasized the importance of the accurate assessment, selection and follow-up of surgical patients with regard to complications, pouchitis, pouch excision, the risk of cancer and the quality of life following IPA surgery [52]. Success of the surgical intervention is determined by quality of life in case of a benign, non-neoplastic disease. In case of UC, abdominal complaints, high number of bowel movements a day, surgical interventions and their consequences are very demanding somatically and psychologically. Social integration of patients, their quality of life and daily routine activities may often be difficult. Regarding disease representation, 92.3% of our patients considered their disease to be caused by psychological factors, 42.3% thought that genetic factors were behind the disease, and 46.2% though that their disease was caused by environmental hazards. In conclusion, patients with UC are well informed, and are aware of the nature and characteristics of their disease. Consequences of wearing a stoma were examined as well, which was significant regarding the “Personal control” subscale of the BIPQ, patients with a

stoma felt less control over their condition. Therefore the presence of an anus praे either temporary or permanent, was psychologically demanding for the patients, it made healing and daily activities more difficult. Besides these results, no difference was found in quality of life of patients living with an ileostoma or a pouch in a prospective cross-sectional observational study [53]. Quality of life was examined regarding laparoscopic surgery and open surgery as well. Examination of psychological differences between the two groups showed that trait anxiety and the average value of “Treatment control” subscale of BIPQ were significantly different, that is patients having open surgery were more anxious and had less faith in the success of the surgical treatment. Based on the total score of gastroenterological questionnaires, there was no difference between the two surgical methods, although perianal and abdominal pain, stress, social and recreational activities were more favorable in the laparoscopic group based on the Functional score system, the SIBDQ and the GIQLI. A German and an Irish study with 10-year follow-up found favorable quality of life after IPAA surgery [54, 55]. Nutritional difficulties, bowel movement problems, as well as daily and night-time incontinence were found in both groups. Incontinence, increased number of bowel movements at night and bowel urgency were found to be negative prognostic factors of quality of life in the literature [56]. Our patients reported >5 stools a day and >1 stool at night weekly in the postoperative period. *Fischera et al.* found high rates of continence and an average of 6 bowel movements a day after laparoscopic IPAA [9]. No difference was found between the two groups regarding early complications; these complications were more common in shorter and thinner patients. Late complications occurred significantly more often in case of emergency and open surgeries. The values of “Personal control” and “Understanding” subscales of BIPQ regarding psychological factors were higher in patients having no late complications, so who felt more control over their disease. Early and late complications correlated with the “Understanding” subscale of BIPQ, so patients having no complication understand their disease more. Logistic regression was used to confirm that the laparoscopic intervention and the “Understanding” subscale of BIPQ were predictive regarding the development of complications, that is the incidence of complications is lower in case of laparoscopic surgeries and in patients understanding their disease better. Significant correlation was found between the results of psychological and gastrointestinal questionnaires, negative emotional condition and mood resulted in lower quality of life, patients were more anxious and depressive, these patients had a negative image of their disease, and had less faith in the success of the surgical interventions (**Figure 2**).



**Figure 2.** Effect of gastroenterological and psychological conditions and surgical technique on quality of life

74.1% of our patients had headaches, 79.1% of these patients had slight to moderate problems with everyday life. Based on the results of BIPQ, headache further worsened the emotional condition of our patients. It should be emphasized that patients having headaches had mainly tension type headaches, stress and psychological tension have primary role in the development of tension headaches [57, 58]. Tension type headache negatively influences quality of life [59].

## 6. CONCLUSION

- i. Our working group was the first to publish short- and long-term results on laparoscopic treatment of UC in Hungary, which proved the success of the method.
- ii. Laparoscopic surgical treatment can be used safely for both emergency and elective cases in UC patients. During the long-term follow-up period, significantly fewer late complications occurred in the laparoscopically operated group of patients.
- iii. Our study is the first to examine quality of life among patients operated with laparoscopy on UC with regard to psychological and gastroenterological conditions. The long-term positive effect of laparoscopic surgery was confirmed regarding quality of life.
- iv. Favourable gastroenterological condition leads to better psychological state and favourable quality of life, which can be negatively influenced by having a stoma, headache or complications.

v. Successful treatment of UC should be performed in centers with close gastroenterological and surgical co-operation.

vi. Psychological guiding is essential. Psychologists, neurologists and social workers may have to be involved in the treatment of these patients.

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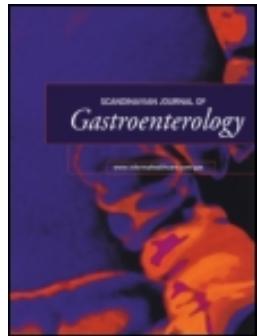
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## Role of laparoscopic surgery in the treatment of ulcerative colitis; short- and mid-term results

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ORIGINAL ARTICLE

## Role of laparoscopic surgery in the treatment of ulcerative colitis; short- and mid-term results

JÁNOS TAJTI JR<sup>1</sup>, ZSOLT SIMONKA<sup>1</sup>, ATTILA PASZT<sup>1</sup>, SZabolcs ÁBRAHÁM<sup>1</sup>, KLAUDIA FARKAS<sup>2</sup>, ZOLTÁN SZEPES<sup>2</sup>, TAMÁS MOLNÁR<sup>2</sup>, FERENC NAGY<sup>2</sup> & GYÖRGY LÁZÁR<sup>1</sup>

<sup>1</sup>Department of Surgery, University of Szeged, Szeged, Hungary, and <sup>2</sup>First Department of Internal Medicine, University of Szeged, Szeged, Hungary

### Abstract

**Objectives.** Laparoscopy is used more widely for the surgery of ulcerative colitis. The objective of this study was a comparison of the surgical and 3-year follow-up results of patients treated with conventional and minimally invasive methods. **Materials and methods.** A total of 45 patients received surgery for ulcerative colitis, 16 as emergency and 29 as elective cases. Laparoscopy was used in 23 and a conventional method in 22 cases. No difference was found between the two groups from the aspects of American Society of Anesthesiologists physical status (ASA) class, mean body mass index (BMI) and age. There were 4 emergency cases in the laparoscopy group, and 12 in the open group. Nineteen elective surgeries were performed in the laparoscopy group, and 10 in the open group. **Results.** There was no significant difference between the groups as concerns the length of hospital or intensive care unit (ICU) stay, the time to bowel function recovery, but the duration of open surgery was significantly shorter. There was no difference between the groups in the rate of early postoperative complications, whereas among potential late complications, the rates of intestinal obstruction (8.7% vs. 45%) and a septic condition (0% vs. 27%) were significantly lower in the laparoscopy group. There was a significant improvement in the quality of life after surgery in both groups, and better cosmetic results were observed in the laparoscopy group. **Conclusion.** Laparoscopy can be used for ulcerative colitis both emergency and elective cases, it provides a good quality of life and the mid-term rate of complications is lower as compared with open surgery.

**Key Words:** ileal pouch-anal anastomosis, laparoscopy, proctocolectomy, ulcerative colitis

### Introduction

The epidemiological data reveal that the incidence of ulcerative colitis (UC) is constantly rising, primarily as a consequence of the spreading of the ‘Western’ lifestyle and urbanization [1]. Its yearly incidence in Europe is  $10/10^5$ , and the Hungarian data are not notably different ( $11.9/10^5$ ) [2,3]. In 2010, the inflammatory bowel disease (IBD) registry of five Hungarian centers included 1390 patients, 539 of whom had UC, but since the estimated prevalence of IBD in Hungary is 25,000, these data relate only to the more severe cases [4].

An estimated 25–45% of patients with UC need surgery at some time [1,5,6]. The purpose of the surgical intervention is to remove the affected bowel segment, which can be achieved with either the conventional, open or the laparoscopic technique. Currently, the generally accepted procedure, which has become the gold standard for the surgical treatment of UC, is total proctocolectomy with the creation of an ileal pouch-anal anastomosis (IPAA) [2,7]. This procedure was first performed with a laparoscopic approach by Peters in 1992 [8]. A number of studies have shown that (although the duration of the procedure is longer) laparoscopic surgery has numerous advantages, such as less postoperative pain, a shorter

Correspondence: György Lázár MD, PhD, DSc, Department of Surgery, University of Szeged, 6720 Szeged, Pf. 427, Hungary. Tel: +3662545701. Fax: +3662545701. E-mail: gylazar@gmail.com

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hospital stay, less time required for recovery of the bowel function, and better cosmetic results. Rather limited experience is available, however, as regard the long-term results of laparoscopic surgery. The objective of this study was a comparison of the surgical and mid-term follow-up results on patients treated for UC with the conventional and the minimally invasive method.

## Patients and methods

Between 1 January 2005 and 31 May 2013, a total of 45 patients (27 women, 18 men) underwent surgery for UC in our institution. Patients who had undergone proctocolectomy and colectomy with the creation of a J-pouch were included in the comparison of minimally invasive surgery and the conventional method, with a mean follow-up of 38 (1–92) months. Sixteen (35.5%) of the surgical interventions were emergency procedures, while 29 (64.5%) were elective interventions. The laparoscopic technique was used in 23 (51.1%) and the conventional method in 22 (48.9%) cases. The mean age of the patients was  $41.29 \pm 14.37$  in the laparoscopy group and  $38.91 \pm 12.58$  years in the open surgery group. No difference was found between the two groups in ASA class ( $2.19 \pm 0.60$  and  $2.14 \pm 0.73$ ,  $p = 0.818$ ) or mean BMI ( $24.03 \pm 5.15$  and  $22.88 \pm 5.74$ ,  $p = 0.490$ ) (Table I). The preoperative laboratory data for the patients who participated in emergency surgery indicated an increased inflammatory response. The hematocrit levels (31.31 vs. 35.31 L/L,  $p = 0.007$ ) and albumin levels (28.93 vs. 39.67 g/L,  $p < 0.001$ ) were significantly lower in the emergency group than in the elective group.

### Surgical technique

Proficient colorectal surgeons operated in both groups. The surgical procedures were performed by three surgeons with about equal rate in the open group, while two surgeons were in the laparoscopic group.

The laparoscopically assisted proctocolectomy + IPAA and the total colectomy + mucous fistula were

Table I. Distribution of Age, American Society of Anesthesiologists physical status (ASA) class and Body Mass Index (BMI) in the laparoscopy and open surgery groups.

	Laparoscopy (n = 23)	Open surgery (n = 22)
Mean age (years)	$41.29 \pm 14.37$	$38.91 \pm 12.58$
Mean ASA	$2.19 \pm 0.60$	$2.14 \pm 0.73$
Mean BMI	$24.03 \pm 5.15$	$22.88 \pm 5.74$

performed with the use of six or seven ports, depending on the auxiliary incision. The resection of the colon and the creation of the anastomosis and the mucous fistula were performed from the cosmetically favorable Pfannenstiel incision. The J-pouch was created from the terminal ileum with a straight stapler(s), and a double stapler technique was used for the ileoanal anastomosis. The staple line was protected with a loop ileostomy in every case. The pouch created as the second surgical step was also achieved from the Pfannenstiel incision. In the cases involving the conventional method, a midline laparotomy was performed to explore the abdominal cavity, in the lower recess of which the mucous fistula was created; the pouch and the ileoanal anastomosis were created in the same way as during the laparoscopic interventions.

Total proctocolectomy with the creation of a J-pouch and protective loop ileostomy was carried out laparoscopically in 13 cases and with the open technique in 5 cases. The first step was total colectomy with mucous fistula and end ileostomy using the minimally invasive technique in 8 cases and the conventional method in 13 cases.

Conversion from laparoscopy to open surgery was required in 3 cases (3/26, 11.53%), because of massive adhesions during elective surgery (1 case) or because of the risk of bowel injury and perforation during emergency surgery (2 cases). These cases were excluded from the subsequent analyses.

The distribution of the various surgical procedure is presented in Table II.

The events following the primary surgery were analyzed in two stages: within 30 days (the early period), and after 30 days (the late period). The length of hospitalization, the number of days in the ICU, the time required for recovery of the bowel

Table II. Distribution of surgery.

		Laparoscopy (n = 23)	Open surgery (n = 22)
Two-stage surgery	Proctocolectomy, J-pouch, ileostomy	13 (56.5%)	5 (23%)
	Ileostomy closure	11	4
Three-stage surgery	Total colectomy, mucous fistula, end ileostomy	8 (34.8%)	13 (59%)
	J-pouch creation, ileostomy	6	12
One-stage surgery	Ileostomy closure	5	11
	Rectum extirpation	2 (8.7%)	0
	Proctocolectomy, end ileostomy	0	2 (9%)
	Colectomy, ileorectostomy	0	1 (4.5%)
	Total colectomy, ileostomy	0	1 (4.5%)

function and the need for transfusion were recorded. The incidence of complications that could be treated with conservative therapy and those that necessitated surgical intervention, such as ileus, abscess, anal bleeding, fistula, anastomotic stenosis or postoperative hernia, and the rate of mortality were assessed. The patients were monitored for the development of pouchitis and cuffitis, the diagnosis of which was confirmed (besides the clinical symptoms) by endoscopy in every case. The change in the quality of life (the general condition, the body weight and the number of stools daily) and the cosmetic result after the surgical interventions were also assessed. The preoperative and current quality of life of the patients were graded on a scale from 1 to 10, where 1 was the best and 10 was the worst quality of life. The cosmetic result was assessed with consideration of the length of the surgical incision on a satisfaction scale ranging from 1 to 5.

### Statistics

The patient population was assessed retrospectively, and the statistical data were processed, and the two-sample t-test, the chi-squared test and the Mann-Whitney test were performed with the SPSS software (IBM SPSS Statistics, Version 20, 2011, Armonk NY, USA).

## Results

### Preoperative results

There was no significant difference in the time (years) from the onset of UC to surgery between the laparoscopic group ( $8.71 \pm 5.28$ ) and the open surgery group ( $8.63 \pm 9.85$ ). In the preoperative period, 16 patients (35.55%) received biological therapy, with infliximab. The preoperative laboratory test results (white blood cell count, C-reactive protein, hemoglobin, hematocrit and albumin) revealed a significant difference between the two groups only in C-reactive protein (Table III). Before the surgical interventions, the mean number of stools daily was  $10.78 \pm$

Table III. Mean preoperative laboratory data in the laparoscopy and open surgery groups.

	WBC (G/L)	CRP (mg/L)	Hgb (g/L)	Htc (L/L)	Albumin (g/L)
Laparoscopy	8.33	16.79	105.43	33.81	37.79
Open surgery	9.06	47.66	109.13	33.96	33.01
	$p = 0.529$	$p = 0.028$	$p = 0.471$	$p = 0.920$	$p = 0.108$

WBC: White Blood Cell; CRP: C-Reactive Protein;  
Hgb: Hemoglobin; Htc: Hematocrit

Table IV. Distribution of duration of surgery (minutes).

	Laparoscopy	Open surgery	
Proctocolectomy, J-pouch, ileostomy	$245.42 \pm 51.28$	$185 \pm 17.80$	$p = 0.040$
Total colectomy, mucous fistula, end ileostomy	$187 \pm 32.39$	$151.67 \pm 23.58$	$p = 0.012$

5.80 and  $9.64 \pm 5.38$ , respectively, in the two groups. The last colonoscopy report before surgery indicated 30 cases (66.67%) of pancolitis, 5 cases (11.11%) of left-sided involvement and 10 cases (22.22%) of distal involvement.

From the aspect of the duration of surgery, the open method was found to be significantly shorter than the laparoscopic intervention in both the emergency and the elective cases (Table IV).

### Postoperative results

There was no significant difference between the groups in the length of hospital stay, the time to the recovery of the bowel function, the number of days spent in the ICU, or the need for transfusion (Table V). There was no death in the perioperative period in either group.

Complications were classified as early (within 30 days) or late (after 30 days) with regard to their onset after primary surgery. There was no difference ( $p = 0.945$ ) between the laparoscopy group and the open surgery group in the rate of severe complications that required reoperation. In the laparoscopy group, two patients needed reoperation in the early period because of ileus, an abdominal wall disruption in the area of the mucous fistula that required immediate surgery in one case, and stoma repair was required in one case. In the early period after open surgery, exploration was performed in one patient because of a septic condition, and reoperation was required because of ileus in three cases. Complications

Table V. Immediate postoperative results in the laparoscopy and open surgery groups.

	Laparoscopy (n = 23)	Open surgery (n = 22)	
Hospital stay (days)	$11.50 \pm 3.85$	$11.63 \pm 3.79$	$p = 0.914$
Time to recovery of bowel function (days)	$1.44 \pm 0.81$	$1.55 \pm 0.69$	$p = 0.656$
Time spent in the ICU (days)	$2.50 \pm 1$	$2.09 \pm 0.83$	$p = 0.437$
Need for blood transfusion (units)	$2.05 \pm 1.77$	$3.13 \pm 1.90$	$p = 0.57$

Table VI. Early postoperative complications (within 30 days).

	Laparoscopy (n = 23)	Open surgery (n = 22)	
<b>Requiring reoperation</b>			
Ileus (2)		Ileus (3)	
Abdominal wall disruption (1)		Septic condition (1)	
Stoma repair (1)			
Total	17.4% (4/23)	18% (4/22)	p = 0.945
<b>Not requiring reoperation</b>	Subileus (3)	Subileus (1)	
		Anal bleeding (1)	
		Dehydration (1)	
		Hydrothorax (1)	
		Urination problems (1)	
Total	13% (2/23)	22% (5/22)	p = 0.396

necessitating reoperation and other complications are listed in Table VI.

During the follow-up period, wound infection was detected in eight patients (34.8% of the cases) in the laparoscopy group, and in seven patients (31.8% of the cases) in the open surgery group; from this respect, there was no significant difference between the groups ( $p = 0.833$ ). Methicillin-resistant staphylococcus aureus infection was confirmed in two patients and one patient, respectively.

During the mean follow-up of 36 months, significantly fewer complications, involving an intestinal obstruction ( $p = 0.005$ ), a septic condition ( $p = 0.007$ ), an anastomotic stenosis, anal bleeding and pouch-vaginal fistula formation ( $p = 0.001$ ), occurred in the laparoscopy group. The rate of development of postoperative hernias was also lower in the laparoscopy group (8.7% vs. 18%), but this difference was not significant statistically ( $p = 0.349$ ) (Table VII).

In the laparoscopy group, surgery was performed because of ileus in one case, and one case of subileus resolved after medical therapy. Abdominal wall reconstruction was carried out electively in two cases because of a hernia in the scar of the previous

ileostomy. Endoscopic dilatation was performed in one case of anastomotic stenosis.

In the conventional surgery group, surgery was performed because of ileus as a late complication in four cases. Four perianal abscesses were explored, three of which were treated by Seton drainage. Perianal exploration was needed in one case because of an abscess in the lesser pelvis. In one patient, excision of the pouch was required because of severe pouchitis and a perianal abscess. Rectum extirpation was necessary in two patients because of an impaired sphincter function and anal bleeding. The abdominal wall was reconstructed in four cases because of a postoperative hernia. Two anastomotic stenoses were dilated surgically, while endoscopic dilatation was performed in three patients. Six cases of subileus, one case of anal bleeding and one case of dehydration were resolved through conservative treatment. Two cases of pouch-vaginal fistula were observed. During the follow-up, two patients died, as a result of an oral cavity tumor or a cardiorespiratory insufficiency; the causes of death were not related to the UC.

Of the 16 patients treated with infliximab, 4 developed an early postoperative complication.

Table VII. Late postoperative complications (after 30 days).

	Laparoscopy (n = 23)	Open surgery (n = 22)	
<b>Septic condition</b>	0	Severe pouchitis (1) → pouch excision Perianal abscess (4) Lesser pelvic abscess (1)	
Total	0% (0/23)	27% (6/22)	p = 0.007
<b>Intestinal obstruction</b>			
Requiring surgical intervention	Ileus (1)	Ileus (4)	
Not requiring surgical intervention	Subileus (1)	Subileus (6)	
Total	8.7% (2/23)	45% (10/22)	p = 0.005
<b>Postoperative hernia</b>	In the ileostomy scar (2)	In the midline laparotomy scar (4)	
Total	8.7% (2/23)	18% (4/22)	p = 0.349
Other	Anastomotic stenosis (1)	Anastomotic stenosis (5) Anal bleeding (2) → rectum extirpation (1) Severe sphincter damage (1) → rectum extirpation Pouch-vaginal fistula (2) Dehydration (1)	
Total	4.3% (1/23)	50% (11/22)	p = 0.001

During the course of the follow-up, there were significantly fewer urgent admissions to a medical unit in the laparoscopy group (1 vs. 6,  $p = 0.034$ ).

The clinical symptoms and endoscopic findings confirmed 15 cases of pouchitis, affecting 41% of the patients with a pouch (6 in the laparoscopic group and 9 in the open surgery group). The inflammation of the pouch was accompanied by cuffitis in 10 cases.

A significant improvement in the quality of life was measured in both groups after the surgery, but there was no significant difference between the two groups.

The postoperative mean number of stools daily at the last medical check-up during the follow-up was  $7.83 \pm 3.28$  and  $7.81 \pm 3.31$  in the two patient groups. There was therefore a decreasing tendency relative to the preoperative results, which proved to be significant in the laparoscopy group. The preoperative and current body weights indicated an increase in both groups (laparoscopy group:  $67.61 \pm 16.19$  kg and  $70.83 \pm 18.31$  kg, open surgery group:  $63.24 \pm 16.15$  kg and  $73.68 \pm 12.73$  kg), which was significant in the open surgery patient population (Table VIII).

The mean length of the midline laparotomy incision in the open surgery group was  $13.9 \pm 7$  cm, and the mean length of the Pfannenstiel incision in the laparoscopy group was  $10.5 \pm 3.5$  cm. From the aspect of the cosmetic result, the patients graded their satisfaction on a five-item scale (not at all satisfied – slightly satisfied – moderately satisfied – rather satisfied – very satisfied), which demonstrated that those who had undergone open surgery were on average ‘rather satisfied’, while the laparoscopic patients were on average ‘very satisfied’.

## Discussion

This study has confirmed that laparoscopic surgical treatment can be used safely for both emergency and elective cases in UC patients. There was no difference between the open surgery and laparoscopy groups as concerns the length of the hospital stay, the number of days spent in the ICU, the blood loss, the time required for the recovery of the bowel function and the number of perioperative complications, but the

duration of laparoscopic surgery proved to be significantly longer. The quality of life of the patients improved significantly in both groups. As differences, the rates of intestinal obstruction, septic and other complications, and medical re-hospitalization were significantly higher among the patients who had undergone open surgery, and the laparoscopic patients on average reported a higher level of satisfaction with the cosmetic result.

The treatment of UC is primarily based on medical/biological therapy. A surgical intervention is considered in the event of the failure of the conservative therapy and the emergence of severe complications of the disease. Proctocolectomy and IPAA creation are adequate alternatives in the surgical treatment of UC, and are currently the most frequently chosen types of surgery [2,9].

The minimally invasive technique has also gained popularity in the treatment of UC and, similarly to the open technique, can be used safely [10]. Its advantages include a shorter hospital stay, less postoperative pain, a shorter time for recovery of the bowel function and a better cosmetic result, but it has the disadvantage of a longer duration of surgery [11]. The current data available in a large international database confirm better rates of both morbidity and mortality in the minimally invasive patient group [12].

Our own results indicate that, other than the cosmetic results, laparoscopic surgery has no clear advantage in the perioperative period. However, the duration of surgery differed significantly in the two patient groups: the laparoscopic interventions took longer to complete. There was no measurable difference in the length of hospital stay, the time until the recovery of the bowel function, the number of days spent in the ICU, the postoperative need for blood transfusion or the wound healing problems. Similarly, Fajardo et al. did not observe a difference in the rate of morbidity during the short-term follow-up of two-stage laparoscopic and open IPAA surgery [13]. A meta-analysis published in 2010 did not find a difference between the conventional open and the minimally invasive procedure from the aspect of complications such as a lesser pelvic abscess,

Table VIII. Pre- and postoperative quality of life, number of stools daily and body weight in the laparoscopy and open surgery groups.

		Preoperative	Current	
Quality of life	Laparoscopy ( $n = 23$ )	$8.88 \pm 1.5$	$2.38 \pm 2.03$	$p < 0.0001$
	Open surgery ( $n = 22$ )	$8.8 \pm 1.74$	$2.6 \pm 2.03$	$p = 0.001$
Number of stools daily	Laparoscopy ( $n = 23$ )	$10.78 \pm 5.80$	$7.83 \pm 3.28$	$p = 0.061$
	Open surgery ( $n = 22$ )	$9.64 \pm 5.38$	$7.81 \pm 3.31$	$p = 0.238$
Body weight	Laparoscopy ( $n = 23$ )	$67.61 \pm 16.19$	$70.83 \pm 18.31$	$p = 0.554$
	Open surgery ( $n = 22$ )	$63.24 \pm 16.15$	$73.68 \pm 12.73$	$p = 0.030$

anastomotic leakage and ileus [14]. Similarly, a recent randomized study likewise confirmed only the cosmetic advantage of the laparoscopic method [15].

Our study led to the finding that the minimally invasive method does not have an advantage as concerns the early complications, but it is demonstrably more advantageous in terms of the incidence of late complications. The rate of medical re-hospitalization was significantly lower in the laparoscopy group (4.34% vs. 27%). Similarly, the rates of intestinal obstruction (8.7% vs. 45%), septic condition (0% vs. 27%) and other complications (4.3% vs. 50%) were also significantly lower in the group of patients who had undergone laparoscopic surgery.

The obvious explanation for the higher rate of hernias in the open surgery group (8.7% vs. 18%) is the more extensive entry opening. The higher rate of ileus and subileus in the open surgery group is probably caused by the higher level of surgical trauma and the adhesions due to the wound surface. Hull et al. observed significantly more cases of adhesion after open IPAA surgery, and a similar result was reported by Indar et al. [16,17]. The research by Bartels et al. revealed that the incidence of adhesions and postoperative hernias was significantly higher following emergency open colectomies performed because of UC [18]. In a US study, however, the incidence of small bowel obstruction after IPAA was not different when the laparoscopic technique was employed [19].

In several studies, prior biological therapy was considered to have a negative effect on the results of the surgical treatment in UC [20,21], although this is not supported by other observations [22–24] or the most recent case-matched study [25]. Our study indicated only four cases of an early postoperative complication among the 16 patients who had received infliximab treatment and therefore suggests that prior biological therapy is not associated with a higher rate of complications.

The most common complication in the long term after IPAA surgery performed because of UC is pouchitis. A total of 15 cases of pouchitis were recorded in our study, corresponding to 41% of the patients with a pouch; there was no difference between the groups. A Swedish study found chronic pouchitis to be the main functional issue during a long-term follow-up after IPAA surgery [26]. The exact etiology of pouchitis is still unknown; no independent risk factor has been recognized. The study by Kalkan et al. pointed to the fulminant colitis leading to the surgery and the steroid dependence as the possible causes of pouchitis, whereas Uchino et al. were of the opinion that a toxic megacolon and the onset of UC before the age of 26 years may predispose to chronic pouchitis [27,28].

In the course of the follow-up, significant improvements were noted in the number of stools daily, the body weight and the quality of life, whereas Fichera et al. did not find a difference between laparoscopy and open IPAA surgery from the aspect of the number of stools daily postoperatively and a similar result was reported from an English study [7,29]. Likewise, Polle et al. did not detect a difference in the quality of life, the morbidity rate or the functional results following open and laparoscopic proctocolectomies, but confirmed a better cosmetic result among laparoscopic female patients [30]. Many publications have reported a better postoperative quality of life following IPAA surgery [31–37].

Our study clearly demonstrates that minimally invasive procedures can be used safely for the surgical treatment of UC in both emergency and elective cases, and these are cosmetically advantageous procedures that are expected to result in a considerably improved quality of life.

Moreover, it is important to emphasize that lower rates of postoperative hernia and ileus are to be expected in the long term after laparoscopic surgery.

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**II.**



# Colitis ulcerosa minimálisan invazív sebészi kezelése – hosszú távú eredmények

Tajti János jr. dr.<sup>1</sup> ■ Simonka Zsolt dr.<sup>1</sup> ■ Paszt Attila dr.<sup>1</sup>  
Ábrahám Szabolcs dr.<sup>1</sup> ■ Farkas Klaudia dr.<sup>2</sup> ■ Szepes Zoltán dr.<sup>2</sup>  
Molnár Tamás dr.<sup>2</sup> ■ Nagy Ferenc dr.<sup>2</sup> ■ Lázár György dr.<sup>1\*</sup>

Szegedi Tudományegyetem, Általános Orvostudományi Kar, <sup>1</sup>Sebészeti Klinika,  
<sup>2</sup>I. Belgyógyászati Klinika, Szeged

**Bevezetés:** A colitis ulcerosa sebészi kezelésében egyre szélesebb körben alkalmazzák a laparoszkópos technikát, azonban hosszú távú magyarországi eredményekkel eddig még nem rendelkeztünk. **Célkitűzés:** A szerzők célja a hagyományos és a minimálisan invazív módszerrel operált betegek műtéti és 47,8 hónapos utánkövetési eredményeinek összehasonlítása. **Módszer:** 2005. január 1. és 2014. december 31. között összesen 56 beteg került műtétre colitis ulcerosa diagnózissal, aikik közül 20-at súrgósséggel, 36-ot tervezetten műtöttek. Laparoszkópos technikával 33, nyitottan 23 műtéttet végeztek. **Eredmények:** A perioperatív időszakban az ápolási idő, passzázsmegindulás, az intensív osztályos és transzfúziós igény és szövődmények terén a csoportok között különbséget nem észleltek. Hosszú távú szövődmények tekintetében az intestinalis obstrukció, a szepikus állapot és az egyéb komplikációk előfordulása szignifikánsan alacsonyabb volt a laparoszkópos műtéten átesett betegek csoportjában. Mindkét csoport életminőségen belül szignifikáns javulást tapasztaltak a műtéttel követően. **Következtetések:** A colitis ulcerosa kezelésében a laparoszkópos módszer biztonságosan alkalmazható, amely jó életminőséget, kedvezőbb kozmetikai eredményt biztosít és hosszú távon alacsonyabb a szövődmények aránya a nyitott műtétekkel összehasonlítva. Orv. Hetil., 2015, 156(39), 1585–1592.

**Kulcsszavak:** colitis ulcerosa, laparoszkópia, ileoanalis anastomosis, J-pouch

## Minimally invasive surgical treatment of ulcerative colitis – long-term results

**Introduction:** For the surgical treatment of ulcerative colitis, laparoscopy is used more widely, but less data are available on long-term results in Hungary. **Aim:** The aim of the authors was to compare the mean 47.8-month follow-up results of patients treated with conventional and minimally invasive surgical methods. **Method:** Between January 1, 2005 and December 31, 2014, 56 patients were treated with surgery (20 emergencies, and 36 elective cases). Laparoscopy was used in 33 and conventional method in 23 cases. **Results:** There was no difference between the two groups in hospital and intensive care unit stay, bowel function recovery, need for transfusion, and complications during the perioperative period. Regarding long-term complications, the occurrence of intestinal obstruction, septic condition and other complications were significantly fewer in the laparoscopy group. The quality of life improved in both groups after the surgery. **Conclusions:** Laparoscopy can be used safely; it provides good quality of life and better cosmetic results, and the long-term rate of complications is lower as compared to open surgery.

**Keywords:** ulcerative colitis, laparoscopy, ileo-pouch anal anastomosis, J-pouch

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## Rövidítések

ASA = American Society of Anaesthesiologists; BMI = testtőmegindex; CRP = C-reaktív protein; CU = colitis ulcerosa; FVS = fehérversejt; Hgb = hemoglobin; Htk = hematokrit; IBD = (inflammatory bowel disease) gyulladásos bélbetegség; IPAA = ileopouch-analisis anastomosis

A minimálisan invazív sebészeti beavatkozás napjainkban egyre nagyobb teret nyer, amely módszer a vastagbélsebészettelben, így a gyulladásos bélbetegségek (inflammatory bowel disease – IBD) kezelésében is megjelent. Az első laparoszkópos vastagbélműtét Moise Jacobs nevéhez fűződik, aki 1990-ben jobb oldali hemicolektomiát végzett minimálisan invazív módon [1]. Epidemiológiai adatok szerint a colitis ulcerosában (CU) szenvendő betegek száma emelkedik, aminek hátterében genetikai és számos környezeti hatást igazoltak. Hazánkban Miheller és mtsai az IBD gyakoriságát 2010-ben 25 000-re becsülték [2]. A széles spektrumú gyógyszeres, valamint biológiai terápiának köszönhetően a CU konzervatív kezeléssel sokáig egyensúlyban tartható, azonban az erre nem reagáló, gyakori relapsusokkal járó, illetve szövődményes esetekben sebészeti beavatkozás válik szükségeséssé, amelynek célja a „célszerv”, a vastagbél eltávolítása. Napjainkban totális proctocolectomia, ileoanalis anastomossal történő J-pouch (IPAA) kialakítása a leginkább elfogadott eljárás, amelynek laparoszkópos kivitelezéséről elsőként Peters munkacsoportja számolt be a kilencvenes évek elején [3, 4].

Az eddigi adatok igazolták, hogy a CU sebészetében a hagyományos műtéti technikával szemben a minimálisan invazív módszer előnye a rövidebb ápolási idő, a kisebb posztoperatív fájdalom, a gyors passzázsrendeződés és a kedvező kozmetikai eredmény a hosszabb műtéti idővel szemben [5].

A CU minimálisan invazív kezelését illetőn magyarországi utánkövetési adatokkal limitált számban rendelkezünk. Vizsgálatunk célja a nyitott és a laparoszkópos módszerrel operált betegek perioperatív és hosszú távú eredményeinek összehasonlítása.

## Módszer és sebészi technika

2005. január 1. és 2014. december 31. között összesen 56 betagnél (31 nő, 25 férfi) végeztünk műtéttet CU diagnózisával. Vizsgálatunkba a klinikailag, radiológiaiag, endoszkóppal és szövettanilag igazolt CU-ban szenvendő betegek kerültek. Az irradiáció okozta vastagbélgyulladás, az álhártyás colitis, a CU talaján kialakult tumoros propagáció esetetől, valamint a laparoszkópos kezdést követő konvertált beavatkozásoktól (3/36, 8,33%, adhéziók és bélserülés veszélye) eltekintettünk.

A primer műtétek utáni időszakot 30 napon belüli, korai és 30 napon túli, késői időszakra bontva elemzettük. Regisztráltuk az ápolási időt, intenzív osztályon töltött napok számát, a passzázsmeindulást és transzfúziós

igényt. Vizsgáltuk a konzervatív terápiával kezelhető és a műtéti beavatkozást igénylő szövődményeket, komplikációkat, mint például ileus, tányog, per anum vérzés, fistula, anastomosisszükület, posztoperatív sérv és mortalitás előfordulását. Kerestük a pouchitis és cuffitis megjelenését, amelyek diagnózisát minden esetben a klinikai tünetek mellett endoszkópos kontroll is igazolta. Vizsgáltuk a műtéti beavatkozásokat követő életminőségbeli változást (általános állapot, testsúly, napi székletszám). A betegek műtét előtti és jelenlegi életminőségének vizsgálatait 1–10-ig terjedő skála alapján hasonlítottuk össze.

A betegek adatainak vizsgálatát retrospektív módszerrel, a statisztika feldolgozását, kétmintás t-próbát,  $\chi^2$ -próbát és Mann–Whitney-tesztet végeztünk SPSS programmal (IBM SPSS Statistics, Version 22, 2014, Chicago, IL, Amerikai Egyesült Államok).

Laparoszkóposan asszisztált műtétekhez 6–7 portot használtunk, míg a vastagbél részekcóját Pfannenstielmetszésből végeztük. A J-pouch kialakításához, a körülbelül 15 cm hosszúságú terminális ileumból, egyenes vágó-varrón gépet, az ileoanalis anastomosis elkészítéséhez kettősstapler-technikát alkalmaztunk. A varratos sort kacsileostomával tehermentesítettük. Hagyományos módszer esetén median laparotomiából exploráltuk a hasüreget.

## Eredmények

Utánkövetésünk átlagosan 47,8 (3–111) hónapig tartott. Az 56 eset közül laparoszkópos technikával 33 (58,9%), hagyományos módszerrel 23 (41,1%) műtét történt, az indikációt tekintve 20 (35,7%) sürgősséggel, míg 36 (64,3%) tervezett úton.

Az akut műtéti beavatkozásokat terápiarefrakter, septicotoxicus állapot miatt végeztük, amelyhez 4 esetben vérzés, 1-1 esetben perforáció, illetve ileus és 2 betagnél súlyos malnutripció is társult. Az elektív beavatkozásokat konzervatív kezeléssel egyensúlyban nem tartható állapot miatt végeztük.

## Perioperatív eredmények

A betegek átlagéletkora a laparoszkópos és a nyitott csoportban  $45,09 \pm 14,49$ , illetve  $38,26 \pm 12,68$  év volt. A két csoportban a testtömegindexet (BMI) ( $22,76 \pm 4,68$  és  $22,59 \pm 5,94$ ) és az American Society of Anaesthesiologists (ASA)-beosztást ( $2,27 \pm 0,57$  és  $2,05 \pm 0,68$ ) illetően különbséget nem találtunk, a betegség diagnosztizálásától a műtéti beavatkozásig átlagosan  $9,05 \pm 7,86$  és  $8,26 \pm 9,93$  év telt el. Áttekintve az extraintestinalis manifestációkat, 5 (8,9%) esetben találtunk szem-, 7 (12,5%) betagnél bőrérintettséget, 18 (32,14%) beteg szenvedett csont- és ízületi fájdalomtól. 3 (5,3%) betagnél merült fel primer szklerotizáló cholangitis lehetősége, 7 (12,5%) esetben zajlott korábban mélyvénás trombózis és 2 betagnél volt tüdőt érintő gümőkór (3,57%), míg az anamnézisekben 2 (3,57%) tumoros megbetegedés (vese- és

szájüregi érintettség) is szerepelt. Betegeink között nem ismert aktív dohányzó, csupán 8 esetben igazolódott korábbi dohányzás, valamint 2 esetben szerepelt appendectomy a körtörténetben. Preoperatív laboreredményeket (fehérvérsejt, C-reaktív protein, hemoglobin, hematokrit, albumin) áttekintve a nyitott csoportban a gyulladásos markerek értéke szignifikánsan magasabbnak bizonyult. Utóbbi eredmény a fokozott szeptikus állapotot járó akut műtétek magasabb arányával magyarázható a hagyományos módszerrel operált betegcsoporthoz (56,52% vs. 21,21%). A műtét előtti időszakban 23 (41,07%) beteg részesült biológiai, infliximabterápiában. A betegek perioperatív eredményeit az *1. táblázat* foglalja össze.

**1. táblázat** Perioperatív eredmények és műtét előtti laboratóriumi vizsgálatok

	Laparoszkópos (n = 33)	Nyitott (n = 23)	
Életkor (év)	45,09±14,49	38,26±12,68	p = 0,074
ASA-beosztás	2,27±0,57	2,05±0,68	p = 0,125
BMI	22,76±4,68	22,59±5,94	p = 0,906
Ápolási idő (nap)	10,75±3,61	11,39±3,78	p = 0,528
Passzázsmegindulás (nap)	1,32±0,66	1,63±0,68	p = 0,129
Intenzív osztályon töltött idő (nap)	2,4±0,89	2,10±0,87	p = 0,545
Vérigény (egység)	2,18±2,0	2,73±1,7	p = 0,283
FVS (G/l)	8,5±3,11	10,42±3,36	p = 0,032
CRP (mg/l)	23,29±36,18	51,51±57,62	p = 0,031
Albumin (g/l)	37,8±7,66	33,46±7,61	p = 0,096
Hgb (g/l)	109,72±19,48	109,52±18,94	p = 0,969
Htk (l/l)	34,27±5	33,95±5,8	p = 0,828

ASA = American Society of Anaesthesiologists; BMI = testtömegindex; FVS = fehérvérsejt; CRP = C-reaktív protein; Hgb = hemoglobin; Htk = hematokrit.

Totális proctocolectomiát végeztünk J-pouch kialakításával és protektív loop ileostomával laparoszkóposan 21, nyitott technikával 5 esetben. A műtéti időtartam 221±51,49, illetve 185±17,79 perc volt. Utánkövetésünk során az ileostoma 17, illetve 5 esetben került zárára, viselése a két csoportban átlagosan 3,8 és 4,4 hónapig tartott.

Első lépcsőként totális colectomiát készítettünk nyákfistulával és végileostomával minimálisan invazív módon 9, hagyományos módszerrel 14 esetben, a beavatkozások 186,88±30,11, valamint 151,54±22,58 perc hosszúságúak voltak, amely utóbbi adat szignifikáns (p = 0,006) rövidebbnek bizonyult. Átlagosan 5,00±1,67 és 5,15±3,02 hónap elteltével végeztük el másodülésben a pouchműtéteket, amelyek száma 6, illetve 13 volt. Utolsó lépésként az ileostomát 6, illetve 12 esetben zártuk,

a primer beavatkozástól számolva 7,83 és 9,25 hónapot követően.

A laparoszkópos csoportban a Crohn-betegségre utaló szövettani lelet miatt 2 esetben a nyákfistulát ileorectostomiává alakítottuk. Laparoszkópos technikával 3 rectumexstirpatót, hagyományos módszerrel 1 colectomiát ileorectalalis anastomosissal, 2 totális proctocolectomiát végileostomával és 1 totális colectomiát végeztünk ileostomával. A műtéti típusok eloszlását a *2. táblázat* foglaltuk össze.

**2. táblázat** Műtéti típusok és műtéti időtartamok

	Laparoszkópos (n = 33)	Nyitott (n = 23)	
Kétszakaszos műtétek	Proctocolectomia, J-pouch ileostoma Műtéti idő (perc) p = 0,187	21 (63,6%) 9 (27,2%) 186,88±30,11 p = 0,006	5 (21,7%) 14 (60,8%) 185±17,79
Háromszakaszos műtétek	Totális colectomia, nyákfistula, végileostoma Műtéti idő (perc)	151,54±22,58	
Egyéb műtétek	Rectumexstirpatio Proctocolectomia, végileostoma Colectomia, ileorectostoma Totális colectomia, ileostoma	3 (9%) 0 0 0	0 2 (8,6%) 1 (4,3%) 1 (4,3%)

A két beteganyag ápolási idejében, intenzív osztályon eltöltött napok számában, transzfúziós igényében, valamint az első széklet megjelenéséig eltelt időben mérhető különbséget nem találtunk (*1. táblázat*).

A kórszövettani feldolgozás az esetek nagy részében (39) súlyos gyulladást véleményezett. Aktív volt a folyamat 8 esetben, idült gyulladás jelei 4 mintában látszottak. Két betegnél felszínes gyulladást és 1 inaktív formát írtak le, valamint 2 esetben a teljes colonot érintő Crohn-betegséget is diagnosztizáltak. Az utóbbi két betegnél primer műtétként laparoszkópos totális colectomiát végeztünk nyákfistulával, majd – tekintettel a patológiai leletre – a tápcsatorna folytonosságát ileorectostomiával állítottuk helyre.

## Szövődmények

A primer műtétekhez képest korai (30 napon belüli) és késői (30 napon túli) csoportra osztva vizsgáltuk a szövődmények, komplikációk megjelenését. A korai időszakban megjelenő szövődményeket reoperációtól

függően két csoportba osztottuk. A laparoszkópos beavatkozásokat követően 5 esetben kényszerültünk ismétlő műtétre: 2 esetben ileus miatti adhaesiolytic, 2 betegnél ileostoma korrekciója és 1 esetben a nyákfistula mentén megjelenő hasfali szétválás miatt történt resutura. Konzervatív kezeléssel 3 betegnek sikerült rendezni subileusos állapotát, alhasi tányog miatt 1 esetben történt ultrahangvezérelt intervenciós drenálás, valamint 1 vérzéssel járó súlyos pouchitis oldódott meg lokális kezelésre. A hagyományos módon operált csoportban a korai időszakban szeptikus állapot miatt 1 betegnél végeztünk exploratiót, 3 esetben történt reoperáció ileus miatt. Míg egyéb, hydrothorax, per anum vérzés, subileus, exsiccosis és vizesi panaszok kapcsán nem műtéti kezelés volt sikeres. A 23., korábban infliximabterápiában részesült beteg közül 6 esetében alakult ki korai szövődmény. A korai időszakban reoperációt igénylő és az egyéb szövődmények terén nem volt statisztikai különbség a két csoportban, ezek eredményeit a 3. táblázat foglalja össze.

**3. táblázat** | Korai posztoperatív szövődmények

	Laparoszkópos (n = 33)	Nyitott (n = 23)	
Reoperációt igénylő	– Ileus (2) – Hasfali dysruptio (1) – Stomakorrekció (2)	– Ileus (3) – Szeptikus állapot (1)	
Összesen	15,1% (5/33)	17,4% (4/23)	p = 0,822
Reoperációt nem igénylő	– Subileus (3) – Alhasi tányog (1) – Pouchitis (1)	– Subileus (1) – Per anum vérzés (1) – Exsiccosis (1) – Hydrothorax (1) – Vizesi panaszok (1)	
Összesen	15,1% (5/33)	21,7% (5/23)	p = 0,527

A késői időszakot áttekintve a laparoszkópos betegcsoportnál szignifikánsan kevesebb szeptikus szövődményt, intestinalis obstrukciót és egyéb szövődményeket észleltünk, amelyeket a 4. táblázatban foglaltunk össze. A minimálisan invazív csoportban szeptikus állapot miatt 3 betegnél történt tányog miatt intervenciós, illetve műtéti beavatkozás. Ileus miatt 1 esetben végeztünk exploratiót, míg 7 subileus oldódott meg gyógyszeres kezelésre. 3 betegnél észleltünk posztoperatív sérvet az ileostoma hegében. 1 esetben akut hasi körkép, az ileum vascularis károsodása miatt végeztünk műtéttet. 1 anastomosisszüklet endoszkópos tágítása történt.

A nyitott módszerrel operált csoportban súlyos pouchitis miatt 1 betegnél a pouch kiirtására kényszerültünk, perianalis tányog kapcsán 9 Seton-drenálást és kismedeneci tányog miatt 1 feltárást végeztünk. Bélelzárodás, hasi panaszok miatt 5 műtét és 9 obszerváció történt. Median laparotomia hegében lévő sérvék miatt 4 hasfali re-

konstrukciót végeztünk. Rectumexstiratio 2 betegnél történt a súlyos zároizom-károsodás és a konzervatív kezelésre nem szűnő vérzés kapcsán. Tágításra 6 anastomosis került, 2 pouch-vaginalis fistulát észleltünk.

Utánkövetéstünk során 2 beteget vesztettünk el szájüregi tumor és cardiorespiratoricus insufficientia következményeként, CU-val összefüggő halálok nem volt.

A vizsgálati időszak alatt belgyógyászati visszavétel 9, illetve 12 esetben volt, amelynek hátterében nagyrészt vérszegénység miatti transzfúziós igény és hasi panaszok voltak. A kontroll endoszkópos vizsgálatok alapján 17 pouchitis igazolódott, amelyhez 10 esetben cuffitis is társult, ez a pouch-csal rendelkező betegek 40%-át érintette.

Szövődmények terén vizsgáltuk a sebgyógyulási zavar megjelenését, amelyet a laparoszkópos csoportban 8 esetben (5 – sebvonvalban, 1 – gáton, 1 – drén helyén, 1 – hasfali resutura helyén), a nyitott beteganyagnál 7 esetben (4 – sebvonvalban, 1 – bezárt ileostoma helyén, 1 – drén helyén, 1 – nyákfistula helyén) észleltünk, közülük 2, illetve 1 betegnél methicillinrezisztens *Staphylococcus aureus*-infekció igazolódott.

## Életminőség

Vizsgáltuk a műtéti beavatkozásokat követő életminőségbeli változást általános állapot, testsúly és napi székletszám tekintetében. A betegek műtét előtti és jelenlegi általános állapotának meghatározását 1–10-ig terjedő szubjektív skála alapján adták meg, ahol 1 a legjobb, míg 10 a legrosszabb életminőséget jelentette. Ebben a tekintetben mindenkorban szignifikáns javulást mérünk a műtétek követő időszakban. A műtétek utáni időszakban mindenkorban testtömeg-növekedést tapasztaltunk, amely a nyitott beteganyagnál szignifikánsnak bizonyult. A posztoperatív időszakban javult, azaz csökkent a napi átlagos székletszám mindenkorban. A két betegcsoport kozmetikai eredményét vizsgálva a betegek ötös skálán (egyáltalán nem elégedett – kicsit elégedett – közepesen elégedett – inkább elégedett – nagyon elégedett) értékeltek, amely alapján a nyitott műtéten átesett betegek az „inkább elégedett”, a laparoszkópos műtéten átesett betegek a „nagyon elégedett” választ adták. Az életminőségbeli változásokat az 5. táblázatban foglaltuk össze.

## Megbeszélés

Vizsgálatunk az első hosszú távú magyarországi tanulmány a CU sebészi kezelését illetően, amely nagy hangsúly fektet a laparoszkópos beavatkozások eredményességének megítélésére is. A minimálisan invazív technika hazánkban is egyre nagyobb teret nyer, amely módszer az IBD kezelésében is széles körben, biztonsággal alkalmazható eljárás [6, 7, 8]. Tanulmányunkat három nagy részre (perioperatív időszak, műtét utáni komplikációk és életminőség) bontva, retrospektív módon vizsgáltuk a

4. táblázat | Késői posztoperatív szövődmények

	Laparoszkópos (n = 33)	Nyitott (n = 23)	
Szeptikus állapot	<ul style="list-style-type: none"> <li>- Kismedencei tányog (1) → intervenciós drenálás</li> <li>- Hasfali tányog (1) → lokális kezelés</li> <li>- Perianalis tányog (1) → Seton-drenálás</li> </ul>	<ul style="list-style-type: none"> <li>- Súlyos pouchitis (1) → pouchexcisio</li> <li>- Perianalis tányog (9) → Seton-drenálás</li> <li>- Kismedencei tányog (1) → műtéti feltáras</li> </ul>	
Összesen	9% (3/33)	47,8% (11/23)	p = 0,001
Intestinalis obstrukció			
- Műtéti beavatkozást igénylő	- Ileus (1)	- Ileus (5)	
- Műtéti beavatkozást nem igénylő	- Subileus (7)	- Subileus (9)	
Összesen	24,2% (8/33)	60,1% (14/23)	p = 0,006
Posztoperatív sérv	- Ileostoma hegében (3)	- Median laparotomia hegében (4)	
Összesen	9% (3/33)	17,4% (4/23)	p = 0,355
Egyéb	<ul style="list-style-type: none"> <li>- Anastomosisstenosis (1)</li> <li>- Akut has, szabad hasi levegő (1) → ileumresectio perforáció miatt</li> </ul>	<ul style="list-style-type: none"> <li>- Anastomosisstenosis (6)</li> <li>- Per anum vérzés (3) → rectumexstirpatio (1)</li> <li>- Súlyos spinchterkárosodás (1) → rectumexstirpatio</li> <li>- Pouch-vaginalis fistula (2)</li> <li>- Exsiccosis (2)</li> </ul>	
Összesen	6% (2/33)	60,1% (14/23)	p = 0,01

5. táblázat | Pre- és posztoperatív életminőségbeli változtatások

		Műtét előtt	Jelenleg	
Életminőség (skála alapján)	Laparoszkópos (n = 33)	8,55±1,5	2,65±1,92	p = 0,000
	Nyitott (n = 23)	8,69±1,74	2,63±1,96	p = 0,000
Napi székletszám	Laparoszkópos (n = 33)	10,51±5,77	8,16±4,21	p = 0,352
	Nyitott (n = 23)	9,73±5,27	8,71±3,14	p = 0,632
Testsúly (kg)	Laparoszkópos (n = 33)	65,33±14,72	72,08±18,37	p = 0,126
	Nyitott (n = 23)	62,45±16,18	73,21±14,7	p = 0,033

CU miatt nyitott, illetve minimálisan invazív módszerrel operált betegcsoportokat. A betegség terápiája elsősorban gyógyszeres és biológiai kezelésben alapszik, sebészeti megoldása, ennek sikertelensége, illetve életet veszélyeztető állapotromlás, akut hasi körkép esetén szükséges. A körkép incidenciája emelkedik, becslések szerint a CU-ban szenvédő populáció 25–40%-ánál kényszerülünk műtéti beavatkozásra [2, 9, 10, 11, 12, 13].

A proctocolectomiát követő első pouchműtétről 1978-ban Parks és munkacsoportja számolt be, amely módszer a CU sebészeti kezelését illetően napjainkra gold standard alternatívává vált, laparoszkópos változatáról elsőként a kilencvenes évek elején tesznek említést [3, 4, 14]. Egy nagy esetszámmal dolgozó japán, valamint egy francia tanulmány is az IPAA-t mint legjobb megoldást emeli ki [13, 15].

Utánkövetésünk átlagosan 47,84 (3–111) hónapig tartott. Az 56 eset közül laparoszkópos technikával 33 (58,9%), nyitottan 23 (41,1%) műtét történt, 20 (35,7%) sürgősséggel, míg 36 (64,3%) tervezett úton. A laparoszkópos beavatkozások közül összesen 3 esetben

(3/36, 8,3%), tervezett műtét kapcsán masszív adhéziók (1 eset), valamint sürgős műtét során észlelt bélserülés, illetve perforáció veszélye miatt (2 eset) kényszerültünk konverzióra, a későbbi elemzésekből ezeket az eseteket kizártuk. Egy amerikai tanulmányban a konverzió okaként a beavatkozások sürgős jellegét, a korábbi hasi műtétek mellett a proctectomiát is megemlíti, valamint az IBD tekintetében a Crohn-betegséget [16].

A betegség megjelenésétől a műtéti beavatkozásig átlagosan 9,05±7,86 és 8,26±9,93 év telt el. A két csoportban a BMI-t és az ASA-klasszifikációt illetően különbséget nem találtunk. Műtét előtti laborértekben a gyulladásos markerek a nyitott beteganyagnál szignifikánsan magasabbnak bizonyultak, amit a csoportban lévő akut műtétek magasabb arányának tulajdonítunk. Extraintestinalis manifesztációra utaló eltérést 42 betegnél észleltünk.

Számos tanulmány foglalkozott a CU és a dohányzás kapcsolatával, amelyek szerint az protektív hatással bír a betegség kialakulásával, fellángolásával szemben [9, 17]. Hasonló megfigyelés igazolódott appendectomy – mint

védőtényező – megfigyelése kapcsán is [9, 18]. Beteganyagunkban nem szerepelt aktív dohányos, kórtörténetükben 8 esetben igazolódott korábbi dohányzás és 2 betagnél szerepelt appendectomy.

A két csoport ápolási idejében, intenzív osztályos és transzfúziós igényében, valamint az első széklet megjeleléseig eltelt időben különbséget nem találtunk. A nyitott módon elvégzett műtétek rövidebb ideig tartottak, amely a nyákfistula-, végileostoma-képzéssel járó colectomiák esetén szignifikánsnak bizonyult.

Az eddig publikált tanulmányok jelentős része a laparoszkópos technika különböző előnyeiről számolt be. Egy ausztrál tanulmány szerint a laparoszkópia rövidebb ápolási idővel bír, gyorsabb a passzázs helyreállása, kozmetikailag előnyösebb, azonban proctocolectomia kapcsán azonos a morbiditása a két műtéti technikának [19]. *Gu és mtsai* a laparoszkópos colectomiát követő laparoszkópos kiegészítő proctectomiákat, IPAA kialakítását vizsgálva alacsony vérvesztésről, a passzázs gyors helyreállásáról és rövid ápolási időről tesznek említést [20]. A nem toxikus colitis miatt végzett colectomiák kapcsán készült holland tanulmány a sebfertőzés és a hasi tányog esetén látja előnyösebbnek a minimálisan invazív technikát [21]. *Koh és mtsai* a CU miatti urgens laparoszkópos műtétek vizsgálata alapján azt biztonságosnak találták, ileus és sebfertőzés terén jobb eredményeket írtak le a nyitott műtétekhez képest [22]. Két amerikai tanulmány hasonlóan kedvező eredményeket közölt ápolási idő, vérigény, kozmetikai eredmény, sebfertőzés terén sürgősséggel végzett laparoszkópos szubtotális colectomiák kapcsán [23, 24]. Egy nagy nemzetközi adatbázis adatai alapján a minimálisan invazív betegcsoport kedvezőbb eredményekkel bír morbiditás és mortalitás szempontjából [6]. Míg egy 2013-ban megjelent randomizált tanulmány a laparoszkópos módszernek csupán a kozmetikai előnyét igazolta [25]. Egy rövid távú utánkövetés nem talált különbséget IPAA-műtéteket követően ápolási idő, passzázsmeindulás és komplikációk terén a két csoport összehasonlítása kapcsán [26].

A posztoperatív szövődményeket megvizsgálva a korai, 30 napon belüli időszakban a laparoszkópos és a nyitott csoport között nem találtunk különbséget a reoperációt igénylő (15,15% vs. 17,39%) és konzervatív kezeléssel orvosolható komplikációk (15,15% vs. 21,7%) között. A műtét előtti időszakban 23 beteg (41,07%) részesült infliximabkezelésben, 6 esetben alakult ki korai szövődmény. Irodalmi adatok alapján megeszűlt vélemények vannak a biológiai terápia és a műtét utáni komplikációk összefüggését illetően, valamint a legfrissebb, ezzel a témaival foglalkozó összefoglaló közlemény alapján még túl korai a biológiai terápiák műtétet befolyásoló hatásának megítélése [27, 28, 29].

Késői szövődmények terén azonban a laparoszkópos műtéti technika egyértelműen kedvezőbb eredményekkel bír szeptikus szövődmények, intestinalis obstrukció és egyéb komplikációk terén, úgymint anastomosisszükület, pouch-vaginalis fistula, per anum vérzés. Sebgyó-

gyulási zavar (24% vs. 30%) tekintetében nem találtunk különbséget.

A nyitott csoportban az intestinalis obstrukciók magasabb aránya (24,2% vs. 60%) a beavatkozás jellegéből adódó nagyobb műtéti traumával és vélhetően az összenövések magasabb rizikójával magyarázható, azonban az erre vonatkozó irodalmi adatok eltérőek. Feltevésünkkel támasztja alá az a két tanulmány, ahol szignifikánsan kevesebb hasúri és kismedencei adhéziót igazoltak laparoszkópos IPAA-t követően, ezáltal csökkentve az ileus és női infertilis kialakulásának lehetőségét [30, 31]. *Dolejs* publikációja szerint a laparoszkópia nem változtatta meg az intestinalis obstrukció rizikóját [32]. Szintén kevesebb, laparoszkópos műtét utáni összenövésről és sérvről számol be egy holland munkacsoport [33]. A laparoszkópos csoportban csupán a protektív ileostomák helyén (9%), míg a nyitott esetekben a nagy behatolási kapuval bíró median laparotomiákban (17,3%) észleltünk műtét utáni sérveket. A *Wu és munkacsoportja* által készített összefoglaló tanulmány nem talált különbséget hasúri tányog, varratelégtelenség és ileus kapcsán a két csoport között [34]. Egy 2014-es összefoglaló közlemény a laparoszkópos IPAA előnyeként az alacsony morbiditást, a rövid ápolási időt és a magasabb fertilitást emeli ki a hosszab műtéti idővel szemben, míg akut esetekben az alacsonyabb szeptikus szövődményt és a sebgyógyulási zavart említi [35]. *Gu és mtsai* laparoszkópos totális colectomiák kapcsán vezető komplikációként distalisconk-elégtelenségből fakadó szeptikus szövődményeket, ileust és sebgyógyulási zavart regisztráltak [36].

Utánkövetésünk során pouchitist a betegek 40%-ánál regisztráltunk, egy esetben a súlyos gyulladás miatt a pouch kiirtására kényszerültünk, 2 pouch-vaginalis fistulát észleltünk. Szövődményeinket áttekintve a pouch gyulladásos folyamata az egyik leggyakrabban észlelt probléma volt. Egy angol összefoglaló közleményben az IPAA-t követő komplikációkat a pouch gyulladása vezeti, hasonló eredményre jutott egy nagy esetszámmal dolgozó finn tanulmány is [37, 38].

Sebészi beavatkozásokat követően szignifikáns életminőségbeli javulást tapasztaltunk, amely eredmény számos irodalmi adattal korrelál [39, 40, 41, 42]. Mindként csoportban csökkent a napi székletszámok átlaga, valamint testsúlygyarapodást tapasztaltunk. A minimálisan invazív beavatkozásokat követően kedvezőbb kozmetikai eredményt értünk el.

Egy olasz tanulmány az IPAA-t követő komplikációk, pouchitis, pouchexcisio veszélye, tumorrizikó, illetve életminőség kapcsán hívja fel a figyelmet a műtétre kerülő betegek pontos kivizsgálásának, szelekciójának és utánkövetésének fontosságára [43].

Vizsgálatunk alapján elmondhatjuk, hogy a CU kezelésében a laparoszkópos módszer tervezett és sürgősségi esetekben is biztonságosan alkalmazható eljárás, amely kedvező hosszú távú eredményekkel bír. A hagyományos, nyitott módszerhez képest alacsony szövődményráta mellett jó életminőséget és előnyösebb kozmetikai

eredményt biztosít. A CU-ban szenvédő populáció egy „nehéz” beteganyag, amelynek kezelése, gondozása dedikált centrumokban javasolt gasztroenterológus és a sebész szoros együttműködésével.

**Anyagi támogatás:** A közlemény megírása, illetve a kapcsolódó kutatómunka anyagi támogatásban nem részesült.

**Szerzői munkamegosztás:** A beteganyag feldolgozását jr. T. J. végezte. A többi szerző a betegek sebészeti, illetve belgyógyászati kezelését, valamint gondozását, utánkövetését végezte. A kézirat végleges változatát valamennyi szerző elolvasta és jóváhagyta.

**Érdekeltségek:** A szerzőknek nincsenek érdekeltségeik.

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(Lázár György dr.,  
Szeged, Szőkefalvi-Nagy u. 6., 6720  
e-mail: gylazar@gmail.com)

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**III.**

# Effect of Laparoscopic Surgery on Quality of Life in Ulcerative Colitis

János Tajti Jr., MD<sup>1</sup>, Melinda Látos, PhD<sup>1</sup>, Klaudia Farkas, MD, PhD<sup>2</sup>,  
Szabolcs Ábrahám, MD, PhD<sup>1</sup>, Zsolt Simonka, MD, PhD<sup>1</sup>, Attila Paszt, MD, PhD<sup>1</sup>,  
Tamás Molnár, MD, PhD<sup>2</sup> and György Lázár, MD, PhD, DSc<sup>1</sup>

## Abstract

**Aim:** To evaluate quality of life after surgery for ulcerative colitis (UC) the gastroenterological and psychological conditions were examined.

**Materials and Methods:** Between January 1, 2005 and March 1, 2016, surgery was performed for UC in a total of 75 patients. Our examinations were performed in 58 cases. Quality of life was examined with questionnaires. Functional Scoring System, Gastrointestinal Quality of Life Index (GIQLI), and Short Inflammatory Bowel Disease Questionnaire (SIBDQ) were used for testing gastroenterological conditions; Spielberger's State-Trait Anxiety Questionnaire, Beck Depression Inventory, and Brief Illness Perception Questionnaire (BIPQ) were performed to consider psychological status.

**Results:** Trait anxiety and the incidence of abdominal pain were significantly lower in patients having undergone laparoscopic surgery. No difference was found between the minimally invasive and conventional methods in the early complications. There were significantly more late complications developing after 30 days in patients who had undergone open surgery. Differences were found in personal control between patients with a stoma and patients without a stoma. Patients with a stoma felt they had less control over their disease. A significant correlation was found between the results of the psychological and gastrointestinal questionnaires.

**Conclusions:** Minimally invasive technique provides a better long-term outcome for patients with UC, fewer complications, and a more balanced emotional condition. Favorable gastroenterological condition leads to better psychological status, which is negatively influenced by stoma or complications.

**Keywords:** colitis, ulcerative, laparoscopy, quality of life, psychology, clinical, stomas, surgical

## Introduction

ULCERATIVE COLITIS (UC) is a chronic inflammatory disease affecting the whole large intestine. The incidence of UC has risen recently. The incidence of Inflammatory Bowel Diseases (IBD) is 11.3/100,000 in Eastern Europe, 14.0/100,000 in Western Europe, and it is estimated to be 24/100,000 in Hungary.<sup>1</sup> Treatment of the disease is primarily drug therapy; however, surgical intervention is required in the case of patients not responding to conservative therapy or in the case of complications.

The gold standard surgical treatment is proctocolectomy and ileal pouch-anal anastomosis (IPAA), using standard,

open, and laparoscopic methods.<sup>2</sup> The aim of surgical intervention is to improve long-term quality of life by removing the target organ, the whole large intestine.<sup>3,4</sup> The benefits of the minimally invasive method in the surgical treatment of UC are the following: length of hospital stay is shorter, postoperative pain is reduced, passage resolves rapidly, and cosmetic results are beneficial.<sup>5</sup> The importance of surgical treatment is supported by two studies that show that patients treated with conservative methods experienced a worse long-term quality of life compared to those receiving surgical treatment.<sup>6,7</sup> As a result, it can be concluded that surgery provides successful treatment for UC in the long term and it is therefore important to inform the patients about it. Limited

<sup>1</sup>Department of Surgery and <sup>2</sup>First Department of Internal Medicine, University of Szeged, Szeged, Hungary.

data are available on quality of life in patients with UC undergoing surgery. Our working group was the first to publish mid- and long-term results on laparoscopic treatment of UC in Hungary, which proved the success of the method.<sup>8,9</sup>

The purpose of our study is to evaluate quality of life for patients who have had surgery due to UC. Quality of life was studied in patients who had undergone laparoscopic and open surgeries, in patients with or without stoma, regarding early and late complications, and in the case of elective and emergency indications. We were looking for a connection between gastroenterological and psychological conditions, daily activities.

## Materials and Methods

Between January 1, 2005 and March 1, 2016, surgery was performed due to UC in a total of 75 patients, the open method was used in 25 cases and the minimally invasive technique in 50. All procedures performed in this study involving human participants were conducted with the approval of the Ethics Committee at the University of Szeged, Hungary (194/2015-SZTE) and were in accordance with the Helsinki Declaration of 1975 (1983) and its later amendments or comparable ethical standards. Our examinations were carried out in 58 of the 75 patients. Questionnaires could not be completed for various reasons for 17 patients (death in 3 cases, language problems occurred in the case of 2 foreign patients, and 12 patients refused to participate in the study or could not be contacted).

The average duration of the follow-up was 46 (1–124) months. Fifty-eight patients (29 female and 29 male) participated in our study; 41 patients had undergone laparoscopic surgery, and 17 patients had had open surgeries. Thirty-nine cases were elective interventions, while 19 were emergency surgery due to unsuccessful conservative treatment or fulminant, septic, or toxic condition. No significant difference was found in the case of the body mass index ( $24.85 \pm 5.12$  versus  $26.82 \pm 5.57$ ) or the American Society of Anesthesiologists (ASA) score ( $2.25 \pm 0.54$  versus  $2.13 \pm 0.74$ ). There was an average 8.2 years from diagnosing the disease to surgery. In the laparoscopic group, 25 proctocolectomies with IPAA and ileostomy were performed, 13 patients had a total colectomy with end ileostomy and mucous fistula, and 3 rectum extirpations were carried out. In the open group, a pouch was created in 4 cases, 9 patients had a total colectomy with mucous fistula, and 4 other colon resections were performed. Seventeen patients had a stoma during the study. To homogenize the groups, 6 patients, who were operated dissimilarly from the standard surgical technique ( $n=3$  rectum extirpation,  $n=3$  other colon resection) were excluded during the comparison of laparoscopic and open surgery groups, and during the analysis of complications.

## Questionnaires

**Functional scoring system.** The functional scoring system is a questionnaire consisting of 12 questions on patients' bowel movements (number of bowel movements during the day and at night, urgency, and perianal soreness), incontinence (during the day and at night and use of protective pads), diet, drug therapy, and potential social disadvantages.<sup>10</sup>

**Gastrointestinal Quality of Life Index.** The Gastrointestinal Quality of Life Index (GIQLI) studies gastroenterological condition (abdominal pain, epigastric fullness, bloating, flatulence, eructation, increased bowel movements, urgency, diarrhea, constipation, nausea, blood in the stool, heartburn, and bowel incontinence), alimentation (appetite, eating speed, and swallowing a bite), physical condition, daily activities, social activities, and psychological condition for 2 weeks before completing the questionnaire.<sup>11</sup>

**Short IBD Questionnaire.** The Short IBD Questionnaire (SIBDQ) studies gastrointestinal symptoms and their effect on social and physical well-being for 2 weeks before completing the questionnaire based on 10 questions.<sup>12</sup>

**Spielberger's State-Trait Anxiety Questionnaire and the Beck Depression Inventory.** Spielberger's State-Trait Anxiety Questionnaire and the Beck Depression Inventory were used to measure the level of anxiety and mood.<sup>13,14</sup>

**Brief Illness Perception Questionnaire.** Illness perceptions and attitude toward healing were studied using the Brief Illness Perception Questionnaire (BIPQ), consisting of eight subscales (consequences, timeline, personal control, treatment control, identity, concern, coherence, and emotional representation).<sup>15</sup>

## Biostatistics

Patients were examined retrospectively, and statistical analysis was performed with the SPSS program (Version 20.0 2014; IBM SPSS Statistics, Chicago, IL). Pearson and Spearman correlations were used to determine relationships between variables. The independent samples *t*-test, Mann-Whitney test, ANOVA, and Chi-square test were used to compare the groups. Values were considered to be statistically significant if *P* was lower than .05.

## Results

### Representation of illnesses

About 92.3% of the patients enrolled in the study considered a psychological factor (psychological causes, family, or work stress) to be in the background of their disease. Around 42.3% of the patients pointed to genetic factors, 46.2% of them mentioned environmental hazards (such as inappropriate diet), and 1 patient noted the Chernobyl nuclear disaster as the cause of the disease.

Patients viewing genetic factors as being in the background of the disease reached significantly higher scores on the BIPQ ( $44.14 \pm 11.64$  versus  $35.73 \pm 13.35$ ; *P* = .022), so they are more threatened by their disease and know less about the nature of it (coherence subscale:  $2.14 \pm 1.58$  versus  $1.10 \pm 1.32$ ; *P* = .013).

### Psychological consequences of having a stoma

There were differences in personal control between patients with a stoma ( $n=17$ ) and patients without a stoma ( $n=41$ ) ( $6.12 \pm 3.33$  versus  $4.12 \pm 2.88$ ; *P* = .045). Patients with a stoma felt they had less control over their disease. No difference was found between the two groups during gastroenterological follow-up examinations.

### Results for emotional state and mood

There was a significant connection between depression and the functional scoring system ( $P=.002$ ;  $r=0.419$ ), GIQLI ( $P<.001$ ;  $r=-0.867$ ), SIBDQ ( $P<.001$ ;  $r=-0.795$ ), and BIPQ ( $P<.001$ ;  $r=0.751$ ), in addition to the consequences, personal and treatment control, identity, concern, and emotional representation subscales ( $P<.05$  in all cases). State anxiety significantly correlated with the total score for the GIQLI ( $P<.001$ ;  $r=-0.624$ ), SIBDQ ( $P<.001$ ;  $r=-0.579$ ), and BIPQ ( $P<.001$ ;  $r=0.615$ ), along with the consequences, personal and treatment control, identity, concern, and emotional representation subscales ( $P<.05$  in all cases). There was a significant connection between trait anxiety and the functional scoring system ( $P=.012$ ;  $r=0.344$ ), GIQLI ( $P<.001$ ;  $r=-0.682$ ), SIBDQ ( $P<.001$ ;  $r=-0.684$ ) and BIPQ ( $P<.001$ ;  $r=0.608$ ), in addition to the consequences, personal and treatment control, identity, concern, and emotional representation subscales ( $P<.001$ ) (Table 1).

### Comparing laparoscopy and open surgery

Trait anxiety was significantly lower in patients having undergone laparoscopic surgery ( $n=38$ ) compared with patients who had had open surgery ( $n=14$ ) ( $P=.018$ ) (average value of trait anxiety in patients with open surgery was 48.71, standard deviation [SD]=10.91; this value was 40.22, SD=9.82 in the laparoscopic group). Both patient groups had  $>5$  stools in the daytime and  $>1$  at night per week, with no significant difference observed between the groups. No difference was noted between the two surgical methods based on the total score on the gastroenterological questionnaires, although the following statistical differences were found when evaluating each questionnaire item individually. Incontinence was registered during the day (25% versus 27%) and at night (39.28% versus 54%) in both patient groups (Table 2). The incidence of abdominal

TABLE 2. TOTAL VALUES FROM THE FUNCTIONAL SCORING SYSTEM

	Laparoscopic (n=28) n (%)	Open (n=11) n (%)
Urgency (inability to defer evacuation $\geq 30$ minutes)	14 (50)	6 (54.5)
Evacuation difficulties	5 (17.85)	3 (27.3)
Soiling or seepage in daytime	7 (25)	3 (27.3)
Soiling or seepage at night	11 (39.28)	6 (54.5)
Perianal soreness	15 (53.57)	9 (81.8)
Protective pad in daytime	7 (25)	3 (27.3)
Protective pad at night	12 (42.85)	3 (27.3)
Dietary restrictions	21 (75)	5 (45.5)
Medication (continuous or occasional)	14 (50)	10 (90.9)
Social handicap	13 (46.6)	4 (36.4)

Based on Oresland et al.<sup>10</sup>

pain was significantly less common ( $1.895 \pm 1.034$  versus  $2.769 \pm 0.927$ ;  $P=.024$ ) in the laparoscopic group based on the GIQLI.

### Complications

No difference was found between the minimally invasive and conventional methods in cases requiring early reoperation (ileus, stoma correction, bleeding, and sepsis) and in cases not requiring reoperation (subileus, bleeding, septic condition, pancreatitis, and dehydration). There were significantly more late complications developing after 30 days (septic condition, intestinal obstruction, postoperative hernia, and “other” complications, such as bleeding, anastomosis stenosis, pouch-vaginal fistula, perforation, and disruption of the abdominal wall) in patients who had undergone open surgery ( $P=.001$ ), of whom the incidence of intestinal obstruction and “other” complications were significantly higher ( $P \leq .001$ ) (Fig. 1). Pouchitis was detected in 17 cases

TABLE 1. PEARSON'S OR SPEARMAN'S CORRELATION BETWEEN CLINICAL AND PSYCHOLOGICAL VARIABLES AND GASTROINTESTINAL QUALITY OF LIFE INDEX

Variables	GIQLI
Psychological variables	
Beck depression inventory	-0.87*
Spielberger's State Anxiety Scale	-0.62*
Spielberger's Trait Anxiety Scale	-0.69*
Brief Illness Perception Questionnaire	-0.84*
Consequences	-0.89*
Timeline	-0.07 (NS)
Personal control	-0.37*
Treatment control	-0.39*
Identity	-0.73*
Concern	-0.71*
Coherence	-0.01 (NS)
Emotional representation	-0.78*
Clinical variables	
Functional scoring system	-0.55*
SIBDQ	0.89*

\* $P < .01$ .

GIQLI, Gastrointestinal Quality of Life Index; NS, non significant; SIBDQ, Short Inflammatory Bowel Disease Questionnaire.

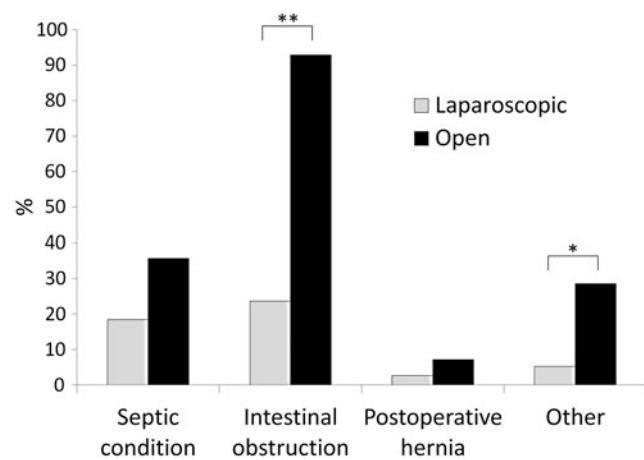


FIG. 1. Late postoperative complications. Among late complications the incidence of intestinal obstruction (\*\* $P \leq .001$ ) and “other” complications (\* $P \leq .05$ ) were significantly higher in patients who had had open surgery than in patients who had undergone laparoscopic surgery.

(35.41% of patients with a pouch). Cuffitis occurred in 13 (27.08%) cases. The personal control ( $3.43 \pm 2.35$  versus  $5.57 \pm 3.31$ ;  $P=.024$ ) was higher in patients with no late complication.

## Discussion

Our study confirmed the long-term positive effect of laparoscopic surgery on quality of life in the surgical treatment of UC. A favorable gastroenterological condition leads to a better psychological state, which can be negatively influenced by the presence of stoma or complications. By positively influencing these factors, using a minimally invasive technique results in better quality of life compared with open surgery.

In the case of a benign, non-neoplastic disease, the success of the surgical intervention is determined by the quality of life. In the case of UC, abdominal complaints, a high number of bowel movements a day, surgical interventions, and their consequences are very demanding somatically and psychologically. The social integration of patients, their quality of life, and their daily routine activities may often be difficult.

Limited data are available on quality of life after surgical treatment of UC. Incidence of the disease is increasing, and performing IPAA after a proctocolectomy has become the gold standard intervention in surgical treatment.<sup>16–18</sup> It is a safe technique with low mortality and morbidity.<sup>19</sup> Our Department was the first in Hungary to examine the minimally invasive technique in the treatment of UC. This method was successful in elective and acute cases as well. Moreover, the occurrence of complications was low compared with the open technique<sup>8,9</sup> After successful surgical interventions, quality of life improved continuously, and pouchitis was considered the main problem.<sup>4</sup>

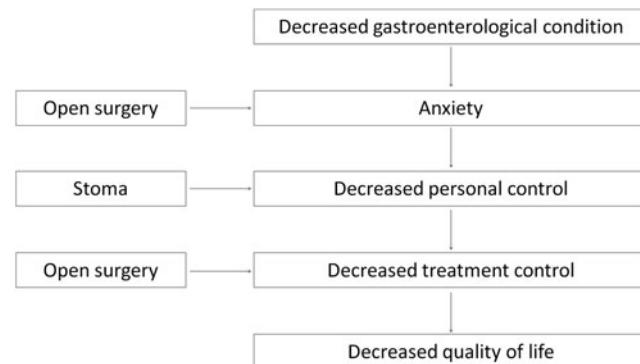
Patients having undergone a surgical intervention between January 1, 2005 and March 1, 2016 due to UC were enrolled in our study. Quality of life was examined with questionnaires considering gastroenterological and psychological conditions and daily activities. Results were analyzed in the laparoscopic group and in patients undergoing open surgery, in patients with or without a stoma, in the case of acute and elective interventions, and with regard to early and late complications. The average duration of the follow-up was 46 months.

In terms of disease representation, 92.3% of our patients considered their disease to be caused by psychological factors, 42.3% thought that genetic factors lay behind the disease, and 46.2% felt that environmental hazards were to blame. In conclusion, patients with UC are well informed and are aware of the nature and characteristics of their disease.

The consequences of wearing a stoma were examined as well. It showed a significant correlation with the BIPQ personal control subscale, meaning that patients with a stoma felt they had less control over their condition. Therefore, the presence of an anus praet, either temporary or permanent, was psychologically demanding for the patients; it made healing and daily activities more difficult. In addition to these results, no difference was found in quality of life among patients living with an ileostoma or a pouch in a prospective cross-sectional observational study.<sup>20</sup>

Quality of life was examined with regard to laparoscopic surgery and open surgery as well. An examination of psychological differences between the two groups showed that trait anxiety was significantly different; that is, patients undergoing open surgery were more anxious. Based on the total score on the gastroenterological questionnaires, there was no difference between the two surgical methods, abdominal pain was more favorable in the laparoscopic group based on the functional scoring system, the SIBDQ and GIQLI. An Irish and a German study with a 10-year follow-up found a favorable quality of life after IPAA surgery,<sup>21,22</sup> and an Indian study concluded that the IPAA was a suitable procedure with regard to functionality and quality of life.<sup>23</sup> Nutritional difficulties, bowel movement problems, and daily and night-time incontinence were noted in both groups. Incontinence, increased number of bowel movements at night, and urgency were determined to be negative prognostic factors of quality of life in the literature.<sup>24</sup> Our patients reported  $>5$  stools during the day and  $>1$  stool at night weekly in the postoperative period. Fichera et al. observed high rates of continence and an average of six bowel movements a day after laparoscopic IPAA.<sup>25</sup> Polle et al. detected no difference in quality of life, functionality, and morbidity between the groups.<sup>26</sup> Pouchitis was reported in 17 (35.41%) cases, and cuffitis occurred in 13 (27.08%) cases. According to a meta-analysis, there was no difference between the two surgical methods with regard to the number of bowel movements a day and pouchitis,<sup>27</sup> while a Swedish study described long-term problems regarding pouchitis.<sup>28</sup> Several other studies noted good quality of life after proctocolectomy.<sup>29–31</sup>

No difference was found between the two groups with regard to early complications. Late complications occurred significantly more often with emergency and open surgeries. With regard to the psychological factors, the values for the BIPQ personal control and coherence subscales were higher in patients with no late complications, meaning that they felt they had more control over their disease. A significant correlation was found between the results of the psychological



**FIG. 2.** Effect of gastroenterological and psychological conditions and surgical technique on quality of life. Deterioration of gastroenterological condition shows connection with decreased psychological status; anxiety, reduced personal and treatment control are more frequent. Furthermore, psychological condition is negatively influenced by the use of open surgical technique and the presence of a stoma. All these factors result in decreased quality of life.

and gastrointestinal questionnaires. Consequently, a negative emotional condition and mood resulted in lower quality of life. Moreover, more anxious and depressed patients had a negative idea of their disease and less faith in the success of surgical interventions (Fig. 2).

An IBD study reported that psychological symptoms have a significant effect on the primary disease and that anxiety increases and social function deteriorates in correlation with the severity of the disease. In addition, it was shown that patients with more control over their disease enjoy a better gastroenterological condition.<sup>32</sup>

## Conclusion

Our study is the first to examine quality of life among patients operated on for UC with regard to psychological and gastroenterological conditions. As a result, it can be concluded that a minimally invasive technique provides a better long-term outcome for patients with UC, fewer complications, and a more balanced emotional condition. Patients who undergo surgery with the standard method have a greater psychological burden and a negative image of their disease. Our study confirmed that a better gastroenterological condition gives rise to a better psychological condition. These factors result in a better quality of life for patients. Successful treatment of UC should be performed in centers with close gastroenterological and surgical co-operation. Psychological guidance is essential; thus, psychologists and social workers may have to be involved in the treatment of these patients.

## Disclosure Statement

No competing financial interests exist.

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Address correspondence to:  
György Lázár, MD, PhD, DSc  
Department of Surgery  
University of Szeged  
Semmelweis Street 8  
Szeged H-6725  
Hungary

E-mail: [lazar.gyorgy@med.u-szeged.hu](mailto:lazar.gyorgy@med.u-szeged.hu)

**IV.**



# TENZIÓS TÍPUSÚ FEJFÁJÁS ÉS COLITIS ULCEROZA

TAJTI Jr. János, LÁTOS Melinda, ÁBRAHÁM Szabolcs, SIMONKA Zsolt, PASZT ATTILA, LÁZÁR György

Szegedi Tudományegyetem, Általános Orvostudományi Kar, Sebészeti Klinika, Szeged



Hungarian

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## TENSION-TYPE HEADACHE IN ULCERATIVE COLITIS

Tajti Jr. J, MD; Látos M, PhD; Ábrahám Sz, MD, PhD;  
Simonka Zs, MD, PhD; Paszt A, MD, PhD;

Lázár Gy, MD, PhD, DSc

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**Célkitűzés** – A tenziós típusú fejfájás igen gyakori, az átlagpopulációban az élettartam-prevalenciája 30–78%, így meglehetősen magas a társadalmi-gazdasági hatása. A gyulladásos bélbetegségek incidenciája folyamatosan emelkedik. Magyarországon colitis ulcerosa miatt műtéttel kapcsolatos életminőségi adatokkal eddig limitált számban rendelkeztünk. Jelen tanulmányunkban a colitis ulcerosa miatt műtéten átesett betegpopuláció életminőségét vizsgáltuk a fejfájás vonatkozásában.

**Módszerek** – 2005. január 1. és 2016. március 1. között 75 betegnél végeztünk colitis ulcerosa miatt műtést. Retrospektív módszerrel végzett utánkövetésünk átlagosan 46 (1–124) hónapig tartott, mely során a Rövid Betegségspercepció Kérdőívet és a Fejfájás Kérdőívet felhasználva regisztráltuk a fejfájás megjelenését.

**Eredmények** – Az elsődleges fejfájásbetegségek (n=27) közül 19 (70,4%) beteg tenziós típusú fejfájásban, 8 (29,6%) beteg migrénben (aura nélküli) szenvendett. A tenziós típusú fejfájásos betegek közül 17 (89,5%) episztodikus, 2 (10,5%) krónikus formába tartozott. A fejfájástól szenvendő betegek szignifikánsan magasabb pontszámot értek el a Rövid Betegségspercepció Kérdőíven.

**Következtetések** – Felmérésünk szerint a tenziós típusú fejfájás a colitis ulcerosában szenvendő betegek között gyakori. Ez felveti a két kórfórmá között a stressznak mint kóroki tényezőnek a szerepét, mely nagymértékben befolyásolja és rontja a betegek életminőségét. A fentiek alapján megfontolandó a colitis ulcerosában szenvendő populáció neurológiai kivizsgálása, szükség szerint pszichiátriai, pszichológiai gondozása.

**Kulcsszavak:** tenziós típusú fejfájás, colitis ulcerosa, műtét, életminőség

**Background and purpose** – Tension-type headache is a very common disease with a high socio-economic impact as its lifetime prevalence is 30–78% in the general population. The incidence of inflammatory bowel diseases is continuously rising. Limited data are accessible on quality of life in patients with surgically treated ulcerative colitis. The aim of our study is to examine quality of life, concerning headache, among patients who had undergone surgery due to ulcerative colitis.

**Methods** – Between 1 January 2005 and 1 March 2016, surgery was performed due to ulcerative colitis in 75 patients. During this retrospective analysis the average duration of the follow-up was 46 (1–124) months. The presence of headache was evaluated by the use of Brief Illness Perception and Headache Questionnaires.

**Results** – Among the primary headache disorders (n=27), tension-type headache occurred in 19 (70.4%) cases, and 8 (29.6%) patients had migraine (without aura). Among tension-type headache cases 17 (89.5%) patients experienced episodic form and 2 (10.5%) suffered from chronic form. Patients with headache had obtained a significantly higher score on Brief Illness Perception Questionnaire.

**Conclusions** – According to our study tension-type headache is common among patients with ulcerative colitis. This observation raises the question whether stress plays role in the pathogenesis of both diseases, which influences and worsens considerably quality of life. Neurological examination, psychological and psychiatric guidance are worth considering in patients with ulcerative colitis.

**Keywords:** tension-type headache, ulcerative colitis, surgery, quality of life

Levelező szerző (correspondent): Prof. dr. LÁZÁR György, Szegedi Tudományegyetem, Általános Orvostudományi Kar, Sebészeti Klinika; 6720 Szeged, Semmelweis u. 8. E-mail: [gylazar@gmail.com](mailto:gylazar@gmail.com)  
<http://orcid.org/0000-0001-7155-2978>

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**A**Nemzetközi Fejfájás Társaság klasszifikációja Alapján a fejfájásbetegségek lehetnek elsődleges vagy másodlagos típusúak. Az elsődleges fejfájások közé soroljuk a migrént, a tenziós típusú fejfájást, a trigeminalis autonóm cephalalgiákat, valamint az egyéb primer fejfájásbetegségeket<sup>1</sup>. A tenziós típusú fejfájás igen gyakori, az átlagpopulációban az élet-tartam-prevalenciája 30–78%, így meglehetősen magas a társadalmi-gazdasági hatása. Jellegzetessége a kétoldali nyomó, szorító (nem lüktető) fájdalom, mely közepeges vagy enyhe intenzitású, 30 perc-től akár hét napig is tart. A fájdalmat nem befolyásolja a rutin fizikai aktivitás. Nem társul hozzá hányninger vagy hánýás, de fotofobia vagy fonofobia kísérheti. Járhat a pericranialis izmok érzékenységével, vagy a nélkül. A fokozott pericranialis nyomásérzékenység típusosan interictalisan jelentkezik, és mértéke fokozódik a fejfájások intenzitásával és gyakoriságával<sup>1</sup>. A tenziós típusú fejfájásnak két fő formája van: az epizodikus (ritka vagy gyakori) és a krónikus. A krónikus tenziós típusú fejfájásra jellemző, hogy egy hónapban 15-nél több fejfájásnap van, legalább egymást követő három hónapon át. A krónikus forma egy súlyos betegség, amely jelentősen rontja az életminőséget és rokkantsághoz vezet. A tenziós típusú fejfájás pontos patomechanizmusa mindmáig ismeretlen, habár a perifériás fájdalommechanizmusok szerepet játszanak az epizodikus forma, míg a centrális fájdalommechanizmusok a krónikus forma kialakulásában.

A gyulladásos bélbetegségek (IBD) megjelenése folyamatosan emelkedik, magyarországi incidenciáját napjainkban 24/100 000-rebecsülük<sup>2</sup>. A betegségnek két fő formája ismert: az egész tápcsontron át érintő Crohn-betegség, valamint a vastagbélre lokalizálódó colitis ulcerosa (CU). Az IBD patogenezise nem teljesen tisztázott, a körkép kialakulásában környezeti, genetikai és immunológiai hatásokat, interakciókat feltételeznek. A CU kialakulásában szerepet játszik az urbanizáció, a „nyugatias” életmóderterjedése, valamint a gyakori stresszes életmóder, pszichés tényezők<sup>3, 4</sup>. Kezelésük elsődlegesen gyógyszeres, azonban annak sikertelensége esetén, illetve a betegség szövődményes eseteiben műtéti beavatkozás válik szükségessé<sup>5</sup>.

A CU sebészi kezelésében a leginkább elfogadott műtéti megoldás a célszerv (a teljes vastagbéltraktus) eltávolításával járó proctocolectomia. A rekonstrukció során a tápcsonora folytonosságát a terminális ileumból képzett ileoanalis „pouch”-csal állítják helyre. A beavatkozásnak hagyományos és laparoszkópos módszere ismert<sup>5</sup>, melyek célja az életminőség hosszú távú javítása<sup>6, 7</sup>. Az életminőséget tekintve a sebészi kezelés előnye igazolódott a gyógyszeresen kezelt betegekkel szemben<sup>8</sup>.

Magyarországon CU miatt műtéttel kapcsolatos életminőségi adatokkal eddig korlátozott számban rendelkeztünk. Hazánkban elsőként számolunk be a CU miatt műtéti beavatkozást követő közép- és hosszú távú klinikai eredményekről<sup>9, 10</sup>.

Jelen tanulmányunkban a CU és különböző műtéti technikákat követő életminőséget érintő tényezők közül a fejfájás megjelenését vizsgáltuk.

## Beteganyag és módszer

2005. január 1. és 2016. március 1. között 75 betegnél végeztünk CU miatt műtétet, melyek közül nyitott módon 25, minimálinvazív technikával 50 beavatkozás történt. Az 58 beteg közül (29 nő, 29 férfi) 41-ben laparoszkópos, 17-ben nyitott műtétre került sor. Vizsgálatunk ideje alatt 17 beteg bélélőhelyezéssel (stoma) élt.

A jelen klinikai vizsgálat a Szegedi Tudományegyetem Etikai Bizottsága által jóváhagyott módon zajlott (194/2015-SZTE). A 75 műtött beteg közül 58 esetben tudtuk kérdőíves vizsgálatunkat elvégezni. Utánkövetésünk átlagosan 46 (1–124) hónapig tartott.

### KÉRDŐÍVEK

#### Rövid Betegségpercepció Kérdőív

A betegségreprezentációkat és a gyógyulással kapcsolatos attitűdöket a Rövid Betegségpercepció Kérdőívvel vizsgáltuk, mely nyolc alskálát (Hatás, Időtartam, Személyes kontroll, Kezelési kontroll, Tünetek identitása, Aggódás, Kohärencia és Érzelmi reprezentáció) tartalmazott<sup>11</sup>.

#### Fejfájás Kérdőív

A betegek fejfájásának jellegét az általunk összeállított 16 kérdéses Fejfájás Kérdőívvel mértük fel. A kérdések a fájdalom gyakoriságát, oldaliságát, lokalizációját, jellegét, erősséget, időtartamát, a kísérő tünetek megjelenését, a betegek fejfájásukról alkotott véleményét, az alkalmazott terápiát, annak hatékonyiságát, valamint az életvezetésre gyakorolt hatását célozták meg, a Nemzetközi Fejfájás Klasszifikáció 3beta verziójának kritériumrendszerre alapján<sup>1</sup>.

### STATISZTIKA

A betegek adatait retrospektív módszerrel tekintetük át. A statisztikai feldolgozást SPSS programmal (IBM SPSS Statistics, Version 20.0 2014, Chicago, IL, USA) végeztük. A változók közötti kapcsolatok feltáráására Pearson- és Spearman-korrelációt hasz-

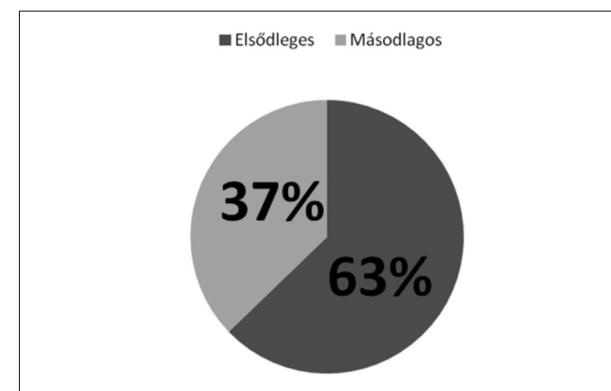
náltunk. A csoportok összehasonlításánál független t-próbát, Mann–Whitney-próbát, ANOVA-t és  $\chi^2$ -próbát alkalmaztunk. Statisztikailag szignifikánsnak tekintettük, ahol a p-érték kisebb volt, mint 0,05.

## Eredmények

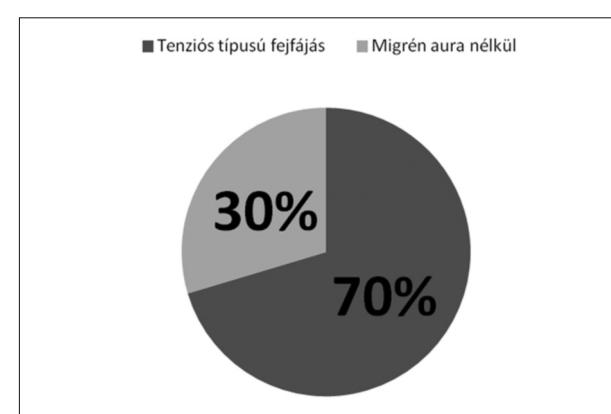
A Nemzetközi Fejfájás Klasszifikáció 3beta verziójának kritériumrendszerét figyelembe véve osztályoztuk a betegek fejfájását<sup>1</sup>. Ezek alapján 43 (74,1%) beteg jelzett fejfájást, amelyek közül 27 (62,8%) elsődleges és 16 (37,2%) másodlagos, azaz szimptomás fejfájás volt (**1. ábra**). Az elsődleges (n=27) fejfájások közül 19 (70,4%) beteg tenziós típusú fejfájásban, 8 (29,6%) beteg aura nélküli migrénben szenvedett, míg a trigeminalis autonóm céphalgiák csoportjába egy beteg sem tartozott (**2. ábra**). A tenziós típusú fejfájásos betegek (n=19) közül 17 (89,5%) episztodikus, 2 (10,5%) krónikus formát mutatott (**3. ábra**). Az életminőséget és a napi életvitelt tekintve a betegek 79,1%-át (n=34) enyhe-közepes mértékben zavarja fejfájása. Fejfájás megjelenésében nincs különbség a laparoszkópos és nyitott módszerrel operált, valamint a stomát viselő vagy nem viselő betegek esetében. A fejfájástól szenvedő betegek szignifikánsan magasabb pontszámot értek el a Rövid Betegségpercepció Kérdőíven a fejfájást nem panaszolókhöz viszonyítva ( $p=0,036$ ; Pearson- és Spearman-korreláció = -0,33).

## Megbeszélés

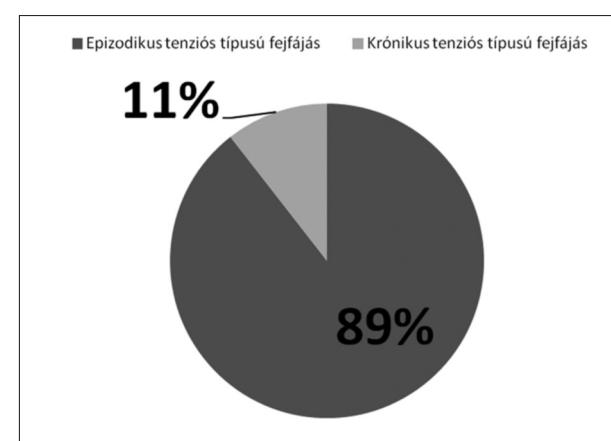
Jelen tanulmányunk Magyarországon elsőként vizsgálja a CU miatt sebészeti kezelésben részesülő betegek körében a fejfájás megjelenését. Eredményeink alapján a CU miatt operált személyekben fejfájást tekintve a tenziós típusú fejfájás jelent meg leggyakrabban, mint elsődleges fejfájásforma. Életminőségüket enyhe-közepes mértékben zavarta a napi életvitelük során. A Rövid Betegségpercepció Kérdőív eredményei alapján az alapbetegséggel járó rosszabb hangulati állapotot a fejfájás tovább rontotta. A tenziós típusú fejfájás kialakulásában elsődleges szerepet tulajdonítanak a stressznak és a pszichés feszülésnek<sup>12, 13</sup>. Ezenfelül a krónikus tenziós típusú fejfájás megjelenése nagymértékben függ a napi lelki traumák gyakoriságától, súlyosságától, valamint az anxietastól<sup>14</sup>. A tenziós típusú fejfájásban szenvedő betegek nehezebben tudják az emociójukat kifejezni és a maladaptív „coping” is gyakoribb<sup>12, 15</sup>. A tenziós típusú fejfájás negatívan befolyásolja az életminőséget<sup>16</sup>.



**1. ábra.** Elsődleges és másodlagos fejfájások megoszlása a műtött colitis ulcerosás betegek körében



**2. ábra.** Elsődleges fejfájástípusok megoszlása a műtött colitis ulcerosás betegek körében



**3. ábra.** Tenziós típusú fejfájásformák megoszlása a műtött colitis ulcerosás betegek körében

Széles körű vizsgálatok alapján igazolást nyert, hogy IBD-ben, így CU-ban szenvedő betegeknél az anxietas és a depresszió igen magas prevalenciával fordul elő<sup>17</sup>. Továbbá igazolt az is, hogy visszatérő vagy elhúzódó stresszel járó események az IBD fel-



lángolását idézik elő<sup>3</sup>. Állatkísérletes megfigyelések a környezeti tényezők stresszként történő megváltozását a CU-szerű colitis oki tényezőjének írták le<sup>18</sup>. Humán megfigyelések alapján a táplálkozás, bizonyos gyógyszeres kezelés (antibiotikumok, D-vitamin, ösztrogéntartalmú hormonális fogamzásgátlók, nem szteroid gyulladásgátlók) rizikótényezőnek számít a CU megjelenésében és gyakori kiújulásában<sup>19, 20</sup>. Kiemelendő, hogy az antioxidánsok táplálékkal történő bevitele kedvező hatást mutatott<sup>21</sup>, míg a nyugat-európai életstílussal járó táplálkozási szokások kártékonyak az IBD vonatkozásában<sup>22</sup>. A stressz feltételezhetően a hypothalamus-hypophysis-mellékvese tengelyen, az autonóm idegrendszer bevonásával játszik szerepet az IBD patogenezisében. Erre utal az is, hogy az emocionális megbetegedések incidenciája kiemelkedően magas CU-ban az átlagpopulációhoz viszonyítva. Ezenfelül az anxietas és a depresszió foka kifejezetten befolyásolja a CU súlyosságát<sup>23</sup>. A neuropeptidek, elsősorban a P-anyag (SP) szerepére a CU

kialakulásában kísérletes bizonyítékok utalnak. Az SP a tachykininek csoportjába tartozik, receptora a neurokinin 1 (NK1). Megfigyelések alapján NK1-receptor-antagonisták a colitis tüneteket jelentősen mérséklik<sup>24</sup>.

## Megbeszélés

Felmérésünk szerint a tenziós típusú fejfájás a CU-ban szenvedő betegek között gyakori. Ez felveti a két körforma között a stressznek mint kóroki tényezőnek a szerepét, mely nagymértékben befolyásolja és rontja a betegek életminőségét. A fentiek alapján megfontolandó a CU-ban szenvedő populáció neurológiai kivizsgálása, szükség szerint pszichiátriai, pszichológiai gondozása.

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*Köszönjük dr. Csáti Anettnek hasznos és kritikus tanácsait.*

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## ERRATUM

Az Ideggyógyászati Szemle 2017. július 29-én megjelent 7–8. összevont számában a 279. oldalon található 2A ábra ábraaláírása hibásan jelent meg. A RÁCZ Lilla, BERÉNYI Ervin, BARSI Péter, BERNÁTH Dávid, CSÉPÁNY Tünde: *Előnyös a másodvonalmi immunmoduláns kezelés sclerosis multiplexben?* című közlemény [Ideggyogy Sz 2017;70(7–8):275–283.] 2A ábra ábraaláírása helyesen (a javított szövegrész félkövérrel jelölve): **Azathioprin és intramuscularis interferon-β1a mellett is aktív állapotot követően négy évig, a terhesség kialakulásáig alkalmazott natalizumabkezelés mellett a betegséget aktivitásmentes állapot jellemzi.**