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Laparoscopic Surgery for the Treatment of Rectal Cancer: Short-Term Results

A. Fetti[1], F. Zaharie[1], M. Geza[1], F. Graur[1], R. Scurtu[2], R. Seiceanu[2], V. Bințințan[2], R. Motocu[2], T. Mocanu[3], L. Fetti[4], C. Ciuce[2], C. Iancu[1]

[1]Regional Institute of Gastroenterology and Hepatology "Prof. Dr. Octavian Fodor", UMF "Iuliu Haţieganu" Cluj-Napoca, Romania
[2]Surgery Department I, UMF "Iuliu Haţieganu" Cluj-Napoca, Romania
[3]Department of Physiology, UMF "Iuliu Haţieganu" Cluj-Napoca, Romania
[4]Cranio-Maxillo-Facial Surgery Department II, UMF "Iuliu Haţieganu" Cluj-Napoca, România

Rezumat

Tratamentul cancerului de rect prin abord laparoscopic: rezultate postoperatorii imediate

Scopul acestui studiu a fost de a stabili eficienţa, siguranţa şi fezabilitatea chirurgiei laproscopice în tratamentul cancerului de rect, prin evaluarea rezultatelor pe termen scurt.
Material şi metodă: În acest studiu clinic prospectiv au fost incluşi 60 de pacienţi cu cancer de rect trataţi prin abord laparoscopic în perioada 2008-2011 în Institutul de Gastroenterologie şi Hepatologie, Departamentul Chirurgie Generală şi Clinica Chirurgie I, Cluj-Napoca.
Rezultate: Intervenţiile chirurgicale efectuate au fost reprezentate de 38 de amputaţii de rect, 21 de rezecţii anterioare de rect şi 1 rezecţie tip Hartmann. Pierderile sanguine au fost în medie de 250 ml (100-800 ml) iar durata medie de spitalizare a fost de 9 zile (4-91 zile). Pierderile sanguine au fost mai mari la pacienţii cu cancer de rect inferior faţă de cei cu cancer situat la nivelul rectului superior (300 ml vs 200 ml, p=0.031). Conversia a fost necesară la 8 pacienţi (13.3%). Rata globală a complicaţiilor postoperatorii a fost de 28.8%. Marginile circumferenţiale de rezecţie au fost pozitive la 1 pacient (1.7%) iar marginile distale de rezecţie au fost negative la toţi pacienţii.
Concluzii: Chirurgia laparoscopică este sigură şi fezabilă în tratamentul cancerului de rect, la pacienţi selecţionaţi, cu rezultate postoperatorii imediate favorabile.

Cuvinte cheie: chirurgie laparoscopică, cancer de rect, rezultate postoperatorii imediate

Corresponding author: Asist. univ. Dr. Alin Fetti
UMF "Iuliu Haţieganu" Cluj-Napoca
Regional Institute of Gastroenterology and Hepatology "Prof. Dr. Octavian Fodor"
Croitorilor Street, no. 19-21, 400162
Cluj-Napoca, Romania
Tel: 0264-432022
E-mail: alin.fetti@yahoo.com

Abstract

The aim of this study was to establish the efficiency, safety and feasibility of laparoscopic surgery for rectal cancer by assessing the short-term outcomes.
Materials and methods: In this prospective clinical study, from 2008 to 2011, 60 patients with laparoscopic resection for rectal cancer were included, treated in "Prof. Dr. Octavian Fodor" Gastroenterology and Hepatology Institute, Department of Surgery and Surgery Clinic I, Cluj-Napoca.
Results: Surgical procedures included 38 abdominal-perineal resections, 21 anterior resections and 1 Hartmann procedure. Average blood loss was 250 ml (100-800 ml) and median length of postoperative hospital stay was 9 days (4-91 days). Blood loss was significantly higher in patients with low rectal cancer than those with upper rectal cancer (300 ml vs 200 ml, p=0.031). Conversion to open surgery was required in 8 patients (13.3%). Overall postoperative complications were 28.8%. Positive

circumferential margins occurred in 1 patient (1.7%), while distal margins were negative in all patients.
Conclusions: Laparoscopic surgery is safe and feasible in selected patients with rectal cancer, with favorable short-term results.
Key words: laparoscopic surgery, rectal cancer, short-term results

Introduction

Minimally-invasive surgical techniques have revolutionized abdominal surgery in the last decade. Laparoscopic surgery has been widely accepted as a treatment method for various benign gastrointestinal diseases, but its use in treating malignant ones is still controversial.

The first colorectal laparoscopic procedure was reported in 1991 (1). In our country, the first laparoscopic abdominal-perineal resection and anterior rectal resection were reported in 1995 (2) and 1996 (3), whereas the first review regarding laparoscopic surgery for rectal diseases was published in 1994 (4). Although this procedure was one of the most important innovations in the surgical field at that time, its use in the treatment of colorectal cancer was limited due to the concerns regarding adequate lymphadenectomy, oncological resection with optimal safety margins as well as the risk of developing metastases at the port site and the lack of long-term results (5,6).

As a result, The National Institute for Clinical Excellence in London declared in 2000 that open surgery is preferred in the treatment of colorectal cancer and the laparoscopic approach should only be used in randomized controlled trials (7). However, recent results of some randomized controlled trials on large number of patients such as COST, COLOR and CLASSIC contradict this statement and claim that laparoscopic surgery in the treatment of colorectal cancer is oncologically safe and feasible with favorable short-term results (8,9,10).

Based on the results of these clinical trials, The American Society of Colorectal Surgeons (ASCRS), approved the use of laparoscopic surgery in the treatment of colorectal cancer for selected patients starting with 2004 (11).

There is still a lot of debate concerning the advantages of laparoscopic surgery in the treatment of colorectal cancer, with contradictory opinions regarding the topic in the field.

Colon cancer is significantly different from rectal cancer from many points of view. It is difficult even for an experienced surgeon to perform a laparoscopic total mesorectal excision and a colorectal anastomosis in a narrow pelvis (12). Most randomized controlled trials did not include patients with rectal cancer located at 15 cm or less from the anal verge because of the technical difficulties in using the laparoscopic approach for these patients (8,9).

The only randomized controlled trial on a large number of patients that included patients with rectal cancer is the CLASSIC trial. The results of this trial concluded that routine laparoscopic surgery in the treatment of colorectal cancer is not justified. It should only be used for carefully selected patients (10).

Excellent oncological results were obtained by total mesorectal excision in open surgery with a recurrence rate of less than 5% for anterior rectal resection (13).

Therefore, it still has to be proven whether laparoscopic rectal surgery can achieve similar oncological results with all the advantages of laparoscopic surgery for the colon.

Materials and Methods

In this prospective study 60 patients diagnosed with rectal cancer who underwent laparoscopic surgery between 2008 and 2011 at the Institute of Gastroenterology and Hepatology – General Surgery Department and Surgery Clinic I Cluj-Napoca were included. Patients hospitalized in emergency with bowel obstruction, patients who had undergone hand-assisted laparoscopic procedures, those with prior abdominal surgeries and those who refused the laparoscopic procedure were excluded from the study.

Most patients presented with stage T1 and T2 tumors and with an ASA score I and II but this study also included patients with stage T3 and T4 tumors who underwent preoperative radiation therapy as well as patients with high ASA score. In general, these categories of patients were excluded from most studies.

The location of the tumor was determined through the distance from the anal verge measured by rectosigmoidoscopy: lower third (1-7 cm), mid third (7.1-12 cm) and upper third (12.1-17 cm).

Preoperative staging included the following examinations: rectosigmoidoscopy, colonoscopy, endorectal ultrasound, abdominal computed tomography and chest X-ray.

11 patients (18.3 %) underwent preoperative radiochemotherapy or only radiation therapy. Mechanical bowel preparation with PEG (polyethylene glycol) was used for 35 patients. Deep vein thrombosis prophylaxis was ensured and antibiotics were administered routinely.

Most surgeries were performed using 5 surgical trocars (two or three 5 mm trocars, a 10 mm port and one or two 12 mm port). After exposing the sigmoid colon, the inferior mesenteric pedicle was identified and ligated, whereas the extent of the lymph node dissection was dictated by the oncological parameters. The mobilization of the splenic flexure and of the descending colon was decided by the surgeon in charge. The rectal dissection advanced along the avascular plane between the rectal fascia and the presacral fascia; preserving this plane is of crucial importance for the total mesorectal excision. Total mesorectal excision was performed for tumors located in the lower and mid third of the rectum whereas for the tumors located in the upper third a partial mesorectal excision was performed with a 5 cm resection margin from the tumor. In anterior rectal resections, the rectum was divided laparoscopically using linear staplers or by inserting the stapler through a suprapubic minilaparotomy which was also used to extract the specimen. In laparoscopic abdominoperineal resection, the specimen was extracted through the perineal incision. A

diverting ileostomy was performed in the cases in which the anastomosis wasn't considered to be totally safe. Conversion to open surgery was defined as an unplanned and longer incision than is routinely performed.

The clinical data analyzed were represented by gender, age, body mass index (BMI), ASA score, type of surgical procedure, tumor site, the distance between the tumor and the resection margins, distal and circumferential margins, number of lymph nodes removed, pTNM staging.

The data regarding the surgical procedure and the postoperative outcomes were represented by the duration of the surgical procedure, blood loss, conversion to open surgery and the reasons for conversion, time to first flatus, time until resumption of liquid and semisolid intake, postoperative hospital stay, postoperative complications and 30 day mortality rate.

Chi Square/Fisher exact tests were used for the statistical analysis of qualitative variables. Continuous numeric parameters were analyzed using the Student/Mann-Whitney test in relation to the normal distribution data, previously tested with the Kolmogorov-Smirnov test. In order to detect independent risk impact variables, univariate analysis was completed by multivariate analysis such as multiple linear regression and calculating the Beta standardized coefficient, by its confidence interval (95%) and statistical significance. The $p < 0.05$ limit of statistical significance was used for all tests applied. SPSS 17.0 (Chicago, Il, SUA) was used for the statistical analysis of the data.

Results

Between 2008 and 2011, 60 patients diagnosed with rectal cancer underwent laparoscopic resections. *Table 1* presents the patients' epidemiological features. 11 patients underwent preoperative radiation therapy. Most patients presented with tumors located in the lower rectum (55%).

Table 1. *Epidemiological features*

Number of patients	60
Gender (male/female)	44(73.3%)/16(26.7%)
Age (years)[1]	60.33 ± 9.43
BMI (kg/m^2)[1]	25.63 ± 3.47
ASA	
I	7(11.7%)
II	40(66.7%)
III	13(21.7%)
Tumor location	
Upper rectum	11 (18.3%)
Mid rectum	16 (26.7%)
Lower rectum	33 (55%)
Preoperative radiation	11 (18.3%)
TNM stage	
I	22 (36.7%)
II	16 (26.6%)
III	18 (30%)
IV	4 (6.7%)

[1]Values are mean ± standard deviation

Table 2. *Operative details and histopathological characteristics*

Type of procedure	
Abdominoperineal resection	38 (63.3%)
Anterior rectum resection with colorectal/ coloanal stapled anastomosis	18 (30%)
Anterior rectum resection with colorectal/ coloanal hand-sewn anastomosis	3 (5%)
Hartmann's procedure	1 (1.7%)
Diverting ileostomy	6 (10%)
Duration of surgery (min)[1]	300 (180-480)
Blood loss (ml)[1]	250 (100-800)
Conversion	8 (13.3%)
Tumor distance from distal margin (cm)[1]	3.4 (1-11)
Distal resection margin involved	0 (%)
Circumferential resection margins involved	1 (1.7%)
Number of lymph nodes retrieved[1]	10.5 (2-35)
Histopathologic lymph nodes stage	
N0	38 (63.4%)
N1	10 (16.7%)
N2	12 (20.1%)

[1]Values are median (range)

Aspects regarding the surgical procedure and histopathological characteristics are shown in *Table 2*. 38 patients (63.3%) underwent abdominoperineal resection, in 21 patients (35%) anterior resection of the rectum was performed and 1 patient (1.7%) underwent a Hartmann procedure. A diverting ileostomy was required in 6 patients (10%) whereas conversion to open surgery was performed for 8 patients (13.3%). The most frequent cause for conversion was the presence of a large tumor as seen in 3 patients (5%), followed by the presence of a locally advanced tumor in 2 patients (3.3%), an anatomically narrow pelvis associated with important visceral adiposity seen in 2 patients (3.3%), intraoperative bleeding generated by injury of the presacral veins in one patient (1.7%). Intraoperative complications occurred in 6 patients (10%), whereas the most common one was the hemorrhage that occurred in 4 cases. Distal resection margins were negative for all patients whereas the circumferential margins were positive in one patient (1.7%) who underwent abdominoperineal resection. The average number of lymph nodes retrieved was 10.5 (2-35 lymph nodes).

Univariate and multivariate analysis of the factors that influence blood loss, the duration of the surgical procedure and hospital stay are shown in *Tables 3, 4, 5*.

Blood loss was significantly less for patients with upper rectal cancer as compared to those with low rectal cancer (200 vs 300 ml; p=0.031). The duration of the surgical procedure was shorter for the patients with upper rectal cancer, but with no statistical significance (240 vs 300 min; p=0.595).

The average hospital stay was 9 days (4-91 days). A shorter hospital stay was registered in the patients with upper rectal cancer as compared to those with low rectal cancer, but with no statistical significance (6 vs 10 days; p = 0.595).

In cases that required conversion to open surgery, blood loss was significantly higher than in those cases that did not require conversion (375 vs 250 ml; p=0.022). The same results

Table 3. *Univariate and multivariate analysis of the factors that influence blood loss*

Univariate			Multivariate		
Factors	**Blood loss (ml)[1]**	**p**	**Beta**	**CI 95%**	**p**
Preoperative radiation		0.60			
present	250(100-350)				
absent	250(100-800)				
Tumor location		0.031	0.2	12.1-102.3	0.120
upper rectum	200(100-300)				
lower rectum	300(100-800)				
Conversion		0.022	0.3	01-170.4	0.043
present	375(200-800)				
absent	250(100-800)				
TNM stage		0.942			
I/II	250(100-800)				
III/IV	250(100-800)				
Gender		0.164			
male	250(100-800)				
female	250(100-400)				
Age		0.053	0.02	-28.3-35.1	0.829
<60 years	240(100-800)				
>60 years	300(100-800)				
ASA score		0.240			
I/II	250(100-800)				
III/IV	300(100-800)				
Body mass		0.143			
normal	250(100-800)				
overweight/obese	250(200-800)				
Intraoperative complications		0.001	0.6	188.9-384.4	0.001
present	600(300-800)				
absent	250(100-500)				

[1]Values are median (range)

Table 4. *Univariate and multivariate analysis of the factors that influence duration of the surgical procedure*

Univariate			Multivariate		
Factors	**Duration of surgery (min)[1]**	**p**	**Beta**	**CI 95%**	**p**
Preoperative radiation		0.019	3.5	48.1-210.8	0.001
present	420(90-480)				
absent	250(90-480)				
Tumor location		0.595			
upper rectum	240(180-420)				
lower rectum	300(150-480)				
Conversion		0.006	3.5	56.8-210.8	0.001
present	420(210-480)				
absent	260(90-480)				
TNM stage		0.236			
I/II	300(90-480)				
III/IV	210(90-480)				
Gender		0.743			
male	300(90-480)				
female	260(90-480)				
Age		0.841			
<60 years	270(150-480)				
>60 years	300(90-480)				
ASA score		0.745			
I/II	300(90-480)				
III/IV	270(150-480)				
Body mass		0.200			
normal	240(90-480)				
overweight/obese	300(90-480)				
Intraoperative complications		0.147			
present	420(180-480)				
absent	285(90-480)				
Diverting ileostomy		0.063	0.2	-23.9-147.5	0.154
present	360(300-480)				
absent	260(90-480)				

[1]Values are median(range)

Table 5. *Univariate and multivariate analysis of the factors that influence hospital stay*

Univariate			Multivariate		
Factors	**Hospital stay (days)[1]**	**p**	**Beta**	**CI 95%**	**p**
Preoperative radiation		0.019	-0.03	-8.9-6.9	0.811
present	8(5-21)				
absent	9(4-91)				
Tumor location		0.595			
upper rectum	6(4-10)				
lower rectum	10(5-91)				
Conversion		0.006	-0.02	-9.8-8.2	0.854
present	10(7-21)				
absent	8(4-91)				
TNM stage		0.236			
I/II	8.5(4-91)				
III/IV	9.5(5-21)				
Gender		0.743			
male	8.5(4-91)				
female	9.5(5-24)				
Age		0.841			
<60 years	9(4-21)				
>60 years	9(5-91)				
ASA score		0.745			
I/II	8(4-24)				
III/IV	19(5-91)				
Body mass		0.031	0.2	1.4-10.8	0.030
normal	8(4-26)				
overweight/obese	9.5(6-91)				
Intraoperative complications		0.147			
prezente	11(7-91)				
absente	8(4-26)				

[1]Values are median (range)

were registered regarding the duration of the procedure (420 vs 260 min; p=0.006) and hospital stay (10 vs 8 days; p=0.006) in patients that required conversion than in those cases in which the procedure was completed laparoscopically.

Patients who underwent preoperative radiation therapy did not present higher blood loss than those who did not require this kind of therapy (250 ml vs 250 ml; p=0.60), but the duration of the surgical procedure was significantly longer for this patients (420 vs 250 min; p=0.019).

Data regarding the postoperative outcomes are presented in *Table 6*. Surgical and non-surgical postoperative complications were registered in 17 patients (28.8%) with 7 patients (11.7%) requiring surgical reintervention.

Hemorrhage was the most common postoperative complication with an incidence of 6.7%. The incidence of anastomotic leakage was 4.6 %. One patient who underwent a laparoscopic retrograde cholecystectomy simultaneously with the laparoscopic procedure for rectal cancer presented bile leakage in the drain which was treated with ERCP and sphincterotomy. The postoperative 30 day mortality rate was 0%.

The independent prediction factors associated with increased blood loss are represented by conversion to open surgery and intraoperative complications (*Table 3*). Preoperative radiation therapy and conversion to open surgery are independent prediction factors for higher duration of the surgical procedure (*Table 4*), whereas obesity is the independent prediction factor associated with prolonged hospital stay. (*Table 5*)

Discussions

In most studies, obese patients, patients with high ASA score and those with large or locally advanced tumors are usually excluded. In this study, favoring selection of patients with normal body mass, with early stage tumors and without associated conditions has been avoided. More than two thirds of the patients included in this study had an ASA score II or III, the average BMI (body mass index) was over 25 and more than half of the patients presented with stage II or III tumors.

In this study, more than half of the patients presented with tumors situated in the lower rectum. Treatment means and surgical techniques for these kinds of tumors are more complex than for those situated in the upper third of the rectum (14).

Preoperative radiation therapy was indicated in 11 patients in the present study. Preoperative radiation ensures a better local control, reducing the rate of local recurrence. It has been shown to downstage and downsize the disease which increases the rate of radical surgery with the possibility of sphincter preservation for the patients with tumors located in the lower rectum (15,16).

A diverting ileostomy was required in 6 patients in this study. However, some surgeons routinely fashion a diverting ileostomy for laparoscopic anterior resections for rectal cancer (17). The presence of a diverting ileostomy does not prevent the development of an anastomotic leakage, but it prevents its negative effects.

Table 6. *Postoperative outcomes*

Time to first flatus (days)[1]	2 (1-8)
Time to resumption of liquid and semisolid intake (days)[1]	2 (1-4)
Hospital stay (zile)[1]	9 (4-91)
Postoperative complications	17 (28.8%)
Type of postoperative complications	
Wound infection	3 (5%)
Bleeding	4 (6.7%)
Prolonged postoperative ileus	2 (3.3%)
Acute urine retention	2 (3.3%)
Anastomotic leakage[2]	1 (4.76%)
Compartment syndrome	2 (3.3%)
Bowel obstruction	1 (1.7%)
Bile leakage	1 (1.7%)
Ischemic stroke	1 (1.7%)
Reintervention for postoperative complications	7 (11.7%)
Mortality	0 (0%)

[1]Values are median (range)

[2]Patients undergoing Hartmann's procedure or abdominoperineal resection were excluded

Conversion to open surgery was required in 8 patients (13.3%) in this study. This conversion rate was also registered in recent randomized controlled trials 11-29% (18). For patients who required conversion to open surgery, the duration of the procedure and blood loss were higher than for those cases in which the procedure was completed laparoscopically. Other studies reported similar results (19,20). Conversion to open surgery led to a longer hospital stay with two days. These data are in accordance with those reported by the multicenter CLASSIC trial (10).

The incidence of positive circumferential margins was 1.7%, whereas the incidence of positive distal resection margins was 0%. The mean distance between the tumor and the distal resection margin was 3.4 cm in this study. These data are in accordance with those reported by other studies, that is a 5% incidence of positive circumferential margins, 1% positive distal resection margins and a 4 cm distance between the tumor and the distal resection margin (21).

The average hospital stay was 9 days in the present study, in accordance with the results reported by the CLASSIC trial, with an average hospital stay of 10 days (10).

The higher blood loss registered in this study, of 250 ml, compared to studies reported by other authors of 200 ml (22), is explained by the fact that more than half of the tumors were located in the lower third of the rectum. Surgical procedures are usually associated with significantly higher blood loss for this location of the tumors as compared to those situated in the upper part of the rectum (22).

Patients with tumors located in the upper rectum presented a shorter duration of the surgical procedure, reduced blood loss and shorter hospital stay. Similar results were reported by other authors as well (22,23).

The duration of the surgical procedure was longer for patients who underwent preoperative radiation therapy as compared to those who underwent surgery alone. However blood loss was similar in the two groups. These data are in accordance with the data reported in the medical literature (24,25). The longer surgical procedure time registered with those patients who underwent preoperative radiation therapy is due to increased tissue edema and vascularity associated with pelvic irradiation, both enhancing the technical difficulties of surgical procedures. Other authors reported similar results (26).

The overall postoperative complication rate was 28.8% in this study. The incidence of anastomotic fistula was of 4.76 %. Authors like Miyajima N. reported a similar complication rate of 26% and the most frequent complication reported in his study was anastomotic leakage, but with a higher incidence of 9.1% than reported in this study (23). The CLASSIC trial reported a complication rate of 39 % for patients diagnosed with rectal cancer who underwent laparoscopic surgery (10).

Drawing some conclusions based on this study is marked by the need of a cautious vision in the absence of long-term results that require further studies.

Conclusions

Laparoscopic surgery represents a safe approach for the treatment of rectal cancer with a postoperative morbidity and mortality rate in accordance with the data in the medical field.

Laparoscopic surgery for rectal cancer is oncologically feasible ensuring an adequate lymphadenectomy as well as the integrity of distal and circumferential resection margins with potential good long-term oncological results.

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