

Rectal cancer: factors predicting short outcomes after radical anterior resection



Ann. Ital. Chir., 2017 88, 6: 505-513
pii: S0003469X17027257

George Ciorogar^{*/**}, Adrian Bartos^{*/**}, Dana Bartos ^{*/**}, Ștefan Cristian Vesa^{***}, Miana Pop^{*/**}, Andrei Herdean^{*/**}, Iulia Beta^{**}, Anca Ciorogar^{*}, Emil Mois^{*/**}, Florin Zaharie^{*/**}, Cornel Iancu^{*/**}

**University of Medicine and Pharmacy "Iuliu Hațieganu" Cluj-Napoca*

***Regional Institute of Gastroenterology and Hepatology "Octavian Fodor" Cluj-Napoca*

****Department of Pharmacology, Toxicology and Clinical Pharmacology, "Iuliu Hațieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania*

Rectal cancer: risk factors predicting short outcomes after radical anterior resection

AIM: *This study analyzes risk factors implicated in postoperative complications and mortality after anterior resection in rectal cancer.*

MATERIAL AND METHODS: *A total number of 378 patients with anterior rectal resection, diagnosed with rectal cancer and admitted at the IIIrd Surgery Clinic, "Octavian Fodor" Regional Institute of Gastroenterology and Hepatology, Romania, between 2009 and 2016. The inclusion criteria were anterior rectal resections with curative visa for rectal cancer. The complications we assessed are the following: anastomotic fistula, intra-abdominal infections, postoperative bowel obstruction and wound infection.*

RESULTS: *There was statistical significance regarding male gender, emergency hospitalization, hypoproteinemia and the resumption of intestinal transit. Anterior rectal resection of tumors located on the middle rectum was associated with high rate of anastomotic fistula. Patients with manual suture of anastomosis developed intraabdominal abscess more frequently. In the multivariate analysis, hypoproteinemia and a number of lymph nodes >1 remained independently associated with the occurrence of wound infection. The 30-day mortality rate was 4.8% with 18 deaths and morbidity rate 20.6% with 78 cases.*

CONCLUSIONS: *Major complications after radical resection for rectal cancer are dependent on multiple variables such as male patients, those admitted in emergency and patients with hypoproteinemia. Location of tumor on middle rectum, manual suture of anastomosis, number of lymph nodes > 1 were associated with high rate of morbidity. Patients with coronary heart disease and diabetes mellitus didn't had statistical significance, but the rate of morbidity and mortality remains high in this groups.*

KEY WORDS: Complications, Radical anterior resection, Rectal cancer, Risk factors

Introduction

Statistics show that an estimated 600,920 Americans will die from cancer in 2017, which means a striking 1,650

deaths every day. Most frequently, cancer mortality is related to either lung and bronchus or colorectal tumors. Every year, the American Cancer Society estimates 39,910 newly diagnosed rectal cancer patients. However, despite these numbers that remain alarming, the death rate for colorectal cancer has decreased by 51% during 1976 and 2014 ¹.

Rectal cancer ranks among the top three cancers in Romania and second and third in incidence as cancer mortality ². Also, in Romania, mortality rates due to colorectal cancer have increased by 2.9% per year during 1985-2005 ³.

Pervenuto in Redazione Aprile 2017. Accettato per la pubblicazione Giugno 2017

Correspondence to: Adrian Bartos, University of Medicine and Pharmacy "Iuliu Hațieganu" Cluj-Napoca, Regional Institute of Gastroenterology and Hepatology "Octavian Fodor" Cluj-Napoca (e-mail: bartos.adi@gmail.com)

Perioperative morbidity in rectal cancer decreases the quality of life, increases hospitalization costs, delays the initiation of adjuvant therapy and, on the long-term, it is a negative prognostic factor ⁴. Both in the United States and in Western Europe, surveillance programs that detect incipient cancer have been developed and neoadjuvant therapy has gained a very important role in cancer treatment. As a result, the rate of rectal cancer has decreased and survival rates have risen. Unfortunately, this is not the case with Eastern Europe, where mortality continues to increase ^{5,6}. Worldwide, the overall rate of morbidity is 20 to 40% and the postoperative rate for mortality is 5% ^{7,8}. This project aims to evaluate the risk factors involved in both morbidity and mortality related to rectal cancer. Particularly, our focus is on rectal tumors treated with anterior rectal resections and risk factors implicated in postoperative complications and mortality.

Material and Methods

A longitudinal, observational, analytical, retrospective, cohort study was conducted on patients diagnosed with rectal cancer and admitted at the IIIrd Surgery Clinic, "Octavian Fodor" Regional Institute of Gastroenterology and Hepatology, Romania, between 2009 and 2016. From a total of 739 patients we selected 378 patients with anterior rectal resection. The study was approved

by the ethics committee of the hospital. Patients were included in the study after signing informed consent. The inclusion criteria were anterior rectal resections with curative visa for rectal cancer. Exclusion criteria were Miles resection, Hartman resection and palliative surgery. The complications we assessed are the following: anastomotic fistula, intra-abdominal infections, postoperative bowel obstruction and wound infection.

The following parameters were assessed: gender; diameter of tumor; location of tumor; admission; T stage; open versus laparoscopic approach, hypoproteinemia, anemia, blood loss, anastomotic suture sewn by hand or mechanical staplers, protective stoma, comorbidities at admission, such as coronary heart disease and diabetes mellitus; resumption of feeding and intestinal function.

The establishment of the tumoral stage was based on several parameters, such as the physical examination, imagery findings, the intraoperative macroscopic aspect and histopathology results.

The treatment of rectal cancer in these patients consisted of anterior rectal resection performed either conventionally or laparoscopically. Protective stoma was performed in patients with neoadjuvant treatment, loose tissue or a positive hydroaeric test during surgery.

The statistical analysis was performed using MedCalc Statistical Software version 17.4 (MedCalc Software bvba, Ostend, Belgium; <http://www.medcalc.org>; 2017). Continuous data were analyzed for normality of distribution using Kolmogorov-Smirnov test, and were char-

TABLE I - Postoperative complications.

Parameter		Without complication (n=300)	With complication (n=78)	P
Gender	Female	118 (39.3%)	22 (28.2%)	0.09
	Male	182 (60.7%)	56 (71.8%)	
Diabetes mellitus		29 (9.7%)	10 (12.8%)	0.4
Coronary heart disease		92 (30.7%)	27 (34.6%)	0.5
Admission	Emergency	24 (8%)	12 (15.4%)	0.05
	Appointment	276 (92%)	66 (84.6%)	
Location	Inferior Rectum	37 (12.3%)	9 (11.5%)	0.1
	Middle Rectum	123 (41%)	41 (52.6%)	
	Superior Rectum	140 (46.7%)	28 (35.9%)	
Hypoproteinemia	25 (8.8%)	20 (26%)	<0.001	
Approach	Conventional	267 (89%)	73 (93.6%)	0.3
	Laparoscopic	33 (11%)	5 (6.4%)	
Suture	Manual	194 (72.9%)	50 (69.4%)	0.6
	Mechanical	72 (27.1%)	22 (30.6%)	
T >2 (extent of tumor)		113 (46.5%)	27 (41.5%)	0.5
N >1 (lymph nodes)		134 (55.1%)	41 (63.1%)	0.3
Tumor diameter (centimeters)		5 (4; 6)	4 (3.3; 6)	0.5
Blood loss		200 (150; 300)	300 (200; 500)	0.007
Resuming food ingestion (days)		2 (2; 3)	2 (1; 3)	0.9
Resuming bowel transit (days)		3 (2; 3)	3 (2; 4)	0.01

acterized by median and 25-75 percentiles. Qualitative variables were described using the frequency and percent. Comparison between groups, regarding continuous variables, was performed using Mann-Whitney test. Differences between groups, regarding nominal data was performed using chi-square test or Fisher test, when appropriate. Survival analysis was carried out using Kaplan-Meier curve. Multivariate analysis was carried on by logistic regression. A p value lower than 0.05 was considered statistically significant.

Results

Gender distribution was homogeneous between the two groups. We had 63% male patients and 37 % female with the mean age of 64 ± 10.4 years. The 30-day mortality rate was 4.8% with 18 deaths and morbidity rate 20.6% with 78 cases.

Male patients, those admitted in emergency and patients with hypoproteinemia were more likely to develop complications of any kind. Also, those who developed complications had important blood loss and resumed bowel movements more slowly (Table I). After the multivariate analysis, the following parameters remained independently associated with complications of any kind: the male gender (OR 1.8, CI95% 0.9-3.5; p = 0.05), emergency

hospitalization (OR 3.1, CI95% 1.3-7.6, p=0.008), hypoproteinemia (OR 2.7, CI95% 1.3-5.5; p=0.006) and the resumption of intestinal transit (OR 1.4, CI95% 1.1-1.8; p=0.008).

The relation between parameters and the presence of anastomotic fistula can be observed in Table II. It is noted that cancer of the superior rectum was significantly more rarely associated with anastomotic fistula (p=0.03). In contrast with inferior and superior rectal cancer, middle rectum has the highest risk of anastomotic fistula (p=0.03). Resumption of bowel transit was slower in those who developed anastomotic fistula (p=0.03). The male group and the mechanical sutures were associated with a higher risk of fistula, and this association was very close to statistical significance (p=0.1; p=0.1 respectively). At the multivariate analysis only cancer location preserved its independent character of factor associated with fistula. Thus, those patients developed fewer fistulas (OR 0.36; CI95% 0.14-0.89; p=0.02). From the total of 378 patients, 56 cases diagnosed with middle or inferior rectal cancer stage T3, N0 or T any, N1-2 following the protocol of NCCN (National Comprehensive Cancer Network), received neoadjuvant treatment in the form of chemoradiotherapy (CRT). The surgical operation was performed 6 to 8 weeks after the end of the neoadjuvant treatment. From the total cases that performed CRT, 21 cases had protective ileostomy. In total, we had 84 pro-

TABLE II - Anastomotic fistula

Parameter		Without fistula (n=349)	With fistula (n=29)	P
Gender	Female	133 (38.1%)	7 (24.1%)	0.1
	Male	216 (61.9%)	22 (75.9%)	
Location	Inferior Rectum	43 (12.3%)	3 (10.3%)	0.03
	Middle Rectum	145 (41.5%)	19 (65.5%)	
	Superior Rectum	161 (46.1%)	7 (24.1%)	
Approach	Conventional	313 (89.7%)	27 (93.1%)	0.7
	Laparoscopic	36 (10.3%)	2 (6.9%)	
T >2 (extent of tumor)		129 (45.4%)	11 (45.8%)	1
N >1 (lymph nodes)		163 (57.4%)	12 (50%)	0.6
Suture	Manual	227 (73.5%)	17 (58.6%)	0.1
	Mechanical	82 (26.5%)	12 (41.4%)	
Hypoproteinemia		41 (12.3%)	4 (13.8%)	0.7
Admission	Emergency	32 (9.2%)	4 (13.8%)	0.5
	Appointment	317 (90.8%)	25 (86.2%)	
Diabetes mellitus		35 (10%)	4 (13.8%)	0.5
Coronary heart disease		112 (31.1%)	7 (24.1%)	0.4
Resuming food ingestion (days)		2 (2; 3)	2 (1; 3)	0.2
Blood loss		200 (150; 300)	200 (200; 400)	0.8
Resuming bowel transit (days)		3 (2; 3)	3 (2.5; 4)	0.03
Tumor diameter (centimeters)		5 (4; 6)	4 (2.5; 6.5)	0.4
Ileostomy		82(23%)	2(6.8%)	0.04

TABLE III - *Intraabdominal abscess*

Parameter		Without intraabdominal abscess (n=371)	With intraabdominal abscess (n=7)	P
Gender	Female	139 (37.5%)	1 (14.3%)	0.2
	Male	232 (62.5%)	6 (85.7%)	
Location	Inferior Rectum	46 (12.4%)	-	0.5
	Middle Rectum	160 (43.1%)	4 (57.1%)	
	Superior Rectum	165 (44.5%)	3 (42.9%)	
Approach	Conventional	333 (89.8%)	7 (100%)	0.7
	Laparoscopic	38 (10.2%)	-	
T >2 (extent of tumor)		136 (44.9%)	4 (80%)	0.1
N >1 (lymph nodes)		173 (57.1%)	2 (40%)	0.6
Suture	Manual	237 (71.6%)	7 (100%)	0.03
	Mechanical	94 (28.4%)	-	
Hypoproteinemia		44 (12.4%)	1 (14.3%)	1
Admission	Emergency	36 (9.7%)	-	1
	Appointment	335 (90.3%)	7 (100%)	
Diabetes mellitus		39 (10.5%)	-	1
Coronary heart disease		116 (31.3%)	3 (42.9%)	0.6
Resuming food ingestion(days)		2 (2; 3)	2 (1.5; 2)	0.4
Blood loss		200 (150; 300)	200 (200; 500)	0.2
Resuming bowel transit		3 (2; 3)	3 (2; 4)	0.4
Tumor diameter (centimeters)		5 (4; 6)	4 (3; 6)	0.3

TABLE IV - *Wound infection*

Parameter		Without wound infection (n=344)	With wound infection (n=34)	P
Gender	Female	128 (37.2%)	12 (35.3%)	0.9
	Male	216 (62.8%)	22 (64.7%)	
Location	Inferior Rectum	43 (12.5%)	3 (8.8%)	0.4
	Middle Rectum	146 (42.4%)	18 (52.9%)	
	Superior Rectum	155 (45.1%)	13 (38.2%)	
Approach	Conventional	307 (89.2%)	33 (97.1%)	0.2
	Laparoscopic	37 (10.8%)	1 (2.9%)	
T >2 (extent of tumor)		128 (45.7%)	12 (42.9%)	0.9
N >1 (lymph nodes)		154 (55%)	21 (75%)	0.06
Suture	Manual	225 (73.1%)	19 (63.3%)	0.3
	Mechanical	83 (26.9%)	11 (36.7%)	
Hypoproteinemia		35 (10.7%)	10 (30.3%)	0.003
Admission	Emergency	32 (9.3%)	4 (11.8%)	0.5
	Appointment	312 (90.7%)	30 (88.2%)	
Diabetes mellitus		33 (9.6%)	6 (17.6%)	0.1
Coronary heart disease		108 (31.4%)	11 (32.4%)	1
Resuming food ingestion (days)		2 (2; 3)	2 (1; 3)	0.6
Blood loss		200 (150; 300)	300 (200; 500)	0.05
Resuming bowel transit (days)		3 (2; 3)	3 (2; 4)	0.1
Tumor diameter (centimetres)		5 (4; 6)	4 (3; 6)	0.4

TABLE V - Postoperative bowel obstruction

Parameter		Without bowel obstruction (n=376)	With bowel obstruction (n=2)	P
Gender	Female	140 (37.2%)	-	0.5
	Male	236 (62.8%)	2 (100%)	
Location	Inferior Rectum	46 (12.2%)	-	0.2
	Middle Rectum	162 (43.1%)	2 (100%)	
	Superior Rectum	168 (44.7%)	-	
Approach	Conventional	340 (90.4%)	-	0.01
	Laparoscopic	36 (9.6%)	2 (100%)	
T >2 (extent of tumor)		140 (45.8%)	-	0.4
N >1 (lymph nodes)		175 (57.2%)	-	0.1
Suture	Manual	244 (72.6%)	-	0.07
	Mechanical	92 (27.4%)	2 (100%)	
Hypoproteinemia	43 (12%)	2 (100%)	0.01	
Admission	Emergency	34 (9%)	2 (100%)	0.009
	Appointment	342 (91%)	-	
Diabetes mellitus		39 (10.4%)	-	1
Coronary heart disease		119 (31.6%)	-	1

TABLE VI - Mortality at 30 days after surgery

Parameter		Survivors (n=360)	Deceased (n=18)	P
Gender	Female	131 (36.4%)	9 (50%)	0.3
	Male	229 (63.6%)	9 (50%)	
Location	Inferior Rectum	43 (11.9%)	3 (16.7%)	0.6
	Middle Rectum	158 (43.9%)	6 (33.3%)	
	Superior Rectum	159 (44.2%)	9 (50%)	
Approach	Conventional	323 (89.7%)	17 (94.4%)	1
	Laparoscopic	37 (10.3%)	1 (5.6%)	
T >2		132 (45.1%)	8 (53.3%)	0.7
N >1		165 (56.3%)	10 (66.7%)	0.6
Suture	Manual	231 (71.7%)	13 (81.3%)	0.5
	Mechanical	91 (28.3%)	3 (18.8%)	
Hypoproteinemia		43 (12.5%)	2 (11.1%)	1
Admission	Emergency	34 (9.4%)	2 (11.1%)	0.1
	Appointment	326 (90.6%)	16 (88.9%)	
Diabetes mellitus		37 (10.3%)	2 (11.1%)	0.1
Coronary heart disease		110 (30.6%)	9 (50%)	0.1
Resuming food ingestion (days)		2 (2; 3)	2 (1; 3)	0.2
Blood loss		200 (150; 300)	250 (200; 375)	0.5
Resuming bowel transit (days)		3 (2; 3)	2.5 (2; 2.75)	0.8
Tumor diameter (centimeters)		5 (4; 6)	5 (4.25; 6.75)	0.3

tective ileostomies with 2 cases (6.8%) of anastomotic fistula, with statistical significance (p=0.04).

The relation between variables and the presence of intraabdominal abscesses can be observed in Table III. Patients with T>2 tumors were more frequently associated with intraabdominal abscesses, but this relationship

was slightly over the limit of statistical significance (p=0.1). This was due to the small number of cases who have developed abscesses. Patients in whom a manual suture was performed, developed an intraabdominal abscess more frequently (p= 0.03).

The comparison between patients with wound infection

and those without this complication is explored in Table IV. Patients with wound infection were more commonly those in the conventional approach group ($p=0.2$), had positive lymph nodes more frequently ($p=0.06$), had reduced levels of plasma proteins ($p=0.003$), and were more frequently diagnosed with type 2 diabetes ($p=0.1$). In the multivariate analysis, hypoproteinemia (OR 5.8, CI95% 2.2-15; $p < 0.001$) and a number of lymph nodes > 1 (OR 1.3, CI95% 1-1.8; $p=0.04$) remained independently associated with the occurrence of wound infection.

Table V presents the association of variables with bowel obstruction. The frequency of bowel obstruction was higher in patients with laparoscopic approach ($p=0.01$), mechanical suture ($p=0.07$), hypoproteinemia ($p=0.009$) and those who were admitted as emergencies ($p=0.009$). Out of the cases with complications, 27 (34.6%) of the patients had coronary heart disease ($p=0.5$) and there were 9 (25%) deceased patients ($p=0.09$). The complications of patients with coronary heart disease were: 2(6%) cases of thrombotic disorders ($p=0.03$), 2(6%) cases of postoperative hemorrhage ($p=0.1$), 2 (6%) cases of urinary retention ($p=0.2$), 7(21.2%) cases of AF ($p=0.2$), 3(9%) cases of intraabdominal abscesses ($p=0.2$), 11(33.3%) cases of wound infection ($p=0.3$), 2(6%) cases of cardiorespiratory decompensation ($p=0.09$) and 4(12.1%) cases of evisceration ($p=0.2$).

The general postoperative complications were: 4 (18%) cases of urinary retention, 16 (48.4%) cases of cardiorespiratory decompensation and 2(9%) cases of thrombotic disorders. Survival analysis did not reveal any factors influencing the mortality at 30 days. Table VI shows the differences between patients that died during the first 30 days after surgery and those who survived.

Discussions

Rectal surgery is undeniably associated with significant morbidity and mortality rates. Several multicenter and single center prospective studies have evaluated patients' short term outcomes after rectal surgery and the rate of major morbidity ranged from 20 to 35 % and the 30-day mortality rate ranged from 2 to 9%⁹⁻¹¹.

Anastomotic fistula (AF) is a major problem in patients who undergo operations for rectal cancer. The overall incidence of AF is 2 to 15% when performed by experienced surgeons and the highest risk is associated with coloanal anastomosis (10 to 20 %) ^{10,11}. In our study, there were 7.6 % (29 cases) of AF, a significantly higher percentage in the male group 75.8% vs the female group 24.2% ($p= 0.1$) and also in the group of patients undergoing conventional surgery (93.1% vs 6.9%; $p=0.7$). However, the male gender does not appear to be a risk factor for AF, but independently is associated with complication of any kind ($p=0.05$). A significantly higher rate of AF in men is also showed in a prospec-

tive study of 196 patients undergoing rectal cancer resections. It appears that the male gender influences the AF because the male pelvis is technically more challenging¹². It is noted in our study that cancer of the superior rectum was significantly more rarely associated with anastomotic fistula, but significantly we had a higher rate of AF in the middle rectum with 19 cases ($p=0.03$). If the location of the tumor is the middle rectum, the optimal treatment consists in anterior rectal resection with total excision of the mesorectum. This procedure leads to the ligation of the superior rectal artery at its origin and the middle rectal artery and it also implies a low anastomosis with the remained inferior rectum. Therefore, the vascularization for the rectal stump is decreased, as the only blood supply is coming from the inferior rectal artery and there is higher risk of AF. The highest risk group for an AF are patients with a low anterior resection and an anastomosis within 5 cm from the anal verge. In the present study, we had 46 (12.1%) cases with low anterior resection and 3 cases of AF. Law reported an anastomotic fistula rate of 10.2% in a range of 196 cases with tumors up to 12 cm from the anal verge¹³. Two studies from Japan and Italy present a rate of AF between 13.1 and 14.4% in patients who undergo rectal resection, one of its reasons being that total excision of the mesorectum results in decreased blood supply to the rectal stump^{14,15}.

An intra-abdominal abscess is a frequent cause of morbidity and mortality following rectal surgery. Antimicrobial therapy is an important element of the prophylaxis and management of intraabdominal infections¹⁶. The patients included in our study had appropriate preoperative therapy that included the administration of third-generation Cephalosporin (2 grams) and Metronidazole (2 grams). We diagnosed 7 (1.8%) intra-abdominal abscess cases, all of them operated with conventional approach and we found that patients with T>2 tumors were more frequently associated with intraabdominal abscesses, but this relationship was slightly over the limit of statistical significance ($p=0.1$), because we had a small number of cases who have developed abscesses. Patients in whom a manual suture was performed, developed an intraabdominal abscess more frequently ($p = 0.03$). A pelvic abscess is classified as a moderate to severe complication and it occurs with a rate <5%¹⁷. In a prospective multicentre study of 4,970 patients comparing open versus laparoscopic surgery for rectal cancer, 206 (6.8 %) cases of intra-abdominal abscesses have been reported in the conventional approach group¹⁸. Thus, open surgery is definitely more likely to be associated with both intra-abdominal and pelvic abscesses, even we didn't have statistical significance ($p=0.7$). Bowel obstruction is a common postoperative morbidity in rectal surgery and it leads to lower quality of life, longer hospital stays, increased hospitalization costs and in some cases, it delays adjuvant treatment¹⁹. The frequency of bowel obstruction was higher in patients with

laparoscopic approach ($p=0.01$), mechanical suture ($p=0.07$), hypoproteinemia ($p=0.009$) and those who were admitted as emergencies ($p=0.009$). Even though these results are with statistical significance, the small number of patients is inconclusive and leaves room for further research. Postoperative BO is associated with the local inflammatory reaction induced by surgical manipulation. Dowson et al. explained that the delicate handling of intestines, using laparoscopic devices, seems to reduce the postoperative inflammatory response. In our study, both patients with bowel obstruction came from the laparoscopic operation group, but in their cases a low anterior rectal resection as performed²⁰.

Surgical wound infection after laparotomy is associated with early morbidity, long hospital stay and high costs. The incidence of WS in colorectal surgery is approximately 5-14%²¹⁻²⁴. Laparoscopic surgery increased rapidly in recent years and with that, the overall rate of WS. Still, studies show that the incidence is higher in patients with conventional surgery²⁵⁻²⁷. Although the patients performed mechanical bowel preparation (MBP) with oral antimicrobial prophylaxis before surgery, in our study, wound infection was also much higher in the conventional approach group (97.0% vs 3%, $p=0.2$) and at patients with positive lymph node. Statistically significant were patients with reduced levels of plasma proteins ($p=0.003$). In the multivariate analysis, hypoproteinemia (OR 5.8, CI95% 2.2-15; $p < 0.001$) and a number of lymph nodes > 1 (OR 1.3, CI95% 1-1.8; $p=0.04$) remained independently associated with the occurrence of wound infection.

Laparoscopic surgery has progressively replaced open rectal surgery in recent years because of its short-term benefits²⁸. In our clinic, we have gained experience with laparoscopic surgery in rectal cancer and we reached 100 interventions, but the number of anterior rectal resections is still relatively small. Our study shows the laparoscopic approach in 6.7% of patients, with 5 complications and the conventional approach in the other 93.6%, with 73 complications ($p=0.3$). Results from surgical literature confirm that laparoscopic surgery provides the same oncological results and similar parietal risk of relapse, but it also brings a number of benefits, such as lower blood loss, a shorter hospital stay and faster recovery compared to the conventional approach^{29,30}.

Neoadjuvant therapy has earned an important role in the management of rectal cancer. The need for radiation treatment has become deeply ingrained in surgical and radiation oncology culture. In our study, 56 patients performed CRT and 21 cases had protective ileostomy. Several risk factors, including sex, intraoperative bleeding, tumor size and neoadjuvant chemoradiotherapy have been reported to be associated with anastomotic fistula in rectal resection³¹. We had 2 cases of anastomotic fistula and both had protective ileostomy ($p=0.04$). Retrospective studies have proven inconclusive as they found no association between the use of neoadjuvant

radiation therapy and the risk of an anastomotic leak^{32,33}. In a randomized controlled study, it is showed that patients who received RCT had better sphincter preservation, a decreased rate of pelvic recurrence and a lower incidence of treatment related toxicities³⁴.

Diversion by a protective stoma remains a controversy regarding whether or not it prevents AF. Providing protective ostomies in every case of rectal resection is associated with a high rate of complications, predominantly during the closure of these ostomies³⁵. In a prospective multicenter study of 2729 patients undergoing a low anterior resection, the overall anastomotic fistula rate was similar in patients with and without a stoma³⁶. In our studies, there was a number of 84 ileostomies. The ostomies were performed in cases with neoadjuvant therapy, loose tissue or because of a positive hydroaeric test and in these cases we first performed rectum suture and then ileostomy. Still, we had 2 anastomotic fistulas ($p=0.04$). Two studies of 579 and 358 patients undergoing anterior resection for rectal cancer, found patients with a protective stoma had significantly fewer AF compared with patients who had no protective stoma^{37,38}. Even a meta-analysis of 13 studies including 8,002 patients with protective stomas had significantly reduced rate of postoperative AF³⁹.

One of the most important risk factors of rectal cancer is diabetes mellitus and insulin resistance, as proven by a 14 studies meta-analysis (8 cohort and 6 case-control). The analysis illustrated a 20% higher risk of rectal cancer in diabetic patients⁴⁰.

We aimed to observe whether diabetes mellitus leads to an increased risk of perioperative surgical morbidity. In our study, there were 39 patients with diabetes and the complications we encountered were, as follows: 10 postoperative complications ($p=0.4$), 2 deceased ($p=0.1$), 4 anastomotic fistulas ($p=0.8$) and 6 wound infections ($p=0.1$). Diabetes has been associated with delayed healing and impaired anastomotic strength^{41,42}. Diabetes ($p=0.037$) and anemia ($p=0.027$) at admission, had statistical significance as risk factors in wound infection. A Cancer Prevention Study-II Nutrition Cohort, showed that individuals with diabetes mellitus had a significantly higher risk of cancer-specific mortality in comparison to those without diabetes⁴³. Still patients with diabetes mellitus had high rate of morbidity, we didn't find statistical significance.

Another risk group are patients with coronary heart disease as they have been associated with an increased risk of rectal cancer and advanced adenomas. Although the mechanisms are unclear, the most viable theory is related to shared risk factors⁴⁴. We wanted to see if coronary heart disease has any association with postoperative morbidity and mortality. From the total of 78 cases with complications, 27 (34.6%) patients also suffered from coronary heart disease ($p=0.5$), in final we had 2 (6%) cases of cardiorespiratory decompensation and mortality rate of 50 % (9 cases $p=0.1$). The American College of

Surgeons (ACS) identified preoperative risk factors that are potential predictors of major postoperative morbidity after rectal resection and one of them was coronary heart disease ⁴⁵.

Conclusion

Major complications after radical resection for rectal cancer are dependent on multiple variables. Male patients, those admitted in emergency and patients with hypoproteinemia were more likely to develop complications of any kind. Resection of the middle rectum, male group, slower resumption of bowel transit developed anastomotic fistula. Patients in whom a manual suture was performed, developed an intraabdominal abscess more frequently. Hypoproteinemia remained independently associated with the occurrence of wound infection. The frequency of bowel obstruction was higher in patients with laparoscopic approach, mechanical suture, hypoproteinemia and those who were admitted as emergencies. Still patients with coronary heart disease and diabetes mellitus didn't had statistical significance, the rate of morbidity and mortality remains high.

Riassunto

Lo studio analizza i fattori di rischio per complicanze postoperatorie e mortalità dopo resezione anteriore del retto su una casistica di 378 pazienti. Si tratta di pazienti ricoverati nella 3^a Clinica Chirurgica dell'Istituto Regionale di Gastroenterologia ed Epatologia "Octavian Fodor" di Romania tra il 2009 e il 2016. Il reclutamento ha riguardato cancri del retto proponibili per la resezione anteriore ad intento curativo. Le complicanze accertate sono state la fistola anastomotica, le infezioni intra-addominali, l'occlusione postoperatoria e le infezioni della ferita.

Di significato statistico è risultato il genere maschile, il ricovero d'urgenza, l'ipoprotidemia e la ripresa del transito intestinale.

I casi di cancro del medio retto sono risultati con alta incidenza di fistola anastomotica. Ascessi intra-addominali si sono verificati più frequentemente nei casi con sutura anastomotica manuale. Nell'analisi multivariata l'ipoprotidemia ed il numero di linfonodi > 1 si sono dimostrati associati indipendentemente con l'evenienza di suppurazione della ferita. La mortalità a 30 giorni è stata del 4,8% con 18 decessi, e la morbilità ha inciso per il 20,6% con 78 casi.

In conclusion le maggiori complicazioni dopo resezione radicale del cancro rettale dipendono da variabili multiple, come il sesso maschile, i ricoveri d'urgenza, e i soggetti malnutriti. Un'alta incidenza di morbilità si è riscontrata nei tumori del medio retto, nelle sutura eseguite manualmente, in caso di linfonodi positivi superiori all'unità.

La coronaropatia ed il diabete non hanno mostrato un significato statisticamente rilevante, ma l'incidenza di morbilità e mortalità rimane alta in questi gruppi.

References

1. Siegel RL, Miller KD, Jemal A: *Cancer statistics, 2017*. CA: A Cancer Journal for Clinicians, 2017; 67:7-30.
2. Coza D, Suteu E, Neamtiu L: *North-Western Cancer Registry. Cancer in North-Western Region of Romania 2009*. Cluj-Napoca; Editura Casa Cartii de Stiinta, 2012; 34-37.
3. Curado MP, Edwards B, Shin HR, et al.: *Cancer Incidence in Five Continents*. Volume IX IARC, Scientific Publications N. 160. International Agency for Research on Cancer Lyon, France 2007.
4. Miyakita H, Sadahiro S, Saito G, et al.: *Risk scores as useful predictors of perioperative complications in patients with rectal cancer who received radical surgery*. Int J Clin Oncol, 2017; 22: 324.
5. Ryerson AB, Ehemann CR, Altekruse SF, et al.: *Annual report to the nation on the status of cancer, 1975-2012, featuring the increasing incidence of liver cancer*. Cancer, 2016; 122: 1312-37.
6. Center MM, Jemal A, Smith RA, Ward E: *Worldwide variations in colorectal cancer*. CA Cancer J Clin, 2009; 59:366-78.
7. Gooiker GA, Dekker JW, Bastiaannet E, et al.: *Risk factors for excess mortality in the first year after curative surgery for colorectal cancer*. Ann Surg Oncol, 2012; 19: 2428-42434.
8. Paun BC, Cassie S, MacLean AR, et al.: *Postoperative complications following surgery for rectal cancer*. Ann Surg, 2010; 251: 807-18.
9. Ragg JL, Watters DA, Guest GD: *Preoperative risk stratification for mortality and major morbidity in major colorectal surgery*. Dis Colon Rectum, 2009; 52:1296-303.
10. Sliker JC, Komen N, Mannaerts GH, et al.: *Long-term and perioperative corticosteroids in anastomotic leakage: A prospective study of 259 left-sided colorectal anastomoses*. Arch Surg, 2012; 147: 447-52.
11. Park JS, Choi GS, Kim SH, et al.: *Multicenter analysis of risk factors for anastomotic leakage after laparoscopic rectal cancer excision: The Korean laparoscopic colorectal surgery study group*. Ann Surg, 2013; 257: 665-71.
12. Law WI, Chu KW, Ho JW, Chan CW: *Risk factors for anastomotic leakage after low anterior resection with total mesorectal excision*. Am J Surg, 2000; 179: 92-6.
13. Law WI, Chu KW, Ho JW, Chan CW: *Risk factors for anastomotic leakage after low anterior resection with total mesorectal excision*. Am J Surg, 2000; 179:92-96.
14. Sartori CA, Dal Pozzo A, Franzato B, et al.: *Laparoscopic total mesorectal excision for rectal cancer: experience of a single center with a series of 174 patients*. Surg Endosc, 2011; 25:508-14.
15. Fukunaga Y, Higashino M, Tanimura S, et al.: *Laparoscopic rectal surgery for middle and lower rectal cancer*. Surg Endosc, 2010; 24:145-51.
16. Okita Y, Kobayashi M, Araki T, et al.: *Impact of Surgical Infection Society/Infectious Disease Society of America-recommended*

- antibiotics on postoperative intra-abdominal abscess with image-guided percutaneous abscess drainage following gastrointestinal surgery. *Surg Today*, 2015; 45: 993-1000.
17. Kim JC, Lim SB, Yoon YS, et al.: *Completely abdominal intersphincteric resection for lower rectal cancer: feasibility and comparison of robot-assisted and open surgery*. *Surg Endosc*, 2014; 28: 2734-44.
18. Lujan J, Valero G, Biondo S, et al.: *Laparoscopic versus open surgery for rectal cancer: results of a prospective multicentre analysis of 4,970 patients*. *Surg Endosc*, 2013; 27:295-302.
19. Nakajima J, Sasaki A, Otsuka K, et al.: *Risk factors for early postoperative small bowel obstruction after colectomy for colorectal cancer*. *World J Surg*, 2010; 34:1086-90.
20. Dowson HM, Bong JJ, Lovell DP, et al.: *Reduced adhesion formation following laparoscopic versus open colorectal surgery*. *Br J Surg*, 2008; 95: 909-14.
21. Baker A, Dicks K, Durkin M, et al.: *Epidemiology of surgical site infection in a community hospital network*. *Infect Control Hosp Epidemiol*, 2016; 37:519-26.
22. Schweizer ML, Cullen JJ, Perencevich EN, et al.: *Costs associated with surgical site infections in veterans affairs hospitals*. *JAMA Surg*, 2014; 149:575-81.
23. Markell, K.W., Hunt, B.M., Charron, P.D. et al.: *Prophylaxis and management of wound infections after elective colorectal surgery: a survey of the American Society of Colon and Rectal Surgeons membership*. *J Gastrointest Surg*, 2010; 14:1090-098.
24. Goto S, Hasegawa S, Hata H, et al.: *Differences in surgical site infection between laparoscopic colon and rectal surgeries: Sub-Analysis of a multicenter randomized controlled trial (Japan-Multinational Trial Organization PREV)*. *Int J Colorectal Dis*, 2016; 31 1775.
25. Yeo H, Niland J, Milne D, et al.: *Incidence of minimally invasive colorectal cancer surgery at National Comprehensive Cancer Network centers*. *J Natl Cancer Inst*, 2015; 107:362.
26. Howard DPJ, Datta G, Cunnick G, et al.: *Surgical site infection rate is lower in laparoscopic than open colorectal surgery*. *Color Dis*, 2010; 12:423-27.
27. Drosdeck J, Harzman A, Suzo A, et al.: *Multivariate analysis of risk factors for surgical site infection after laparoscopic colorectal surgery*. *Surgical Endoscopy and Other Interventional Techniques* 2013; 27: 4574-580.
28. Zhao D, Li Y, Wang S, Huang Z: *Laparoscopic versus open surgery for rectal cancer: A meta-analysis of 3-year follow-up outcomes*. *Int J Colorectal Dis*, 2016; 31: 805-11.
29. van der Pas MH, Haglind E, Cuesta MA, et al.: *Laparoscopic versus open surgery for rectal cancer (COLOR II): Short-term outcomes of a randomised, phase 3 trial*. *Lancet Oncol*, 2013; 14: 210-18.
30. Pascual M, Salvans S, Pera M: *Laparoscopic colorectal surgery: Current status and implementation of the latest technological innovations*. *World J Gastroenterol*. 2016; 22(2): 704-17.
31. Eberl T, Jagoditsch M, Klingler A, Tschmelitsch J: *Risk factors for anastomotic leakage after resection for rectal cancer*. *Am J Surg*, 2008; 196: 592-98.
32. Kingham TP, Pachter HL: *Colonic anastomotic leak: risk factors, diagnosis, and treatment*. *J Am Coll Surg*, 2009; 208:269-78.
33. Matthiessen P, Hansson L, Sjødahl R, Rutegård J: *Anastomotic-vaginal fistula (AVF) after anterior resection of the rectum for cancer-occurrence and risk factors*. *Colorectal Dis*, 2010; 12: 351-57.
34. Sauer R, Becker H, Hohenberger W, et al.: *Preoperative versus postoperative chemoradiotherapy for rectal cancer*. *New Engl J Med*, 2004; 351:1731-40.
35. Prochazkova V, Sakra L, Cervinka V, et al.: *The importance of protective ileostomy during rectal resection*. *Eur Surg*, 2016; 48 (Suppl 2):175-77.
36. Gastinger I, Marusch F, Steinert R, et al.: *Protective defunctioning stoma in low anterior resection for rectal carcinoma*. *Br J Surg*, 2005; 92:1137.
37. Hüser N, Michalski CW, Erkan M, et al.: *Systematic review and meta-analysis of the role of defunctioning stoma in low rectal cancer surgery*. *Ann Surg*, 2008; 248:52-60.
38. Räsänen M, Renkonen-Sinisalo L, Carpelan-Holmström M, et al.: *Low anterior resection combined with a covering stoma in the treatment of rectal cancer reduces the risk of permanent anastomotic failure*. *Int J Colorectal Dis*, 2015; 30:1323-328.
39. Gu W, Wu S: *Meta-analysis of defunctioning stoma in low anterior resection with total mesorectal excision for rectal cancer: Evidence based on thirteen studies*. *World J Surg Onc*, 2015; 13:9.
40. Yuhara H, Steinmaus C, Cohen SE, et al.: *Is diabetes mellitus an independent risk factor for colon cancer and rectal cancer?* *Am J Gastroenterol*, 2011; 106: 1911-21.
41. Verhofstad MH, Hendriks T: *Diabetes impairs the development of early strength, but not the accumulation of collagen, during intestinal anastomotic healing in the rat*. *Br J Surg* 1994; 81(7):1040-45.
42. Wagner OJ, Egger B: *Influential factors in anastomosis healing [in German]*. *Swiss Surg*, 2003; 9(3):105-13.
43. Dehal AN, Newton CC, Jacobs EJ, et al.: *Impact of diabetes mellitus and insulin use on survival after colorectal cancer diagnosis: The cancer prevention study-II nutrition cohort*. *J Clin Oncol*, 2012; 30:53-9.
44. Chan AO, Jim MH, Lam KF, et al.: *Prevalence of colorectal neoplasm among patients with newly diagnosed coronary artery disease*. *JAMA*, 2007; 298:1412-419.
45. Speicher PJ, Ligh C, Scarborough JE, et al.: *A simple scoring system for risk-stratifying rectal cancer patients prior to radical resection*. *Tech Coloproctol*, 2014; 18: 459-65.