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The Role of Ileostomy in the Prevention and Treatment of Anastomotic Leakage after Elective Rectal Cancer Surgery – A Retrospective Analysis of Specific Risk Factors, Outcomes, and Complications

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Abbreviations:
AL: anastomotic leakage;
ASA: American Society of Anesthesiology;
TME: total mesorectum excision.

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Rezumat

Rolul ileostomiei în prevenirea și tratamentul fistulelor anastomotice după chirurgia electivă a cancerului rectal – o analiză retrospectivă a factorilor de risc specifici, a rezultatelor și complicațiilor

Context: Obiectivul acestei lucrări este de a evidenția rolul şi locul ileostomiei de protecție din perspectiva riscului de fistulă anastomotică.
Material şi Metodă: Acesta este un studiu retrospectiv a 74 (46.54%) de rezecții rectale joase şi ultrajoase dintr-un număr de 159 de cazuri de cancer de rect operate într-un interval de 7 ani (2015-2021). Cazurile au fost împărțite în două grupuri: grupul A cu ileostomie de protecție (47 de cazuri = 63,51%) şi grupul B, fără ileostomie de protecție (27 de cazuri = 35,49%).
Rezultate: Tipul de anastomoză în cazul pacienților cu fistule anastomotice a fost colorectală în 15 cazuri şi ileorectală pentru 2 cazuri, ambele din grupul A, cu sutură mecanică sau manuală. Ileostomia a fost singura modalitate de protecție a anastomozei. Complicațiile datorate ileostomiei înregistrate în grupul A au fost leziunile cutanate peristomale (8 cazuri), eventrația precoce peristomală (2 cazuri) şi deshidratarea severă cu insuficiență renală acută (7 cazuri). Suprimarea ileostomiei s-a practicat în 42 de cazuri (89,36%), intervalul de timp scurs între momentul intervenției şi închidrea ileostomiei fiind de 4,28 de luni cu limite între

12 zile şi 10 luni. Tratamentul fistulelor anastomotice a fost conservator în 13 cazuri (76.47%), şi chirurgical în 4 cazuri. În cazul reintervențiilor s-a recurs la desființarea anastomozei urmată de colostoma stângă şi închiderea ileostomiei în 3 cazuri (2 cazuri din grupul A şi 1 caz din grupul B) sau ileostomie terminală într-un caz din grupul A. Rata mortalității la pacienții cu fistulă anastomotică a fost 7,40%, cu două decese înregistrate la pacienți din grupul B.
Concluzii: Pentru a reduce complicațiile sale specifice, ileostomia trebuie efetuată la pacienți bine selectați. Printre cei cu factori de risc pentru apariția fistulei se numără bărbații, vârstnicii şi cei care au comorbidități importante, chimioterapia neoadjuvantă, tumori joase la mai puțin de 5 cm de orificiul anal extern, sau tumori circumferențiale stenozante şi cu infiltrat inflamator peritumoral.

Cuvinte cheie: ileostomie, chirurgia cancerului rectal, fistula anastomotică

Abstract
Background: The objective of this paper is to highlight the role and place of ileostomy from the perspective of the risk of anastomotic leakage (AL).
Materials and method: This was a retrospective study of 74 (46.54%) low and ultra-low anterior resections from 159 cases of rectal cancer operated on in a seven-year interval (2015–2021). The cases were divided into two groups: Group A with protective ileostomy (47 cases = 63.51%) and Group B without protective ileostomy (27 cases = 35.49%).
Results: The type of anastomosis was low colorectal for 15 cases and ileorectal for two cases, both in Group A, with either mechanical or manual sutures. Continuous loop ileostomy was the only fecal diversion procedure used for protection. The ileostomy-specific complications recorded in Group A were peristomal skin lesions (8 cases), early peristomal hernia (2 cases), and severe dehydration with acute renal-insufficency (7 cases). The closure of the ileostomy was performed in 42 cases (89.36%), with the time between the primary operation and the closure being 4.28 months on average, with limits between 12 days and 10 months. AL treatment was conservative in 13 (76.47%) cases and surgical in four cases, with the types of operations performed at reintervention being take-down of the anastomosis + left terminal colostomy + ileostomy closure in three cases (2 in Group A and 1 in Group B) and terminal ileostomy in one case in Group A.
Conclusions: To reduce its specific complications, ileostomy should be performed in well-selected patients. Those with risk factors for leakage include males, the elderly, and those having important comorbidities, neoadjuvant chemoradiotherapy, low tumors below 5 cm from the anal verge, or complete circumferential stenosis and peritumoral inflammatory infiltrate.

Key words: ileostomy, rectal cancer surgery, anastomotic leakage

Introduction

Surgery is the main therapeutic option for rectal cancer, and the introduction of total mesorectum excision (TME) was first reported by Heald in 1982. Anterior resection with TME later became the standard technique in the curative treatment of rectal cancer, resulting in a decrease in the recurrence rate, an increase in the disease-free rate, and a five-year overall survival (1,2,4-8).

Later, the evolution of surgical techniques and instrumentation (e.g., laparoscopic and robotic surgery, as well as mechanical sutures with circular stapling), along with the reduction of oncological safety limits (from 5 to 1-2

cm) and the improvement of adjuvant and neoadjuvant therapy protocols, allowed for lower anterior rectal resection (low-and ultra-low) with sphincter preservation, which emerged as the main therapeutic option of the last 20 years (4,8-12).

With an incidence varying between 1% and 39%, depending on the report, AL is burdened by high morbidity and mortality due to sepsis and peritonitis.

Proximal fecal diversion (ileostomy and/or colostomy) was introduced a few decades ago with the aim of ensuring the protection of lower colorectal anastomosis by keeping it free of feces and preventing the occurrence of AL in patients with low and ultra-low anterior resection. It decreases the incidence of AL, decreases the extent and severity of sepsis in symptomatic AL, allows for conservative treatment, and decreases the rate of morbidity and mortality due to fistula.

The objective of the present paper was to perform a retrospective analysis of a group of patients undergoing radical elective surgery for rectal cancer, with or without a protective ileostomy, and to highlight the role and place of the ileostomy from the perspective of the risk of AL and the complications specific to the procedure.

Materials and Methods

This research consisted of a retrospective study carried out on 74 (46.54%) low and ultra-low anterior resectons with sphincter preservation, selected from a number of 159 cases of rectal cancer operated on at the 1st Surgery Clinic in Craiova within a seven-year interval (2015-2021). The inclusion criteria were patients with and without protective ileostomy and with an age over 18 years, adenocarcinoma confirmed pathologically by biopsy, tumors located up to 15 cm from the anal verge, and scheduled surgery, but with or without neoadjuvant radiochemotherapy.

Exclusion criteria were synchronous colonic tumors, distant metastases, and other types of operations (e.g., Miles-type rectal amputation, Hartmann or Hartmann-like operation, and supratumoral discharge colostomies) imposed by evolutive complications of rectal cancer (e.g., obstruction, tumor perforation, perforations diastatic, or locally advanced tumors).

The preoperative procedures carried out in all patients consisted of mechanical preparation with polyethylene-glycol (4 liters the day before surgery), infection prophylaxis (1 dose of second-generation cephalosporins 30 minutes before induction of anesthesia, repeated if the intervention lasted longer than 3 hours), and thromboembolism prophylaxis with low-weight molecule heparins (LWMH) at least 12 hours before surgery.

The diagnosis of leakage was established clinically (through the observation of fever, chills, prolonged ileus, abdominal rigidity/guarding, leakage of feces through the drain tube or the wound, anastomotic dehiscence found at digital tact), proctoscopy, and a computer tomography (CT) scan with water-soluble contrast.

As a result of the existing controversies in the literature, in the last 10 years, two teams with different attitudes have emerged in our clinic regarding the use of protective ileostomy associated with anterior rectal resections with sphincter preservation. The cases studied were divided into two groups: Group A with protective ileostomy (47 cases = 63.51%) and Group B without protective ileostomy (27 cases = 35.49%).

The data required for the study, extracted from the clinical observation files and operative and necropsy protocols, were entered in an individual file for each patient and then centralized and statistically processed using the Microsoft Excel® software; the mean and standard deviation were calculated, and a T-test was performed to determine the statistical significance of the difference between means, with a p-value < 0.05 considered statistically significant.

The study had the approval of the University and Scientific Ethics and Deontology Commission of the University of Medicine and Pharmacy of Craiova No. 122/30.07.2021.

Results

Demographic Data

For the entire studied group (74 patients), the average age was 65.05 years, ranging from 27 to 88 years, with the majority of patients (50 cases, 67.56%) belonging to >61 year-old group (*Table 1*). Regarding the gender distribution, we recorded a net predominance of the male gender (43 men vs. 31 women, sex ratio = 1.38).

Table 1. Age-group distribution

Age	Ileostomy	No ileostomy	Total
21–30	1		1
31–40	3		3
41–50	2	2	4
51–60	12	4	16
61–70	18	10	28
71–80	10	7	17
> 80	1	4	5
Total	47	27	74
Range	27–81 y	49–88 y	
Average	61.62 y	68.48 y	
St. dev.	11.39	10.06	
p			0.0113

Anatomic-clinical parameters of patients with low anterior rectal resection with and without protective ileostomy

Although different in number (47 in Group A vs. 27 in Group B), the two groups were relatively homogeneous in structure. There were significant differences regarding the age of the patients, where we noted the predominance of older patients with ASA scores of 3 in the group without ileostomy. Another significant difference was the location of the tumor: 53.19% in group A vs. 85.18% in group B were located in the middle rectum, and 46.81% in group A vs. 14.81% in group B in the lower rectum (p = 0.009).

Comorbidities

A total of 64 (83.79%) patients presented important comorbidities (*Table 2*), which were

Table 2. Comorbidities

Comorbidities	Total cases	Group A resection + ileostomy (n = 47)	Group B resection without ileostomy (n = 27)	p
Obesity	12 (16.2%)	8	4	0.804
Diabetes mellitus	7 (9.45%)	5	2	0.589
Cardiovascular	37 (50%)	12	25	0.001
- Coronary heart disease	5	2	3	0.256
- Arterial hypertension	29	14	15	0.0268
- Atrial fibrillation	7	5	2	-
- Valvulopathies	2	-	2	-
- Heart failure	2	-	2	-
- Lower limb venous insufficiency	2		1	-
Respiratory	7 (9.45%)	5	4	0.486
- Pulmonary fibrosis/asthma	5/2	1	4	
Digestive	15 (20.27%)	11	4	0.377
- Hiatal hernia + GERD	4	2	2	
- Chronic gallbladder lithiasis	1	1	-	
- Liver steatosis/chronic hepatitis	6	6	-	
- Polyposis/diverticulosis	3	1	2	
- Acute pancreatitis	1	1	-	
Renal	14 (18.91%)	7	7	0.241
- Renal lithiasis	5	2	3	
- Prostate adenoma	5	5	-	
- Hydronephrosis	1	-	1	
- Acute/chronic kidney failure	3	-	3	
Hernia/incisional hernia	7 (9.45%)	7	-	NS
Genital	2 (2.70%)	-	2	NS
No comorbidities	12 (16.21%)	12	-	

unique in 18 (24.32%) cases, and associations of two or more comorbidities in the remaining 46 cases (75.68%); the absence of comorbidities was recorded only in 12 cases (16.21%), all belonging to Group A (with ileostomy).

Cardiovascular diseases represented the main comorbidity and were present in 37 (50.0%) cases, with significant differences (p = 0.001) between the two groups, both as a whole (12 cases in Group A vs. 25 cases in Group B, p = 0.001), as well as specifically for hypertension, which was more frequent in Group B (p = 0.0268). For the other comorbidities (i.e., diabetes, obesity, renal, respiratory, or digestive diseases) found in both groups, we did not register statistically significant differences.

Clinico-pathological parameters of patients with anastomotic leakage (AL) after low and ultra-low anterior resection with sphincter preservation

As shown in *Table 3*, 17 (22.9%) patients presented with postoperative AL, and their incidence was substantially equal in the two groups, with 23.40% (11 cases) in Group A, and 22.22% (6 cases) in Group B. The incidence of AL was higher in men in both groups (M/F = 8/3 Group A vs. 5/1 Group B). Regarding age, AL was more frequent in the elderly in Group B (mean age 71.50 years for Group B vs. 58.10 years for Group A).

Neoadjuvant radio-chemotherapy was involved in the appearance of AL in both groups; its contribution as a factor favoring AL was significant (p = 0.0134) for chemotherapy and highly significant (p = 0.002) for radiotherapy.

No significant differences were recorded in terms of AL occurring in tumors located on the middle rectum, while these became highly significant (p = 0.001) for tumors located on the lower rectum (36.36% Group A vs. 75.0% Group B). The incidence of AL was almost identical in the two groups for tumors with a diameter (D) < 5 cm (6 for Group A vs. 5 for Group B, p = 0.939), while for tumors > 5 cm, the incidence of AL was higher in Group A. Circumferential stenosis as a favoring factor of AL was found in 63.63% of cases in Group A and 33.33% in Group B (p = 0.0105).

All patients underwent elective surgery (scheduled surgery), with the incidence of AL almost similar in the two groups (11 for Group A vs. 6 for Group B, p = 0.907). The approach was classical in 57 cases (37 for Group A with 9 AL and 20 for Group B with 4 AL, p = 0.001) and laparoscopic in 17 cases (10 for Group A with 2 AL and 7 for Group B with 2 AL, p = 0.465).

For the type of surgery, anterior resection was applied in 14 cases (8 for Group A and 6 for Group B), inter-sphincteric resection in one case in Group A, and total colectomy in two cases, both of which were in Group A. The type of anastomosis was low colorectal for 15 cases (9 for Group A and 6 for Group B) and ileorectal for two cases, both in Group A, with either mechanical sutures (35 cases with 9 AL in Group A and 24 cases with 5 AL in Group B, p = 0.138) or manually (12 cases with 2 AL group A vs. 3 cases with 1 AL group B, p = 0.477).

AL treatment was conservative in 13 (76.47%) cases (8 from Group A and 5 from Group B) and surgical in four cases (3 for Group A and 1 for Group B), with the types of operations performed at reintervention being take-down of the anastomosis + left terminal colostomy + ileostomy closure in three cases (2 in Group A and 1 in Group B) and terminal ileostomy in one case in Group A.

The mortality rate in patients with AL was 7.40%, with two deaths recorded in patients from Group B.

The average length of hospital stay was 36.09 ± 20.88 days in Group A and 32.66 ± 7.65 days in Group B.

Data Related to Ileostomy

As shown in *Table 4*, continuous loop ileostomy was the only fecal diversion procedure used for protection. The output of the ileostomy was low (<500 ml/24 hours) in 21 (44.68%) cases, medium (500–1000 ml/24 hours) in 20 (42.53%) cases, and high (> 1000 ml/24 hours) in six (12.76%) cases.

Table 3. Anatomo-clinical parameters of AL cases

Anatomo-clinical parameters of patients with AL after low and ultra-low anterior resections	**Group A resection + ileostomy (n = 47)**	**Group B resection without ileostomy (n = 27)**	**P**
Total AL (%)	11 (23.40%)	6 (22.22%)	0.769
Sex			0.532
- Males	8 (72.72%)	5 (83.33%)	
- Females	3 (30.00%)	1 (16.67%)	
Age	58.10±11.03	71.50±10.02	0.029*
Diabetes	0 (0.00%)	3 (50%)	NS
Arterial hypertension	4 (40%)	4 (66.66%)	NS
Coronary heart disease/myocardial infarction	0 (0.00%)	1 (16.66%)	NS
Preoperative chemotherapy			
- Total	37 (78.72%)	10 (37.03%)	
- AL	8 (72.72%)	4 (66.6%)	0.0134*
Preoperative radiotherapy			
- Total	18 (38.29%)	9 (37.03%)	
- AL	8 (72.72%)	4 (66.66%)	0.002*
Topography of tumor			
- Middle rectum	25 (53.19%)	22 (81.48%)	
- AL	3 (12.00%)	3(13.63%)	0.896
- Low rectum	22 (46.81%)	4 (18.52%)	
- AL	8 (36.36%)	3 (75.00%)	0.001*
Tumor's size			
- < 5 cm	25 (53.19%)	19 (70.34%)	
- AL	6 (24.0%)	5 (26.31%)	0.939
- > 5 cm	22 (48.81%)	8 (29.66%)	
- AL	5 (22.42%)	1 (12.54%)	0.604
Circumferential stenosing tumor			0.0105*
- Yes	7 (63.63%)	2 (33.33%)	
- No	4 (34.37%)	4 (66.66%)	
Inflammatory infiltrate			0.138
- Yes	9 (81.81%)	4 (66.66%)	
- No	2 (18.19%)	2 (33.33%)	
Timing of surgery			
- Elective	47 (100%)	27 (70.38%)	
- AL	11 (23.40%)	6 (22.22%)	0.907
Approach			
- Open	37 (74.46%)	20 (70.07%)	
- AL	9 (81.81%)	4 (66.66%)	0.0001*
- Laparoscopic	10 (25.54%)	7 (39.93%)	
- AL	2 (18.9%)00	2 (33.33%)	0.465
Type of surgery			0.164
- low and ultra-low anterior resection	8 (72.72%)	6 (100%)	
- Intersphincteric resection	1 (9.09%)	0 (0.00%)	
- Total proctectomy	2 (18.18%)	0 (0.00)	
Anastomosis			0.020*
- Ileo-rectal	2 (18.18%)	0 (0.00%)	
- Low colorectal	9 (81.82%)	6 (100%)	
Suture			
- Mechanic	35 (74.46%)	24 (88.88%)	
- AL	9 (22.85%)	5 (20.83%)	0.138
- Hand-sewn	12 (25.54%)	3 (11.12%)	
- AL	2 (16.66%)	1 (33.33%)	0.477
AL management			0.138
- Conservative	8 (72.72%)	5 (83.33%)	
- Surgical	3 (27.28%)	1 (16.66%)	
Reoperations	2 (18.18%)	1 (16.66%)	0.938
Length of hospital stay	36.09±20.88	32.66±7.65	0.706
Mortality (N of deaths with AL)	0 (0.00%)	2 (7.40%)	

Table 4. Postoperative morbidity and mortality

Parameters	Group A resection + ileostomy	Group B resection without ileostomy
Output of ileostomy		
- Low (< 500 ml/24 ore)	21 (44.68%)	
- Medium (500–1000 ml/24 ore)	20 (42.53%)	
- High (> 1000 ml/24 ore)	6 (12.76%)	
Specific complications of ileostomy	17 (36.17%)	
- Peristomal skin lesions	8 (17.02%)	
- Early parastomal hernia	2 (4.25%)	
- Dehydration with acute renal failure	7 (14.89%)	
Complications after ileostomy closure	6 (14.28%)	
- Wound infection	3 (7.14%)	
- Incisional hernia	1 (2.38%)	
- Clostridium difficile infection	2 (4.76%)	
Other local complications		
- Wound dehiscence	4 (8.50%)	5 (18.51%)
- Incomplete evisceration		2 (7.40%)
Morbidity	21 (44.68%)	7 (25.92%)
Postoperative mortality	3 (6.38%)	3 (11.11%)
- After AL	-	2 (7.40%)
- After ileostomy closure	2 (4.25%)	-
Causes of death		
- Urosepsis	1 (2.38%)	-
- MSOF		2 (7.40%)
- Clostridium difficile infection	2 (4.6%)	1 (3.70%)

The postoperative morbidity rate was different between the two groups, reaching 44.68% (21 cases) in Group A and 25.92% (7 cases) in Group B. The ileostomy-specific complications recorded in Group A (17 cases) were peristomal skin lesions (8 cases), early peristomal hernia (2 cases), and severe dehydration with acute renal-insufficency (7 cases). Among the local postoperative complications specific to abdominal surgery, we recorded wound infection suppuration in nine cases (4 cases in group A and 5 cases in group B) and incomplete evisceration in two cases in Group B.

The closure of the ileostomy was performed in 42 cases (89.36%), with the time between the primary operation and the closure being 4.28 months on average, with limits between 12 days and 10 months. The procedures used to close the ileostomy were segmental enterectomy in 38 cases, with end-to-end entero-enteroanastomosis in 32 cases and side-to-side in six cases; wedge enterectomy was used in three cases, and in one case, definitive ileostomy was used. Four postoperative complications were recorded after closing the ileostomy, including wound infection in three cases and eventration in one case.

The global postoperative mortality was 8.10% (6 deaths, 3 in each group), with a different mortality rate for the two groups (6.38% in Group A and 11.11% in Group B). The causes of death were urosepsis (1 case in Group A), multiple systemic organic failure (MSOF; 2 cases in Group B), and Clostridium difficile infection in three cases, of which one case in Group B and two cases in Group A occurred after ileostomy closure.

Discussion

Nowadays, rectal resection with sphincter preservation is the operation of choice for rectal cancer, and ileostomy is the procedure of choice for the protection of high-risk colorectal anastomoses. Performed in well-selected patients, with indications imposed by the risk factors involved in the occurrence of anastomotic fistulas (i.e., men and elderly with important comorbidities, neoadjuvant chemoradiotherapy, low tumors located below 5 cm from the anal verge, complete circumferential stenosis and peritumoral inflammatory infiltrate, difficult resections and high-risk anastomoses, tension, and poor vascularization), ileostomy, even if it does not prevent the leakage, considerably reduces the contamination of the peritoneum and the severity of sepsis, favors conservative treatment, and reduces the rate of reinterventions and the mortality rate in clinically manifest leakages.

Although it has considerably improved patient's satisfaction and quality of life, low anterior rectal resections with sphincter preservation, are burdened with significant morbidity and mortality, with AL being the most severe evolutive complication that continues to appear despite the improvements in surgical techniques and equipment (11,14). AL has a negative impact on the local and general evolution of the patient, decreases the survival rate, and favors the occurrence of local relapses (1,2,10,12,14-19). The incidence of AL differs depending on the morphological

characteristics of the tumor (e.g., topography, dimensions, macroscopic form, staging, etc.), the type of reconstruction, and the level of the anastomosis, as well as the presence or absence of the proximal fecal diversion (diverting stoma; DS), varying broadly between 3-39% depending on the author (1,7,11,12,14,15,19, 22-26).

The data of our study fall within the limits of those in the literature, with 21 complications recorded in patients with ileostomy (general morbidity 44.68%), of which 17 complications were specific to ileostomy (8 peristomal skin lesions, 7 severe electrolyte imbalances with acute renal failure, and 2 early parastomal hernias), with a specific morbidity rate of 36.17%. Apart from these, the discomfort and lower quality of life in ileostomized patients, as well as the psychological impact related to the need for a second operation to close the stoma, are disadvantages that must be taken into account when deciding to perform a protective ileostomy in patients with low and ultra-low anterior resections.

In the absence of a standardized guideline regarding the indications of DS, and in agreement with the majority of authors, our comparative study assessed the value of AL risk factors and the opportunity to use them as major criteria for the indication of an ileostomy in low and ultra-low anterior resections (*Table 3*). Ileostomy was mainly used in men (63.29% in Group A vs. 51.85% in Group B), starting from the fact that most authors consider being male as a risk factor for AL, which was confirmed in our study by the higher incidence of AL in patients with low and ultra-low anterior resections without ileostomy (Group B), compared to those with ileostomy (83.33% vs. 72.72%).

There were significant differences in the ages of the patients who underwent ileostomy. Although advanced age is considered a major risk factor for AL, in our study, ileostomy was performed more frequently in younger patients (average age 61.62 years in Group A vs. 68.48 years in Group B, $p = 0.121$). Seo (14) attributes the higher incidence of ileostomy in younger patients to the fact that neoadjuvant radiotherapy preceding low and ultra-low anterior resections is indicated, especially in younger patients. We avoided ileostomy in the elderly on the grounds that some of the complications of ileostomy (e.g., dehydration and major electrolytic imbalances complicated with acute renal failure in high-flow ileostomies) represent a major risk, are difficult to control, and are burdened by a high mortality rate.

The impact of neoadjuvant chemo-radiotherapy as a favoring factor of AL was significant ($p = 0.0134$) for chemotherapy and highly significant ($p < 0.002$) for neoadjuvant radiotherapy in the present study, with AL being registered in 72.72% of cases irradiated preoperatively in the group with protective ileostomy, and 66.66% in the one without; similar data were recorded for neoadjuvant chemotherapy).

The morphological characteristics of the tumor detected intraoperatively (i.e., location, dimensions, macroscopic shape, and presence of inflammatory infiltrate) are included in the literature among the decision criteria for performing a protective ileostomy in rectal resections with sphincter preservation. Most authors recommend performing an ileostomy in tumors of the lower rectum, with difficult or uncertain low colorectal or colo-anal anastomoses (anastomoses in tension, poor vascularity, inconclusive methylene blue test, or positive air-leak test) (3,8,11,13,14,20,26,44). In our study, we found no difference between the 2 groups concerning the incidence of AL after low and ultra-low anterior resections for tumors located on the middle rectum: 12% group A vs 13,36% group B, $p=0.896$. For tumors located on the lower rectum the incidence was higher in patients without ileostomy and the difference was highly significant (36.6% in group A vs 75% group B, $p=0.001$).

Regarding tumor sizes, we did not record significant differences in terms of the number of resections with sphincter preservation and the incidence of AL for tumors with $D < 5$ cm (25 cases in Group A vs. 19 in Group B, with an incidence of AL of 24% and 26.31% respec-

tively, p =0.939). At the same time, for tumors with D > 5 cm, we recorded differences both in terms of the number of cases (22 in Group A vs. 8 in Group B) and the incidence of AL (22.72% in Group A vs. 25.54% in Group B). We found the macroscopic form of the tumor to be much more relevant, which was infiltrative - stenotic ± ulcerated in most cases in both groups (72.35% in Group A and 66.66% in Group B), with a significantly higher incidence (p = 0.0105) of AL in both groups for complete circumferential stenosis; the explanation can be found in the fact that the vitality of the supra-stenotic segment of the colon can be compromised by the dilatation upstream of the stenosis, which can be considered a risk factor for the occurrence of AL. Furthermore, the excessive peritumoral inflammatory infiltration, present in both groups, can be considered an additional risk factor with an impact on the quality of the anastomosis and deserves to be taken into account in the choice of ileostomy as a method of anastomosis protection.

Significant differences were recorded regarding the approach (p = 0.0001), with the majority of AL appearing after open surgery, where the incidence of fistulas was relatively close in the two groups (24.32% in Group A vs. 20.0% in Group B) compared to the laparoscopic approach, in which the incidence of AL was significantly higher in the group without ileostomy (20.0% in Group A vs. 28.57% in Group B). The majority of AL were encountered after low rectal resection (8 in Group A and all 6 in Group B), while inter-sphincteric resection was hampered by the occurrence of AL in one case, and total proctectomy in two cases, all in Group A. Credited almost unanimously as one of the main technical advances that allowed lowering the level of resection and anastomosis, making low rectal resection with sphincter preservation the standard operation in rectal cancer, mechanical suture, even if it is easier and safer, does not exclude the occurrence of AL. In fact, it was the main type of anastomosis used in most cases in both groups, without registering significant differences regarding the incidence of AL (22.85% vs. 20.83%, p = 0.138); AL was encountered in 16.16% of cases in the group protected by ileostomy and 33.33% in the group without ileostomy (p = 0.477).

Our study confirms the data from the literature reporting that the presence of ileostomy makes conservative treatment the main therapeutic option for AL occurring after rectal cancer surgery, including vacuum therapy or endoscopic therapy (5,8,20,43,44). Eight (72.72%) AL from Group A and five (83.33%) from Group B were closed by conservative treatment. We did not record significant differences regarding the rate of reinterventions (18.18% in Group A vs. 16.66% in Group B), although this decrease is one of the arguments mentioned in the literature in favor of ileostomy (8,12,14,16,19,20,24,29-31).

The morbidity rate was 44.68% in the group with ileostomy and 25.92% in the group without ileostomy, but the differences regarding the structure of morbidity in the two groups were significant; thus, 17 patients from Group A presented complications specific to ileostomy (peristomal skin lesions in 8 cases, early parastomal hernia in 2 cases, and hydroelectrolitic imbalances ± acute renal failure), with a morbidity rate of 36.17%, located within the limits of 3–93% mentioned in the literature (3,21,26,32-35). The morbidity due to local complications specific to open abdominal surgery (wound infection, wound dehiscence) was 25.93% in the group without ileostomy and only 8.5% in the group with ileostomy.

Regarding the closure of the ileostomy, although there is still no consensus regarding its appropriate timing, most authors advocate early closure in the first three months after the primary surgery (1,3,26,48) if there is certainty of healing of the anastomosis confirmed by irrigography and/or proctoscopy (26). Moreover, some authors recommend early closure in patients who do not require adjuvant therapy, and late closure (after 7 months) in those who require it or in those who have received neoadjuvant radio-chemo-therapy (3, 20, 48, 49). Early closure significantly reduces the rate of ileostomy

complications and improves quality of life. AL and/or neoadjuvant radio-chemotherapy are the main circumstances that require late closure of the ileostomy, and both are responsible for the higher rate of local complications specific to the ileostomy and intestinal and anal dysfunctions, prolonging the recovery time and delaying the initiation of adjuvant therapy (3,47,50,51). The closure of the ileostomy in our study was performed in 42 cases (89.36%), with the interval between the primary operation and the closure being 4.28 months, on average, with limits between 12 days and 10 months. Six postoperative complications (*Table 4*) were recorded after closure (wound infection in 3 cases, postoperative incisional hernia in 1 case, and Clostridium difficile infection in 2 cases), the morbidity rate being 14.28% and within the limits of the literature data, which reports a morbidity of 17-48% (3,14,52). Ileostomy reconstruction, reported in the literature at rates between 0.4 and 12.1% (53), was not necessary in any of our cases.

Despite the fact that patients with ileostomy require a second hospitalization to close it, we did not record significant differences between the two groups in terms of the average length of hospital stay, which was 23.55 days in Group A vs. 22.63 days in Group B as a whole ($p = 0.817$) and 36.09 days in Group A vs. 32.66 days in Group B for patients with AL ($p = 0.706$), a fact also reported in the literature (17).

Regarding postoperative mortality, the rates were 6.38% in Group A and 11.11% in Group B (3 deaths in each group), with the remark that none of the deaths recorded in the group with ileostomy were due to AL, while two of the deaths recorded in the group without ileostomy were determined by the unfavorable evolution of AL. We also emphasize the fact that in two cases in Group A, the cause of death was a fulminant *Clostridium difficile* infection that occurred after the ileostomy was closed, a fact also reported in the literature (45,46).

Conclusions

Rectal resection with sphincter preservation is currently the surgery of choice for middle and lower rectal cancer, and ileostomy is the procedure of choice for the protection of high-risk colorectal anastomoses. To reduce its specific complications, the procedure should be performed in well-selected patients, with indications imposed by the risk factors involved in the occurrence of anastomotic fistulas (i.e., men, elderly, important comorbidities, neo-adjuvant chemoradiotherapy, low rectal tumors located below 5 cm from the anal verge, complete circumferential stenosis and peritumoral inflammatory infiltrate, difficult resections and high-risk anastomoses, tension, and poor vascularization). In our study, although we found no strong evidence that ileostomy avoids conservative treatment and reduces the rate of reoperation, ileostomy significantly reduced the mortality rate in clinically manifest leakages.

Conflicts of Interest

The authors declare no conflict of interest.

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Informed Consent Statement

Informed consent was obtained from all subjects involved in the study.

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