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“CAROL DAVILA” University of

Medicine and Pharmacy

Bucharest

DOCTORAL SCHOOL

MEDICINE

DOCTORAL THESIS ABSTRACT

PhD coordinator:

PROF. UNIV. DR.VICTOR STRÂMBU

PhD student:
Răvaș Maria-Manuela

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SEPTIC COMPLICATIONS OF RECTAL CANCER SURGERY

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List of Abbreviations and Symbols

NCCN – National Comprehensive Cancer Network

IOB – Bucharest Oncology Institute

MRI – Magnetic Resonance Imaging

CT – Computed Tomography

PET/CT – Positron Emission Tomography combined with CT

SPSS – Statistical Product and Service Solutions

TME – Total Mesorectal Excision

TEO – Transanal Endoscopic Operation

TAMIS – Transanal Minimally Invasive Surgery

APR – Abdominoperineal Resection

LAR – Low Anterior Resection

TAD – Transanal Drainage Tube

non-TAD – Without Transanal Drainaige Tube

HTN – Hypertension

DM – Diabetes Mellitus

CRC – Colorectal Cancer

TAE – Transanal Excision

TEM – Transanal Endoscopic Microsurgery

TaTME – Transanal Total Mesorectal Excision

AL – Anastomotic Leak Fistula

ASA – American Society of Anesthesiologists

Gy – Gray

CEA- Carcinoembryonic antigen

MMR- Mismatch Repair System

IARC- Agency for Research on Cancer

Introduction

Rectal cancer is one of the most common malignancies worldwide and in Romania, representing a major cause of oncological morbidity and mortality. In recent decades, advances in early diagnosis and the development of multimodal treatment have significantly contributed to improving patient prognosis and quality of life. The evolution of local treatments (minimally invasive surgical techniques and radiotherapy) and systemic therapies has led to increased rates of sphincter preservation and a reduction in postoperative complications.

The motivation for selecting this topic stems from the persistently significant rate of postoperative septic complications, which remains a challenging stage in postoperative management. Anastomosis represents a key step in surgical treatment, enabling the preservation of digestive continuity. However, it is associated with a risk of anastomotic dehiscence, leading to increased morbidity, the need for reinterventions, prolonged hospitalisation, and ultimately increased postoperative mortality. In this context, the present work aims to analyse the incidence of septic complications, with a focus on local septic complications (fistula, pelvic abscess) reported across different types of surgical interventions and approaches.

The study evaluates the relationship between postoperative complications and patient-related factors, including comorbidities, place of origin, sex, and age. In addition, a narrative review was conducted highlighting the advantages and disadvantages of each surgical approach, as well as the role of minimally invasive techniques in reducing the rate of septic complications. The importance of preoperative rehabilitation (prehabilitation) is also emphasised, along with the negative impact of sarcopenia on postoperative recovery and the role of indocyanine green fluorescence in assessing anastomotic perfusion.

The limitations of the study include its retrospective design and the variability of surgical experience, factors that may influence postoperative outcomes. Nevertheless, the research highlights the need for the development of individualised risk assessment and

prevention strategies for septic complications, aiming to improve survival and maintain patient quality of life.

I. General Part

1. Rectum and Anal Canal: Embryology, Histopathology, Etiopathogenesis

The rectum ("intestinum rectum" or straight intestine) and the anal canal represent the terminal portion of the digestive tract and have a mixed embryological origin.

Superiorly, the endodermal cloaca is divided into the urogenital sinus (anterior) and the rectal ampulla (posterior), while the lower part of the anal canal develops from the proctodeum, an ectodermal invagination. The two segments unite at the level of the pectinate line, which represents the embryological boundary between the endodermal and ectodermal portions of the anal canal. Inferior to the pectinate line, the anatomical anal canal is described, whereas inferior to the anorectal line, the surgical anal canal is defined [1].

From an anatomical perspective, the superior limit of the rectum is represented by the rectosigmoid junction, which descends into the pelvic cavity following the concavity of the sacrum, crosses the pelvic diaphragm, and continues inferiorly with the anal canal. Morphologically, the absence of haustra, mesocolon, and epiploic appendages distinguishes it from the sigmoid colon.

The anatomical relationships of the rectum are essential for oncological surgical procedures. The rectal compartment is limited anteriorly, in females, by the parametrium and the posterior vaginal wall (rectovaginal space), and in males by the rectovesicoprostatic septum or Denonvilliers' fascia. Posteriorly, the rectum is related to the sacrum and coccyx, while laterally it is in relation with the levator ani muscles and pelvic structures.

Topographically, the rectum has a pelvic portion and a perineal portion, and at the level of Kohlrausch's transverse fold there is a peritoneal reflection forming the rectouterine (Douglas) pouch. Thus, the rectum includes both a peritoneal and an extraperitoneal portion. In the subperitoneal segment, it is surrounded by loose connective tissue, which allows greater distensibility (rectal ampulla). At this level, two fascial layers are distinguished: the presacral fascia (parietal endopelvic fascia), covering the sacrum and presacral

neurovascular structures, and the rectal fascia (visceral endopelvic fascia), which encloses the mesorectum [2–6].

A central concept of this thesis is the avascular plane described by Heald as the “holy plane”, located between the mesorectal fascia and the presacral fascia. Respecting this plane enables total mesorectal excision (TME), which is considered the gold standard in the surgical treatment of rectal cancer. The mesorectum contains vessels, lymphatics, adipose tissue, and regional lymph nodes, and its complete removal reduces the risk of local recurrence. Dissection outside this plane may increase the risk of bleeding, nerve injury, positive circumferential resection margins, and postoperative complications. Therefore, knowledge of fascial anatomy is fundamental for performing optimal surgery in rectal neoplasms [4–6].

The vascular supply of the rectum is mainly provided by the superior, middle, and inferior rectal arteries. The superior rectal artery, a continuation of the inferior mesenteric artery, represents the main blood supply. The rectosigmoid junction is considered a relatively poorly vascularised area, described as Sudeck’s critical point, with potential vulnerability to ischemia and consequently anastomotic dehiscence.

Venous drainage of the rectum is characterized by a porto-caval anastomosis, through connections between the portal and systemic venous systems. Lymphatic drainage varies according to the level relative to the pectinate line: superior regions drain toward the inferior mesenteric and intrapelvic lymph nodes, while inferior regions may drain toward the superficial inguinal lymph nodes.

The innervation of the rectum and anal canal includes both autonomic and somatic components. Sympathetic and parasympathetic fibres regulate motility, secretion, and the tone of the internal and external anal sphincters. The hypogastric plexuses play an important role in urinary and sexual function control; thus, their injury may lead to significant functional complications. Defecation is a complex process involving rectal distension, spinal reflexes, relaxation of the internal anal sphincter, and voluntary control of the external anal sphincter [7].

2. Rectal Neoplasm

2.1 Etiopathogenesis, Diagnosis, Staging, Multimodal Management, and Septic Complications

Colorectal cancer is one of the leading causes of morbidity and mortality worldwide and represents the third most frequent malignancy in both women and men. Risk factors include excessive alcohol consumption, smoking, unhealthy diet, sedentary lifestyle, and obesity, all of which significantly increase the lifetime risk of developing the disease. In Romania, the association of these factors with the lack of effective screening programs frequently leads to late diagnosis and limited access to preventive measures, thereby requiring more complex therapeutic strategies [8–10].

The etiopathogenesis of colorectal cancer is complex and is driven by the accumulation of genetic and epigenetic alterations. The main involved mechanisms include chromosomal instability, defects in DNA repair systems, and CpG island hypermethylation, all of which progressively lead to adenoma formation and subsequently to invasive carcinoma. Frequent mutations occur in the APC, KRAS, TP53, and PIK3CA genes, as well as microsatellite instability associated with the mismatch repair (MMR) system. These alterations have important prognostic and therapeutic implications.

APC mutation is considered an early event in carcinogenesis, promoting uncontrolled cellular proliferation. The KRAS gene influences cellular proliferation and survival, and its mutations may induce resistance to certain therapies. TP53 is a key tumour suppressor gene involved in cell cycle control and apoptosis, and its loss of function facilitates tumour progression. Currently, the management of rectal cancer integrates anatomical, histopathological, and molecular data.

Microsatellite instability and MMR defects have both diagnostic and therapeutic relevance, being associated with differential responses to immunotherapy. Additional molecular alterations such as BRAF V600E, TGFBRII, BAX, and IGFIIR mutations, as well as involvement of the CIMP pathway in tumour suppressor gene inactivation, highlight the biological heterogeneity of the disease. Sex-related differences in incidence have also been

reported, possibly linked to X chromosome related mechanisms, with colorectal cancer being more frequent in men. However, in the analysed clinical studies, these differences were not statistically significant for septic complications, although higher rates were observed in males in certain cohorts. Furthermore, PIK3CA mutations may increase sensitivity to immunotherapy through activation of the PI3K pathway and PD-L1 overexpression, suggesting a potential predictive role in patient selection [11–13].

2.2 Diagnosis, Staging, and Multimodal Management

The diagnosis of rectal neoplasm is based on a multidisciplinary approach that includes clinical evaluation, endoscopic investigations, imaging studies, and histopathological examination. This thesis emphasises the important role of the tumour board, in which surgery, medical oncology, radiotherapy, imaging, and pathology specialists contribute to establishing the optimal therapeutic strategy [14].

Clinical examination includes inspection of the perianal region and digital rectal examination. Rectal examination provides information regarding tumour location, mobility, consistency, extent, and its relationship with the sphincter complex. In low rectal tumours, these findings are essential for deciding whether sphincter preservation is feasible [15].

Colonoscopy with biopsy is the method that confirms the diagnosis and allows the evaluation of synchronous lesions. Laboratory investigations include complete blood count, biochemical profile, and carcinoembryonic antigen (CEA), the latter being particularly useful for monitoring therapeutic response and recurrence [16].

Pelvic MRI is considered the gold standard for loco-regional staging and for evaluating potential hepatic metastases. CT of the chest, abdomen, and pelvis is used for the detection of distant metastases, while PET/CT is reserved for selected cases [17].

TNM staging is essential for treatment selection. The thesis describes T, N, and M categories and their correlation with disease stages. In addition, relevant histopathological criteria are mentioned, such as tumour grade, lymphovascular invasion, perineural invasion, and resection margin status [18].

Surgical treatment aims to achieve complete R0 resection with negative margins and total mesorectal excision (TME), the gold standard procedure performed through dissection

in the avascular plane between the mesorectal fascia and the parietal fascia, with preservation of the autonomic nerve plexuses [19].

For early-stage tumours, transanal local excision or minimally invasive techniques such as TAE, TEM, TEO, or TAMIS may be used in carefully selected cases. For locally advanced tumours, treatment is multimodal, including neoadjuvant therapy, radical surgery, and, depending on the case, adjuvant therapy.

The "watch and wait" strategy is described for patients achieving a clinical complete response after neoadjuvant treatment; however, it requires strict surveillance. This concept highlights that modern rectal cancer management may also include non-operative approaches, but only under strict selection criteria and close monitoring [20].

2.3 Postoperative Septic Complications

Septic complications in rectal surgery are classified in this thesis into local pelvic septic complications, surgical site infections, and systemic septic complications. Among these, anastomotic fistula and pelvic abscess are of major importance as they directly influence postoperative outcomes and may require additional therapeutic interventions [21–23].

Anastomotic fistula is defined as a defect at the level of the anastomosis allowing communication between the intestinal lumen and extraluminal spaces. This defect may lead to local or systemic infections, including pelvic abscess, peritonitis, and sepsis [24,25].

The Clavien–Dindo classification is used to standardise the severity of postoperative complications. Grades I–II are managed medically, grade III requires surgical, endoscopic, or radiological intervention, grade IV corresponds to organ dysfunction, and grade V represents patient death [26,27].

II. Personal Contribution

3. Working Hypothesis and General Objectives of the Study

The general objective of the present study is to assess the incidence and severity of septic complications in rectal surgery, as well as to analyse the associated risk factors involved in their occurrence. The study aims to highlight the impact of septic complications

on postoperative outcomes, prognosis, and hospital length of stay, thereby contributing to the optimisation of the surgical management of patients following rectal surgical interventions.

In order to achieve this general objective, several specific objectives were established. First, the study aims to analyse the relationship between associated comorbidities, tumour characteristics, and patients' demographic features, such as age, sex, and place of residence, and the frequency of postoperative septic complications. The study also evaluates the influence of these complications on postoperative clinical evolution, including hospital length of stay and the need for additional therapeutic interventions.

Another important objective is the classification of postoperative complications according to the standardised Clavien–Dindo system, in order to provide an objective and comparable assessment of their severity. The analysis focuses particularly on local pelvic septic complications, assessing their incidence in relation to different types of surgical procedures performed in rectal surgery.

Furthermore, the research aims to compare the main surgical techniques used in the treatment of rectal pathology in terms of feasibility, safety, and risk of developing local septic complications. In this context, both surgical interventions and digestive protective procedures were evaluated, with the goal of identifying the most effective strategy for reducing postoperative septic morbidity.

Through the analysis of these aspects, the study seeks to formulate relevant conclusions regarding predictive factors for septic complications and to identify optimal surgical approaches capable of reducing their incidence and improving postoperative outcomes in rectal surgery.

4. General Research Methodology

4.1 Study Population

The study is based on a retrospective, single-centre cohort of 226 patients diagnosed with rectal cancer at different stages of the disease, admitted to the Surgical Oncology Clinic of the "Al. Trestioreanu" Oncology Institute in Bucharest over a 5-year period starting in 1

february 2018. Patients with complete clinical, biological, and histopathological data, as well as information regarding postoperative evolution, were included.

Inclusion criteria comprised patients diagnosed with rectal neoplasm, patients admitted and surgically treated in the analysed clinic, and patients aged over 18 years.

Exclusion criteria included patients with surgical emergencies managed in other surgical clinics, patients under 18 years of age, and patients with incomplete surgical data.

4.2 Statistical Data Processing

Data were extracted from the Hipocrate system and processed using Microsoft Excel, with complete information collected for each patient. Continuous variables analysed included age, length of hospital stay, and tumour distance from the anal margin; ordinal variables included tumour stage and degree of differentiation; and nominal qualitative variables included sex and place of residence (urban/rural). All these were considered independent variables. The dependent variable was the occurrence of postoperative septic complications following rectal surgical interventions.

IBM SPSS Statistics software was used for data analysis and processing. Several statistical tests and methods were applied depending on the type of variables and study objectives. The Mann–Whitney test was used to compare differences between independent groups when data were not normally distributed. Fisher's exact test was used to assess associations between categorical variables in small samples, while the Chi-square test was applied to evaluate relationships between categorical variables.

4.3 Incidence of Septic Complications

Postoperative septic complications were classified into several categories, including superficial (supra-aponeurotic) septic complications, local complications (fistula, abscess), systemic complications (sepsis), and stoma-related septic complications *(Fig. 4.1)*.

In the analysed cohort, these complications were more frequent in patients with mid-rectal tumours, particularly in those over 50 years of age, with the highest incidence observed in patients over 60 years. A single case of postoperative sepsis was recorded in a male patient over 60 years of age.

Associated comorbidities, particularly obesity, were frequently observed in patients with local and stoma-related septic complications. Additionally, patients from urban areas showed a higher rate of septic complications.

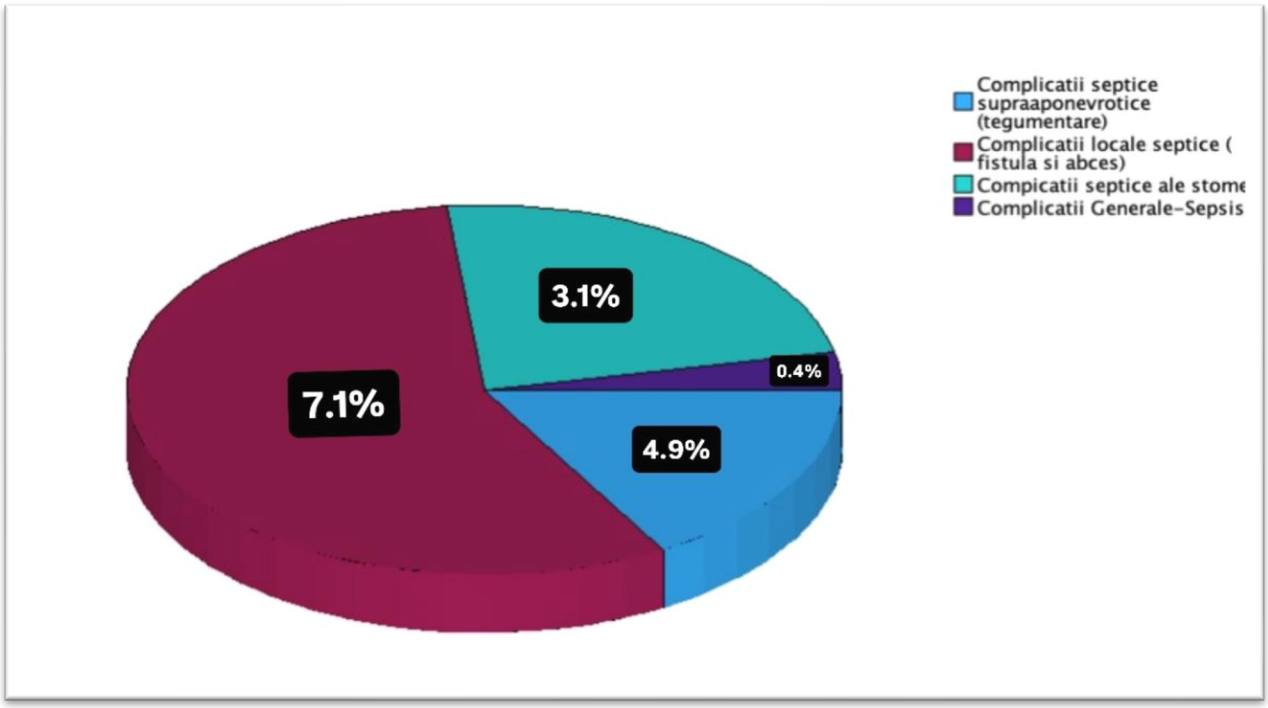

Figure 4.1 Septic complications in rectal surgery in the study cohort

5. Surgical Management of Rectal Cancer: Does Robotic Surgery Emerge as the Best Alternative A Narrative Revie

5.1 Introduction

Colorectal cancer (CRC) is the third most frequently diagnosed malignant neoplasm worldwide, accounting for 9.6% of all cancer cases, and the second leading cause of cancer-related mortality, according to the GLOBOCAN study [28].

The introduction of robotic techniques in rectal surgery has revolutionised certain postoperative outcomes in specific situations, such as low rectal cancer, where precision is essential, particularly for ultra-low anastomoses. It has been demonstrated that robotic surgical interventions may facilitate the radical resections required for T4 tumours and local recurrences, offering the potential for improved oncological outcomes [29].

This narrative review presents a brief history of open, laparoscopic, and robotic surgical approaches, as well as their advantages and disadvantages. Particular emphasis is placed on robotic surgery, highlighting its specific role in the management of rectal cancer [30].

5.2 Materials and Methods

A literature review was conducted according to PRISMA guidelines, using the PubMed, Web of Science, and Google Scholar databases, with the keywords “rectal”, “cancer”, and “surgery”. Studies were selected to highlight the evolution of rectal cancer treatment, with a focus on minimally invasive and robotic surgery.

Rectal cancer surgery has evolved progressively, beginning with the first abdominoperineal resection performed by Lisfranc in 1826. Later, Miles standardised radical abdominoperineal resection in 1908, while Hartmann (1921) proposed an approach with potential sphincter preservation. In 1948, Dixon demonstrated that colorectal anastomoses were safe for high rectal tumours, without increasing recurrence or mortality [31,32].

The most important progress was the introduction of total mesorectal excision (TME) by Heald in 1982, which subsequently became the current gold standard in rectal surgery [20,31,32]. Laparoscopic surgery was introduced in 1990 by Jacobs [33], and later robotic surgery (da Vinci system, approved in 2000) brought superior precision, followed by the continuous development of alternative platforms [34–37].

Transanal techniques evolved from TAE (1984), with limited indications, to TEM and subsequently TAMIS (2009), which improved access, precision, and recovery, and were later integrated into modern robotic approaches [38–40].

Open surgery is a well-established technique, indispensable in cases of massive haemorrhage, offering direct access and versatility, but being more traumatic, with an increased risk of infection and slower recovery. Minimally invasive surgery reduces both postoperative septic complications and intraoperative bleeding, and provides improved pelvic visualisation, resulting in better preservation of pelvic plexuses.

Robotic vs Laparoscopic Surgery

The ROLARR trial (2017) showed lower blood loss and a lower conversion rate in robotic surgery, but similar oncological outcomes [41]. The REAL study demonstrated higher sphincter preservation rates (83.1% vs 76.9%), fewer positive margins (4.0% vs 7.1%), and a lower conversion rate (1.7% vs 3.9%) in the robotic group [42].

In contrast, the COLRAR study did not demonstrate significant differences in mesorectal excision quality (TME) or postoperative complications [43]. Other studies reported a lower complication rate in robotic surgery (37.2% vs 51.2%), but a longer operative time (324 vs 214 minutes) [44], and confirmed reduced conversion rates, including in abdominoperineal resection (40.5% vs 64.3%) [45].

In patients with T4 tumours, robotic surgery showed good oncological outcomes, with a 3-year survival of 87.5% and a local recurrence rate of 4.0% [46]. Overall, the data suggest benefits mainly in the short term and in complex cases [41–56].

Robotic vs Open Surgery

The COLOR II, COREAN, ACOSOG Z6051, and ALaCaRT trials failed to demonstrate the inferiority of open surgery regarding oncological outcomes. Several meta-analyses have shown that robotic surgery reduces blood loss, infection rates, and hospital stay duration, with higher rates of negative margins and more effective lymphadenectomy [32,57–59].

Robotic vs Transanal Surgery

Compared with TaTME and other transanal techniques, short-term outcomes are similar, but differences depend on surgical team experience and patient selection [60]. Other data suggest advantages of robotic surgery in sphincter preservation, while TaTME may offer advantages in hypogastric plexus preservation [61].

Costs and Limitations

Robotic surgery is significantly more expensive than laparoscopic surgery (18,300 ± 13,900 USD vs 16,000 ± 14,800 USD) [62] or open surgery (16,316.85 USD vs 11,213.94 USD) [63]. Another important limitation is the long learning curve and increased operative time. Studies report operative time variations (190–324 minutes) depending on surgical experience [42–45,55,56,64].

5.3 Conclusions

Robotic surgery offers certain technical and functional advantages, particularly for patients with advanced or recurrent low rectal neoplasms, obese patients, and those with a narrow pelvis, by reducing conversion rates, decreasing complications, and improving nerve preservation. However, oncological outcomes are generally similar to those of laparoscopic surgery, while costs and the learning curve represent important limitations. Moreover, minimally invasive surgery cannot replace open surgery; therefore, the choice of technique must be individualised according to the patient, disease stage, and surgical team experience.

6. Impact of Transanal Drainage Tube Placement on Anastomosis Leakage Incidence After Rectal Cancer Surgery

6.1 Introduction

Low rectal neoplasms account for a significant proportion of colorectal cancer cases [65]. The surgical management of rectal cancer has evolved through the use of minimally invasive techniques; however, anastomotic fistula remains one of the most important postoperative complications, with an incidence ranging between 1.3% and 23%. In order to reduce the rate of these complications, particularly in low anastomoses (<6 cm), protective methods are used, with ileostomy being the most common option [66]. Several meta-analyses suggest that the transanal tube may represent an effective protective method, reducing the incidence of anastomotic fistula after low anterior resection. Furthermore, although some studies indicate that diverting stoma may reduce the severity of major complications such as peritonitis and sepsis, it does not appear to significantly reduce the incidence of anastomotic fistula [52,67–71].

The aim of this retrospective study was to evaluate the effectiveness of the transanal drainage tube (TAD) as a protective method after low anterior resection in rectal cancer. In the literature, there are few studies comparing, within the same patient cohort, TAD with other protective methods such as ileostomy, colostomy, or no protection. Moreover, the influence of tube characteristics (material and diameter) on postoperative outcomes remains insufficiently investigated. Therefore, a single-centre cohort from the IOB was analysed, in which a consistent 32F silicone tube was used. The study included 171 patients diagnosed with rectal neoplasm who underwent Dixon-type resection. The effectiveness of TAD was evaluated by analysing postoperative complications, with a focus on local septic complications.

6.2 Materials and Methods

The study was designed as a retrospective, single-centre cohort study conducted on 171 patients diagnosed with rectal cancer in the Department of Surgery of the "Prof. Dr. Alexandru Trestioreanu" Bucharest Oncology Institute (IOB). Patients were followed for 5 years, starting from 1 February 2018, the year in which the surgeries were performed.

The transanal drainage tube (TAD) was introduced in our hospital on 1 February 2018 as a protective method. In this context, patients who underwent tumour resection with colorectal anastomosis were divided into four distinct groups: patients with ileostomy, patients with colostomy, patients with transanal tube (TAD), and patients without any protective measure (non-TAD).

6.3 Results

The results focused on postoperative complications occurring within the first 30 days after low anterior resection (LAR), with the primary endpoint being the incidence of anastomotic fistula (AF), and the secondary endpoint being the overall comparison of complications among the TAD, non-TAD, ileostomy, and colostomy groups.

Complications were classified as early (<7 days) and late (>7 days), septic (AF, abscess), and general (parastomal hernia, seroma). Anastomotic fistula was defined according to guidelines based on clinical, biological, and imaging criteria. Anastomotic dehiscence was classified into grades A (no therapeutic impact), B (requires treatment), and C (requires surgical reintervention).

Compared with the non-TAD group, patients in the TAD group had significantly fewer early surgical complications (OR 0.23, p = 0.004) and fewer overall complications (10.6% vs. 33.3%, p = 0.0085), suggesting a protective effect of TAD. No significant differences were observed for early septic complications (p = 0.121) or late septic complications; however, late general complications were less frequent in the TAD group, without statistical significance (OR 0.27, p = 0.100). Overall, total complications were significantly reduced in the TAD group (OR 0.15, p < 0.001) (Table 6.1).

Compared with ileostomy, TAD showed no significant differences in early or late septic complications. However, ileostomy was associated with more late general complications (p = 0.0008), and total complications were significantly lower in the TAD group (OR 0.20, p = 0.003). Overall, TAD demonstrated more favourable clinical outcomes compared with ileostomy (Table 6.2).

Compared with colostomy, TAD was associated with fewer total complications (OR 0.46, p = 0.049). In contrast, colostomy showed a higher rate of total complications (OR 2.15, p = 0.049). A significant difference was also observed for stoma-related late complications, in favour of TAD (OR 0.33, p = 0.03) *(Table 6.3).*

Table 6.1 Postoperative complications: TAD vs. non-TAD

Group	TAD (n = 47)	NON-TAD (n = 54)	Value p
Early general surgical complication	3 (6.40%)	11 (20.40%)	0.004
Early septic surgical complications	0 (0%)	4 (7.40%)	0.121
Late general surgical complications	2 (4.30%)	8 (14.80%)	0.1003
Late septic surgical complications	1 (2.10%)	1 (1.85%)	1
Total septic complications	1 (2.10%)	5 (9.25%)	0.0001
Total septic complications	5 (10.60%)	18 (33.3%)	0.0085

Table 6.2 Postoperative complications: TAD vs. ileostomy

Group	TAD (n = 47)	Ileostoma (n = 45)	Value p
Early general surgical complication	3 (6.40%)	4 (8.9%)	0.711

Early septic surgical complications	0 (0%)	2 (4.4%)	0.236
Late general surgical complications	2 (4.30%)	14 (31.10%)	0.00078
Late septic surgical complications	1 (2.10%)	3 (6.7%)	0.356
Total septic complications	1 (2.10%)	5 (11.11%)	0.107
Total complications	5 (10.60%)	17 (37.80%)	0.0031

Table 6.3 Postoperative complications: TAD and colostomy

Grup	TAD (n = 47)	Colostomy (n = 25)	Value p
Early general surgical complication	3 (6.40%)	4 (16%)	0.207
Early septic surgical complications	0 (0%)	1 (4%)	0.347
Late general surgical complications	2 (4.30%)	4 (16%)	0.173
Late septic surgical complications	1 (2.10%)	1 (4%)	0.645
Total septic complications	1 (2.10%)	2 (4.44%)	0.275

6.4 Discussion

Low rectal tumours are associated with an increased risk of anastomotic dehiscence. Clinical studies have demonstrated that in these cases, the probability of developing an anastomotic fistula is 6.5 times higher compared to more proximally located tumours [72]. Risk factors include low tumour location, ischaemia, anastomotic tension, and patient comorbidities (diabetes, hypertension, obesity, smoking, chronic kidney disease), as well as systemic or local treatments. The severity of anastomotic fistula is classified into grades A–C, ranging from minor forms without therapeutic impact to severe cases requiring surgical reintervention [67].

In this study, three patient groups with different protective methods and one group without any protective measure were analysed. The results showed a lower incidence of anastomotic fistula and total complications in the TAD group compared with the other groups, suggesting a potential protective effect. Compared with the non-TAD group, TAD significantly reduced early and total complications, demonstrating an overall protective effect. Compared with ileostomy, TAD showed similar results for septic complications, but fewer total and late complications. Compared with colostomy, TAD was associated with

fewer total and late complications. Thus, ileostomy, although a classical protective method, was associated with more late complications, and some studies suggest that it does not prevent severe anastomotic fistula. In our study, the incidence of anastomotic fistula was 4.6%, with one grade C case occurring in the ileostomy group, highlighting that no method is completely protective.

TAD appears to reduce intraluminal pressure and the risk of anastomotic fistula, but without completely eliminating the risk. Several meta-analyses in the literature show variable results; however, most support a reduction in fistula incidence in TAD groups [39,73–84]. The method is simple, safe, and easy to apply, thereby avoiding potential stoma-related complications (hernia, prolapse, obstruction).

In our study, TAD was used in the form of a 32F (10 mm) silicone tube, considered superior to smaller-calibre tubes 8 mm (24F) due to more efficient drainage and improved tolerance [85]. Initially, an 8 mm tube was used in our clinic without positive results, as it proved inefficient. The study has limitations related to its retrospective, single-centre design and variability in surgical techniques, which necessitate prospective randomised studies for validation.

6.5 Conclusions

Protective stoma is associated with a higher rate of complications, and postoperative anastomotic dehiscence may have severe consequences, including life-threatening risk, particularly in low anastomoses below the Douglas pouch.

The transanal drainage tube (TAD) represents a simple and feasible alternative to stoma, with a protective role for the anastomosis, providing favourable outcomes without significant complications in the analysed group. Compared with intestinal diversion (ileostomy, colostomy), TAD offers the advantage of a lower morbidity profile.

The use of a 32F silicone tube with multiple lateral holes is recommended for optimal drainage efficiency. However, large-scale prospective randomised studies are required to validate its widespread use.

7. Comparison of morbidity and mortality of abdominoperineal resection vs low anterior resection in rectal cancer

7.1 Introduction

According to the American Cancer Society, in 2025 approximately 46,950 new cases of rectal cancer were reported in the United States, including about 27,950 in men and 19,000 in women. Rectal cancer accounts for approximately 29% of all colorectal cancers, according to the International Agency for Research on Cancer (IARC) [86].

Total mesorectal excision (TME), with preservation of the anal sphincter when possible, represents the gold standard in the surgical treatment of rectal neoplasms [87].

The main surgical options are low anterior resection (LAR/AR) and abdominoperineal resection (APR). LAR allows sphincter preservation but is associated with a risk of anastomotic fistula, whereas APR avoids this risk but involves specific morbidity related to the stoma and the perineal wound [87,88].

Anastomotic fistula is one of the most severe postoperative complications, significantly increasing mortality and the risk of local recurrence [89]. Postoperative sepsis is a major complication frequently associated with gastrointestinal surgery, with significant mortality and a substantial economic burden [90,91].

Risk factors include age, male sex, and comorbidities such as diabetes and hypertension [92]. Differences between LAR and APR regarding septic complications remain insufficiently clarified due to study variability and the lack of standardized criteria.

In this context, the present study aims to compare septic morbidity and mortality after LAR versus APR and to identify factors associated with postoperative sepsis.

7.2 Materials and Methods

The study was designed as a retrospective, single-centre analysis, including 226 patients diagnosed with rectal cancer and treated in the Department of Surgery of the Oncology Institute of Bucharest “Prof. Dr. Alexandru Trestioreanu” over a 5-year period. Patients who underwent low anterior resection (LAR) with restoration of intestinal

continuity, as well as those who underwent abdominoperineal resection (APR) with permanent stoma formation, were included.

Fisher's exact test was used to compare categorical variables between subgroups. A p-value < 0.05 was considered statistically significant. The Mann–Whitney U test was used to compare continuous variables between groups. All statistical analyses were performed using SPSS (Statistical Package for the Social Sciences), version 26.0 (IBM Corp., Armonk, NY, USA).

7.3 Results

The study included 226 patients with rectal cancer: 24.3% underwent abdominoperineal resection (APR), while 75.7% underwent low anterior resection (LAR). The mean age was 63.1 years, with no differences between groups, and males predominated (66.3%). Diabetes mellitus was significantly more frequent in the APR group (30% vs 9.9%). Neoadjuvant treatment was also more commonly used in the APR group: chemotherapy (88% vs 71.3%) and radiotherapy (92% vs 74.9%).

Hospital length of stay was similar between groups (11.35 vs 13.5 days), and mortality was 1.4% in the LAR group and 0% in the APR group. Anastomotic fistula occurred only in the LAR group (4.67%). Overall postoperative complications were comparable between groups, with rates generally ranging between 7–16%, without statistically significant differences.

Early postoperative complications (<7 days) occurred in 7.2% of APR patients and 12.9% of LAR patients, with no significant difference. Early septic complications were 8.0% in APR and 4.1% in LAR. Between days 7–30, general complications were slightly more frequent in LAR (16.4% vs 14.5%), while septic complications were more frequent in APR (9.1% vs 3.5%), but without statistical significance.

Overall, septic complications affected 7.62% of patients and were more frequent in APR (OR = 2.38), with borderline statistical significance (p = 0.06). Total postoperative complications were also more frequent in APR (54.5% vs 36.8%), likewise with borderline statistical significance (p = 0.06). Overall, complications were more frequent in the APR group. Early, general complications were 7.2% in APR vs 12.9% in LAR, while septic

complications were 8.0% vs 4.1%. Late, general complications were similar (14.5% vs 16.4%), but septic complications were higher in APR (9.1% vs 3.5%).

In summary, APR was associated with higher rates of septic complications (16.4% vs 7.6%) and total complications (54.5% vs 36.8%), without statistical significance ($p = 0.06$).

7.4 Discussion

In this study, no statistically significant differences were identified between APR and LAR regarding septic complications, hospital length of stay, or overall postoperative complications, with results being consistent with other studies in the literature [93–95]. However, sphincter preservation is feasible in most patients, although with an increased incidence of low anterior resection syndrome in ultra-low anastomoses, which remains an important clinical issue [96].

Anastomotic fistula (AL) may require reinterventions, prolonged hospitalisation, and is associated with poorer oncological outcomes [97]. A meta-analysis including 20 studies showed that AL induces local inflammation and fibrosis, affecting intestinal motility [98]. Anastomotic fistula has been reported in the literature in approximately 14% of cases and is associated with low anterior resection syndrome [95]. In the present study, the incidence of AL in the LAR group was 4.6%, including both early (<7 days) and late (7–30 days) cases, with one death associated with early septic complications.

Hypertension (HTN), diabetes mellitus(DM), and obesity have been identified as risk factors for anastomotic fistula [99–102]. Hypertension promotes tissue ischemia through microangiopathy, impairing anastomotic healing, while diabetes increases the risk of dehiscence through micro- and macrovascular alterations [100]. Obesity is associated with systemic inflammation and intraoperative technical difficulties, increasing the risk of AL, particularly in low anterior resections [101,102].

Sarcopenia increases chemotherapy toxicity and is associated with poorer clinical outcomes. Patients with greater skeletal muscle mass tend to have better tolerance to oncological treatments and, consequently, a more favourable prognosis. Chemotherapy may contribute to skeletal muscle depletion through pro-atrophic mechanisms, mitochondrial dysfunction, and reduced muscle protein synthesis. Therefore, pro-anabolic

strategies targeting skeletal muscle have shown promising results in preserving muscle mass in oncologic patients [103].

Indocyanine green (ICG) fluorescence imaging is a rapid and cost-effective technique for intraoperative assessment of intestinal perfusion. This method allows real-time visualisation of rectal wall vascularisation, particularly at the anastomotic level, and has been associated with reduced rates of severe complications, including anastomotic fistula (AL), pelvic abscess, and delayed initiation of adjuvant therapy [104].

Prehabilitation is a relatively recent approach aimed at improving patients' physical, nutritional, and psychological status prior to surgery. Reported benefits include reduced hospital length of stay, decreased postoperative complication rates, and improved quality of life [105].

Further studies are required to define optimal rehabilitation protocols and to establish the most effective implementation strategies in clinical practice in order to optimise the management of colorectal cancer patients [106]. The risk of anastomotic fistula remains significantly influenced by patient comorbidities. In this context, the creation of a diverting stoma should be considered, particularly in high-risk patients, to reduce the incidence and severity of postoperative complications [107,108].

Radiotherapy aims both to increase resectability in locally advanced tumours and to improve local disease control in early-stage disease.

In the present study, no statistically significant differences were observed between different radiotherapy dose regimens (25 Gy, 45 Gy, and 50.4 Gy), with tumour regression observed across all analysed groups. Similar results have been reported in other studies, which demonstrated comparable outcomes between 45 Gy and 50.4 Gy regimens. Additionally, radiotherapy has been associated with an increased incidence of gynaecological malignancies, while a decreased incidence of prostate cancer has been reported in these patients [95,109–113].

Thus, APR is more frequently associated with parastomal hernias and perineal wound healing problems, whereas ultra-low anastomoses carry a higher risk of anastomotic fistula and low anterior resection syndrome [93,95,114,115].

The study conclusions indicate that, although differences in septic complications between abdominoperineal resection (APR) and low anterior resection (LAR) were not statistically significant, the trend suggests a higher risk of septic complications in the APR group. It also highlights that factors such as age over 50 years and the presence of comorbidities may contribute to an increased risk of postoperative sepsis, although this association was not statistically significant.

We therefore support the use of low anterior resection (LAR) whenever possible and propose the development of a risk score for local septic complications in order to individualise management strategies and reduce their incidence.

7.5 Conclusions

Rectal surgery is still associated with a relevant risk of septic complications, especially in distal rectal tumors where fistula and pelvic abscesses are more frequent and severe. No significant difference in septic morbidity was observed between APR and LAR, suggesting that surgical approach alone is not the main determinant of infection risk. Patient comorbidities and technical factors play a key role, supporting the need for individualized surgical planning and risk stratification tools.

Final Conclusions and Personal Contribution

Although surgical techniques for rectal cancer have significantly evolved, postoperative septic complications remain frequent and continue to increase both postoperative morbidity and mortality. Strengthening healthcare infrastructure and developing both screening and rehabilitation programs are essential to reduce infection rates and optimize outcomes.

In the overall cohort analysed in this thesis, the highest incidence of septic complications was recorded in male patients. Postoperative septic complications were more frequently observed in patients with tumours located in the mid-rectum, particularly in those over 50 years of age, with the highest incidence seen in patients over 60 years. Accordingly, the single case of postoperative sepsis occurred in a male patient over 60 years of age. Associated comorbidities, especially obesity, were more frequently correlated with the occurrence of local septic complications and stoma-related complications. Patients from urban areas also showed a higher rate of septic complications. However, the differences

observed according to age, sex, place of residence, and comorbidities did not reach statistical significance, suggesting a cumulative effect of risk factors in the occurrence of postoperative septic complications.

In the first study, a literature review was conducted regarding the role of different surgical approaches and their influence on the incidence of postoperative septic complications. Minimally invasive surgery shows a clear upward trend, with a progressive shift towards robotic surgery. The analysis of available studies highlights both the advantages and limitations of the robotic approach. In total mesorectal excision, robotic surgery has demonstrated superiority, particularly in obese patients with a narrow pelvis, due to improved instrument ergonomics, greater precision of dissection, and superior visualization. These advantages translate into higher rates of complete mesorectal excision, increased lymph node harvest, lower rates of positive margins, and better preservation of pelvic nerve plexuses, especially in ultra-low and locally advanced tumours. However, laparoscopic surgery provides similar oncological outcomes in selected cases, while being more cost-effective and associated with shorter operative time. Minimally invasive surgery remains the approach associated with the lowest infection rates and faster postoperative recovery. Nevertheless, open surgery still plays an essential role in selected complex or emergency cases, such as massive haemorrhage, where conventional surgical access cannot be replaced.

In the second study, the role of different protective methods in reducing the incidence of septic complications after anterior resections was analysed. The main method evaluated was the transanal drainage tube (TAD), and its outcomes were compared with other protective strategies in order to determine their impact on postoperative septic complication rates. The results highlighted the importance of both the type and diameter of the tube used; thus, 32F (10 mm) tubes were associated with the best outcomes. In our clinic, a 24F (8 mm) tube was initially used, but it frequently became obstructed and proved ineffective. Similarly, data from the literature emphasize the importance of using a 10 mm (32F) tube. The TAD group was compared with patients without protective measures, as well as with those undergoing colostomy or ileostomy. While intestinal diversion (stoma) is associated with its own complications, the TAD group did not experience significant device-related morbidity. The results demonstrated a significant reduction in overall postoperative complications and a trend toward a decreased rate of anastomotic fistula in the TAD group,

suggesting that this represents a simple, safe, and less invasive alternative to temporary stomas. However, the risk of anastomotic fistula is influenced not only by the protective method but also by patient comorbidities, general condition, and surgical technique. Ultimately, large prospective randomized trials are required to provide stronger evidence supporting the widespread clinical use of the transanal drainage tube.

In the third study, attention was focused on analysing the incidence of local septic complications in abdominoperineal resection versus low anterior resection. The main conclusion of this research is that, although no statistically significant differences were observed between APR and LAR regarding postoperative local septic complications and postoperative mortality, the overall trend indicates a higher rate of total septic complications in abdominoperineal resection. Overall, these results support the use of low anterior resection whenever it is oncologically feasible in the treatment of rectal cancer.

Regardless of the surgical procedure performed or the protective method used, none completely eliminates the risk of septic complications; however, they may contribute to reducing their incidence. The occurrence of complications is multifactorial, being influenced both by patient-related factors, such as preoperative biological status and comorbidities, and by the surgical technique employed.

Personal Contribution

My personal contribution included database collection, statistical analysis, and interpretation of results. I also drafted the methodology and discussion sections and reviewed manuscripts for the preparation of articles subsequently published in national and international journals. In total, three articles were published: one review article in *Chirurgia*, and two original articles in *Life* and *The Journal of Medicine and Life (JML)*.

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List of Published Works

1. **Maria-Manuela Răvaş**, Virgiliu-Mihail Prunoiu, Eugen Brătucu, Marincaş M, Simion L, Manea LM, et al. *Surgical Management of Rectal Cancer: Does Robotic Surgery Emerge as the Best Alternative A Narrative Review.* **Chirurgia** [Internet]. 2025 Feb 28;120(1):48**. Indexată ISI**; FI-0.8/2025, Q3, capitolul V, https://www.revistachirurgia.ro/surgical-management-of-rectal-cancer-does-robotic-surgery-emerge-as-the-best-alternative-a-narrative-review/

2. **Maria-Manuela Răvaş**, Marincaș M, Eugen Brătucu, Vrgiliu Prunoiu, Simion L, Manea LM, et al. *Impact of Transanal Drainage Tube Placement on Anastomosis Leakage Incidence After Rectal Cancer Surgery*. **Life** [Internet]. 2025 Dec 19;16(1):5–5. **Indexată ISI**; FI-3,4/2025, Q1, capitolul VI, https://www.mdpi.com/2075-1729/16/1/5

3. **Răvaș MM**, Moisa HA, Brătucu E, Prunoiu V, Brătucu MN. Comparison of morbidity and mortality of abdominoperineal resection vs low anterior resection in rectal cancer. JML [Internet]. 2026 Apr;(3). **Indexată PubMed**; IF- 1.6, Q3, capitolul VII, https://medandlife.org/wp-content/uploads/JML-2026-0001.pdf