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COLORECTAL CANCER: MANUAL SUTURING VERSUS MECHANICAL SUTURING

DOCTORAL THESIS ABSTRACT

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TABLE OF CONTENTS

Introduction

Colorectal cancer is one of the most common malignancies worldwide, ranking third in incidence and second in cancer-related mortality [1]. The development of the disease is determined by the complex interaction between genetic factors, lifestyle, and alterations in the intestinal microbiota [4,5].

Advances in screening and diagnostic techniques, particularly colonoscopy and modern imaging methods, have improved the early detection of the disease, although access to screening programs remains uneven worldwide [9–11].

Surgery remains the primary treatment with curative intent, and the creation of a safe intestinal anastomosis represents a key factor for a favorable postoperative outcome [12]. Despite diagnostic and therapeutic progress, postoperative complications—particularly anastomotic dehiscence—continue to represent a major challenge in the management of this pathology [2,14].

However, the management of colorectal cancer remains complex, being influenced by tumor heterogeneity, treatment resistance, and the increasing incidence of early-onset forms, which highlights the need for the continuous development of diagnostic and therapeutic strategies [2,14].

GENERAL PART

Chapter 1. Current State of Knowledge

1.1 Epidemiology and Risk Factors

Colorectal cancer shows significant geographic and socioeconomic variations, with high incidence rates in Europe, North America, and Oceania, and lower rates in Africa and the Eastern Mediterranean region [16,17]. These differences are influenced by access to screening, lifestyle factors, and the level of socioeconomic development [18–22]. At the same time, an increasing incidence of early-onset colorectal cancer has been observed, particularly among individuals under the age of 50, highlighting the need for more effective prevention and early detection strategies [23,24].

The development of colorectal cancer results from the interaction between modifiable and non-modifiable risk factors. Modifiable risk factors include obesity, physical inactivity, alcohol consumption, smoking, and unhealthy dietary habits [25–32]. Among non-modifiable factors, age, male sex, genetic predisposition, and family history play a major role [16,33]. In addition, inflammatory bowel diseases, diabetes mellitus, certain chronic infections, and alterations in the intestinal microbiota contribute to colorectal carcinogenesis [34,35].

1.2 Molecular Pathways and Tumor Biology in Colorectal Cancer

Colorectal cancer is characterized by complex tumor biology involving key signaling pathways such as Wnt/β-catenin, Notch, Hedgehog, and Hippo/YAP-TAZ [4,36,37]. Dysregulation of these pathways promotes uncontrolled cell proliferation, resistance to apoptosis, tumor plasticity, and metastatic potential [38–46]. These molecular mechanisms explain the biological heterogeneity of the disease and provide new perspectives for targeted therapies.

1.3 The Role of the Tumor Microenvironment

The tumor microenvironment plays a crucial role in colorectal cancer progression through interactions between tumor cells, fibroblasts, immune cells, and the extracellular matrix [47,48]. Cytokines and growth factors stimulate tumor invasion, angiogenesis, and resistance to treatment, contributing to the development of an aggressive and adaptable tumor ecosystem [47–49].

1.4 Screening, Diagnosis, and Staging

Early detection of colorectal cancer relies primarily on colonoscopy, considered the gold standard, as well as non-invasive tests such as the fecal immunochemical test (FIT) and multitarget fecal DNA testing [9,50,51]. Recent advances include blood-based biomarkers, microbiome analysis, CT colonography, and the use of artificial intelligence to improve the detection rate of premalignant lesions [52–55]. Modern staging relies on imaging techniques such as CT, MRI, and PET-CT, which allow a more accurate evaluation of local tumor extension and metastatic disease [58–62].

1.5 Surgical Management of Colorectal Cancer

Surgery remains the main curative treatment for colorectal cancer. In colon cancer, complete mesocolic excision (CME) represents an important oncological standard, while in rectal cancer total mesorectal excision (TME) has significantly reduced local recurrence rates [10,63–66]. Minimally invasive techniques, including laparoscopic and robotic surgery, offer important benefits in postoperative recovery while maintaining oncological outcomes comparable to open surgery [67–73].

In selected cases, organ-preserving strategies such as transanal endoscopic microsurgery (TEM), transanal minimally invasive surgery (TAMIS), or the “watch-and-wait” approach may represent valuable alternatives to radical surgery [74–77]. In addition, ERAS protocols and the intraoperative use of indocyanine green fluorescence imaging contribute to reducing complications and optimizing surgical outcomes [81–84].

1.6 Systemic Therapy and Targeted Approaches

Systemic treatment of colorectal cancer has evolved significantly through the integration of targeted therapies and immunotherapy. Conventional chemotherapy remains the cornerstone of treatment in advanced disease, while anti-EGFR, anti-VEGF, and BRAF inhibitors have improved outcomes in molecularly selected patients [87–89]. Immunotherapy has demonstrated particular efficacy in MSI-H/dMMR tumors, while liquid biopsy and circulating tumor DNA (ctDNA) provide important opportunities for monitoring minimal residual disease and personalizing treatment strategies [87,90–94].

1.7 Emerging Therapeutic Strategies

New therapeutic directions include the use of ctDNA for molecular monitoring, combined immunotherapy approaches for MSS tumors, nanomedicine, gene editing, and the integration of CRISPR technologies in oncology [91–99]. These approaches reflect the transition toward precision oncology, in which treatment is guided by tumor biology and the individual molecular profile of each patient.

Chapter 2. Colorectal Anastomoses

Surgical resection remains the main curative treatment for localized colorectal cancer, and the creation of a safe intestinal anastomosis is essential for achieving favorable postoperative outcomes [101–105]. However, anastomotic dehiscence continues to represent one of the most severe postoperative complications, being associated with increased morbidity and mortality, prolonged hospitalization, and the need for surgical reintervention [102,106,107]. Its reported incidence ranges from 2% to 19%, with the highest rates observed in low rectal anastomoses [108,109]. Early diagnosis and prompt management are essential for improving patient prognosis [110–112].

In colorectal surgery, intestinal continuity can be restored using two main techniques: manual anastomosis and mechanical anastomosis. Manual anastomosis offers superior technical control and allows adaptation to the patient's anatomical and tissue characteristics, being particularly useful in complex situations. However, it requires longer operative time and significant surgical expertise [113–116]. Mechanical anastomosis, performed using stapling devices, is faster and more reproducible and is especially advantageous in minimally invasive surgery. Nevertheless, it may be associated with the risk of leakage at the staple line, particularly in fragile or compromised tissues [114,116,118].

The literature has not clearly established the superiority of one technique over the other in preventing anastomotic dehiscence. Some studies and meta-analyses support an advantage of mechanical anastomosis, particularly in low rectal resections [117,119–121], while other research highlights the benefits of manual suturing in cases involving fragile tissues or inflammatory conditions [122–124]. Additionally, randomized studies have reported no clinically significant differences between the two techniques [125].

In conclusion, the choice of anastomotic technique should be individualized according to the patient's clinical status, local tissue characteristics, type of surgical procedure, and the surgeon's experience. Both manual and mechanical anastomoses remain valid options in colorectal surgery, each presenting specific advantages and limitations [123–125].

Chapter 3. Justification of the Research Topic and Study Objectives

Colorectal cancer is one of the most common malignancies worldwide and represents a major cause of morbidity and mortality [99–101]. Although advances in diagnosis and treatment have improved patient prognosis, surgical resection remains the primary curative treatment for localized disease [6,100].

The creation of a safe intestinal anastomosis is essential for the success of surgical intervention. Anastomotic fistula represents one of the most severe postoperative complications and is associated with increased morbidity, prolonged hospitalization, and significant mortality [105–108]. The choice of anastomotic technique—manual or mechanical—remains a subject of debate in colorectal surgery, as each method presents specific advantages and limitations [110–114].

The hypothesis of this study is that postoperative outcomes in colorectal cancer surgery are influenced by the interaction between patient-related clinical factors and the surgical technique used.

The main objective of the research was to evaluate the factors influencing postoperative outcomes, with particular emphasis on the role of the anastomotic technique and the identification of risk factors associated with postoperative complications. Specific objectives included the analysis of patients' clinical characteristics, the comparative evaluation of manual and mechanical anastomoses, and the assessment of the impact of the surgical technique on postoperative complications, operative time, and postoperative recovery.

Chapter 4. General Research Methodology

The research presented in this doctoral thesis was designed as a retrospective observational clinical study aimed at analyzing the factors influencing postoperative outcomes in colorectal cancer surgery, with particular emphasis on the role of intestinal anastomosis technique and the identification of risk factors associated with postoperative complications.

The study was conducted over a period of four years (January 2021 – December 2024) in a general surgery department specialized in the treatment of colorectal oncologic pathology. All surgical procedures were performed electively by the same surgical team in order to reduce technical variability.

The study population included patients diagnosed with colorectal cancer who underwent colorectal resections with intestinal anastomosis. Two patient cohorts were analyzed within the research:

- 195 patients used for the analysis of risk factors associated with postoperative complications;
- 100 patients with rectal cancer used for the comparative analysis between manual and mechanical anastomosis.

In the comparative study, patients were divided into two equal groups: 50 patients who underwent manual anastomosis and 50 patients who underwent mechanical anastomosis performed using a circular stapler.

Adult patients with a confirmed diagnosis of colorectal cancer who underwent elective colorectal resection with intestinal anastomosis and had complete clinical data available were included in the study. Patients with previous major colorectal surgery, severe comorbidities contraindicating surgery, or incomplete medical documentation were excluded.

The analysis included clinical and demographic parameters (age, sex, body mass index, ASA score, comorbidities, neoadjuvant treatments), tumor characteristics (location, size, stage), and surgical parameters (type of procedure, anastomotic technique, operative time, surgical approach, and height of the anastomosis).

Postoperative complications evaluated included anastomotic fistula, postoperative hemorrhage, pelvic abscesses, surgical wound infections, seromas, and hematomas. The diagnosis of anastomotic fistula was established based on clinical examination, imaging investigations (CT), or intraoperative confirmation.

Postoperative evolution was assessed by analyzing the length of hospital stay, recovery of bowel function, postoperative pain intensity (VAS scale), and quality of life evaluated using the EORTC QLQ-C30 questionnaire. Patients were followed at 30 days, 6 months, and 12 months postoperatively.

Statistical analysis included descriptive and inferential methods. The Chi-square test was used for categorical variables and the Student's t-test for continuous variables, with statistical significance set at $p < 0.05$.

The study was conducted in accordance with the principles of the Declaration of Helsinki, with approval from the institutional ethics committee and with full respect for patient data confidentiality.

Chapter 5. Study I – Risk Factors for Postoperative Complications in Colorectal Cancer Surgery

Colorectal surgery represents the central component of curative treatment for colorectal cancer; however, postoperative outcomes may be influenced by numerous clinical and technical factors. Despite advances in surgical techniques, perioperative management, and multimodal oncological treatments, postoperative complications remain a significant issue in colorectal surgery, being reported in approximately 30% of cases [6,125]. These complications may lead to increased morbidity and mortality, prolonged hospitalization, and the need for surgical reintervention [125].

Colorectal cancer is one of the leading causes of cancer-related mortality worldwide, and surgical treatment remains essential for disease control in localized stages [101]. Postoperative outcomes are influenced by multiple factors, including tumor biology, patient comorbidities, immune and nutritional status, and the complexity of the surgical procedure. Among the most severe complications is anastomotic fistula, a major complication associated with peritoneal contamination, septic complications, and increased postoperative mortality.

To analyze these factors, a retrospective study was conducted including 195 patients diagnosed with colorectal cancer who underwent surgical treatment between January 2021 and December 2024. The study evaluated patients' clinical and demographic characteristics, associated comorbidities, tumor features, type of surgical intervention, anastomotic technique used, and the occurrence of postoperative complications.

The mean age of the patients was 66 years, with a predominance of male patients in the study population. A significant proportion of patients presented important comorbidities, the most frequent being cardiovascular diseases, followed by chronic respiratory insufficiency and chronic renal insufficiency. From an oncological perspective, most patients were diagnosed in stages I–III of the disease, although approximately one quarter presented metastatic disease (stage IV).

Various types of colorectal resections were performed within the studied cohort, adapted to tumor location, the most frequent being anterior rectal resection, sigmoid resections, and hemicolectomies. Digestive continuity was restored using different anastomotic techniques, including manual suturing and the use of linear or circular staplers.

Postoperative complications were recorded in 41 patients (21%). Among these, anastomotic fistula was identified in 16 patients (8.2%), representing one of the most severe complications. Other complications included postoperative hemorrhage, surgical wound healing disorders, evisceration, and intra-abdominal abscesses. The average length of hospital stay was 21 days, increasing to 33 days in patients who developed postoperative complications. The overall mortality rate was 11.7%, being higher among patients who required surgical reintervention.

Statistical analysis identified several factors significantly associated with the occurrence of postoperative complications. High tumor grade and advanced disease stage were correlated with higher complication rates ($p = 0.004$ and $p = 0.001$). In addition, major comorbidities such as cardiovascular diseases, chronic respiratory insufficiency, and chronic renal insufficiency were associated with increased perioperative risk.

The surgical approach also significantly influenced postoperative outcomes. Patients operated using laparoscopic surgery had a lower complication rate compared with those undergoing open surgery (7.1% vs. 28%, $p = 0.003$). Similarly, mechanical anastomoses were associated with a lower frequency of complications compared with manual suturing (10% vs. 42.1%, $p = 0.009$), suggesting a potential advantage of mechanical techniques in colorectal surgery.

Tumor location also had an impact on postoperative outcomes. Resections performed for tumors located in the left colon were associated with a higher complication rate compared with resections in the right colon ($p = 0.013$). This difference may be explained by the greater technical complexity of distal resections and the higher risk of anastomotic fistula in this region.

Overall, the results of this study highlight the multifactorial nature of postoperative complications in colorectal cancer surgery. Tumor-related factors, patient comorbidities, the type of surgical approach, and the anastomotic technique significantly influence postoperative outcomes. The use of minimally invasive techniques and the careful selection of the anastomotic method may contribute to reducing morbidity and improving postoperative recovery.

Although the study presents the inherent limitations of a retrospective design, the results provide relevant information from clinical practice and emphasize the importance of individualized perioperative risk stratification, optimized patient selection, and careful postoperative monitoring to improve surgical outcomes in colorectal cancer.

Chapter 6. Study II – Comparative Analysis of Mechanical and Manual Anastomosis in Rectal Cancer Surgery

Colorectal cancer represents one of the leading causes of oncologic morbidity and mortality worldwide, and the curative treatment of localized disease relies primarily on surgical resection [99–101]. The success of the intervention depends not only on oncological radicality but also on the creation of a safe anastomosis, as anastomotic dehiscence remains one of the most severe postoperative complications, being associated with sepsis, surgical reinterventions, prolonged hospitalization, and increased mortality [105–109].

In this context, the present study aimed to perform a comparative analysis of manual and mechanical anastomosis in rectal cancer surgery. A retrospective descriptive study was conducted on a cohort of 100 patients with rectal cancer treated surgically between January 2021 and December 2024. Patients were divided into two equal groups: 50 patients who underwent manual anastomosis and 50 patients who underwent mechanical anastomosis performed using a circular stapler. The analysis included postoperative complications, anastomotic fistula rate, operative time, recovery of bowel function, postoperative pain, length of hospitalization, survival, and quality of life.

The results demonstrated a clear advantage of the mechanical technique in terms of operative efficiency. The mean time required to perform the anastomosis was 15 ± 5 minutes for mechanical anastomosis compared with 30 ± 5 minutes for manual anastomosis, while the total operative time was also shorter in the mechanical group (2.3 hours versus 2.9 hours; $p < 0.01$). These findings suggest that the use of stapling devices can contribute to optimizing operative time and surgical workflow.

Regarding anastomotic fistula, the incidence was higher in the manual anastomosis group (22%) compared with the mechanical group (12%), although the difference did not reach statistical significance ($p = 0.29$). Most fistulas occurred during the early postoperative period and were more frequent in low anastomoses located 5–6 cm from the anal verge in both groups. Preoperative radiotherapy was present in a large proportion of patients who developed fistulas, suggesting a negative influence of radiation-induced tissue changes on anastomotic healing.

The analysis of fistula management showed that most cases were treated conservatively; however, the need for surgical reintervention was higher in the manual anastomosis group (36% versus 17%). Other postoperative complications, such as pelvic abscesses, postoperative hemorrhage, and surgical wound complications, were also slightly more frequent in the manual anastomosis group, although the differences were not statistically significant.

An important aspect of the study was the use of indocyanine green (ICG) fluorescence to evaluate anastomotic perfusion in five cases from each group. In all these cases, no anastomotic fistulas were recorded, suggesting a possible protective role of intraoperative perfusion assessment, although the small number of cases does not allow definitive conclusions.

Regarding functional recovery, manual anastomosis was associated with a faster return of bowel function, with 82% of patients passing flatus by the fourth postoperative day compared with the mechanical group. However, the overall length of hospitalization was comparable between groups, with a slight advantage observed in the mechanical group.

The analysis of morbidity and mortality showed lower values in the mechanical anastomosis group, where morbidity was 38% and mortality 2%, compared with 46% and 4% in the manual group. Moreover, at 12 months postoperatively, patients in the mechanical group demonstrated better quality of life, reflected by a higher HQI score (87 vs. 75; $p < 0.01$), as well as a slightly improved survival rate.

Overall, the study suggests that mechanical anastomosis provides important advantages in terms of reduced operative time, a tendency toward lower rates of anastomotic fistula, reduced morbidity, and improved medium-term quality of life. On the other hand, manual anastomosis maintains its relevance in complex cases where careful adaptation to the patient's anatomical and tissue characteristics is required [121,125]. Therefore, the choice of the optimal technique should be individualized according to the clinical context, local conditions, and the surgeon's experience.

Chapter 7. General Discussions

7.1 Surgical Techniques for Colorectal Anastomosis

Restoring intestinal continuity after colorectal resection represents a critical step of the surgical procedure, as the integrity of the anastomosis directly influences postoperative morbidity and oncological outcomes. Anastomotic dehiscence is one of the most severe complications, being associated with increased morbidity, mortality, and a higher risk of tumor recurrence [105,116,125].

In colorectal surgery, two main techniques are used: manual anastomosis and mechanical anastomosis. Manual anastomosis allows adaptation of the suture to local tissue conditions and is particularly useful in complex situations such as inflammation or post-radiation fibrosis [110,121]. Mechanical anastomosis enables rapid and standardized construction of the anastomosis and is frequently used in low rectal resections and minimally invasive surgery [111,113,118].

Comparative studies have shown no clear superiority between the two techniques, as the success of the anastomosis is mainly influenced by factors such as tissue perfusion, anastomotic tension, and patient-related characteristics [111,122]. In this context, intraoperative evaluation of intestinal perfusion using indocyanine green fluorescence represents a modern method that may increase the safety of colorectal anastomoses.

7.2 Operative Efficiency

An important advantage of mechanical anastomosis is the reduction of operative time due to the rapid and reproducible formation of the staple line [111]. Shorter operative duration may reduce perioperative stress and optimize hospital resource utilization, particularly in high-volume surgical centers.

Although mechanical staplers involve higher initial costs, cost-effectiveness studies have demonstrated that they may reduce overall healthcare expenses by shortening operative time and hospital stay [31].

7.3 Anastomotic Dehiscence

Anastomotic dehiscence remains one of the most important complications in colorectal surgery, with a reported incidence ranging from 2% to 19%, occurring more frequently in low rectal anastomoses [116].

Anastomotic healing depends on adequate tissue perfusion, collagen synthesis, and angiogenesis. Risk factors include advanced age, obesity, malnutrition, smoking, diabetes mellitus, and low tumor location [116]. Recent research also suggests a potential role of the intestinal microbiota in the process of anastomotic healing [61].

7.4 Impact of Preoperative Radiotherapy

Neoadjuvant radiotherapy is frequently used in locally advanced rectal cancer to reduce the risk of local recurrence [103]. However, it may negatively affect anastomotic healing through vascular changes and tissue fibrosis, which reduce tissue perfusion and elasticity.

Preoperative radiotherapy is therefore considered an independent risk factor for anastomotic fistula, particularly in low rectal anastomoses.

7.5 Postoperative Recovery

The restoration of bowel function is an important indicator of recovery after colorectal surgery. In the present study, the return of bowel transit was slightly faster in patients with manual anastomosis, possibly due to lower tissue compression.

Enhanced Recovery After Surgery (ERAS) protocols have significantly improved postoperative recovery through early mobilization, multimodal analgesia, and early enteral nutrition [103].

7.6 Postoperative Complications

Postoperative complications remain relatively frequent in colorectal surgery and include surgical wound infections, pelvic abscesses, and anastomotic fistulas [116].

In the present study, the overall complication rate was similar between manual and mechanical anastomosis, suggesting that both techniques are safe when performed by experienced surgical teams [18,105]. Modern strategies such as minimally invasive surgery and intraoperative

evaluation of intestinal perfusion may further contribute to reducing these complications [103–105].

Chapter 8.

Personal Contributions

8.1 Clinical Analysis of Risk Factors for Postoperative Complications

One of the main contributions of this thesis consists of the clinical analysis of risk factors involved in the occurrence of postoperative complications after colorectal resections with anastomosis. The retrospective study included 100 patients with rectal cancer divided into two equal groups: manual anastomosis and mechanical anastomosis.

The results showed an overall complication rate of 46% in the manual anastomosis group and 38% in the mechanical anastomosis group, suggesting a slightly more favorable postoperative evolution when mechanical staplers were used. Postoperative mortality was 4% in the manual group and 2% in the mechanical group.

Data analysis highlighted the role of several important factors in the occurrence of complications, particularly neoadjuvant radiotherapy and low anastomotic location, both being associated with an increased risk of anastomotic fistula.

8.2 Comparative Evaluation of Anastomotic Techniques

Another important contribution of the thesis is the comparative evaluation of manual and mechanical anastomosis in rectal cancer surgery.

The results showed that mechanical anastomosis significantly reduces the time required to construct the anastomosis (15 ± 5 minutes versus 30 ± 5 minutes for manual technique) and decreases the total operative time (2.3 hours versus 2.9 hours). Regarding anastomotic fistula, the incidence was 22% in the manual group and 12% in the mechanical group, without statistically significant differences.

Patients in the manual anastomosis group showed a slightly faster recovery of bowel function, whereas quality of life at 12 months was significantly better in patients treated with mechanical anastomosis.

8.3 Identification of Predictive Factors for Anastomotic Fistula

The analysis of the data allowed the identification of several predictive factors for the occurrence of anastomotic fistula, including:

- low rectal anastomoses
- neoadjuvant radiotherapy
- extensive tissue manipulation
- prolonged operative time

Most fistulas occurred during the early postoperative period. Regarding their management, conservative treatment was effective in most cases; however, reinterventions were more frequent in the manual anastomosis group.

8.4 Strategies for Optimizing Surgical Outcomes

Based on the results obtained, the thesis proposes several strategies for optimizing surgical outcomes in colorectal cancer:

- individualized selection of the anastomotic technique
- intraoperative assessment of intestinal perfusion
- use of mechanical staplers in high-volume surgical centers
- adaptation of the manual technique in cases with fragile or irradiated tissues
- careful monitoring of low rectal anastomoses

The implementation of these measures may contribute to reducing the incidence of postoperative complications.

8.5 Study Limitations

The main limitations of the study are related to its retrospective design, the relatively small sample size, and the inability to fully control all clinical variables.

In addition, the study did not include detailed stratification according to tumor stage or patients' nutritional status. Despite these limitations, the research provides relevant data regarding

the factors influencing postoperative outcomes and may serve as the basis for future prospective multicenter studies.

Chapter 9. Conclusions

This doctoral thesis aimed to perform a comparative evaluation of manual and mechanical anastomotic techniques in colorectal cancer surgery, as well as to identify risk factors associated with postoperative complications, particularly anastomotic fistula.

The results of the research demonstrated that both surgical techniques can be safely used when performed by experienced surgical teams; however, relevant differences exist between the two methods in terms of operative efficiency, postoperative evolution, and long-term functional outcomes. The study confirms the multifactorial nature of anastomotic dehiscence and highlights the importance of an individualized surgical approach tailored to each patient's characteristics.

Conclusions

1. **Mechanical anastomosis significantly reduces operative time**, with the time required to construct the anastomosis being approximately half that of manual suturing, contributing to improved surgical workflow and reduced exposure of the patient to anesthesia.
2. **The incidence of anastomotic fistula was lower in the mechanical anastomosis group** compared with the manual group, suggesting that stapling devices may provide more uniform tissue approximation and improved stability of the anastomotic line.
3. **Manual anastomosis was associated with faster recovery of bowel function**, probably due to reduced tissue compression and the absence of pressure exerted by mechanical stapling devices on the intestinal wall.
4. **Preoperative radiotherapy and low anastomotic location represent major risk factors for anastomotic fistula**, highlighting the impact of radiation-induced vascular and fibrotic changes on tissue healing.
5. **Quality of life at 12 months postoperatively was superior in patients with mechanical anastomosis**, suggesting that improved anastomotic stability and reduced complication rates may positively influence long-term clinical outcomes.

6. **The intraoperative use of indocyanine green (ICG) fluorescence to evaluate intestinal perfusion** represents a promising method for reducing the risk of anastomotic dehiscence by allowing real-time identification of areas with inadequate vascularization.
7. **The choice of anastomotic technique should be individualized**, taking into account patient characteristics, tumor location, tissue quality, and the surgeon's experience, as both manual and mechanical techniques present specific advantages in different clinical situations.

Overall, this thesis provides a relevant scientific contribution to the understanding of the factors influencing the success of colorectal anastomoses and emphasizes the importance of a personalized and multidisciplinary surgical approach in the treatment of colorectal cancer. The integration of modern technologies and careful evaluation of risk factors may contribute to improving anastomotic safety and patient prognosis.

Selective Bibliography

1. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality world- wide for 36 cancers in 185 countries. CA Cancer J Clin. 2024;74(3):229-263.
2. Siegel RL, Giaquinto AN, Jemal A. Cancer statistics, 2024. CA Cancer J Clin. 2024;74(1):12-49.
3. Jafari A, Hosseini FA, Jalali FS. A systematic review of the economic burden of colorectal cancer. Health Sci Rep. 2024;7(8):e70002.
4. Li Q, Geng S, Luo H, Wang W, Mo YQ, Luo Q, et al. Signaling pathways involved in colorectal cancer: pathogenesis and targeted therapy. Signal Transduct Target Ther. 2024;9(1):266.
5. Tudorache M, Treteanu AR, Gradisteanu Pircalabioru G, Lixandru-Petre IO, Bolocan A, Andronic O. Gut Microbiome Alterations in Colorectal Cancer: Mechanisms, Therapeutic Strategies, and Precision Oncology Perspectives. Cancers (Basel). 2025;17(14):2294.
6. Radu P, Zurzu M, Tigora A, Paic V, Bratucu M, Garofil D, et al. The Impact of Cancer Stem Cells in Colorectal Cancer. Int J Mol Sci. 2024;25(8):4140.
7. Radu P, Zurzu M, Paic V, Bratucu M, Garofil D, Tigora A, et al. CD34-Structure, Functions and Relationship with Cancer Stem Cells. Medicina (Kaunas). 2023; 59(5):938.
8. Pathak PS, Chan G, Deming DA, Chee CE. State-of-the-art management of colorectal cancer: Treatment advances and innovation. Am Soc Clin Oncol Educ Book. 2024;44(3):e438466.
9. Khan A, Hasana U, Nadeem IA, Khatri SP, Nawaz S, Makhdoom QU, et al. Advances in colorectal cancer screening and detection: a narrative review on bio- markers, imaging and preventive strategies. J Egypt Natl Canc Inst. 2025;37(1):20.
10. Fadlallah H, El Masri J, Fakhereddine H, Youssef J, Chemaly C, Doughan S, et al., Colorectal cancer: Recent advances in management and treatment. World J Clin Oncol. 2024;15(9):1136-1156.

11. Zhang T, Guo Y, Qiu B, Dai X, Wang Y, Cao X. Global, regional, and national trends in colorectal cancer burden from 1990 to 2021 and projections to 2040. Front Oncol. 2025;14:1466159.

12. Iordache IE, Herlo L, Popescu R, Costea DO, Alexandrescu L, Suceveanu AP, et al. Cutting Edge: A Comprehensive Guide to Colorectal Cancer Surgery in Inflammatory Bowel Diseases. J. Mind Med. Sci. 2025;12(1):6.

13. Chen E, Chen L, Zhang W. Robotic-assisted colorectal surgery in colorectal cancer management: A narrative review of clinical efficacy and multidisciplinary integration. Front Oncol. 2025;15:1502014.

14. Li Y, Cheng Z, Li S, Zhang J. Immunotherapy in colorectal cancer: statuses and strategies. Heliyon. 2024;11(1):e41354.

15. Chen H, An Y, Wang C, Zhou J. Circulating tumor DNA in colorectal cancer: biology, methods and applications. Discov Oncol. 2025;16(1):439.

16. Roshandel G, Ghasemi-Kebria F, Malekzadeh R. Colorectal cancer: epidemiology, risk factors, and prevention. Cancers (Basel). 2024;16(8):1530.

17. Sawicki T, Ruszkowska M, Danielewicz A, Niedźwiedzka E, Arłukowicz T, Przybyłowicz KE. A review of colorectal cancer in terms of epidemiology, risk factors, development, symptoms and diagnosis. Cancers (Basel). 2021;13(9):2025.

18. O'Sullivan DE, Sutherland RL, Town S, Chow K, Fan J, Forbes N, et al. Risk factors for early-onset colorectal cancer: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2022;20(6):1229-1240.e5.

19. Tsokkou S, Konstantinidis I, Papakonstantinou M, Chatzikomnitsa P, Liampou E, Toutziari E, et al. Sex differences in colorectal Cancer: epidemiology, risk factors, and clinical outcomes. J Clin Med. 2025;14(15):5539.

20. Miranda BCJ, Tustumi F, Nakamura ET, Shimanoe VH, Kikawa D, Waisberg J. Obesity and colorectal cancer: a narrative review. Medicina (Kaunas). 2024;60(8):1218.

21. Nguyen L, Shanmugan S. A review article: the relationship between obesity and colorectal cancer. Curr Diab Rep. 2024;25(1):8.

22. Marcellinaro R, Spoletini D, Grieco M, Avella P, Cappuccio M, Troiano R, et al. Colorectal cancer: current updates and future perspectives. J Clin Med. 2023; 13(1):40.

23. Matsuda T, Fujimoto A, Igarashi Y. Colorectal cancer: epidemiology, risk factors, and public health strategies. Digestion. 2025;106(2):91-99.

24. Karam F, El Deghel Y, Iratni R, Dakroub AH, Eid AH. The gut microbiome and colorectal cancer: an integrative review of the underlying mechanisms. Cell Biochem Biophys. 2025;83(3):2637-2650.

25. Gonzalez-Gutierrez L, Motiño O, Barriuso D, de la Puente-Aldea J, Alvarez-Frutos L, Kroemer G, et al. Obesity-associated colorectal cancer. Int J Mol Sci. 2024; 25(16):8836.

26. Xu P, Tao Z, Yang H, Zhang C. Obesity and early-onset colorectal cancer risk: emerging clinical evidence and biological mechanisms. Front Oncol. 2024; 14:1366544.

27. Hatime Z, El Kinany K, Huybrechts I, Murphy N, Gunter MJ, Khalis M, et al. Association of Physical Activity and Sedentary Behavior with Colorectal Cancer Risk in Moroccan Adults: A Large-Scale, Population-Based Case-Control Study. Asian Pac J Cancer Prev. 2022;23(6):1859-1866.

28. Yin JL, Li YZ, Wang R, Song XJ, Zhao LG, Wang DD, et al. Dietary patterns and risk of multiple cancers: umbrella review of meta-analyses of prospective cohort studies. Am J Clin Nutr. 2025;121(2):213-223.

29. Akter S, Islam Z, Mizoue T, Sawada N, Ihira H, Tsugane S, et al. Smoking and colorectal cancer: a pooled analysis of 10 population-based cohort studies in Japan. Int J Cancer. 2021;148(3):654-664.

30. Tsukanov VV, Vasyutin AV, Tonkikh JL. Risk factors, prevention and screening of colorectal cancer: a rising problem. World J Gastroenterol. 2025;31(5):98629.

31. Marginean SS, Zurzu M, Garofil D, Tigora A, Paic V, Bratucu M, et al. Evaluation of Key Risk Factors Associated with Postoperative Complications in Colorectal Cancer Surgery. J. Mind Med. Sci. 2025;12(1):22.

32. Shivshankar S, Patil PS, Deodhar K, Budukh AM. Epidemiology of colorectal cancer: a review with special emphasis on India. Indian J Gastroenterol. 2025; 44(2):142-153.

33. Yamada A, Kondo T. Hereditary Colorectal Cancer: Clinical Implications of Genomic Medicine and Precision Oncology. J Anus Rectum Colon. 2025;9(2): 167-178.

34. Papier K, Bradbury KE, Balkwill A, Barnes I, Smith-Byrne K, Gunter MJ, et al. Diet-wide analyses for risk of colorectal cancer: prospective study of 12,251 incident cases among 542,778 women in the UK. Nat Commun. 2025;16(1):375.

35. Chalif J, Goldstein N, Mehra Y, Spakowicz D, Chambers LM. The role of the microbiome in cancer therapies: current evidence and future directions. Hematol Oncol Clin North Am. 2025;39(2):269-294.

36. Yan L, Shi J, Zhu J. Cellular and molecular events in colorectal cancer: biological mechanisms, cell death pathways, drug resistance and signalling network interactions. Discov Oncol. 2024;15(1):294.

37. Yang Z, Wang X, Zhou H, Jiang M, Wang J, Sui B. Molecular complexity of colorectal cancer: pathways, biomarkers, and therapeutic strategies. Cancer Manag Res. 2024;16:1389-1403.

38. Feng H, Yang Y, Chen H, Zhang Z, Zeng J, Huang Y, et al. Jiedu Xiaozheng Yin extract targets cancer stem cells by Wnt signaling pathway in colorectal cancer. J Ethnopharmacol. 2025;337(Pt 1):118710.

39. Zeng S, Wang J, Shi Z, Zhao H, Gao J, Li J. The Wnt/β-catenin signaling pathway in colorectal cancer: mechanism and intervention of traditional Chinese medicine and chemical compound. Front Pharmacol. 2025;16:1560714.

40. Xue C, Chu Q, Shi Q, Zeng Y, Lu J, Li L. Wnt signaling pathways in biology and disease: mechanisms and therapeutic advances. Signal Transduct Target Ther. 2025;10(1):106.

41. Zhang, H., Hang, W., Jing, Z., Liu, B., Wang, X., Li, Y., Luo, H., Lv, H., Tao, X., Timashev, P. and Li, Y., 2025. The role of notch signaling pathway in cancer: mechanistic insights, therapeutic potential, and clinical progress. Frontiers in Immunology, 16, p.1567524.

42. Sun J, Chen Y, Xu Z, Wang W, Li P, Notch signaling in the tumor immune micro-environment of colorectal cancer: mechanisms and therapeutic opportunities. J Transl Med. 2025;23(1):315.

43. Omran MM, Fouda MS, Mekkawy SA, Tabll AA, Abdelaziz AG, Omran AM, et al. Molecular biomarkers and signaling pathways of cancer stem cells in colorectal cancer. Technol Cancer Res Treat. 2024; 23:15330338241254061.

44. Geyer N, Gerling M. Hedgehog signaling in colorectal cancer: all in the stroma? Int J Mol Sci. 2021;22(3):1025.

45. Zhang L, Zhang F, Liang H, Qin X, Mo Y, Chen S, et al. Hippo/YAP signaling pathway in colorectal cancer: regulatory mechanisms and potential drug exploration. Front Oncol. 2025;15:1545952.

46. Mohammadpour S, Torshizi Esfahani A, Sarpash SK, Vakili F, Zafarjafarzadeh N, Mashaollahi A, et al. Hippo Signaling Pathway in Colorectal Cancer: Modulation by Various Signals and Therapeutic Potential. Anal Cell Pathol (Amst). 2024; 2024:5767535.

47. Kasprzak A. The role of tumor microenvironment cells in colorectal cancer (CRC) cachexia. Int J Mol Sci. 2021;22(4):1565.

48. Wozniakova M, Skarda J, Raska M. The role of tumor microenvironment and immune response in colorectal cancer development and prognosis. Pathol Oncol Res. 2022;28:1610502.

49. Li J, Li ZP, Ruan WJ, Wang W. Colorectal cancer screening: the value of early detection and modern challenges. World J Gastroenterol. 2024;30(20): 2726-2730.

50. Lopes SR, Martins C, Costa Santos I, Teixeira M, Gamito É, Alves AL. Colorectal cancer screening: a review of current knowledge and progress in research. World J Gastrointest Oncol. 2024;16(4):1119-1133.

51. Liu SC, Zhang H. Early diagnostic strategies for colorectal cancer. World J Gastroenterol. 2024;30(33):3818-3822.

52. Duan C, Sheng J, X Ma. Innovative approaches in colorectal cancer screening: advances in detection methods and the role of artificial intelligence. Therap Adv Gastroenterol. 2025;18:17562848251314829.

53. Zhu M, Zhai Z, Wang Y, Chen F, Liu R, Yang X, et al. Advancements in the application of artificial intelligence in the field of colorectal cancer. Front Oncol. 2025;15:1499223.

54. Sun K, Wang Y, Qu R, Yang Q, Luo R, Jiang Z, et al. Comprehensive application of artificial intelligence in colorectal cancer: a review. iScience. 2025; 28(7):112980.

55. Maksim R, Buczyńska A, Sidorkiewicz I, Krętowski AJ, Sierko E. Imaging and metabolic diagnostic methods in the stage assessment of rectal cancer. Cancers (Basel). 2024;16(14):2553.

56. Sikkenk DJ, Henskens IJ, van de Laar B, Burghgraef TA, da Costa DW, Somers I, et al. Diagnostic performance of MRI and FDG PET/CT for preoperative loco- regional staging of colon cancer: systematic review and meta-analysis. AJR Am J Roentgenol. 2024;223(5):e2431440.

57. Patanè V, Atripaldi U, Sansone M, Marinelli L, Del Tufo S, Arrichiello G, et al. MRI-based radiomics for preoperative T-staging of rectal cancer: a retrospective analysis. Int J Colorectal Dis. 2025;40(1):174.

58. Gong X, Ye Z, Shen Y, Song B. Enhancing the role of MRI in rectal cancer: advances from staging to prognosis prediction. Eur Radiol. 2025;35(9):5714- 5732.

59. Engel R, Kudura K, Antwi K, Denhaerynck K, Steinemann D, Wullschleger S, et al. Diagnostic accuracy and treatment benefit of PET/CT in staging of colorectal cancer compared to conventional imaging. Surg Oncol. 2024; 57:102151.

60. Elahi R, Karami P. Mohammadreza Amjadzadeh 3 4, Mahdis Nazari 2 Radiomics- based artificial intelligence (AI) models in colorectal cancer (CRC) diagnosis, metastasis detection, prognosis, and treatment response prediction. Abdom Radiol (NY). 2025 Sep 24. Online ahead of print.

61. Smith HG, Nilsson PJ, Shogan BD, Harji D, Gambacorta MA, Romano A, et al. Neoadjuvant treatment of colorectal cancer: comprehensive review. BJS Open. 2024;8(3):zrae038.

62. Shinji S, Yamada T, Matsuda A, Sonoda H, Ohta R, Iwai T, et al. Recent advances in the treatment of colorectal cancer: a review. J Nippon Med Sch. 2022;89(3): 246-254.

63. Glimelius B. Recent advances in rectal cancer treatment–are we on the right track? Ups J Med Sci. 2024;129. eCollection 2024.

64. Islam, M.S., Abdullah, K.S.M., Sadat, C.M.A. and Islam, M.I., 2024. Surgical innovations and outcomes in the management of rectal cancer: A departmental study on advanced techniques and postoperative care. Asia Pacific Journal of Cancer Research, 1(1), pp.14-22.

65. Song XJ, Liu ZL, Zeng R, Ye W, Liu CW. A meta-analysis of laparoscopic surgery versus conventional open surgery in the treatment of colorectal cancer. Medicine (Baltimore). 2019; 98(17):e15347.

66. Naseri A, Khosravi-Mashizi M, Soleymani S, Shirinzadeh-Dastgiri A, Rahmani A, Neamatzadeh H. Advancements in Minimally Invasive Surgery for Colorectal Cancer: A Paradigm Shift. Asian Pac J Cancer Prev. 2025;26(5):1479-1481.

67. Manisundaram N, Childers CP, Hu CY, Uppal A, Konishi T, Bednarski BK, et al. Rise in Minimally Invasive Surgery for Colorectal Cancer Is Associated With Adoption of Robotic Surgery. Dis Colon Rectum. 2025;68(4):426-436.

68. Mirza W, Dadan S, Khan HM, Yasmin S. Robotic versus laparoscopic surgery for rectal cancer: a systematic review and meta-analysis of randomized trials evaluating functional recovery, complication risk, and oncologic quality. J Robot Surg. 2025;19(1):457.

69. Willis F, Amati AL, Reichert M, Hecker A, Vilz TO, Kalff JC, et al. Current evidence in robotic colorectal surgery. Cancers (Basel). 2025;17(15):2503.

70. Fan Q, Fu Z, Xiong D. Advantages and prospects of robotic surgery for colo- rectal cancer. Intelligent Surgery, 2025.

71. Kumar A, Gautam V, Sandhu A, Rawat K, Sharma A, Saha L. Current and emerging therapeutic approaches for colorectal cancer: A comprehensive review. World J Gastrointest Surg. 2023;15(4):495-519.

72. Angenete E. The Expansion of Organ Preservation. Dis Colon Rectum. 2025; 68(10):1130-1131.

73. Zhang Z, Wu R, Ke Z, Xia F, Li G, Wan J, et al. Total neoadjuvant therapy in high- risk rectal cancer: organ preservation and survival outcomes in a single-center retrospective cohort. Ther Adv Med Oncol. 2025;17:17588359251332466.

74. Negoi I, Monson JRT, Bustamante-Lopez L, Garoufalia Z, D'Andrea V, Emile SH. Editorial: Organ preservation for rectal cancer patients. Front Surg. 2025; 12:1600115.

75. Al Dhaheri M, Mubarak R, Toffaha A, AbuNada M, Parvaiz A, Kurer M. Organ Preserving or Radical Surgery? A Systematic Review and Meta-Analysis of Transanal Local Excision Versus Total Mesorectal Excision After Neoadjuvant Therapy for Rectal Cancer. J Surg Oncol. 2025;132(8):1337-1355.

76. Chandra P, Sacks GD. Contemporary surgical management of colorectal liver metastases. Cancers (Basel). 2024;16(5):941.

77. Karaoğlan BB, Öz DK, Araz MS, Akyol C, Utkan G. Advancements in the management of synchronous colorectal liver metastases: a comprehensive review of surgical, systemic, and local treatment modalities. Curr Oncol Rep. 2024; 26(7):791-803.

78. Shouki B, Abdelsalam A, Sharm Abdullah Al, Kanan A, Sherhi Ahmed Al, Emad D, et al. Management of metastatic colorectal cancer: consensus in the Gulf Cooperation Council countries. Ther Adv Med Oncol. 2025;17: 17588359241299324.

79. Kannan V, Ullah N, Geddada S, Ibrahiam A, Shakir Al-Qassab ZM, Ahmed O, et al. Impact of "Enhanced Recovery After Surgery" (ERAS) protocols vs. traditional perioperative care on patient outcomes after colorectal surgery: a systematic review. Patient Saf Surg. 2025;19(1):4.

80. Riscanevo-Bobadilla C, Barbosa RE, Guerrero IM, Valbuena D, Naranjo MP, Hernández M, et al. Enhanced Recovery After Surgery (ERAS) protocol attenuates stress and

accelerates recovery in patients after radical resection for colorectal cancer: Experience at Clínica Universitaria Colombia. Rev. Colomb. Cir. [online]. 2024;39(2):218-230.

81. McEntee PD, Singaravelu A, McCarrick CA, Murphy E, Boland PA, Cahill R. et al. Quantification of indocyanine green fluorescence angiography in colorectal surgery: a systematic review of the literature. Surg Endosc. 2025;39(4):2677- 2691.

82. Khalafi S, Botero Fonnegra C, Reyes A, Hui VW. Developments in the use of Indocyanine green (ICG) fluorescence in colorectal surgery. J Clin Med. 2024; 13(14):4003.

83. Romero-Zoghbi SE, Krumina E, López-Campos F, Couñago F. Current and future perspectives in the management and treatment of colorectal cancer. World J Clin Oncol. 2025;16(2):100807.

84. Gahunia S, Wyatt J, Powell SG, Mahdi S, Ahmed S, Altaf K. Robotic-assisted versus laparoscopic surgery for colorectal cancer in high-risk patients: a systematic review and meta-analysis. Tech Coloproctol. 2025;29(1):98.

85. Delle Cave D. Advances in molecular mechanisms and therapeutic strategies in colorectal cancer: a new era of precision medicine. Int J Mol Sci. 2025;26(1):346.

86. Loupakis F, Chiara Cremolini, Gianluca Masi, Sara Lonardi, Vittorina Zagonel, Lisa Salvatore, et al. Initial therapy with FOLFOXIRI and bevacizumab for metasta- tic colorectal cancer. N Engl J Med. 2014;371(17):1609-18.

87. El Hage M, Su Z, Linnebacher M. Addressing challenges in targeted therapy for metastatic colorectal cancer. Cancers (Basel). 2025;17(7):1098.

88. LaPelusa M, Qiao W, Iorgulescu B, San Lucas F, Patel K, Bhamidipati D, et al. Long-Term Efficacy of Pembrolizumab and the Clinical Utility of ctDNA in Locally Advanced dMMR/MSI-H Solid Tumors. Nat Commun. 2025;16(1):4514.

89. Ma D, Gao X, Wang L, Yin H, Feng L, Zhu Y. Circulating tumor DNA for MRD detection in colorectal cancer: recent advances and clinical implications. Biomark Res. 2025;13(1):89.

90. Sanz-Garcia E, Peinado P, Peláez A, Gonzalez Lopez-Aranda E, Álvarez-Gallego R, Muñoz C, et al. Circulating tumor DNA using a plasma-only assay predicts survival in patients with oligometastatic colorectal cancer after definitive therapy. J Gastrointest Oncol. 2025;16(2):580-590.

91. Parikh AR, Van Seventer EE, Siravegna G, Hartwig AV, Jaimovich A, He Y, et al. Minimal residual disease detection using a plasma-only circulating tumor DNA assay in patients with colorectal cancer. Clin Cancer Res. 2021;27(20):5586- 5594.

92. Tie J, Cohen JD, Wang Y, Christie M, Simons K, Lee M, et al. Circulating tumor DNA analyses as markers of recurrence risk and benefit of adjuvant therapy for stage III colon cancer. JAMA Oncol. 2019;5(12):1710-1717.

93. Addissouky, T.A., El Sayed, I.E.T., Ali, M.M., Alubiady, M.H.S. and Wang, Y., 2024. Precision medicine and immunotherapy advances transforming colorectal cancer treatment. Journal of Cancer Biology, 5(2), pp.38-43..

94. Ahmad, U., Harun, S., Diagne, M.M., Abdullah, S., Yusoff, K. and Veerakumarasivam, A., 2025. Oncolytic mechanisms and immunotherapeutic potential of Newcastle disease virus in cancer therapy. arXiv preprint arXiv:2505.06067.

95. Akpe V, Cock IE. Advances in Cancer Treatment Through Nanotheranostics and Emerging Therapies. Journal of Nanotheranostics. 2025 Oct 23;6(4):29.

96. Khorshid Sokhangouy S, Alizadeh F, Lotfi M, Sharif S, Ashouri A, Yoosefi Y, et al. Recent advances in CRISPR-Cas systems for colorectal cancer research and therapeutics. Expert Rev Mol Diagn. 2024;24(8):677-702.

97. Deng S, Vlatkovic T, Li M, Zhan T, Veldwijk MR, Herskind C. Targeting the DNA damage response and DNA repair pathways to enhance radiosensitivity in colorectal cancer. Cancers (Basel). 2022;14(19):4874.

98. Yang L, Wei W, Yuan X, Guo E, Peng P, Wang J, et al. Targeting DNA Damage Repair to Enhance Antitumor Immunity in Radiotherapy: Mechanisms and Opportunities. Int J Mol Sci. 2025;26(8):3743.

99. Organization WH. Cancer Today. Global Cancer Observatory 2020.

100. Dekker E, Tanis PJ, Vleugels JLA, Kasi PM, Wallace MB. Colorectal cancer. Lancet. 2019;394(10207):1467-1480.

101. Baidoun F, Elshiwy K, Elkeraie Y, Merjaneh Z, Khoudari G, Sarmini MT, et al. Colorectal Cancer Epidemiology: Recent Trends and Impact on Outcomes. Curr Drug Targets. 2021;22(9):998-1009.

102. Ali F, Keshinro A, Weiser MR. Advances in the treatment of locally advanced rectal cancer. Ann Gastroenterol Surg. 2020;5(1):32-38.

103. Keller DS, Berho M, Perez RO, Wexner SD, Chand M. The multidisciplinary management of rectal cancer. Nat Rev Gastroenterol Hepatol. 2020;17(7):414-429.

104. Smits LJH, van Lieshout AS, Grüter AAJ, Horsthuis K, Tuynman JB. Multidisciplinary management of early rectal cancer – The role of surgical local excision in current and future clinical practice. Surg Oncol. 2022;40:101687.

105. Degiuli M, Elmore U, De Luca R, De Nardi P, Tomatis M, Biondi A, et al. Risk factors for anastomotic leakage after anterior resection for rectal cancer (RALAR study): A nationwide retrospective study of the Italian Society of Surgical Oncology Colorectal Cancer Network Collaborative Group. Colorectal Dis. 2022;24(3):264-276.

106. Sripathi S, Khan MI, Patel N, Meda RT, Nuguru SP, Rachakonda S. Factors Contributing to Anastomotic Leakage Following Colorectal Surgery: Why, When, and Who Leaks? Cureus. 2022;14(10):e29964.

107. Delaney CP. Anastomotic Leaks in Colorectal Surgery. Clin Colon Rectal Surg. 2021;34(6):355-356.

108. Aker M, Askari A, Rabie M, Aly M, Adegbola S, Patel K, et al. Management of anastomotic leaks after elective colorectal resections: The East of England experience. A retrospective cohort. Int J Surg. 2021;96:106167.

109. Cwalinski J, Hermann J, Paszkowski J, Banasiewicz T. Dehiscence of colorectal anastomosis treated with noninvasive procedures. Wideochir Inne Tech Maloinwazyjne. 2023;18(1):128-134.

110. Kryzauskas M, Poskus E, Dulskas A, Bausys A, Jakubauskas M, Imbrasaite U, et al. The problem of colorectal anastomosis safety. Medicine (Baltimore). 2020;99(2):e18560.

111. Neutzling CB, Lustosa SAS, Proenca IM, da Silva EMK, Matos D, et al. Stapled versus handsewn methods for colorectal anastomosis surgery. Cochrane Database Syst Rev. 2012;(2):CD003144.

112. Tomori K, Eto K, Haruki K, Sugano H, Imaizumi Y, Kumamoto T, et al. Comparison of Strength of Anastomosis Between Four Different Techniques for Colorectal Surgery. Anticancer Res. 2020;40(4):1891-1896.

113. Lahes S, Fischer C, Igna D, Jacob P, Glanemann M. Stapled versus hand sewn anastomoses after bowel resection in patients with Crohn disease. BMC Surg. 2024;24(1):130.

114. Azevedo C, Costa Pereira C, Vilela Pinto N, Antunes A, Marques I, Costa Pereira J. Laparoscopic staple line invagination in low colorectal anastomosis – A Video Vignette. Colorectal Dis. 2023;25(7):1552-1553.

115. Atallah S, Kural S, Banda N, Banda A, Bawaney F, Cabral F, et al. Initial clinical experience with a powered circular stapler for colorectal anastomosis. Tech Coloproctol. 2020;24(5):479-486.

116. McDermott FD, Heeney A, Kelly ME, Steele RJ, Carlson GL, Winter DC. Systematic review of preoperative, intraoperative and postoperative risk factors for colorectal anastomotic leaks. Br J Surg. 2015;102(5):462-479.

117. Balkarov AA, Ponomarenko AA, Alekseev MV, Rybakov EG, Frolov SA, et al. Reinforcement of staple line of colorectal anastomosis for leakage prevention: a systematic review and meta-analysis. Khirurgiia (Mosk). 2019;(8):53-58.

118. Paun BC, Cassie S, MacLean AR, Dixon E, Donald Buie W. Postoperative complications following surgery for rectal cancer. Ann Surg. 2010;251(5):807-818.

119. Vaughan-Shaw PG, Fletcher J, El-Sayed C, Sarmah P, Gregoir T, Potter M. The Dukes' Club Fundamentals of Colorectal Surgery video series: End-to-end single layer handsewn ileocolic anastomosis – a video vignette. Colorectal Dis. 2021;23(7):1940.

120. Sanchez-Medina R, Suárez-Moreno R, Aguilar-Soto O, Cuéllar-Gamboa L, Avila-Vargas G, Di Silvio-López M. Manual mechanical anastomosis colorectal surgery. Cir Cir. 2003;71(1):39-44.

121. Varela C, Nassr M, Razak A, Kyu Kim N. Double-layered hand-sewn anastomosis: a valuable resource for the colorectal surgeon. Ann Coloproctol. 2022;38(3):271-275.

122. Karliczek A, Harlaar NJ, Zeebregts CJ, Wiggers T, Baas PC, van Dam GM. Surgeons lack predictive accuracy for anastomotic leakage in gastrointestinal surgery. Int J Colorectal Dis. 2009;24(5):569-576.

123. Slesser AA, Pellino G, Shariq O, Cocker D, Kontovounisios C, Rasheed S, et al. Compression versus hand-sewn and stapled anastomosis in colorectal surgery: a systematic review and meta-analysis of randomized controlled trials. Tech Coloproctol. 2016;20(10):667-676.

124. Kshirsagar VV, Mp H. A Comparative Study of Hand-Sewn and Stapled Anastomosis in Gastrointestinal Surgeries. Cureus. 2024;16(10):e71264.

125. Bashir Mohamed K, Haangard Hansen C, Krarup PM, Fransgård T, Tvilling Madsen M, Gögenur I. The impact of anastomotic leakage on recurrence and long-term survival in patients with colonic cancer: A systematic review and meta-analysis. Eur J Surg Oncol. 2020;46(3):439-447.

List of Published Scientific Papers

1. Marginean SS, Radu PA, Zurzu M, et al. **Advances and Ongoing Challenges in Colorectal Cancer.** *Chirurgia (Bucur).* 2026;121(1):27–42. doi:10.21614/chirurgia.3262. https://www.revistachirurgia.ro/pdfs/2026-1-27.pdf

• Article published in the journal Chirurgia, indexed in ISI Web of Science, impact factor 0.8.
• The article is based on Chapters 1–2 of the thesis (pages 1–25).

2. Marginean SS, Zurzu M, Garofil D, Tigora A, Paic V, Bratucu M, Popa F, Surlin V, Cartu D, Strambu V, et al. **Evaluation of Key Risk Factors Associated with Postoperative Complications in Colorectal Cancer Surgery.** *Journal of Mind and Medical Sciences.* 2025;12:22.
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• Article published in **Journal of Mind and Medical Sciences**, indexed in **ISI Web of Science**, impact factor **1.6**.
• The article is derived from Chapter 5 – Study I: Risk Factors for Postoperative Complications in Colorectal Cancer Surgery (pages 34–50).

3. Marginean SS, Petru AR, Garofil D, et al. **Mechanical vs. Manual Anastomosis in Colorectal Cancer Surgery: A Comparative Analysis.** *Chirurgia (Bucur).* 2024;119(6):611–625. doi:10.21614/chirurgia.3073.
https://revistachirurgia.ro/pdfs/2024-6-611.pdf

• Article published in the journal **Chirurgia**, indexed in **ISI Web of Science**, impact factor **0.6**.
• The article is derived from Chapter 6 – Study II: Comparative Analysis of Mechanical and Manual Anastomosis in Rectal Cancer Surgery (pages 52–83).