

The Impact of Minimally Invasive Surgery in Patients with Colorectal Cancer and Type 2 Diabetes Mellitus

Nicoleta Leopa¹, Mihaela Pundiche^{1,2*}, Cristina Dan¹, Teodor Ștefan Nițu^{1,2}, Stefan Paitici³, Andreea Badea², Alina Doina Nicoară^{2,4}, Răzvan Cătălin Popescu^{1,2}

¹Department of General Surgery, Emergency Hospital of Constanța, Romania

²Ovidius University, Faculty of Medicine and Pharmacy Constanța, Romania

³Department of General Surgery, Emergency Hospital of Craiova, Romania

⁴Department of Internal Medicine, Emergency Hospital of Constanța, Romania

*Corresponding author:

Mihaela Pundiche, M.D.

Ovidius University

Faculty of Medicine and Pharmacy

Department of General Surgery

Emergency Hospital of Constanța

No 145 Tomis Boulevard, 900591

Constanța, Romania

E-mail: mihaelapundiche@yahoo.com

Rezumat

Impactul chirurgiei minim invazive la pacienții cu cancer colorectal și diabet zaharat de tip II

Introducere: Chirurgia laparoscopică este acum recunoscută pe scară largă ca un tratament standard foarte sigur și eficient pentru cancerul colorectal. Diabetul provoacă mortalitate și morbiditate importantă la populația generală, iar în mod particular la pacienții care asociază o patologie oncologică. În perioada post-operatorie, pacienții diabetici prezintă un risc semnificativ mai mare de a dezvolta complicații importante. Scopul acestui studiu a fost de a analiza impactul intervenției chirurgicale minim invazive la pacienții cu cancer colorectal și diabet zaharat de tip 2.

Metodă: În perioada ianuarie 2018-2022, 482 de pacienți diagnosticați cu cancer colorectal au fost înrolați în studiu, iar dintre aceștia 52 au fost eligibili pentru includere. Au fost identificate caracteristicile generale, precum și prezența diabetului înainte de diagnosticarea cancerului de colon. S-au efectuat analize Kaplan-Meier în funcție de tipul de intervenție chirurgicală, gen, stadiu de boală și comorbidități asociate.

Rezultate: În studiu au fost incluși 52 de pacienți, împărțiți în două grupuri: 24 operați laparoscopic și 28 operați deschis. Recuperarea postoperatorie a fost mai rapidă la pacienții operați laparoscopic, acest lucru fiind evidențiat și de un număr mai mic de zile de spitalizare postoperatorie. În privința complicațiilor postoperatorii, pacienții operați deschis au avut o rată mai mare de complicații minore și majore conform clasificării Clavien-Dindo, iar supraviețuirea pe termen lung a pacienților operați laparoscopic a fost mai lungă.

Concluzii: Chirurgia laparoscopică este recomandată pacienților cu cancer colorectal și diabet zaharat tip 2, pacienții având complicații postoperatorii minime și o perioadă de recuperare postoperatorie mai rapidă.

Cuvinte cheie: chirurgie laparoscopică, cancer colorectal, diabet zaharat, complicații, supraviețuire

Received: 11.01.2025

Accepted: 20.02.2025

Abstract

Background: Laparoscopic surgery is now widely recognized as a very safe and effective standard treatment for colorectal cancer as compared with laparotomy. Diabetes causes significant mortality and morbidity in the general population, and in particular in patients who associate an oncological pathology. In the postoperative period, diabetic patients have a significantly higher risk of developing important complications. The aim of this study was to analyze the impact of minimally invasive surgery in patients with colorectal cancer and type 2 diabetes mellitus.

Methods: Between January 2018-2022, 482 patients diagnosed with colorectal cancer were enrolled in the study, of whom 52 were eligible for inclusion. General characteristics and the presence of diabetes before colon cancer diagnosis were identified. Kaplan-Meier analyses were performed according to type of surgery, gender, stage of disease, and associated comorbidities.

Results: Fifty-two patients were included in the study, divided into two groups: 24 underwent laparoscopic surgery and 28 open surgery. Postoperative recovery was faster in patients who underwent laparoscopic surgery, this being also evidenced by a lower number of postoperative hospitalization days (6.67 ± 1.97 vs 9.21 ± 2.36 , $p < 0.001$). Regarding postoperative complications, patients with open surgery, had higher rate of minor and major complications according to the Clavien-Dindo classification (67.9% vs 25%), and the long-term survival of patients who underwent laparoscopic surgery was higher.

Conclusions: Laparoscopic surgery is recommended for patients with colorectal cancer and type 2 diabetes, the patients having minimal postoperative complications and a faster postoperative recovery period.

Key words: laparoscopic surgery, colorectal cancer, diabetes mellitus, complications, survival

Introduction

Laparoscopic surgery (LS) has become an efficient and safe solution for cases of colorectal cancer (CRC), with results comparable to open surgery (OS) from an oncological point of view, but with already known benefits: faster postoperative recovery, a lower rate of postoperative complications, faster socio-professional reinsertion (1-3). Type II Diabetes Mellitus (T2DM) and Colorectal Cancer (CRC) represent diseases with an increasingly important population and socio-economic impact, but also with an impact on the duration and quality of life; the two conditions having high morbidity and mortality (4,5).

T2DM is a frequently identified comorbidity in patients requiring surgery, with approximately 15% of surgeries being performed in patients with diabetes (6). During their lifetime, one out of two patients who associate diabetes will require a surgical intervention (7). Long-term exposure to diabetes can lead to major perioperative complications, causing significant postoperative mortality and morbidity (8). Patients with diabetes frequently have microvascular and macrovascular disease that affects their perioperative results. Because of their advanced age and the inherent increased risk of the procedure, patients undergoing CRC surgery may be

especially negatively affected (9). It has long been known that hyperglycemia and infection are related; research has also linked endothelial cell dysfunction, which is caused by oxidative stress and inflammatory markers, to thrombosis (10,11).

Diabetes is the etiopathogenic factor involved in the occurrence of several diseases, including cancer (12,13). People with T2D have a higher risk of developing cancer, as well as a higher mortality rate; diabetes is a risk factor for cancer in general, and for colorectal cancer in particular (14).

The aim of this study was to analyze the clinical-pathological differences and long-term postoperative survival of patients with CRC and T2DM correlated with the type of surgical approach.

Material and Methods

Study Group

Between January 2018-2022, a case-control retrospective study was conducted on adult patients from South-Eastern Romania who were admitted to the Surgical Department for elective surgery and had been diagnosed with T2DM and colorectal cancer. The inclusion criteria were as follows: 1) Patients diagnosed with T2DM and CRC; 2) elective cases; 3) surgical resection within oncological limits, followed by anastomosis. The exclusion criteria were as follows: 1) Non-elective surgery for

CRC; 2) any personal cancer history. The patients who met the requirements for inclusion were split into two groups: Group I consisted of 28 patients who underwent open surgery, and Group II consisted of 24 patients who underwent laparoscopic surgery. The study flow is shown in *Fig. 1*.

The World Health Organization defines type 2 diabetes as having a plasma glucose level of ≥ 7.0 mmol/l and an inability of the body to manufacture insulin as needed (15). Using the Clavien-Dindo classification, postoperative complications were categorized. The minor complications were classified as Grade I and II according to the Clavien-Dindo classification. (16) Overall survival, which was defined as the interval between operation and evaluation or death, was calculated at five years. Records were kept of the clinical and pathological information (tumor staging, TNM classification, perineural, venous, and lymphatic invasion). Every six months during the first two years and then once a year after that, patients were monitored using complete blood counts, serum tumor markers, abdominal-pelvic and thoracic computed tomography, and colonoscopies.

Study Endpoints

Study endpoints: to analyze the postoperative complications and to perform a comparison

between the open and laparoscopic approaches with the assessment of long-term survival.

Ethical Approval

In compliance with the Declaration of Helsinki on human testing, the study was authorized by the Local Ethics Commission for the Approval of Clinical and Research Developmental Studies. All patients gave their informed consent when they were enrolled (approval no. 11/4.7.2024).

Statistical Analysis

SPSS version 28 was used for statistical analysis. Categorical variables are represented as counts, and the results are displayed as a median with range or mean $\pm$ standard deviation. The clinical and pathological parameters were compared using the χ^2 test. The Kaplan-Meier test was used to assess the mean overall survival (OS). A statistically significant difference was defined as $P < 0.05$. Additionally, 95% CIs and odds ratios were calculated.

Results

Included for analysis were 52 patients: 24 laparoscopically operated patients and 28 patients who

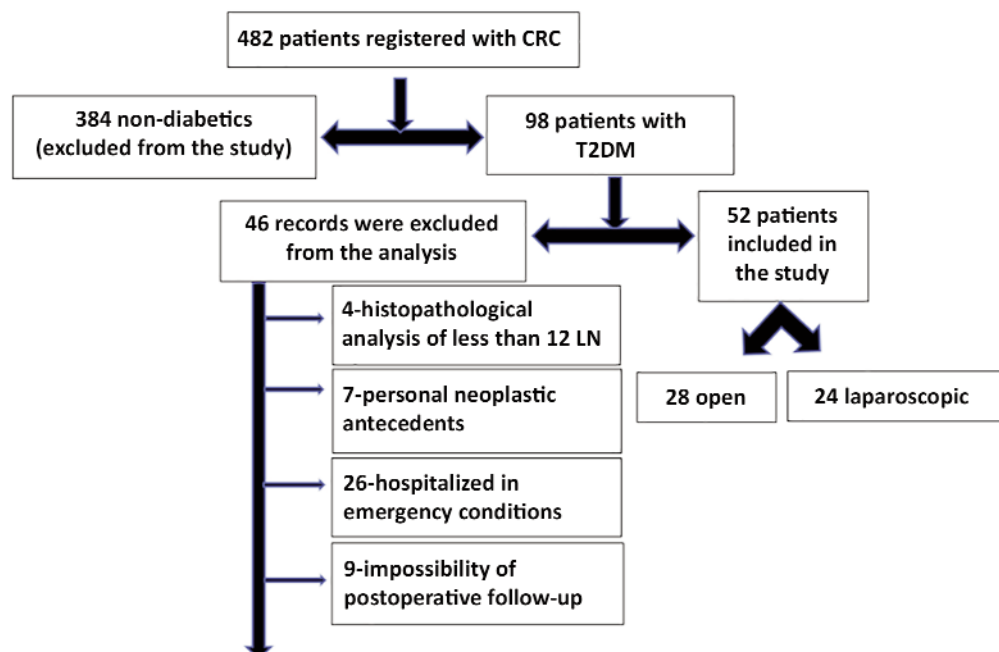


Figure 1. Flowchart visualizing recruitment of participants. Of 482 interested subjects, 52 were eligible for study inclusion.

received open surgery. The basic parameters of the patients are presented in *Table 1*. The patients operated on in the laparoscopic manner (LS) were compared according to age (within 5 years) with the participants operated on by the open manner (OS). The average age of LS patients was 61.04 ± 11 years, the average age of OS subjects was 66.54 ± 11.2 years.

One of the most frequent comorbidities of patients in both groups was hypertension, better represented by those with LS (29.2% vs 17.9%, $p=0.049$). Most patients in the study were classified as overweight (LS: 24.19 ± 3.61 , OS: 27.65 ± 4.64 , $p=0.011$). Most of the patients were preoperatively treated with oral antidiabetics (75% LS vs 53.6% OS), and the most frequent complication of diabetes was angiopathy (LS: 25%, OS: 32.1%). Between the two study groups, there were no significant statistical differences regarding age ($p=0.130$), type of treatment for T2DM ($p=0.094$),

and duration of treatment for T2DM before surgery ($p=0.058$).

The comparison of surgical outcomes between laparoscopic and open approach are presented in *Table 2*. The mean operative time was 225.42 ± 30.07 min for LS and 198.93 ± 19.12 for OS, with $p < 0.001$. The average blood loss was 136.25 ± 30.07 for LS and 158.93 ± 45.24 for OS. There were statistically significant differences between the 2 groups in terms of intensive care unit (ICU) stay (LS: 1.08 ± 0.28 , OS: 1.79 ± 0.57 , $p < 0.001$), time to the first flatus (LS: 2.92 ± 0.78 vs OS: 4 ± 0.98 , $p < 0.001$) or to the first bowel movement (LS: 2.75 ± 0.74 , OS: 3.86 ± 1.01 , $p < 0.001$). Postoperative hospitalization was longer in patient who underwent OS (9.21 ± 2.36) compared to LS (6.67 ± 1.97) ($p < 0.001$) and no postoperative mortality rate or readmission were observed.

Postoperative complications in patients with CRC and T2DM are presented in *Table 3*. The

Table 1. Baseline demographics and comorbidity of the patients

Variables	Laparoscopic (n=24)	Open (n=28)	p-value
Age (y)	61.04 ± 11	66.54 ± 11.2	0.130
BMI (kg/m ²)	24.19 ± 3.61	27.65 ± 4.64	0.011
Hb (g/dL)	10.89 ± 1.93	11.05 ± 0.66	0.008
Hypertension*	7 (29.2)	5 (17.9)	0.049
Type of treatment for T2DM*			0.094
OAD	18 (75)	15 (53.6)	
Insulin	6 (25)	13 (46.4)	
Duration of treatment for T2DM (y)	6.63 ± 2.93	8.64 ± 5.20	0.058
Complications of T2DM*			<0.001
Uncomplicated	16 (66.7)	11 (39.3)	
Angiopathy	6 (25)	9 (32.1)	
Retinopathy	1 (4.2)	2 (7.1)	
Neuropathy	0	2 (7.1)	
Nephropathy	1 (4.2)	3 (10.7)	
Skin infections	0	1 (3.6)	

Variables are expressed as mean $\pm$ SD (Standard Deviation), unless indicated otherwise.

*Number of cases, with percentages in parenthesis. Values in *italics* indicate statistical significance ($p < 0.050$). y, years; BMI, Body Mass Index; T2DM, Type 2 Diabetes Mellitus; OAD, Oral Antidiabetics.

Table 2. Comparison of surgical outcomes between laparoscopic and open approach

Variables	Laparoscopic (n=24)	Open (n=28)	p-value
Operation time (min)	225.42 ± 30.07	198.93 ± 19.12	<0.001
Estimate blood loss (ml)	136.25 ± 30.07	158.93 ± 45.24	0.094
ICU stay (pod)	1.08 ± 0.28	1.79 ± 0.57	<0.001
First bowel movement (pod)	2.75 ± 0.74	3.86 ± 1.01	<0.001
First flatus (pod)	2.92 ± 0.78	4 ± 0.98	<0.001
First mobilization (pod)	2.54 ± 0.83	3.71 ± 0.88	<0.001
Postoperative hospital stay	6.67 ± 1.97	9.21 ± 2.36	<0.001
30-day mortality	0	0	ns
Readmission	0	0	ns

Variables are expressed as mean $\pm$ SD (Standard Deviation). Values in *italics* indicate statistical significance ($p < 0.050$). min, minutes; ml, milliliters; ICU, intensive care unit; pod, postoperative day.

Table 3. Postoperative complications depending on the type of surgical intervention.

Variables	Laparoscopic (n=24)	Open (n=28)	OR [95%CI]	p-value
Any postoperative complication	6 (25)	19 (67.9)	0.171 [0.042-1.029]	0.002
Reoperation	1 (4.2)	1 (3.6)	0.967 [0.905-1.033]	0.201
Anastomotic leakage	1 (4.2)	1 (3.6)	0.967 [0.905-1.033]	0.201
Infectious complications				
Surgical site infection	0	2 (7.1)	-	ns
Intra-abdominal abscess	0	2 (7.1)	-	ns
Septicemia	0	0	-	ns
Systemic complications				
Urinary complications	1 (4.2)	1 (3.2)	0.174 [0.20-3.115]	0.171
Pulmonary complications	1 (4.2)	2 (7.1)	0.772 [0.40-5.441]	0.047
Cardiac complications	1 (4.2)	0	-	ns
Mechanical failure of wound healing	0	6 (21.4)	-	ns
Ileus	2 (8.3)	3 (10.7)	0.227 [0.043-1.197]	0.052
Clostridium difficile colitis	0	1 (3.2)	-	ns

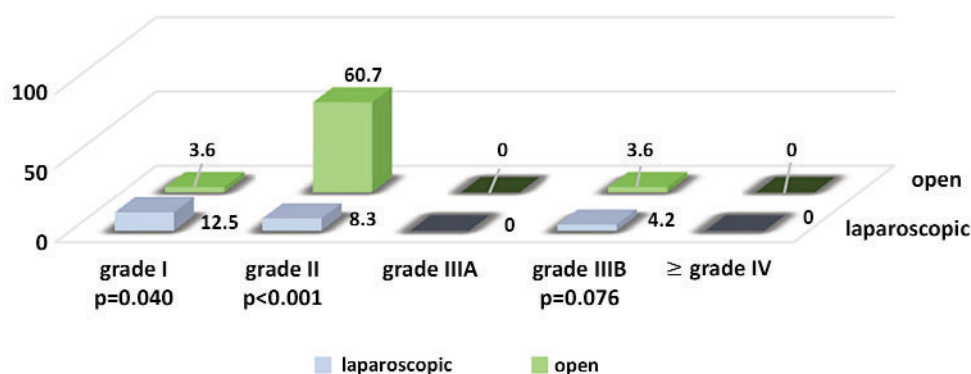
Variables are expressed as number of cases, with percentages in parenthesis.
Values in italics indicate statistical significance ($p < 0.050$).

occurrence of postoperative complications was significantly lower in patients without LS compared to patients with OS ($p=0.002$). According to the Clavien-Dindo classification, major complications were identified in one patient from the laparoscopic group and in one patient operated on openly, both patients having anastomotic leakage with intra-peritoneal abscess requiring reintervention. The minor complication rate for patients with LS was 20.8% ($n=5$): grade I (12.5%) and grade II (8.3%), and for patients with OS: 64.3% (grade I: 3.6%, grade 2: 60.7%) (Fig. 2).

From the group of patients with LS, 2 patients developed postoperative ileus and only in 4.2% of cases was a systemic complication identified. Patients undergoing open surgery had more minor complications, the most common being: surgical site infection (7.1%, treated with antibiotics), intra-abdominal abscess (7.1%, treated by ultrasound-

guided drainage and antibiotics), wound infection ($n=6$; treated with antibiotics); systemic complications being in a similar percentage in both study groups.

The overall survival rates in patients with CRC and T2DM according to Kaplan-Meier curve is analyzed in Fig. 3. Overall Survival in patients with LS was higher compared to those with OS (Fig. 3A). Survival gradually decreased with increasing tumor stage, with the exception of stage 2 where survival was shorter than in stage 3 disease (Fig. 3B). Overall survival in patients with CRC and T2DM was similar compared for men and women, with a slight increase in survival in favor of women (Fig. 3C). Regarding long-term survival of patients with CRC and T2DM, according to the Kaplan-Meier survival curve, patients who had high blood pressure as a comorbidity had a longer long-term survival (Fig. 3D).

**Figure 2.** Dindo-Clavien classification for laparoscopic and open procedures in patients with CRC and T2DM

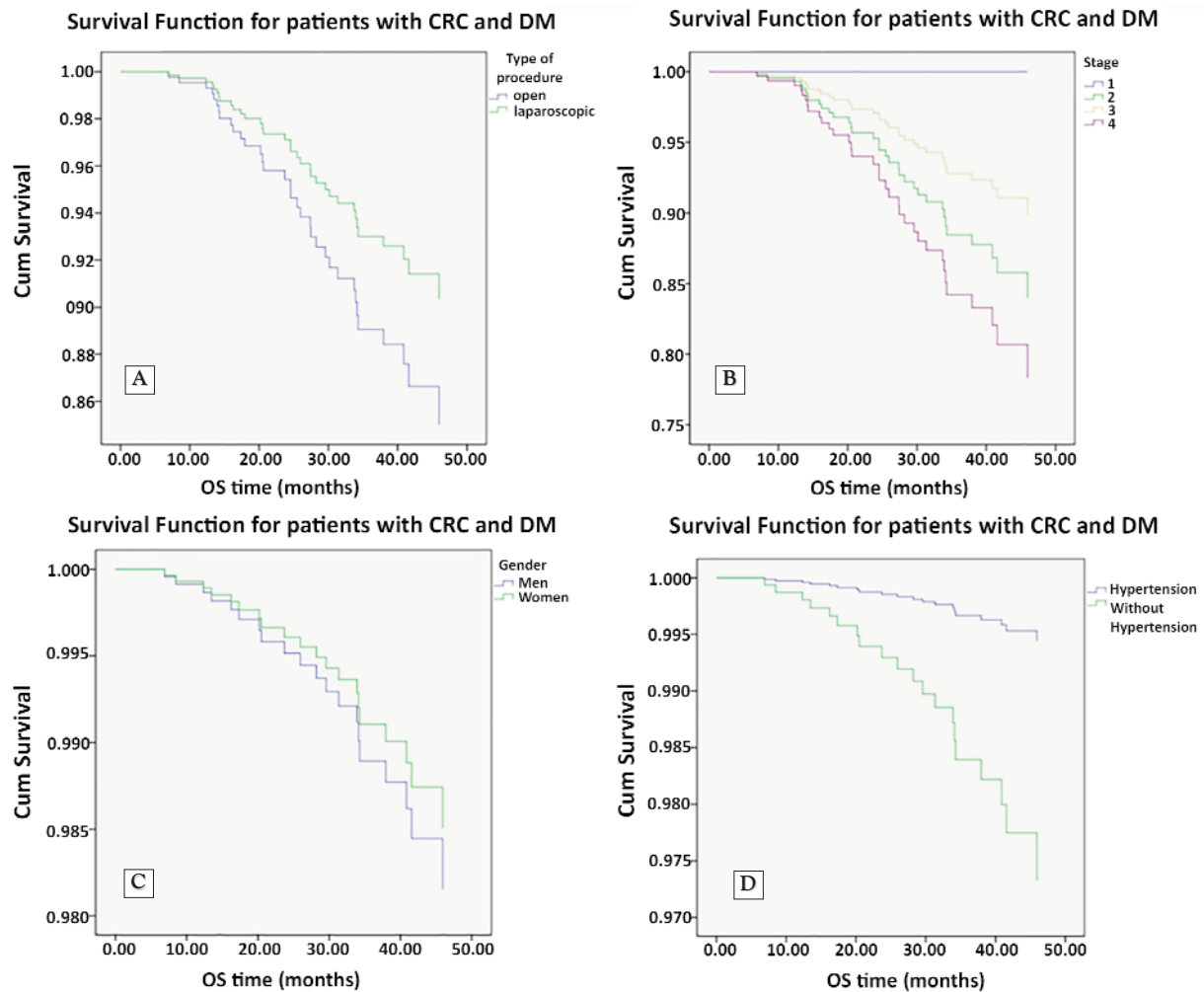


Figure 3. Kaplan-Meier overall survival analysis in patients with colorectal cancer and type 2 diabetes mellitus (A) Overall survival depending on the type of surgical approach, (B) Overall survival depending on the stage of the disease, (C) Overall survival depending on the gender of patients, (D) Overall survival depending on the association of hypertension.

Discussion

After colorectal surgery, patients with diabetes are more likely to experience postoperative complications and a higher rate of morbidity and mortality (17). Minimally invasive surgery, regardless of the patients' associated comorbidities, has proven its superiority (18). The findings of the current study demonstrated that for diabetic patients, the recommendation of a minimally invasive technique helps to reduce the rate of postoperative complications. The most common complications identified in this study were minor, regardless of the type of surgical approach, complications that required conservative treatment. Among the minor complications, the most frequently identified were wound infections in

patients undergoing open surgery. Patients who underwent minimally invasive surgery developed fewer minor complications compared to patients who underwent open surgery.

Diabetic patients are more prone to developing infectious complications in general, but especially after major surgery (19,20). In this context, major complications were also identified in the current study, but in a very low percentage, and with complications such as anastomotic leakage, which required surgical reintervention. Regarding BMI, the patients in the group of LS were classified with an average that places them in the normal weight category, and the patients in the group of OS in the overweight category. The difference between the average of the two groups is relatively small, but at

the same time statistically significant. In this sense, considering the results of the study, we do not exclude the involvement of obesity on postoperative complications and long-term survival.

Studies in the literature present strong evidence that diabetes is independently and closely associated with an increased risk of mortality in CRC surgery (3). Myenteric neuron destruction from chronic diabetes mellitus, a major source of gastrointestinal problems associated with diabetes, was identified as the cause of postoperative ileus (21). More patients in the OS group (10.7%) had ileus than in the LS group (8.3%), and they received more prokinetic medications.

Diabetes increases the risk of developing systemic problems, mostly pulmonary and urinary, and this risk is increased in patients with oncological pathologies and those in the postoperative phase (22,23). In this study, systemic complications were identified in patients regardless of the type of surgical approach. Patients who underwent minimally invasive surgery developed urinary complications in a similar number to patients who underwent open surgery. Regarding postoperative pulmonary complications, patients who underwent open surgery were more likely to develop such complications. The rate of systemic cardiac complications in patients who underwent laparoscopic surgery was higher, and no patient after open surgery developed post-operative cardiac complications.

Postoperative recovery after laparoscopic surgery is significantly reduced, compared to patients who have undergone open surgery (24). Even though the operating time is slightly longer for a minimally invasive procedure, the subsequent stay in an intensive care unit and postoperative hospitalization are significantly shorter for these patients (25). The present study demonstrated that patients operated laparoscopically had a significantly shorter time to resume bowel transit and postoperative recovery, this aspect being highlighted by a significantly lower number of post-operative hospitalization days compared to patients operated on openly.

Because of its many advantages, such as decreased postoperative complications, a connection to early mobilization, and a decreased risk of ileus, opiate use, and discomfort, minimally invasive surgery need to be taken into consideration for diabetic patients (26). Long-term survival by disease stage in the present study revealed a higher long-term survival for patients in stage 3 compared to stage 2, possibly due to the mandatory initiation of adjuvant oncology therapy in stage 3,

compared to stage 2 where only selected patients benefited from oncology treatment. The association of hypertension with diabetes and cancer led to a higher survival of patients compared to those who did not have hypertension. A possible explanation is that patients under cardiological follow-up were diagnosed earlier, followed up in the perioperative period with much more attention.

Interestingly, the results of the current study indicate an increase in survival of diabetic and colorectal cancer patients who underwent minimally invasive surgery, compared to patients undergoing open surgery, this aspect possibly being explained by the association with reduced perioperative complications, postoperative recovery, and faster socio-professional reinsertion.

When diabetic individuals acquire colorectal cancer, the best course of action, rigorous glycemic control right after surgery, and the dosage of pre-operative antidiabetic medication should all be thoroughly examined (27). Insulin reduces post-operative infections in patients with hyperglycemia and a higher risk of infectious complications (28).

Laparoscopic surgery and decreasing septic operative time (by performing mechanical anastomoses) are advised for diabetic patients. The glycemic profile should be taken into consideration in postoperative therapeutic management, along with extra precautions against thrombosis (e.g., the use of an intermittent pneumatic compression device within a below-knee cast, early preoperative mobilization, and administration of anticoagulants) and greater attention to the surgical wound. Although there are oncological advantages to standardizing techniques, lowering the incidence of postoperative problems may require more individualized surgery.

One of the limitations of the study is the limited number of cases that were analyzed after fulfilling the inclusion and exclusion requirements and also the difference between the BMI of the two study groups. Using these results alone to make adjustments to the preoperative care of DM patients would be premature. These results need to be confirmed by more research.

Conclusion

The laparoscopic approach is recommended for patients with colon or rectal cancer and especially those with type II diabetes mellitus as it lowers the complication rate and increases long-term survival. Diabetes significantly and negatively

impacted overall survival in patients with colorectal cancer. Laparoscopic surgery is recommended for patients with CRC.

Author's Contributions

Conceptualization: NL, MP, RCP; methodology: NL, RCP, MP; software: NL; validation: NL, RCP, MP, CD, TSN, SP, ADN, AB; formal analysis: NL; investigation: NL, MP, RCP, CD, TSN, SP, ADN, AB; resources: NL, RCP, MP, TSN, CD; data curation: NL; writing-original draft preparation: MP, NL; writing-review and editing: NL, MP, RCP; visualization: NL, RCP, MP, CD, TSN, SP, ADN, AB; supervision: NL, MP, RCP; administration: NL, RCP, MP. All authors have read and agreed to the published version of the manuscript.

Conflicts of Interests

The authors declare no conflicts of interests.

Ethical Statement

In compliance with the Declaration of Helsinki on human testing, the study was authorized by the Local Ethics Commission for the Approval of Clinical and Research Developmental Studies. All patients gave their informed consent when they were enrolled (approval no. 11/4.7.2024).

References

- Kagawa Y, Yamada D, Yamasaki M, Miyamoto A, Mizushima T, Yamabe K, et al. The association between the increased performance of laparoscopic colon surgery and a reduced risk of surgical site infection. *Surg Today*. 2019;49(6):474-481.
- Durak D, Alkurt EG, Turhan VB, Tutan B, Sahiner IT, Kendirci M. Comparison of Short-Term Results of Laparoscopic and Open Surgeries for Colorectal Cancer: A Single-Center Experience. *Cureus*. 2022;14(5):e24635.
- Popescu RC, Leopa N, Dumitru E, Mitroi AF, Tocia C, Dumitru A, et al. Influence of type II diabetes mellitus on postoperative complications following colorectal cancer surgery. *Exp Ther Med*. 2022;24(4):611.
- (WHO). World Health Organization. Global Report on Diabetes; WHO: Geneva, Switzerland, 2017; Available online: <http://www.who.int/diabetes/global-report/en/> (Accessed in 01.02.2022).
- Dumitru E, Dumitru IM, Popescu R, Resul G, Bulbuc I, Rugina S. Simultaneous occurrence of two rare diseases: actinomycosis and melanoma of the rectum. *J Gastrointest Liver Dis*. 2014;23(1):95-98.
- Clement S, Braithwaite SS, Magee MF, Ahmann A, Smith EP, Schafer RG, et al. Management of diabetes and hyperglycemia in hospitals. *Diabetes Care*. 2004; 27(2):553-91.
- Khazai NB, Hamdy O. Inpatient Diabetes Management in the Twenty-First Century. *Endocrinol Metab Clin North Am*. 2016;45(4):875-894.
- Kopp Lugli A, Marti WR, Salm L, Mujagic E, Bundi M, von Strauss M, et al. The Role of HbA1c as a Positive Perioperative Predictor of Surgical Site and Other Postoperative Infections: An Explorative Analysis in Patients Undergoing Minor to Major Surgery. *World J Surg*. 2022;46(2):391-399.
- Coursin DB, Connery LE, Ketzler JT. Perioperative diabetic and hyperglycemic management issues. *Crit Care Med*. 2004;32(4 Suppl):S116-25.
- Khazai NB, Hamdy O. Inpatient Diabetes Management in the Twenty-First Century. *Endocrinol Metab Clin North Am*. 2016;45(4):875-894.
- Dumitru A, Matei E, Cozaru GC, Chisoi A, Alexandrescu L, Popescu RC, et al. Endotoxin Inflammatory Action on Cells by Dysregulated-Immunological-Barrier-Linked ROS-Apoptosis Mechanisms in Gut-Liver Axis. *Int J Mol Sci*. 2024; 25(5):2472.
- Popescu RC, Botea F, Dumitru E, Mazilu L, Micu LG, Tocia C, et al. Extended Lymphadenectomy for Proximal Transverse Colon Cancer: Is There a Place for Standardization? *Medicina (Kaunas)*. 2022;58(5):596.
- Tocia C, Dumitru A, Mateescu B, Negreanu L, State M, Cozaru GC, et al. Tissue and Circulating MicroRNA-31, MicroRNA-200b, and MicroRNA-200c Reflects Disease Activity in Crohn's Disease Patients: Results from the BIOMIR Study. *J Gastrointest Liver Dis*. 2023;32(1):30-38.
- Savu E, Vasile L, Serbanescu MS, Alexandru DO, Gheonea IA, Pirici D, et al. Clinicopathological Analysis of Complicated Colorectal Cancer: A Five-Year Retrospective Study from a Single Surgery Unit. *Diagnostics (Basel)*. 2023; 13(12):2016.
- Federation., World Health Organization & International Diabetes. Definition and diagnosis of diabetes mellitus and intermediate hyperglycaemia: report of a WHO/IDF consultation. World Health Organization. <https://apps.who.int/iris/handle/10665/43588>. (Accessed 20.10.2023).
- Bolliger M, Kroehnert JA, Molineu F, Kandiolier D, Schindl M, Riss P. (2018). Experiences with the standardized classification of surgical complications (Clavien-Dindo) in general surgery patients. *Eur Surg*. 2018; 50(6):256-261.
- Sandini M, Mattavelli I, Nespoli L, Uggeri F, Gianotti L. Systematic review and meta-analysis of sutures coated with triclosan for the prevention of surgical site infection after elective colorectal surgery according to the PRISMA statement. *Medicine (Baltimore)*. 2016;95(35):e4057.
- Pasam RT, Esemuede IO, Lee-Kong SA, Kiran RP. The minimally invasive approach is associated with reduced surgical site infections in obese patients undergoing proctectomy. *Tech Coloproctol*. 2015;19(12):733-743.
- Tan DJH, Yaow CYL, Mok HT, Ng CH, Tai CH, Tham HY, et al. The influence of diabetes on postoperative complications following colorectal surgery. *Tech Coloproctol*. 2021;25(3):267-278.
- Lin X, Li J, Chen W, Wei F, Ying M, Wei W, et al. Diabetes and risk of anastomotic leakage after gastrointestinal surgery. *J Surg Res*. 2015; 196(2):294-301.
- Biondo S, Miquel J, Espin-Basany E, Sanchez JL, Gorda T, Ferrer-Artola AM, et al. A Double-Blinded Randomized Clinical Study on the Therapeutic Effect of Gastrografin in Prolonged Postoperative Ileus After Elective Colorectal Surgery. *World J Surg*. 2016;40(1):206-214.
- Targher G, Byrne CD, Tilg H. MASLD: a systemic metabolic disorder with cardiovascular and malignant complications. *Gut*. 2024;73(4):691-702.
- Ghioldis AC, Sărbu V, Pundiche M, Dan C, Butelchin C, Olteanu C, et al. Clostridium Difficile Infection in Rectal Cancer Patients after Diverted Loop Ileostomy Closure. *Chirurgia (Bucur)*. 2024;119(1):36-43.
- Petrelli F, Ghidini M, Rausa E, Ghidini A, Cabiddu M, Borgonovo K, et al. Survival of Colorectal Cancer Patients With Diabetes Mellitus: A Meta-Analysis. *Can J Diabetes*. 2021;45(2):186-197.e2.
- Strombom P, Widmar M, Keskin M, Gennarelli RL, Lynn P, Smith JJ, et al. Assessment of the Value of Comorbidity Indices for Risk Adjustment in Colorectal Surgery Patients. *Ann Surg Oncol*. 2019;26(9):2797-2804.
- Meng F, Song L, Wang W. Metformin Improves Overall Survival of Colorectal Cancer Patients with Diabetes: A Meta-Analysis. *J Diabetes Res*. 2017; 2017:5063239.
- Tsilidis KK, Kasimis JC, Lopez DS, Ntzani EE, Ioannidis JP. Type 2 diabetes and cancer: umbrella review of meta-analyses of observational studies. *BMJ*. 2015; 350:g7607.
- Pearson-Stuttard J, Papadimitriou N, Markozannes G, Cividini S, Kakourou A, Gill D, et al. Type 2 Diabetes and Cancer: An Umbrella Review of Observational and Mendelian Randomization Studies. *Cancer Epidemiol Biomarkers Prev*. 2021;30(6):1218-1228.