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CONTENTS

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RESEARCH ARTICLE

Effect of Mismatch Repair and Human Epidermal Growth Receptor 2 Expression on Prognosis in Colon Adenocarcinoma

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ABSTRACT

Aim: Colon adenocarcinomas are common worldwide and are among the most common causes of cancer-related deaths despite recent advances. In our study, we aimed to investigate the effect of the expression of human epidermal growth receptor 2 (HER2) and mismatch repair (MMR), which are used in the treatment of other solid organ tumors, on prognosis in colon adenocarcinoma.

Method: HER2 and MMR expressions were examined by immunohistochemical examination by identifying colon adenocarcinoma diagnosed and treated in our center between 2010 and 2019. Clinicopathological features and disease-free survival (DFS) were compared with the expressions.

Results: The mean DFS was 49.71 months in patients with HER2 score 3 and 104.45 months in patients with microsatellite instability. A HER2 score of 3 in patients with colon adenocarcinoma increases the mortality risk 3.36 times in multivariate analysis. Microsatellite instability was not associated with clinicopathological features and prognosis.

Conclusion: HER2 was found to be an independent prognostic factor in patients with colon adenocarcinoma.

Keywords: Colon adenocarcinoma, human epidermal growth receptor 2, mismatch repair, microsatellite instability, prognosis

Introduction

Colon cancer is among the top five most common organ tumors.[1] Despite its molecular characteristics, tumor stage remains the gold standard in terms of prognosis.[2] Colon cancer is a prevalent form of tumor worldwide, and while molecular characteristics are important in predicting prognosis, tumor stage remains the primary determinant.[1,2] Tumors can be classified as either microsatellite stable (MSS) or microsatellite instable (MSI), depending on the status of the mismatch repair (MMR) system. Deficiency in the MMR system is caused by inactivation of genes responsible for MMR, namely MLH1, MSH2, MSH6, and PMS2. MMR immunohistochemical staining results were compatible with the genetic results. MSI tumors can be further categorized as MSI with or without germline mutations in DNA.[3] The frequency of MSI tumors is approximately 15% (12% are sporadic, and 3% are inherited).[4] MSI tumors have been reported at a rate of 24% in advanced metastatic tumors.[5,6] Patients with MSI colon cancer have histological and molecular features, such as high lymph node involvement and poorly differentiated colon cancer.[7] However, patients with MSI tumors are more sensitive to immune checkpoint inhibitors than are patients with low microsatellite instability in colon cancer.[8] However, it should be noted that the prognosis may be heterogeneous in patients with MSI tumors. This is especially important in stage 2 patients, and this group of patients with a poor outcome may require adjuvant chemotherapy to prevent relapse after surgery.[5]

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Studies have shown that overexpression of human epidermal growth receptor 2 (HER2) in colon cancer may be associated with lower disease-free survival (DFS) and overall survival (OS).[9-11] HER2 is a tyrosine kinase-related epidermal growth factor receptor (EGFR) located on 17q12.[12] Efforts have been made to target HER2 with trastuzumab for the treatment of gastric and breast cancers, and this approach has shown effectiveness. Consequently, there have been drug-targeting efforts in colorectal cancers.[11-13] HER2 has been incorporated into the treatment of patients with metastatic colon cancer with appropriate HER2 status.[15] Additionally, the relationship between HER2 and clinicopathological prognostic factors is contradictory.[9,14] These conflicting findings suggest that the role of HER2 in colon cancer requires further investigation.

In this study, the relationship between MMR and HER2 status, clinicopathological findings, and survival in patients with colon adenocarcinoma is retrospectively examined in light of literature information.

Materials and Method

Patients diagnosed with colon cancer and followed up in the oncology clinic between 2010 and 2019 were identified from the pathology department and hospital records. The study was conducted in cases with surgical resection material.Approval for the study was obtained from the Hittite University Clinical Research Ethics Committee (approval number: 2023-168, dated: 26.12.2023).

A total of 146 patients diagnosed with colon adenocarcinoma were identified based on pathology records. Confidentiality of patient information was ensured.

Histologic Study

The histopathological features of 146 patients were examined by two expert pathologists (BY and YB) who were blinded to the patients' clinical information. The examination was conducted using the tumor node metastasis 8th classification.[16] The study focused on a specific group of patients and did not include those diagnosed with other rare types, such as neuroendocrine carcinoma or pure mucinous carcinoma. Tumors of type pT1 were not detected, and since there were not enough patients in the pT2 and pT3 groups, pT2-3 and pT4 were grouped to be able to work statistically. Furthermore, patients whose materials could not be accessed and those with no tissue left for examination (n=24) were also excluded. Patients who received neoadjuvant treatment were excluded from the study. All patients could receive surgical treatment. Formalin-fixed paraffin-embedded tumor tissues from 122 patients with adenocarcinoma meeting the study criteria were sectioned serially at 4-micron thickness for hematoxylin-eosin, MMR (MLH1, MSH2, MSH6, PMS2), and HER2 analysis (Figure 1).

Clinicopathological data, sex, patient age at diagnosis, tumor location, diameter, depth (pT), lymph node metastasis, organ metastasis, tumor grade, angiolymphatic invasion, perineural invasion, and clinical stage were determined. DFS time and the number of deaths were recorded until the study termination date (June 2023).

Stage and tumor depth ratios were grouped separately according to the distribution of the cases, and the differences in the ratios between HER2 scores, MMR status, and prognosis were analyzed according to the size of the ratios in the cross-table.

Immunohistochemical Study

The following immunohistochemical staining was performed using the Dako platform (Dako Omnis closed system immunohistochemical staining device), in accordance with the manufacturer's instructions. The following Dako platform clones were used: Clone A048529 for HER2, Clone FE11 for MSH2, Clone ES05 for MLH1, Clone EP49 for MSH6, and Clone EP51 for PMS2. A previously detected positive tumor tissue was selected as the HER2 control. MMR colon tumor tissue samples were selected as MMR-positive controls. Since the immunohistochemical method was used in the study, MMR examinations were grouped as MSI/MSS. The slides underwent evaluation using a Nikon Eclipse Ni microscope. Tumor areas were examined sequentially at low-to-high magnification. The artifacts and necrotic areas were not evaluated.

Statistical Analysis

A statistical analysis was conducted using IBM SPSS Statistics version 22 software (SPSS Inc., Chicago, IL, USA). The mortality effects were examined using Cox regression analysis. The Kolmogorov-Smirnov test was used for the normality analysis of variables. When the dependent variable was quantitative,

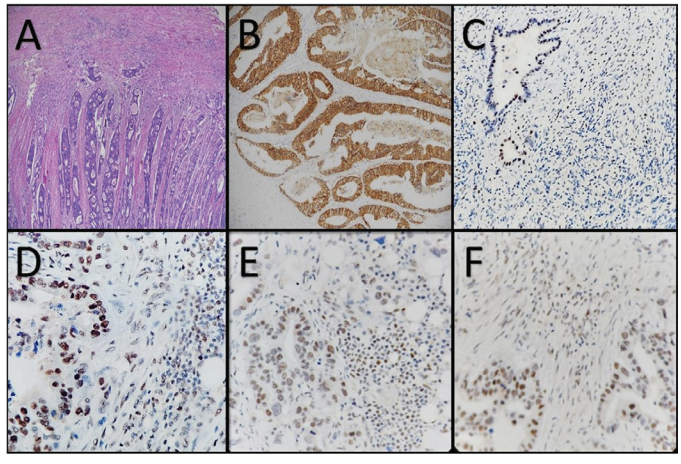

Figure 1. Colorectal cancer H&E staining and mismatch repair immunohistochemistry staining; A-Colon adenocarcinoma H&E, 10X, B-HER2 score 3 staining, 20X, C-PMS2 positive staining, 40X, D-MLH1 positive staining, 40X, E-MSH2 positive staining, 40X, F-MSH6 positive staining, 40X
HER2: Human epidermal growth receptor 2, H&E: Hematoxylin and eosin

two independent groups were compared using the Mann-Whitney U test, and more than two independent groups were compared using the Kruskal-Wallis test. If the variables were distributed normally, median values were determined using Kaplan-Meier survival analysis. Descriptive statistics were performed using Kaplan-Meier analyses and evaluated with log-rank tests. The chi-squared independence test was used to investigate whether the two qualitative variables influenced each other. A p-value of <0.05 was considered significant.

Results

Table 1 shows the descriptive statistics for the clinicopathological characteristics.

The expression rates of MLH1, MSH2, MSH6, and PMS2 in MMR cases were 84%, 97.5%, 91.8%, and 89.3%, respectively. The HER2 expression rate was 5.7%.

The MMR status did not affect survival or other prognostic factors. The mean life expectancy for those with MSI tumors was 104.45 [95% confidence interval (CI): 80.43-128.46] months, while that for those without MSS tumors was 92.78 (95% CI: 81.73-103.83) months. There was no statistically significant difference in survival rates between patients with and without MSI tumors (log-rank =0.295, p=0.587).

At pathological stage 3, a statistically significant difference was observed between HER2 rates and DFS time rates (p=0.025) (Figure 2). There was no statistically significant difference between the HER2 rates and survival rates at clinical stages 2, 3, and 4 (p>0.05). Similarly, no statistically significant difference was observed between the HER2 rates and survival rates at pathological stage 4 (p>0.05).

There was no statistically significant difference between the HER2 rates and survival rates when clinical and pathological stages 3 and 4 were combined with clinical stage 2 (p>0.05) (Table 2). However, a statistically significant difference was found between the HER2 rates and survival time rates when combined pathological stages 3 and 4 were compared (p=0.034); (Table 2).

In the univariate model, none of the variables was statistically significant (p>0.05). These variables included sex, localization, tumor diameter, histological grade, lymphovascular invasion, perineural invasion, lymph node metastasis (N1), tumor depth, and MSI status.

The results of the univariate model indicated that certain factors were statistically significant, including age (<65 vs. >65 years), lymph node metastasis (N2), distant metastasis, and HER2 expression (p=0.033, p=0.029, p=0.004, and p=0.021, respectively). The corresponding hazard ratios (HRs) (95% CI) for age, lymph node metastasis (N2), distant metastasis, and HER2 scores (3/0) were 1,030 (1,002-1,058), 3,506 (1,569-7,837), 2,636 (1,351-5,143), and 3,023 (1,180-7,742), respectively.

Table 1. Statistical distributions of clinicopathological features

		Mean ± SD (min.-max.)
Age		67.71±12.54 (25-93)
Sex	Male	72 (59%)
	Female	50 (41%)
Tumor diameter		5 (2-15)
Tumor localization	Right colon	59 (48.4%)
	Left colon	63 (51.6%)
Tumor grade	Good	29 (23.8%)
	Moderately	86 (70.5%)
	Poorly	7 (5.7%)
Lymphovascular invasion	No	61 (50%)
	Yes	61 (50%)
Perineural invasion	No	63 (51.6%)
	Yes	59 (48.4%)
Number of metastatic lymph nodes		0 (0-16)
Clinic stage	2	67 (54.9%)
	3	34 (27.9%)
	4	21 (17.2%)
pT2-3, pT4	pT2-3	95 (77.9%)
	pT4	27 (22.1%)
pN	0	68 (55.7%)
	1	45 (36.9%)
	2	9 (7.4%)
pM	0	101 (82.8%)
	1	21 (17.2%)
MMR	MSI	20 (16.4%)
	MSS	102 (83.6%)
HER2	0	115 (94.3%)
	3	7 (5.7%)
DFS	Alive	83 (68%)
	Ex	39 (32%)

min.-max.: Minimum-maximum, MMR: Mismatch repair, HER2: Human epidermal growth receptor 2, DFS: Disease-free survival

Non-significant variables in the univariate model were excluded from the multivariate model. Lymph node metastasis (N2) was not statistically significant (p>0.05) in the multivariate model. However, age, distant metastasis, and HER2 expression were statistically significant (p=0.001, p=0.032, and p=0.019, respectively) in the multivariate model. The HR (95% CI) for

age, distant metastasis, and HER2 (3/0) scores were found to be statistically significant. This study suggests that age is positively associated with mortality risk, as DFS times decrease with age. Patients with M-stage disease had a significantly higher mortality risk than those without M-stage disease. Moreover, patients with a HER2 score of 3 had a higher mortality risk than those with a score of 0.

The mean survival of those with a HER2 score of 0 was 98.81 (88.32-109.3) months (95% CI), and those with a HER2 score of 3 had a mean survival of 49.71 (9.88-89.54) months (95% CI), with a statistically significant difference in survival between HER2 rates (log-rank =5,955, p=0.015) (Table 3).

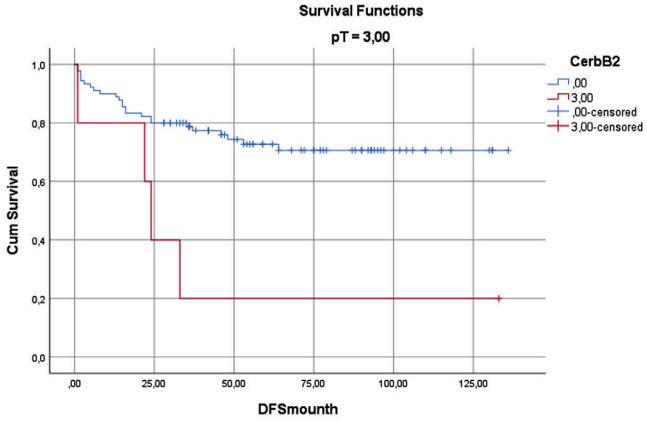

Figure 2. Kaplan-Meier curves of disease-free survival in HER2-positive and HER2-negative patients with pathologic stage 3
HER2: Human epidermal growth receptor 2

Discussion

In colon cancers, the average 5-year survival rate is approximately 65%, and in the presence of distant metastasis, the prognosis decreases to 13%.[17] As in solid organ tumors, patient-specific treatments and immunotherapy are used to improve the prognosis of colon cancer. In this study, we aimed to investigate the effect of HER2 and MMR expressions on prognosis in patients with colon adenocarcinoma diagnosed and treated in our clinic in light of literature information.

In the last 10 years, survival times in metastatic colon cancers have increased from 10 to 20 months as a result of alternative treatments and immunotherapy.[18] Microsatellite instability is detected in 15% of metastatic colon cancers, and 3% is associated with Lynch syndrome.[4,19,20] In our study, the rate of MSI cancer was 20%, which is close to the rates reported in the literature. The MSI status is currently used in patients with colon cancer for neoadjuvant treatment resistance and immunotherapy.[13] Current guidelines for MSI cancer recommend that it be studied in all patients and do not mention its prognostic impact.[21] In solid tumors, pembrolizumab (immunotherapy) was first approved for patients with MSI cancer.[22] Currently, the use of pembrolizumab in patients with MSI tumors is a subgroup that benefits from treatment.[23] Although studies have reported that MSI tumors have better prognostic factors and earlier stages,[13,23] no statistical significance was found in terms of survival in most studies.[18,24,25] In studies comparing MSI and MSS colon cancers, MSI cancers were found to have high mutation and neoantigen load, frequent immune cell infiltration, high response to

Table 2. Comparisons between survival time rates and c-erbB2 rates for clinic stage 2, 3, and 4 and pathologic stage 3 and 4 conditions

				DFS time		p-value
				Alive	Ex	
Clinic stage	2	HER2	0	48 (98%)	15 (83.3%)	0.056[b]
			3	1 (2%)	3 (16.7%)	
	3 ve 4	HER2	0	33 (97.1%)	19 (90.5%)	0.551[b]
			3	1 (2.9%)	2 (9.5%)	
Pathological stage	pT3 ve pT4	HER2	0	81 (97.6%)	34 (87.2%)	0.034[b]
			3	2 (2.4%)	5 (12.8%)	

[a]Chi-squared test, [b]Fisher's exact test

Table 3. Results of univariate and multivariate Cox regression analysis of the effect of HER2 and MSI on mortality

		Univariate		Multivariate	
		p-values	HR (CI 95%)	p-values	HR (CI 95%)
MMR	MSS/MSI	0.590	-	-	-
HER2	3/0	0.021	3,023 (1,180-7,742)	0.019	3,368 (1,217-9,320)

HR: Hazard ratio, CI: Confidence interval, Cox regression: Backward Wald, MMR: Mismatch repair, HER2: Human epidermal growth receptor 2

immunotherapy, and better survival.[5,13,22] The characteristics of MSI tumors are associated with proximal localization, advanced T stage, N0, and stage 2-3 tumors.[18,22] Survival was longer in MSI tumors than in MMS tumors, although the difference was not statistically significant.[7,18,24] However, the effects of immunotherapy on colorectal tumors have not yet been clarified. Kang et al.[7] reported a mean 5-year survival of 95.8 months in MSI cancer, 74.5 months in MSS cancer, and a mean follow-up of 37.5 months. In our study, the mean follow-up period was 47 months, and the mean survival time in patients with MSI cancer was 104.45 months. According to Afrăsânie et al.,[18] stage 2-3 MSI cancer is a good prognostic factor, but the prognosis is not significant in metastatic disease. In our study, no statistically significant relationship was found between clinicopathological parameters and prognosis and MSI status.

Study Limitations

The effect of the limitations in the number of patients on our results should be considered.

Meta-analysis studies on colon cancer have shown that the incidence of HER2 is highly variable, ranging from 0.5% to 49%.[9,25,26] In a study by Dienstmann et al.[19] on metastatic colon cancers, the rate of HER2 was 2%. In the present study, HER2 expression was observed at a rate of 5.7%. HER2 has been associated with aggressive tumor behaviors, such as lymphatic metastasis, distant metastasis, perineural invasion, and distal localization; however,[27] in our study, we could not detect a significant relationship between HER2 and clinicopathological findings. Studies have also indicated its association with anti-EGFR resistance.[28,29] Anti-EGFR treatment in patients with metastasis worsens the prognosis and decreases the survival rate of HER2-positive patients. Yonesaka et al.[30] found a poor clinical effect of de novo HER2 amplification in 233 patients treated with cetuximab. In patients with amplified HER versus non-amplified HER2, median progression-free survival and OS decreased by 5 months versus 3 months, and OS was 30.5 months versus 10.2 months.[30] Therefore, knowledge of HER2 expression is necessary to organize the treatment protocol. According to the National Comprehensive Cancer Network® guidelines, the prognostic role of HER2 overexpression has not been supported in studies, and HER2-targeted therapies are still being investigated; testing is recommended in patients with metastatic colon cancer.[21] In large meta-analyses on the relationship between HER2 and survival, no relationship with survival was found.[15] Although there were different results related to survival in different studies, it was found to be a prognostic survival marker in both the univariate and multivariate analyses in our study. Its effect on survival should be investigated in larger studies that compare different treatment protocols.

Conclusion

In our study, HER2 was identified as an independent prognostic factor for patients with colon cancer, regardless of the presence of metastatic disease. Patients with a HER2 score of 3 had a 3,368 times higher risk of death. Additionally, no association was found between the clinicopathological features and survival in patients with MSI cancer. The limited sample size in our study may account for this observation. The fact that we only included patients in our clinic in our study causes selection bias as a limitation. Both HER2 and MSI status appear to be essential in the management of colorectal cancer, especially in advanced patients, and in identifying patients who are eligible for treatment.

Ethics

Ethics Committee Approval: Approval for the study was obtained from the Hittite University Clinical Research Ethics Committee (approval number: 2023-168, dated: 26.12.2023).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: B.Y., Y.B., G.G., Concept: B.Y., Y.B., G.G., Design: B.Y., Y.B., G.G., Data Collection or Processing: B.Y., Y.B., K.H., Analysis or Interpretation: B.Y., Y.B., K.H., Literature Search: B.Y., Y.B., K.H., Writing: B.Y., Y.B., E.R.

Conflict of Interest: No conflict of interest was declared by the authors.

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RESEARCH ARTICLE

Approach of Colorectal Surgeons to Lower Rectal Adenocarcinomas: Results from the Turkish Society of Colon and Rectal Surgery Database

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ABSTRACT

Aim: This study aimed to analyze surgical preferences and outcomes among patients with lower rectal tumors in Türkiye using data from the national Colorectal Cancer Database of the Turkish Society of Colon and Rectal Surgery (TSCRS).

Method: A retrospective analysis was conducted on 158 patients with lower rectal tumors who underwent surgery between July 2018 and March 2022, with data prospectively collected from the TSCRS database. Variables included demographic characteristics, neoadjuvant therapy administration, surgical techniques, and postoperative outcomes.

Results: Among the 158 patients (mean age: 57.8 years; 58.2% men), 95.6% received neoadjuvant therapy. Approximately half the patients underwent open surgery, and the other half underwent minimally invasive surgery (MIS). The T-stage distribution differed significantly (p=0.009); early-stage cancers (stages I-II) were more frequently treated with MIS, whereas advanced stages (stages III-IV) were predominantly managed with open surgery. Conversion from laparoscopic to open surgery occurred in five patients (5.9%). Abdominoperineal resection was more common in patients who underwent open surgery. Hand-sewn anastomosis was performed more frequently in patients undergoing MIS. The operative time was longer for MIS than for open surgery (249±85 min vs. 169±52 min). The circumferential resection margin positivity rate was 3.2%, and tumor perforation occurred in 4.5% of cases.

Conclusion: The treatment of lower rectal cancer increasingly relies on a multidisciplinary approach integrating neoadjuvant therapies and diverse surgical techniques. Turkish surgeons adopt a tailored approach based on patient characteristics, leading to similar adoption rates for both surgical techniques. These findings highlight the dynamic and evolving nature of lower rectal cancer management, particularly in the context of neoadjuvant treatment strategies.

Keywords: Low anterior resection, lower rectal cancer, minimally invasive surgery, multidisciplinary approach, neoadjuvant therapy

Introduction

Colorectal cancer remains one of the most common malignancies worldwide, ranking third in prevalence both nationally and globally. It accounts for approximately 10% of all cancer diagnoses and is the second leading cause of cancer-related mortality worldwide.[1,2] Although it primarily affects individuals aged ≥50 years, there is a concerning rise in cases among younger populations.[3] Notably, about one-third of these diagnoses are classified as rectal cancer.[2]

The optimal management strategy for rectal adenocarcinoma depends on multiple factors, with paramount consideration given to tumor location within the rectum and disease extent. In cases where patients present with limited invasive cancer confined to a polyp without adverse features, polypectomy

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alone may be a sufficient treatment modality. Conversely, for individuals with locally advanced disease, such as fixed, bulky tumors, nodal involvement, or evidence of extramural venous invasion on staging magnetic resonance imaging, a neoadjuvant approach is recommended. Additionally, in selected patients who achieve a complete response to neoadjuvant therapy, the watch-and-wait strategy-postponement of surgery with close surveillance-may be an option.[4] However, surgery remains the cornerstone of curative treatment for rectal adenocarcinoma.[5]

In determining the appropriate surgical treatment for rectal cancer, several critical factors should be considered, including tumor distance from the anal verge or from the lower border of the tumor to the top of the anorectal ring (which guides sphincter preservation decisions), invasion into the lateral pelvic walls or adjacent intra-abdominal organs, tumor size, regional lymph node involvement, pelvic anatomy, preoperative anorectal sphincter function, and the patient's ability to tolerate transabdominal surgery.[6]

Given the diverse nature of rectal cancer and the multifaceted considerations involved in treatment decisions, treatment modalities may vary considerably. Substantial differences in clinical approaches to lower rectal tumors exist between institutions. Although international guidelines are generally adhered to, notable variations occur, particularly in low anterior resection/abdominoperineal resection (APR) rates, anastomosis techniques, and stoma rates. Ongoing research aims to further elucidate optimal management approaches. In Türkiye, data regarding surgeons' preferences for treating lower rectal tumors are currently lacking. This study aims to address this gap by analyzing national data on surgical preferences and clarifying the approaches employed by colorectal surgeons in managing lower rectal adenocarcinoma.

Materials and Method

Patient Selection

This study was approved by the Ankara University Medical School Institutional Review Board (approval number: i03-285-24, dated: 25.04.2024). Data were obtained from the national Colorectal Cancer Database (CCD) of the Turkish Society of Colon and Rectal Surgery (TSCRS). The TSCRS-CCD was established in 2018, with 18 centers providing data. To participate in this database, centers must perform at least 50 colorectal cancer surgeries annually and conduct multidisciplinary tumor board meetings for tumor-related surgeries. The preoperative, operative, and short-term (30-day) postoperative data of patients who underwent curative colon or rectal resection for colorectal cancer are prospectively recorded in this database.

In the TSCRS-CCD, data entry is performed by responsible colorectal surgeons from each contributing center, and the entered data are subsequently verified by the CCD working study group.

This study included patients with lower rectal adenocarcinomas who underwent surgery between July 2018 and March 2022. Patients aged ≥18 years were included, whereas those with tumors located >5 cm from the anal verge or diagnosed with squamous cell carcinoma were excluded.

Variables Examined

The surgical preferences of the surgeons, along with patient demographic data and pathological outcomes, were analyzed. The demographic data included age, gender, preferred neoadjuvant therapy, operation type, and surgical technique. The patients were categorized into two groups based on the surgical techniques used: open surgery and minimally invasive surgery (MIS; laparoscopic or robotic). These groups were compared and analyzed in terms of age, gender, body mass index, American Society of Anesthesiologists score, clinical stage, T staging, neoadjuvant therapy, tumor distance to the anal verge, operation type, intraoperative blood loss, circumferential resection margin (CRM), mesorectal plane completeness, history of prior abdominal surgery, anastomosis type, presence of stoma, and operative time.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation, and categorical variables were expressed as percentages. The Fisher's exact test or chi-square test was used to assess the significance of categorical variables, whereas the t-test or Mann-Whitney U test was used for continuous variables. Statistical analyses were conducted using SPSS version 21.0. A p-value <0.05 was considered statistically significant.

Results

A retrospective analysis was conducted on data from 158 patients (36.9%) with lower rectal cancer, selected from a total of 428 patients with rectal cancer registered in the database. The mean age was 57.8±12.6 years, and 92 patients (58.2%) were men.

Among the total cohort, 151 patients (95.6%) received neoadjuvant treatment. Approximately 40% of the patients underwent APR, whereas the remaining patients underwent surgeries concluded with anastomosis. Abdominoperineal resection was more commonly performed in patients undergoing open surgery. Regarding the surgical technique, approximately half the patients underwent open surgery, whereas the remaining half underwent MIS (Table 1).

When comparing the results of open surgery and MIS, a statistically significant difference was observed in the T-stages. Specifically, among patients in stages I-II, 30 patients (41.1%) underwent open surgery, whereas 56 patients (65.9%)

underwent MIS (p=0.009). In stages III-IV, the distribution shifted toward open surgery, with 43 patients (58.9%) undergoing open surgery and 29 patients (34.1%) undergoing MIS. The number of T0 patients was 16 in the open surgery group and 20 in the MIS group. Except for one patient (open surgery), all cases demonstrated a pathological complete response (Table 2).

Table 1. Characteristics of the patients (n=158)

Variables	Value
Age (years)	57.8±12.6
Men, n (%)	92 (58.2%)
Neoadjuvant therapy, n (%)	
CRT	139 (88%)
CT	5 (3.2%)
RT	7 (4.4%)
None	7 (4.4%)
Operation type, n (%)	
LAR	93 (58.9%)
APR	63 (39.9%)
Total proctocolectomy	2 (1.2%)
Operation technique, n (%)	
Open	73 (46,2%)
Laparoscopic	77 (48,7%)
Robotic	8 (5.1%)

CRT: Chemoradiotherapy, CT: Chemotherapy, RT: Radiotherapy, LAR: Low anterior resection, APR: Abdominoperineal resection

In five patients (5.9%), laparoscopic surgery was converted to an open procedure. No conversions to open surgery occurred during robotic procedures. Positive circumferential resection margins were observed in five patients (3.2%), whereas tumor perforation occurred in seven patients (4.5%) during surgery (Table 3).

The hand-sewn anastomosis rate was 7.9% in patients who underwent open surgery, increasing to 40.4% in those who underwent MIS. Additionally, the mean operative time was 169±52 minutes for open surgery and 249±85 minutes for MIS. There was no statistically significant difference between the two groups in the number of harvested lymph nodes, rates of distal surgical margin positivity, or postoperative complication rates (Table 3).

Discussion

The treatment of rectal cancer requires a multidisciplinary approach. Although surgery remains the cornerstone of treatment, neoadjuvant therapy, particularly for distal rectal tumors and locally advanced disease, has become an essential component of rectal cancer management. Despite the availability of various surgical techniques, none have been demonstrated to be superior in terms of oncological outcomes, and all continue to be widely used. In Türkiye, as in the rest of the world, rectal cancer treatment is guided by decisions made by multidisciplinary tumor councils. Our study reflects that surgeons adopt a tailored approach for each patient, aligning with this multidisciplinary strategy.

Table 2. Demographics outcomes comparing minimally invasive vs. open surgery for lower rectal cancer (n=158)

Variables	Open	Minimally invasive	p-value
Age (years)	58.3±11.9	57.5±13.3	0.691
Gender (M/F)	38/35	54/31	0.15
BMI (kg/m^2)	26.1±4.9	26.9±4.6	0.331
ASA score, n (%)			
1-2	62 (84.9%)	74 (87.1%)	0.819
3-4	11 (15.1%)	11 12.9%)	
Clinical stage, n (%)			
1	5 (7.1%)	10 (16.4%)	0.194
2	12 (17.1%)	14 (23%)	
3	44 (62.9%)	33 (54.1%)	
4	9 (12.9%)	4 (6.6%)	
Pathological T-stage, n (%)			
0-1-2*	30 (41.1%)	56 (65.9%)	**0.009**
3-4	43 (58.9%)	29 (34.1%)	
Neoadjuvant therapy, n (%)	72 (98.6%)	79 (92.9%)	0.124
Distance to anal verge (cm)	3.4±1.5	3.4±1.2	0.947

*The number of T0 patients is 16 in the open surgery group and 20 in the minimally invasive surgery group. BMI: Body mass index, ASA: American Society of Anesthesiologists

Minimally invasive surgery has made substantial advancements, particularly in the last quarter century, and has increasingly become the preferred option over open surgery in colorectal procedures. Its safety, feasibility, and oncologic equivalence have been established, with well-documented clinical benefits over open approaches.[7] Moreover, MIS is considered superior to the open approach because of the various postoperative outcomes, including reduced surgical site infections, shorter hospital stays, and less blood loss. It is also associated with enhanced short-term non-oncologic outcomes compared with open surgery for rectal cancer.[8-11] However, no significant difference has been observed in short-term and long-term oncologic outcomes.[10,11] Minimally invasive surgery is a safe and effective option for patients with colorectal cancer, providing similar oncologic outcomes in both the short and long term when compared with the open approach.[12]

Although our study did not include long-term oncological outcomes, there were no differences between the groups in

Table 3. Peri-operative outcomes comparing minimally invasive vs. open surgery for lower rectal cancer (n=158)

Variables	Open (n=73)	Minimally invasive (n=85)	p-value
APR, n (%)	35 (47.9%)	28 (32.9%)	0.152
Intraoperative bleeding (mL)	125±78	145±132	0.252
CRM (+)	3 (4.1%)	2 (2.4%)	0.663
Intraoperative tumor perforation	5 (6.9%)	2 (2.4%)	0.248
Mesorectal plane, n (%)			
Complete or nearly complete	47 (100%)	58 (93.5%)	0.132
Incomplete	0	4 (6.5%)	
Lymph node count	14.52±11.23	15.86±8.73	0.41
Metastatic lymph node count	2.4±5.47	1.2±3.68	0.12
Distal surgical margin positivity, n (%)*	5 (13.1%)	6 (10.5%)	0.75
Previous abdominal surgery, n (%)			
Yes	48 (65.8%)	63 (85.9%)	**0.004**
No	25 (34.2%)	12 (14.1%)	
Anastomosis, n (%)			
Hand-sewn	3 (7.9%)	23 (40.4%)	**0.001**
Stapled	32 (84.2%)	33 (57.9%)	
Stoma (excluding APR), n (%)	39 (100%)	49 (84.5%)	**0.01**
Operation time (min.)	169±52	248±85	**<0.001**
Postoperative complications, n (%)			
Superficial SSI	10 (13.6%)	5 (5.9%)	0.182
Deep SSI	8 (10.9%)	5 (5.9%)	0.398
Intra-abdominal abscess	1 (1.4%)	8 (9.4%)	0.033
Evisceration	2 (2.7%)	2 (2.4%)	1.0
Prolonged ileus	7 (9.6%)	7 (8.2%)	1.0
Anastomotic leak	5 (6.8%)	1 (1.2%)	0.114
Urinary complications	6 (8.2%)	6 (7.1%)	1.0
Bleeding	1 (1.4%)	1 (1.2%)	1.0
Obstruction	2 (2.7%)	0	0.241
Non-surgical**	2 (2.7%)	4 (4.7%)	0.681
Timing of surgery after neoadjuvant treatment (weeks)	10±3.5	10.5±6	0.576

*Excluding APR. Open (n=38), minimally invasive (n=57). **Open surgery: 1 atelectasis, 1 encephalopathy. Minimally invasive surgery: 1 myocardial infarction, 1 pulmonary edema, 1 pleural effusion, and 1 acute kidney injury. APR: Abdominoperineal resection, CRM: Circumferential resection margins, SSI: Surgical site infection., min.: Minute

terms of pathological evaluation, including specimen quality, lymph node yield, and resection margins. This suggests that the role of MIS in rectal surgery is well established and no longer open to debate.

Unfortunately, this study included only a limited number of patients undergoing robotic surgery. Current literature suggests that robotic surgery offers the advantages of laparoscopic surgery and may even be superior in certain aspects. According to the results of the REAL study, which compared robotic and laparoscopic surgery in rectal cancer, robotic surgery resulted in better oncological quality of resection, less surgical trauma, and improved postoperative recovery.[13] Additionally, robotic surgery provided several advantages over laparoscopic surgery, including substantially lower conversion rates to open surgery, shorter hospital stays, decreased risk of urinary retention, and improved survival rates to hospital discharge or 30-day overall survival rates.[14]

However, a meta-analysis showed that robotic surgery yields results similar to, rather than better than, laparoscopic surgery in terms of hospital stay, blood loss, time to first flatus, conversion rates to open surgery, number of removed lymph nodes, complication rates, and CRM positivity rates. Another meta-analysis comparing open, laparoscopic, and robotic surgery for rectal cancer found no differences in oncologic outcomes or recovery parameters among the three techniques. However, robotic surgery demonstrated improved distal resection margin distance.[15] Despite these similarities, robotic surgery was associated with longer operative times and higher costs.[16]

Overall, robotic surgery has been shown to offer comparable or better clinical outcomes compared with both laparoscopic and open surgery.[17] In our study, none of the patients undergoing robotic surgery exhibited CRM positivity, intraoperative tumor perforation, or distal surgical margin positivity. Moreover, no statistically significant differences were observed between the groups in terms of postoperative complications. These results are likely attributable to the small sample size, which may have limited the statistical power of the study. However, operative times were significantly longer in patients undergoing robotic surgery.

The criteria for selecting patients for neoadjuvant treatment in rectal cancer are well established. Traditionally, long-course chemoradiotherapy (CRT) followed by consolidation therapy has been recommended for lower rectal tumors. The majority of patients in this study were treated with long-term CRT in accordance with the guidelines at the time of surgery, but a small number received only short-term radiotherapy (RT). Although studies have shown that RT and CRT yield similar results in reducing the risk of local recurrence, evidence suggests that adding chemotherapy to the treatment regimen may be more beneficial for patients requiring downstaging before surgery, particularly in cases where tumors have invaded the mesorectal fascia.[18-21] In this study, clinics administered consolidation chemotherapy after RT or CRT in accordance with their own protocols. However, the latest National Comprehensive Cancer Network guideline recommends total neoadjuvant therapy (TNT) for locally advanced rectal cancer.[22]

As demonstrated by cornerstone studies comparing open and laparoscopic rectal surgeries, APR rates vary, ranging from 7.3% to 23% in open surgery and 7.6% to 29% in laparoscopic surgery.[23-25] In the Robotic Versus Laparoscopic Resection for Rectal Cancer study, which compared robotic and other surgical techniques, the APR rate was 21.9% among 237 robotic cases and 19.2% among 234 laparoscopic cases.[26] In our study, the APR rate was 32.9% in the minimally invasive group and 50% in the open surgery group, likely due to patient selection bias, as patients at higher T-stages were more frequently selected for open surgery.

In this study, the hand-sewn anastomosis rate in open surgery was 7.9%, increasing to 40.4% in MIS. Although no comparable data are currently available in the literature, the increased frequency of manual anastomosis in MIS may be attributed to the enhanced visibility, allowing surgeons to achieve lower levels in the rectum, potentially exceeding the suitable levels for stapled anastomosis. As a result, hand-sewn anastomosis may have been preferred at a higher rate in these patients.

Study Limitations

The strengths of our study include its multicentric nature and the distinction of being the first study in Türkiye utilizing the TSCRS database. However, several limitations should be considered. The study did not include all clinics in Türkiye; only those actively engaged in colorectal cancer care were part of the research. Additionally, the lack of long-term follow-up meant that oncological outcomes could not be assessed. Furthermore, factors such as patients' neoadjuvant treatment regimens and the impact of comorbidities on surgical technique selection are not available in the database, which represents a limitation. Another limitation is that postoperative complications were not classified according to the Clavien-Dindo classification, and an important limitation of this dataset is the absence of data for patients with rectal cancer undergoing non-operative management.

Moreover, the TSCRS database does not include specific treatment details, such as intersphincteric resection, extralevator abdominoperineal excision, the use of stomas, toxicity profiles, and TNT regimens. As these data were unavailable, they could not be included in the study. The absence of such information limits the ability to comprehensively evaluate the full spectrum of treatment approaches and their outcomes.

Furthermore, patients received tailored treatments based on evaluations by multidisciplinary tumor councils at their respective clinics. Although such personalized treatments likely yielded better patient outcomes, they also introduced a selection bias into the study. Lastly, due to the limited number of patients who underwent robotic surgery, these cases could not be analyzed separately and were grouped together with laparoscopic surgeries under the MIS group.

CONCLUSION

In conclusion, the treatment of rectal cancer, particularly for distal and locally advanced tumors, increasingly relies on a multidisciplinary approach that integrates neoadjuvant therapies and diverse surgical techniques. Neither approach has demonstrated superiority over the other in terms of short-term oncological outcomes. Additionally, because Turkish surgeons prefer a tailored approach based on each patient's specific needs, the preference rates for open and minimally invasive surgeries appear to be similar. Despite the absence of long-term oncological data, current findings affirm the efficacy of minimally invasive approaches, which offer well-established advantages documented in the literature. Neoadjuvant treatment strategies continue to evolve, reflecting the dynamic nature of rectal cancer management.

Ethics

Ethics Committee Approval: This study was approved by the Ankara University Medical School Institutional Review Board (approval number: i03-285-24, dated: 25.04.2024).

Informed Consent: This study was conducted using data from TSCRS Database, which consists of de-identified patient information. Therefore, obtaining individual informed consent was not required.

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Footnotes

Authorship Contributions

Surgical and Medical Practices: M.A.K., E.A., Concept: M.A.K., E.A., Design: M.A.K., E.A., Data Collection or Processing: M.A.K., E.A., Analysis or Interpretation: K.S., Literature Search: K.S., Writing: K.S., M.A.K.

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RESEARCH ARTICLE

Impact of Structured Education on the Stress Levels and Health Perceptions of Caregivers of Patients Undergoing Colorectal Cancer Surgery: Quasi-Experimental Study

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ABSTRACT

Aim: This study evaluated the impact of structured education on the stress levels and health perceptions of caregivers of patients undergoing colorectal cancer surgery.

Method: A pretest-posttest quasi-experimental design was used. This study was done in a university hospital's general surgery department. Caregivers of patients with colorectal cancer got stress management and health perception education. A qualified researcher led face-to-face sessions with a booklet and PowerPoint presentation. Pretests and posttests were taken on the 1st day of hospitalization and shortly before release. The Caregiver Stress Scale (CSS) was used to assess stress levels, and the Perception of Health Scale (PHS) was used to evaluate caregivers' health perceptions. Data analysis was performed using the SPPS 29.0 package program.

Results: The study included 65 caregivers. The mean age of the patients was 61.85±14.85 years, with 80.0% diagnosed with colon cancer. Caregivers had a mean age of 52.93±10.67 years; 36.9% had a primary school education, 41.5% were employed, and 73.8% provided care for at least four weeks. The pre-education mean CSS score was 9.26±1.38, decreasing to 6.36±3.77 post-education ($p<0.001$). The mean PHS score considerably rose from 44.49±2.93 to 53.58±7.01 ($p<0.001$). Stress and health perception were positively impacted by patient education, care equipment, caregiver education, marital status, employment status, and caregiving duration ($p<0.05$).

Conclusion: Structured education reduced stress and improved health perceptions in colorectal cancer caregivers. This intervention filled a research gap by emphasizing caregiver well-being over patient-centered education. Caregivers need resilience-building strategies and caregiver-centered education in colorectal cancer care.

Keywords: Caregiver stress, caregiver, colorectal cancer, health perception, structured education, psychological stress

Introduction

Colorectal cancer is the second leading cause of cancer-related deaths worldwide. In 2020, the World Health Organization reported 1.9 million new colorectal cancer cases and 930,000 deaths. The highest incidence rates are observed in Europe, Australia, and New Zealand, whereas Eastern Europe has the highest fatality rates. By 2040, colorectal cancer cases are projected to increase by 63% to 3.2 million annually, with fatalities rising by 73% to 1.6 million per year.[1] In Türkiye, this global trend is also evident. According to the 2018 Ministry of Health data, colorectal cancer is the third most common malignancy in both sexes. GLOBOCAN 2022 identified colorectal cancer as the fourth most frequent cancer worldwide. Despite its high prevalence, public awareness of colorectal

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cancer screening remains low, underscoring the need for targeted awareness programs.

Advancements in medical technology and a deeper understanding of colorectal cancer pathophysiology have expanded treatment options, including endoscopic procedures, surgery, radiation, immunotherapy, targeted treatments, and palliative chemotherapy.[2,3] These innovations have carried patient care from hospitals to home settings, making caregivers essential in managing complex medical needs such as medication administration, symptom management, and coordination with healthcare professionals. However, caregiving places a significant physical, emotional, and financial burden on caregivers, leading to persistent stress, fatigue, and diminished overall well-being.[2,3]

This increasing caregiving burden negatively impacts caregivers' physical and mental health, as well as their self-perception. Balancing symptom management, emotional support, medical follow-ups, and daily care can reduce caregivers' quality of life.[4] Studies indicate that increased caregiving responsibilities are associated with poorer health perception and negative health behaviors.[5] Health outcomes depend on an individual's perception of their biological, psychological, and social well-being. A lower health perception often leads to reduced healthcare utilization, lower quality of life, and an increased risk of illness.[6]

Although caregivers play a crucial role in postoperative care, research primarily focuses on education programs aimed at improving the patient's care and social adaptation. However, there is a notable gap in the literature regarding interventions designed to empower caregivers themselves. Most existing studies emphasize patient-centered education, whereas this study focuses on caregivers, aiming to strengthen their coping mechanisms and improve their well-being. Addressing this gap is essential for enhancing caregiver support systems and ensuring sustainable care for patients with colorectal cancer.

Objective

This study aims to evaluate the effect of structured education on the stress levels and health perceptions of caregivers of patients undergoing colorectal cancer surgery.

The study hypotheses were as follows:

$H1._1$. There is a significant difference in mean scores on the Caregiver Stress Scale (CSS) before and after structured education for caregivers of patients undergoing colorectal cancer surgery.

$H1._2$. There is a significant difference in the mean scores on the Perception of Health Scale (PHS) before and after structured education for caregivers of patients undergoing colorectal cancer surgery.

Materials and Methods

Design

A prospective quasi-experimental, non-randomized study was conducted.[7] Randomization was not used due to the potential for interactions between caregivers, which could lead to information exchange and influence the effects of the intervention, making it difficult to maintain group independence. This research was conducted as a single group pre-test/post-test quasi-experimental study. The Transparent Reporting of Evaluations with Non-randomized Designs (TREND) checklist was utilized to standardize the reporting of non-randomized controlled trials. Figure 1 illustrates the comprehensive study design.

Setting

The study was conducted through face-to-face interviews with caregivers of patients admitted to the general surgery inpatient clinic of a Dokuz Eylül University Hospital between April 1, 2024, and June 30, 2024. Data was collected by trainee nurses on the research team.

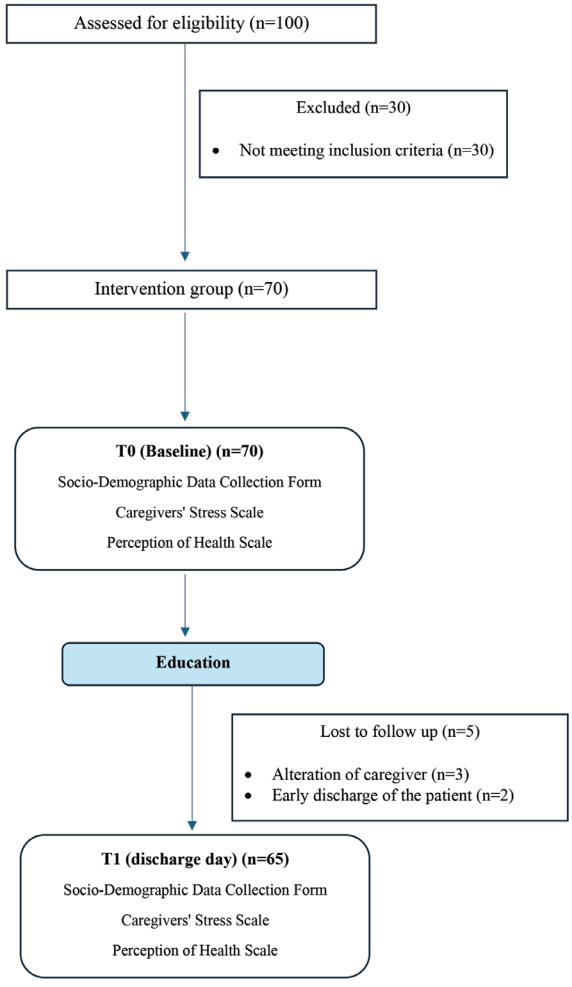

Figure 1. Flow diagram of enrolled patients

Participants

The sample of the study consisted of caregivers of patients who would undergo colorectal cancer surgery. A purposive sampling method was used. The inclusion criteria were as follows: caregivers of patients who would undergo colorectal cancer surgery; caregivers who voluntarily agreed to participate in the study; caregivers who could speak, understand, and write in Turkish; caregivers with a complete person, place, and time orientation; and caregivers over 18 years of age. The exclusion criteria were as follows: caregivers of patients with metastatic colorectal cancer and caregivers with acute health problems (respiratory system diseases, gastrointestinal system diseases, infectious diseases, etc.).

Sample Size

The study's sample size was calculated using G*Power 3.1.9.2 at a 95% confidence interval. Cohen's d was calculated based on the d-value. A Cohen's d-value greater than 0.8 was considered substantial.[8] The sample size calculated according to this value was 52 participants, with a theoretical power of 0.80. Considering a 25% loss rate, 65 caregivers were included in the study. A post-hoc power analysis was then performed based on the caregiver stress parameter. In this analysis, the power was determined to be 1.00.

Intervention Group

All investigators produced structured educational content according to established guidelines.[8-12] The developed education content was reviewed by the senior author, an expert in the field. The focus of this structured education content was to increase caregiver resilience. The education material included the following topics: categories of caregivers, caregiver responsibilities, assessment of patient care needs, home care, institutional care settings, caregiver self-care strategies (stress management, balancing work and caregiving, family resolution, and family life management), and evaluation of alternative care options. Two experts were then verbally consulted, and a preliminary study was conducted with one caregiver. Once the education content was finalized, it was printed as a booklet. At the same time, a PowerPoint presentation was prepared as visual teaching material to be used during the education. After all processes were completed, the first researcher trained the trainee nurses on how to provide structured education and the data collection process before data collection began. A structured education trial was conducted with each of them to ensure that all trainee nurses provided standardized training to caregivers.

The first researcher was an assistant professor of surgical nursing who conducted research focused on colorectal surgery. The trainee nurses were senior students who had completed a surgical nursing course and worked as trainee nurses in inpatient clinics. The senior author was a professor of surgical nursing with expertise in colorectal surgery.

Data Collection

Patients admitted to the general surgery inpatient clinic for colorectal cancer surgery were identified through the inpatient list of the clinic. The caregiver was informed, and consent was obtained after visiting the patient's clinic, during which the CSS and HPS were completed. Upon completing these scales, the caregiver received education through visual education materials and written brochures for colorectal cancer surgery. The education was provided by trainee nurses from the research team who had received training on structured education. An optimal and quiet location within the ward was selected for the education. The caregivers were asked to fill in the CSS and PHS on the day the patient was discharged. Figure 1 shows the study's data collection process.

Measurement Instruments

Data collection involved using the sociodemographic data collection form, the CSS, and the PHS.

Sociodemographic Data Collection Form

The study included questions regarding the sociodemographic characteristics of the participating caregivers. The assessment encompassed inquiries about the caregiver's age, gender, degree of closeness to the patient, marital status, educational background, profession, employment status, caregiving responsibilities, duration of care provided, support received, presence of chronic illness, and regular medication usage.[13-17] The assessment encompassed inquiries regarding the patient, including age, gender, diagnosis, planned surgery, and presence of stoma.

Caregiver Stress Scale

The scale was developed by Robinson[17] in 1983 to assess the caregiving burden experienced by caregivers. The CSS helps identify families potentially facing caregiving concerns rapidly. The burden measurements in caregiving comprise 13 items. At least one item each exists concerning the work situation, financial situation, physical condition, social situation, and time. A positive response to seven or more items on the scale signifies an elevated stress level. This evaluation tool can assess people of all ages who have taken on the duty of caring for an older adult. The scale was evaluated with a cohort of 132 individuals who supported hospitalized older adults, and it was found to be appropriate for caregivers across all age groups. The scale designed to assess the subjective burden of caregivers for patients with cancer was utilized with family caregivers of patients aged 65 and older who had received hip and heart surgery. The original version of the scale comprises 13 items derived from 10 everyday stressors identified through interviews with adult children caring for

elderly parents, alongside 3 stressors identified from a review of pertinent literature. All 13 items on the scale represent a stressor. The scale score is derived by aggregating the 0 and 1 responses from the 13 items. The scale exhibited a Cronbach's alpha value of 0.86. Robinson[17] Uğur and Fadıloğlu[18] conducted a validity and reliability study of the scale in 2006, involving 132 patients and their relatives, to examine the caregiving burden experienced by individuals providing home care to oncology patients. Cronbach's alpha coefficient was determined to be 0.77.[18] Permission to use the scale was obtained from Uğur and Fadıloğlu[18] on October 27, 2023. Cronbach's alpha coefficient in this study was determined to be 0.85.

Perception of Health Scale

This scale, developed initially by Diamond et al.[19] and subsequently adapted into Turkish by Kadıoğlu and Yıldız,[20] comprised 15 items and utilized a 5-point Likert-type format. The scale's total scores range from 15 to 75, with higher scores reflecting a greater level of health perception and lower scores indicating a diminished level of health perception. Questions 1, 5, 9, 10, 11, and 14 are affirmative, whereas questions 2, 3, 4, 6, 7, 8, 12, 13, and 15 are negative assertions. The scale comprises four sub-dimensions: control center, precision, significance of health, and self-awareness. The initial study of the scale indicated a Cronbach's alpha coefficient of 0.77 for the general population. Permission to use the scale was obtained from Kadıoğlu and Yıldız,[20] on October 29, 2023. Cronbach's alpha coefficient in this study was determined to be 0.82.

Statistical Analysis

Data from the study was analyzed using the Statistical Package for the Social Sciences software, version 29.0. The Kolmogorov-Smirnov test, kurtosis, skewness values, and QQ plot were analyzed to assess the normality of the data distribution. The evaluation of kurtosis and skewness values followed the methodology outlined in the article by Zhou and Shao.[21] Descriptive characteristics included numerical values, percentages, means, standard deviations, and minimum and maximum values. Correlation, variance, and t-tests were used to analyze the influence of caregiver and patient characteristics on caregiver stress and health perceptions. A pairwise t-test examined differences in caregivers' stress and health perceptions before and after the education.

Ethical Approval

Permission was obtained from the Dokuz Eylül University Non-interventional Research Ethics Committee (approval number: 2023/40-21, dated: 13.12.2023). Permission was obtained from the department of general surgery (number: E-968337284-100-822054, dated: 08.12.2023). The research adhered to ethical guidelines, with caregivers informed of the purpose of the study in accordance with the tenets of the Declaration of Helsinki, followed by signing informed consent forms.

Results

Descriptive Characteristics of the Patients

The mean age of the patients was 61.85±14.85 years, with 55.4% identifying as women and 60% having completed primary education. Colon cancer was present in 80% of patients, whereas 20% had rectal cancer. Partial colectomy was performed in 61.5% of patients, and 23.1% had a stoma. In 90.8% of patients, only a peripheric intravenous intravenous catheter (PIV) was present as care equipment (Table 1).

When the stress level and health perception of caregivers were compared with the descriptive characteristics of the patients, age, gender, diagnosis, presence of chronic disease, type of surgery, and presence of stoma had no significant effect on caregiver stress levels and health perceptions ($p>0.05$). A significant relationship was found between education level and health perception ($p=0.002$). Caregivers with primary education had the lowest level of health perception, whereas those with higher education had the highest level. The type of catheter used in the patient was found to be effective on the stress level of caregivers ($p=0.005$). A significant difference was found in terms of stress level between the caregivers of patients with only PIV catheters and those of patients with central venous catheters (CVC) and drains (Table 1).

Descriptive Characteristics of the Caregivers

The mean age of caregivers was 52.93±10.67 years, with 66.2% identifying as women and 36.8% having completed primary education. About 40% of caregivers were spouses of the patients, whereas 58.5% were unemployed. Additionally, 38.5% had chronic illnesses, and 35.4% were taking medication regularly. More than half (53.8%) of caregivers were responsible for other individuals in addition to the patient. The duration of caregiving was 4 weeks or less for 73.8% of participants, whereas only 13.8% received support during the caregiving process (Table 2).

When the descriptive characteristics of caregivers were compared with stress level and health perception, it was observed that age, gender, degree of closeness with the patient, presence of chronic disease, regular medication use, and receiving support during the care process did not significantly affect caregiver stress levels and health perceptions ($p>0.05$). A significant relationship was found between education and stress levels ($p=0.003$). Caregivers with primary education had the highest stress level, and those with higher education had the lowest. A significant

Table 1. Comparison of the patient's descriptive characteristics with caregivers' stress and perception of health

Descriptive characteristics of patients	n, %	Mean ± SD	Pre-education Caregiver Stress Scale Test statistic p-value	Post-education Caregiver Stress Scale Test statistic p-value	Pre-education Perception of Health Scale Test statistic p-value	Post-education Perception of Health Scale Test statistic p-value
Years	65, 100.00	61.85±14.85	r=-0.064 p=0.612	r=-0.114 p=0.367	r=-0.055 p=0.664	r=-0.021 p=0.867
Gender						
Female	36, 55.40		t=1.400	t=1.475	t=0.102	t=0.070
Male	29, 44.60		p=0.166	p=0.145	p=0.918	p=0.944
Education						
Primary education	39, 60.00					
Secondary education	15, 23.10		F=0.840	F=0.715	F=0.065	F=6.828
Higher education	11, 16.90		p=0.436	p=0.493	p=0.937	**p=0.002***
Diagnosis						
Rectum cancer	13, 20.00		t=-0.434	t=-0.255	t=0.476	t=0.415
Colon cancer	52, 80.00		p=0.668	p=0.801	p=0.640	p=0.683
Chronic disease						
Yes	28, 43.10		t=-0.235	t=0.569	t=0.635	t=-0.642
No	37, 56.90		p=0.815	p=0.571	p=0.528	p=0.523
Type of surgery						
Total colectomy	2, 3.10					
Partial colectomy	40, 61.50					
Hemicoectomy	3, 4.60		F=1.253	F=0.376	F=0.348	F=0.029
Lower anterior resection	20, 30.80		p=0.299	p=0.771	p=0.791	p=0.993
Existence of stoma						
Yes	15, 23.10		t = 0.202	t=0.033	t=1.443	t=0.408
No	50, 76.90		p = 0.842	p=0.974	p=0.160	p=0.688
Maintenance equipment						
PIV	59, 90.80					
PIV and CVC	2, 3.10					
PIV and foley catheter	2, 3.10		F=4.773	F=1.606	F=0.392	F=2.477
PIV and drain	2, 3.10		**p=0.005***	p=0.197	p=0.759	p=0.070

*p<0.05. PIV: Peripheric intravenous catheter, CVC: Central venous catheter, r: Correlation test, t: t-test in independent groups, F: Analysis of variance test, SD: Standard deviation

difference was found between marital status and health perception (p=0.016). Single caregivers had the highest level of health perception. There was a significant difference between employment status and health perception (p=0.007). The health perceptions of employed caregivers were higher than those of non-employed caregivers. A significant relationship was found between the duration of care and stress level (p=0.011). Caregivers who provided care for four weeks or less had the lowest stress level, whereas caregivers who provided care for 9 weeks or more had the highest stress level (Table 2).

The Impact of Structured Education on Stress Levels and Health Perceptions of Caregivers

The caregivers' mean pre-structured education CSS score was 9.26±1.38, whereas the post-education score significantly decreased to 6.36±3.77 (t=7.080, p=0.000), indicating a statistically significant reduction in stress levels (Table 3). Similarly, the caregivers' mean PHS score increased significantly from 44.49±2.93 before education to 53.58±7.01 after education (t=-9.557, p=0.000) (Table 3). Statistically significant increases were observed in the subdimensions of health perception, including self-awareness (t=-9.410,

Table 2. Comparison of the caregivers' descriptive characteristics with caregivers' stress and perception of health

Descriptive characteristics of patients	n, %	Mean ± SD	Pre-education Caregiver Stress Scale Test statistic p-value	Post-education Caregiver Stress Scale Test statistic p-value	Pre-education Perception of Health Scale Test statistic p-value	Post-education Perception of Health Scale Test statistic p-value
Years	65, 100.00	52.93±10.67	r=-0.029 p=0.822	r=-0.137 p=0.278	r=0.013 p=0.915	r=-0.078 p=0.535
Gender						
Female	43, 66.20		t=-0.427	t=-0.387	t=-1.276	t=-0.855
Male	22, 33.80		p=0.671	p=0.701	p=0.209	p=0.397
Education						
Primary education	24, 36.90					
Secondary education	20, 30.80		F=0.559	F=0.091	F=0.834	F=6.409
Higher education	21, 32.30		p=0.575	p=0.913	p=0.439	**p=0.003***
Proximity to the patient						
Parent	3, 4.60					
Spouse	26, 40.00					
Child	21, 32.30		F=0.463	F=0.243	F=0.803	F=0.257
Relative	15, 23.10		p=0.709	p=0.866	p=0.497	p=0.856
Marital status						
Married	55, 84.60		t=-0.095	t= -0.986	t=1.865	t=-2.687
Single	10, 15.40		p = 0.933	p = 0.344	p=0.081	**p=0.016***
Work status						
Working	27, 41.50		t=0.686	t=0.470	t=1.002	t=2.809
Not working	38, 58.50		p=0.496	p=0.640	p=0.311	**p=0.007***
Chronic disease						
Yes	23, 35.40		t=0.090	t=-0.216	t=0.974	t=0.835
No	42, 64.60		p=0.928	p=0.830	p=0.334	p=0.408
Regular use of medication						
Yes	23, 35.40		t=-0.003	t=-0.441	t=0.799	t=-1.141
No	42, 64.60		p=0.998	p=0.661	p=0.428	p=0.260
Status of the person for whom he/she is responsible						
Yes	35, 53.80		t=-0.028	t=-0.908	t=0.066	t=-0.899
No	30, 46.20		p=0.978	p=0.367	p=0.947	p=0.372
Maintenance period	48, 73.80					
4 weeks						
4-6 weeks	3, 4.60		F=4.840	F=3.429	F=0.217	F=3.251
9 weeks and over	14, 21.50		**p=0.011***	**p=0.039***	p=0.806	**p=0.045***
Receive support during the care process						
Yes	9, 13.80		t=-0.822	t=-0.105	t=-1.156	t=1.426
No	66, 86.20		p=0.432	p=0.919	p=0.271	p=0.182

*p<0.05. r: Correlation test, t: t-test in independent groups, F: Analysis of variance test, SD: Standard deviation

Table 3. The impact of structured education on caregivers' stress levels and health perceptions

Variable	Pre-education (Mean ± SD)	Post-education (Mean ± SD)	t[a]	p-value
Caregiver Stress Scale	9.26±1.38	6.36±3.77	**7.080**	**0.000***
Perception of Health Scale	44.49±2.93	53.58±7.01	**-9.557**	**0.000***
Center of control	15.04±1.72	14.67±4.04	0.662	0.492
Self-awareness	8.66±1.16	11.26±1.73	**-9.410**	**0.000***
Certainty	11.56±1.11	13.98±3.99	**-4.859**	**0.000***
Importance of health	9.21±1.48	13.66±1.33	**-19.600**	**0.000***

*p<0.05, SD: Standard deviation , t[a]: Paired-samples t-test

p=0.000), certainty about health (t=-4.859, p=0.000), and perceived importance of health (t=-19.600, p=0.000) (Table 3). These results indicate that structured education effectively reduced caregivers' stress levels and improved their health perceptions across multiple dimensions.

Discussion

This study examined how structured education for colorectal cancer surgical caregivers affected stress and health perceptions. Structured education greatly lowered caregivers' stress and improved their health views, as shown in the literature.[22-26] Structured education improved caregivers' health processes involvement, according to this study.

The Impact of Organized Education on Caregiver Stress Levels

The results show that structured education significantly reduced caregiver stress. Research suggests that chronic illness caregivers experience high stress.[4,13,14] Caregivers watching surgery may feel stressed due to uncertainty and fear. This study found that caregivers with high stress levels before education had lower stress thereafter. The instructional content provided insight on caregiving issues, decreasing uncertainty and stress. Additionally, answering caregivers' questions and offering emotional support during schooling reduced stress. Educational content focused on caregiving reduced caregiver issues; research shows that structured cancer caregiver education reduces stress, anxiety, and sadness. Information and support programs also lessen caregiver stress.[15,16] A randomized controlled experiment found that needs-based education reduced the anxiety of families who had patients with cancer better than organized education.[27] Similarly, caregiver education in pediatric oncology improved clinical outcomes, such as reducing CVC infections and emergency department visits.[28] These findings highlight the importance of tailoring educational programs to caregivers' specific needs to maximize their effectiveness in reducing stress and improving caregiving outcomes.

The Impact of Structured Education on Caregivers' Health Perception

Health perception is a key concept that describes how people view their health and how this affects their health practices.[6] Our study found that structured education improved caregivers' health perceptions, except for locus of control. This shows that education increases health awareness and stress management. The educational content improved caregivers' health assessment and motivation to live healthily. Improved health perception reduces caregiver role tensions and exhaustion. A cancer caregiver study showed the complex link between caregiver views, patient health, and caregiver well-being. Caregivers' health and ability assessments may differ from patients' self-reports, affecting caregiver burden.[29] Caregivers' impressions of patients' interpersonal and mental issues are linked to lower quality of life, depression, and anxiety.[30] Living with the patient and assessing their interpersonal and psychological issues affect caregiver health. Social support affects patient and caregiver health in a reciprocal manner.[31] Caregiver health affects patient care, emphasizing the importance of caregiver health in cancer care.[32] Cancer caregivers need targeted assistance and treatments to improve patient and caregiver outcomes. Information and support on the disease process boost caregivers' self-efficacy and health perceptions, according to research.[33] Psychoeducational components dominate caregiver education programs, but more comprehensive techniques to meet all caregiver requirements are needed.[34] Caregiver evaluations of patients' problems, especially interpersonal and psychiatric ones, greatly affect their quality of life and health.[30,35] Targeted support and information help caregivers understand and manage patients' social and psychological issues, improving caregiver health and the caregiver–patient relationship.

The Impact of Patient Demographic Variables on Caregiver Stress and Health Perception

The study indicated that age, gender, diagnosis, chronic condition, operation type, and stoma had no significant effect.

However, education level affected health perception, with lower education being associated with lower health awareness and self-efficacy. Complex catheters such as CVCs and drains increased effort and technical abilities, causing caregiver stress. The literature emphasizes that patient variables, especially perceived general health status, impact the care burden, depression, and anxiety of colorectal cancer caregivers.[36,37] This study found that although different characteristics of patients than those found in the literature affected caregivers, the health status and care-related activities of colorectal cancer surgery caregivers were affected by patient variables.

The Impact of Caregiver Demographic Variables on Caregiver Stress and Health Perception

The study found that education, marital status, employment status, and length of caregiving affected caregiver stress and perceived health, whereas age, gender, patient affiliation, chronic disease, and support did not. Lower education increases stress due to health management difficulties, whereas higher education improves problem-solving. Single caregivers may benefit from better social support and increased well-being through employment, financial stability, and social interaction. However, long-term caregiving increases stress and requires psychosocial support. As mentioned in the literature,[36] caregiver characteristics, time spent on caregiving, and expenses incurred were identified as contributing to caregiver burden.

Study Limitations

This study has limitations. Despite the acceptable power, the small sample size may have affected population representation. Self-reported measures may have introduced response bias into the study. Additionally, due to caregiver interaction, randomization was not performed, which may have influenced the results. Finally, follow-up was short, and the long-term effects of structured education on caregiver stress and health views were not examined. Future research should include diverse and larger populations, ensure randomization, and examine long-term outcomes to address these limitations.

Conclusion

This study found that structured education reduced stress and improved health perceptions in colorectal cancer caregivers. It was also found that patient characteristics, education level, and care equipment, as well as caregiver characteristics, education level, marital status, employment status, and duration of caregiving, affected caregiver stress and health perception. Colorectal cancer treatment is continuous and complex; therefore, caregiver education should be part of routine healthcare. Further research should examine the long-term effects of structured education programs and specific interventions for various caregiver groups. The chronic and diverse nature of colorectal cancer makes caregiving difficult. In addition to physical caregiving, these problems include mental stress from prognostic uncertainty, which affects caregivers. Caregiver well-being and caregiving ability depend on increasing their adaptability and coping resilience. Education and support programs should focus on techniques to increase caregiver resilience and help them cope with the challenges of caregiving. The effects of these interventions on caregiver mental health and support structures that improve their access to healthcare should be further studied. With resilience therapies, caregivers can manage stress, maintain emotional well-being, and successfully care for patients throughout the challenging process of colorectal cancer treatment.

Ethics

Ethics Committee Approval: Permission was obtained from the Dokuz Eylül University Non-interventional Research Ethics Committee (approval number: 2023/40-21, dated: 13.12.2023).

Informed Consent: Informed consent was obtained.

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Footnotes

Authorship Contributions

Concept: N.G.Ö.Ö., M.B., Ö.A., S.Ö., E.T., F.V., Design: N.G.Ö.Ö., Data Collection or Processing: N.G.Ö.Ö., M.B., Ö.A., S.Ö., E.T., Analysis or Interpretation: N.G.Ö.Ö., F.V., Literature Search: N.G.Ö.Ö., M.B., Ö.A., S.Ö., E.T., F.V., Writing: N.G.Ö.Ö., M.B., Ö.A., S.Ö., E.T., F.V.

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RESEARCH ARTICLE

Minimally Invasive Mesh Rectopexy versus Perineal Rectosigmoidectomy in the Elderly: a Retrospective Comparative Analysis

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ABSTRACT

Aim: The aim of this study was to compare early and intermediate perioperative outcomes after rectal prolapse repair in elderly patients undergoing either minimally invasive mesh rectopexy or perineal rectosigmoidectomy (PR).

Method: This retrospective comparative analysis evaluated the outcomes of elderly patients (age ≥70 years) who underwent surgical correction of full-thickness rectal prolapse at a single tertiary hospital between 2010 and 2023. Patients included in the study had undergone either minimally invasive rectopexy (MIR) or PR (Altemeier procedure). The primary outcomes assessed were 30-day mortality and complication rates.

Results: A total of 55 patients were included, with 42 who underwent MIR and 13 who underwent PR. The average age of all the patients was 79.8±6.4 years, and the average body mass index was 22.5±3.7. Most patients (49, 89.1%) were women. Patients who underwent MIR had a significantly lower 30-day complication rate than those who underwent PR (11.9% vs. 53.8%, respectively; p=0.001). No deaths occurred in either group within 30 days of the procedure. Patients who underwent PR had similar recurrence rates to those who underwent MIR, with a median interval to the first documented recurrence of 6.0 months (range: 0.2-24.5 months). The rate of normal bowel function achieved at the most recent follow-up was significantly higher in patients who underwent MIR than in those who underwent PR (76.2% vs. 30.8%, respectively; p=0.003).

Conclusion: The MIR approach to prolapse repair is safe and feasible in elderly patients, with a lower 30-day complication rate and comparable mortality rates than PR. Additionally, early functional outcomes are better after MIR.

Keywords: Rectal prolapse, rectopexy, perineal rectosigmoidectomy, minimally invasive surgical techniques, perioperative care

Introduction

Rectal prolapse is a debilitating condition characterized by the full-thickness protrusion of the rectum through the anal canal. Although it can occur at any age, it most commonly develops in elderly women beyond the seventh decade of life. Surgical repair is required for definitive management, and perineal approaches have traditionally been considered "safer" for elderly patients. However, this claim has limited supporting data, and perineal approaches have been associated with higher long-term recurrence rates than transabdominal repairs.[1,2] Historically, surgical dogma has supported the notion that perineal approaches, such as perineal rectosigmoidectomy (PR; Altemeier) and mucosal sleeve resection (Delorme), should be reserved for elderly or high-risk patients deemed poor candidates for surgery.[2,3] Conversely, intra-abdominal approaches have been preferred for younger, healthier patients.[4-6]

In recent years, these views have been challenged as surgical and anesthetic techniques have improved. Multiple studies suggest that transabdominal rectopexy may be safer for elderly, high-risk patients than previously believed.[7-10] Additionally, minimally invasive abdominal procedures in the elderly have

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been shown to be safe compared with both open and perineal approaches.[11-14] Contemporary data indicate that major complication and mortality rates are similar for minimally invasive rectopexy (MIR) and PR in both younger and older patients, suggesting that age alone should not dictate the choice of treatment.[15]

Recent large-scale studies evaluating early perioperative outcomes after prolapse repair in elderly patients have reported comparable early postoperative outcomes between laparoscopic transabdominal approaches and traditional perineal approaches.[10,16] However, despite these improved outcomes, perineal repairs remain the most commonly performed procedures for rectal prolapse in elderly patients, although the use of minimally invasive approaches has increased.[10] The aim of this study was to compare perioperative outcomes in elderly patients undergoing rectal prolapse repair with either minimally invasive mesh rectopexy or PR.

Materials and Methods

This was a retrospective cohort study evaluating the outcomes of elderly patients (age ≥70 years) undergoing the surgical correction of full-thickness rectal prolapse. Patients included in the study underwent surgical repair at a single tertiary hospital between 2010 and 2023 either through MIR or PR (Altemeier). Patients who underwent robotic or laparoscopic mesh rectopexy via either anterior or posterior approaches were categorized into the MIR group.

All procedures were performed by board-certified colorectal surgery attendings with appropriate experience and expertise in rectal prolapse management. A retrospective chart review was performed to obtain relevant demographic and preoperative data. This study approved by the University of Southern California Institutional Review Board (approval number: HS-17-00058-CR008, dated: 7/11/2024). Additionally, intraoperative, perioperative, and postoperative outcomes were collected using the electronic health record and available procedural and operative reports. Only patients with at least one follow-up visit were included, and those who underwent a Delorme procedure were excluded from the analysis.

The primary outcomes evaluated included 30-day mortality and complication rates. Individual complications were analyzed, and a composite variable-"any complication"-was defined for cases where any complication was reported within 30 days of surgery.

Intraoperative variables assessed included operative duration, concurrent pelvic prolapse procedures performed, estimated blood loss (EBL), and intraoperative complications. Additional operative details specific to MIR were also evaluated, including the type of repair (ventral vs. posterior), minimally invasive approach used (robotic vs. laparoscopic), type of mesh utilized, and whether conversion to an open procedure was required.

The length of stay (LOS) at the hospital was recorded for each group. Other postoperative outcomes assessed included patient-reported functional outcomes, prolapse recurrence rates, time to recurrence (if applicable), and 30-day readmission rates.

Statistical Analysis

All statistical analyses were performed using IBM SPSS software version 28.0 (IBM Corp., Armonk, NY, USA). Continuous variables were described using the mean and standard deviation, whereas categorical variables were reported as frequencies and percentages. The student's *t*-test was used to compare continuous variables between two groups, and the chi-squared test was used to compare categorical variables. For comparisons involving three or more groups, analysis of variance was conducted. A two-tailed p-value of <0.05 was considered statistically significant.

Results

A total of 55 patients were included in the study, with 42 who underwent MIR and 13 who underwent PR. The average age of all the patients was 79.8±6.4 years, and the average body mass index (BMI) was 22.5±3.7. The majority of patients (49, 89.1%) were women.

Patients who underwent PR had a significantly higher average BMI than those who underwent MIR (25.0±3.9 vs. 21.9±3.4, respectively; p=0.016). Patients who underwent PR also had higher rates of medical comorbidities than patients who underwent MIR. Specifically, patients who underwent PR had significantly higher rates of diabetes, chronic obstructive pulmonary disease (COPD), congestive heart failure (CHF), coronary artery disease or prior myocardial infarction (CAD/MI), arrhythmia, and chronic kidney disease (CKD) and were more likely to be on chronic blood-thinning medications (Table 1). All the patients reviewed were classified as American Society of Anesthesiologists (ASA) class 2 or 3 (40% and 54.5%, respectively), with three patients (5.5%) classified as ASA class 4. Patients who underwent PR had higher rates of ASA class 3 and 4 than patients who underwent MIR, although this difference did not reach statistical significance (p=0.108). No other demographic differences were observed between the two groups. Further details of the demographic and comorbid conditions are presented in Table 1.

The average operative duration was significantly longer for MIR than for PR (155.5±73.9 vs. 87.1±41.5 minutes, respectively; p=0.003). However, hospital LOS was nearly identical between the two groups (2.64±0.96 vs. 2.62±1.66 days, respectively; p=0.954). Three patients (5.5%) underwent an additional concurrent pelvic organ prolapse procedure-one patient who underwent MIR (2.4%) and two patients who underwent PR (15.4%) (p=0.071).

The average EBL was low in both groups but was significantly lower for MIR than for PR (17.9±23.7 vs. 41.0±58.0 mL, respectively; p=0.050). Intraoperative complications were rare, with only one patient (1.8%) experiencing an intraoperative complication, specifically, an iatrogenic bladder injury in a patient who underwent MIR, which was successfully managed with primary repair intraoperatively. Details of the intraoperative variables between the two groups are presented in Table 2.

Of the 42 patients who underwent MIR, 32 (76.2%) underwent ventral mesh rectopexy (VMR), whereas 10 (23.8%) underwent posterior mesh rectopexy (PMR). Twenty-seven patients (64.3%) underwent a laparoscopic approach, whereas the remaining 15 (35.7%) underwent a robotic approach. Nine patients (21.4%) received a synthetic mesh, 32 (76.2%) received a biologic mesh, and 1 patient (2.4%) had a hybrid mesh incorporating both biologic and synthetic components. No patients (0%) required intraoperative conversion to an

Table 1. Demographics and comorbid conditions

Outcome, [n (%)]	Overall (n=55)	Minimally invasive (n=42)	Altemeier (n=13)	p-value
Age	79.8 (6.4)	79.8 (6.7)	79.9 (5.6)	0.986
Body mass index (kg/m^2), avg. (SD)	22.5 (3.7)	21.9 (3.4)	25.0 (3.9)	**0.016**
Women	49 (89.1)	39 (92.9)	10 (76.9)	0.107
Tobacco use	4 (7.3)	3 (7.1)	1 (7.7)	0.964
Alcohol use	14 (25.5)	11 (26.2)	3 (23.1)	0.822
Diabetes	10 (18.2)	5 (11.9)	5 (38.5)	**0.030**
Hypertension	31 (56.4)	23 (54.8)	8 (61.5)	0.667
Hyperlipidemia	7 (12.7)	6 (14.3)	1 (7.7)	0.533
COPD	5 (9.1)	2 (4.8)	3 (23.1)	**0.045**
Congestive heart failure	2 (3.6)	0 (0)	2 (15.4)	**0.010**
CAD/MI	6 (10.9)	2 (4.8)	4 (30.8)	**0.009**
PAD	3 (5.5)	2 (4.8)	1 (7.7)	0.684
Arrhythmia	4 (7.3)	1 (2.4)	3 (23.1)	**0.012**
CVA/TIA	7 (12.7)	5 (11.9)	2 (15.4)	0.742
CKD/ESRD	4 (7.3)	1 (2.4)	3 (23.1)	**0.012**
Liver disease/Cirrhosis	2 (3.6)	1 (2.4)	1 (7.7)	0.371
Thyroid disease	7 (12.7)	7 (16.7)	0 (0)	0.115
Colorectal cancer	3 (5.5)	1 (2.40	2 (15.4)	0.071
Other cancer	10 (18.2)	9 (21.4)	1 (7.7)	0.262
Psychiatric diagnosis	4 (7.3)	2 (4.8)	2 (15.4)	0.197
Malnutrition	3 (5.5)	3 (7.1)	0 (0)	0.322
Rheumatologic disorder	10 (18.2)	10 (23.8)	0 (0)	0.052
Blood thinners	20 (36.4)	11 (26.2)	9 (69.2)	**0.005**
Prior abdominal surgery	32 (58.2)	22 (52.4)	10 (76.9)	0.117
ASA class				0.108
Class 1	0 (0)	0 (0)	0 (0)	
Class 2	22 (40.0)	19 (45.2)	3 (23.1)	
Class 3	30 (54.5)	22 (52.4)	8 (61.5)	
Class 4	3 (5.5)	1 (2.4)	2 (15.4)	

avg.: Average, SD: Standard deviation, COPD: Chronic obstructive pulmonary disease, CAD: Coronary artery disease, MI: Myocardial infarction, PAD: Peripheral artery disease, CVA: Cerebrovascular accident, TIA: Transient ischemic attack, CKD: Chronic kidney disease, ESRD: End-stage renal disease, ASA: American Society of Anesthesiologists

open procedure. Further details of the intraoperative MIR variables are presented in Table 3.

Overall, the 30-day postoperative complication rate for all patients was 21.8%. Patients who underwent MIR had a significantly lower early complication rate than those who underwent PR (11.9% vs. 53.8%, respectively; p=0.001). The most commonly reported complication was urinary retention (9.1%), followed by ileus/constipation (5.5%). Other complications, each occurring at a rate of 1.8%, included delirium, arrhythmia, rectal bleeding, respiratory failure, and sepsis. Of these, only urinary retention was significantly higher in patients who underwent PR than in patients who underwent MIR (23.1% vs. 4.8%, respectively; p=0.045). The rates of other complications were similar between the two groups.

Overall, two patients (3.6%) were readmitted within 30 days of discharge, both of whom had undergone PR, whereas no patients who underwent MIR required readmission (15.4% vs. 0%, respectively; p=0.010). There were no deaths (0%) in either group within 30 days of the procedure. Further details of the 30-day postoperative outcomes are presented in Table 4.

A binary logistic regression analysis was performed to examine the association between treatment type (MIR vs. PR) and 30-day postoperative complications, adjusting for the presence of diabetes, COPD, CHF, CAD/MI, arrhythmia, and CKD/ESRD. The results indicated that patients who underwent PR had significantly higher odds of experiencing postoperative complications than those who underwent MIR [adjusted odds ratio (OR)=28.42, 95% confidence interval=2.70-298.75, p=0.005]. None of the other comorbidities significantly affected the likelihood of postoperative complications within 30 days.

For all the patients included, the median follow-up interval was 4.6 months (range: 0.6-80.3 months). Eight patients (14.5%) experienced a documented prolapse recurrence during follow-up. Patients who underwent PR had a higher recurrence rate than patients who underwent MIR (30.8% vs. 9.5%, respectively); however, this difference did not reach statistical significance (p=0.058). The median interval to the first documented recurrence was 6.0 months (range: 0.2-24.5 months), which was similar between the two groups.

A separate binary logistic regression analysis was performed to assess factors associated with recurrence. Although diabetes

Table 2. Perioperative variables

Outcome	Overall (n=55)	Minimally invasive (n=42)	Altemeier (n=13)	p-value
Operative duration, min. [avg. (SD)]	139.3 (73.4)	155.5 (73.9)	87.1 (41.5)	**0.003**
Concurrent pelvic prolapse procedure, [n (%)]	3 (5.5)	1 (2.4)	2 (15.4)	0.071
EBL, mL [avg. (SD)]	22.4 (33.6)	17.9 (23.7)	41.0 (58.0)	**0.050**
Intraoperative complication, [n (%)]	1 (1.8)	1 (2.4)	0 (0)	0.574
Hospital LOS [avg. (SD)]	2.63 (1.14)	2.64 (0.96)	2.62 (1.66)	0.954

min.: Minute, avg.: Average, SD: Standard deviation, mL: Milliliter, EBL: Estimated blood loss, LOS: Length of stay

Table 3. Minimally invasive approach intraoperative variables

	Overall (n=42)
Procedure performed, [n (%)]	
Ventral mesh rectopexy	32 (76.2)
Posterior mesh rectopexy	10 (23.8)
Approach, [n (%)]	
Laparoscopic	27 (64.3)
Robotic	15 (35.7)
Mesh used, [n (%)]	
Synthetic	9 (21.4)
Biologic	32 (76.2)
Hybrid	1 (2.4)
Conversion to open, [n (%)]	0 (0)

(adjusted OR=2.46, p=0.428), COPD (adjusted OR=3.715, p=0.368), and type of procedure (adjusted OR=6.27, p=0.056) showed trends toward higher odds of recurrence, none reached statistical significance. Other comorbidities, including CAD, CKD, arrhythmia, and CHF, also did not significantly impact the recurrence risk.

The rate of normal bowel function at the most recent follow-up visit was 65.5% for all patients and was significantly higher for patients who underwent MIR than for those who underwent PR (76.2% vs. 30.8%, respectively; p=0.003). The individual patient-reported functional outcomes assessed included regular bowel movements, obstructive defecation, fecal incontinence, constipation, and diarrhea. Patients who underwent MIR reported a significantly higher rate of regular bowel movements than patients who underwent PR (78.6% vs. 46.2%, respectively; p=0.025) and a significantly lower rate of constipation (0% vs. 38.5%, respectively; p<0.001). The rates of other functional outcomes were similar between the two groups. Further details of the functional outcomes and recurrence rates are presented in Table 5.

Discussion

In recent years, growing evidence has supported the use of transabdominal approaches for rectal prolapse repair over traditional perineal approaches, including for elderly and frail patients. The results of the current study are consistent with these findings, demonstrating that MIR is a safe surgical treatment for full-thickness rectal prolapse in the elderly, with lower postoperative complication rates, lower early readmission rates, and improved long-term functional outcomes than PR. Additionally, the study found comparable mortality and early to intermediate recurrence rates between the two groups.

The most recent clinical practice guidelines from the American Society of Colon and Rectal Surgeons suggest that the gold-standard surgical procedure should be transabdominal rectal

Table 4. 30-day postoperative outcomes

Outcome	Overall (n=55)	Minimally invasive (n=42)	Altemeier (n=13)	p-value
Any 30-day complication, [n (%)]	12 (21.8)	5 (11.9)	7 (53.8)	**0.001**
Urinary retention	5 (9.1)	2 (4.8)	3 (23.1)	**0.045**
Ileus/Constipation	3 (5.5)	1 (2.4)	2 (15.4)	0.071
Delirium	1 (1.8)	1 (2.4)	0 (0)	0.574
Arrhythmia	1 (1.8)	0 (0)	1 (7.7)	0.070
Rectal bleeding	1 (1.8)	0 (0)	1 (7.7)	0.070
Respiratory failure	1 (1.8)	1 (2.4)	0 (0)	0.574
Sepsis	1 (1.8)	0 (0)	1 (7.7)	0.070
Readmission, [n (%)]	2 (3.6)	0 (0)	2 (15.4)	**0.010**
Mortality, [n (%)]	0 (0)	0 (0)	0 (0)	1.000

Table 5. Patient-reported postoperative functional outcomes

Outcome	Overall (n=55)	Minimally invasive (n=42)	Altemeier (n=13)	p-value
Any recurrence, [n (%)]	8 (14.5)	4 (9.5)	4 (30.8)	0.058
Interval to recurrence, months [med. (range)]	6.0 (0.2-24.5)	6.5 (0.1-12.5)	6.0 (1.5-24.5)	1.000
Total follow-up, months [med. (range)]	4.6 (0.6-80.3)	4.1 (0.6-80.3)	8.1 (0.9-17.8)	0.487
Functional outcomes				
Regular bowel movements	39 (70.9)	33 (78.6)	6 (46.2)	**0.025**
Obstructive defecation	1 (1.8)	1 (2.4)	0 (0)	0.574
Any fecal incontinence	12 (21.8)	8 (19.0)	4 (30.8)	0.371
Any constipation	5 (9.1)	0 (0)	5 (38.5)	**<0.001**
Diarrhea	2 (3.6)	1 (2.4)	1 (7.7)	0.371
Overall normal bowel function[a]	36 (65.5)	32 (76.2)	4 (30.8)	**0.003**

[a]Normal bowel movements reported without incontinence, constipation, or diarrhea at the time of the most recent follow-up. med.: Median

fixation with or without mesh in acceptable-risk patients.[17] This recommendation has also been supported by other societies and expert panels; however, these guidelines do not specifically target elderly patients. Notably, there is growing evidence that minimally invasive transabdominal approaches are being increasingly used to treat rectal prolapse in the elderly.[9,10] However, these same studies indicate that the perineal approach remains the most frequently performed procedure in this population. Interestingly, in the present study, a greater number of patients were treated with minimally invasive transabdominal approaches than with perineal approaches, which contrasts with previously observed trends. Since all patients in this study were managed at a single tertiary hospital, this contrast may be attributed to management bias within the group.

Regarding postoperative outcomes, the current study found that the overall 30-day complication rate for elderly patients who underwent MIR was significantly lower than for those who underwent PR. These findings were observed despite an average patient age of nearly 80 years and a substantial number of comorbid conditions in both groups, suggesting that MIR may be safer than PR. However, this finding must be interpreted with caution, as the PR group in this study had higher rates of multiple comorbid conditions, including diabetes, cardiovascular disease, and pulmonary disease, than the MIR group. This raises concerns about potential selection bias, which may have influenced the observed results. Nevertheless, the higher prevalence of comorbid conditions in the PR group is not unexpected and is consistent with findings from other studies assessing similar outcomes.[18,19] Despite this concern, the contemporary literature consistently reports lower rates of early postoperative complications with minimally invasive approaches, suggesting that our results are consistent with previous findings despite differences between the two groups.[10,16,20,21] Additionally, there were no (0%) 30-day mortalities reported in the current study. It is well established that mortality rates for these procedures are generally low, and multiple large database studies assessing mortality have found no significant difference in early postoperative mortality rates between patients undergoing perineal versus transabdominal approaches.[9,10,16,22]

Unsurprisingly, patients who underwent PR had significantly shorter operative durations than those who underwent MIR, which is one of the consistent benefits of the perineal approach. However, despite the longer procedure time, MIR was associated with lower average EBL compared with PR and had the same average hospital LOS. The evaluation of patients who underwent MIR in the current study showed that three-quarters of the patients underwent VMR, whereas approximately one-quarter underwent PMR. Although both options have been shown to have low recurrence rates,[23] the posterior approach has historically been associated with higher complication rates. Despite the inclusion of PMR in the MIR group, the 30-day complication rate remained acceptable and was overall lower than that of the PR group.

Importantly, the use of minimally invasive VMR has gained considerable popularity and support in recent years due to its low long-term recurrence rates, low mesh-related complication rates, and notable improvements in constipation symptoms than other commonly used techniques.[23,24] In the current study, most MIR procedures involved the use of biologic mesh. Although studies have shown that overall mesh-related complication rates are low for both biologic and synthetic mesh, biologic mesh may ultimately be safer due to lower rates of mesh erosion while maintaining similar durability of repair to synthetic mesh.[25-27]

One of the most important findings of this study was the improved functional outcomes observed in patients who underwent MIR compared with those who underwent PR. In fact, three-quarters of the patients who underwent MIR reported normal bowel function without any new, persistent, or worsening bowel complaints at their most recent follow-up visit. Other studies have shown similar findings, and it is well established that transabdominal approaches result in better long-term functional outcomes and lower recurrence rates. However, one unexpected finding was that patients who underwent PR reported higher rates of at least temporary constipation during follow-up. This contrasts with other studies assessing functional outcomes after transabdominal and perineal repairs.[28] As such, this finding should be interpreted with caution, as this was a retrospective study assessing long-term outcomes via chart review and reporting was not standardized for either group.

Regarding recurrence, the current study showed that the MIR group had a lower observed rate of prolapse recurrence; however, this finding did not reach statistical significance. It is possible that with a larger sample size, a statistically significant difference may have been observed, but at minimum, our study demonstrated comparable recurrence outcomes. Previous studies have shown that transabdominal approaches are generally preferred for appropriately selected patients due to their lower long-term recurrence rates than perineal approaches, a factor that remains paramount when evaluating prolapse repair outcomes.[1]

Study Limitations

This study has several key limitations that must be acknowledged. First, its retrospective design inherently limits the ability to establish causality between observed differences among groups and increases the potential for selection bias. Additionally, multiple surgeons contributed to the data, leading to inherent heterogeneity in surgical practice. Second, the

study's small sample size, coupled with the disproportionate number of patients undergoing MIR compared with PR, increases the likelihood of type II errors. Furthermore, the lack of long-term follow-up data and the absence of standardized follow-up reporting hinder the ability to correlate findings with long-term clinical outcomes. Despite these limitations, the study's evaluation of early 30-day morbidity and mortality rates provides reliable and clinically important insights.

Conclusion

The MIR approach to prolapse repair is safe and feasible in elderly patients, with a lower 30-day complication rate and comparable mortality rates than PR. Additionally, early functional outcomes were overall better after MIR. Although growing evidence continues to support the use of minimally invasive transabdominal approaches in elderly patients, their widespread adoption in surgical practice has been slow. Further large prospective studies with long-term follow-up are needed to better evaluate the findings of this study and to help establish best practice for elderly patients undergoing rectal prolapse repair.

Ethics

Ethics Committee Approval: This study approved by the University of Southern California Institutional Review Board (approval number: HS-17-00058-CR008, dated: 7/11/2024).
Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: K.G.C., S.E.K., M.P.D., J.S., S.W.L., Concept: K.G.C., S.E.K., M.P.D., J.S., S.W.L., Design: B.W., A.G., S.W.L., Data Collection or Processing: J.M., A.S., B.W., A.G., Analysis or Interpretation: J.M., A.S., B.W., K.G.C., S.W.L., Literature Search: J.M., A.S., B.W., Writing: J.M., A.S., K.G.C., S.W.L.

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LETTER TO THE EDITOR

Peritoneal Carcinomatosis: Management Challenges

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Anahtar Kelimeler: Karsinomatoz, onkoloji, patoloji, peritoneal, cerrahi, tedavi

Dear Editor,

Our interest in the management of peritoneal carcinomatosis (PC) increased after reading the review by Canda and Sever,[1] published in this journal, which focused on important innovations in this field. They discussed the inherent limitations of preclinical experimental methods (*in vitro*, *in vivo*, and *in silico*), including aspects of new molecular mechanisms involved in cancer management outcomes. Therefore, it seems opportune to add brief comments on more recent literature about PC treatment, emphasizing the significance of the mentioned article, particularly for non-specialist healthcare workers.[2-6]

PC occurs in the course of abdominal cancers, is associated with a poor prognosis, and has few treatment options.[1-6] However, potential therapeutic tools related to interleukin-6 (IL-6) and its soluble receptor have emerged, including for ovarian, gastric, pancreatic, colorectal, and appendiceal cancers, as well as mesotheliomas.[2] The authors highlighted that the IL-6 pathway may play a role in peritoneal cancer dissemination, mesothelial adhesion and invasion, stromal invasion and proliferation, and immune response modulation.[2] Eugster et al.[3] reported the utilization of a 3D-printed composite platform for the sustained release of the tyrosine kinase inhibitor gefitinib, a small-molecule drug used to treat PC and post-surgical adhesions. These biodegradable liposome-loaded hydrogel microbeads may address the challenge of rapid clearance of small molecules, which can limit the effectiveness of intraperitoneal treatments.[3]

Gurusamy et al.[4] studied the effects of hyperthermic intraoperative peritoneal chemotherapy (HIPEC) plus cytoreductive surgery (CRS) with or without systemic chemotherapy, compared with chemotherapy alone, in PC from colorectal, gastric, or ovarian cancers. They concluded the following: the effect of CRS + HIPEC in gastric PC remains uncertain; CRS + HIPEC should be the standard for advanced ovarian carcinoma; and CRS + systemic chemotherapy should be the standard for colorectal PC, with HIPEC administered only as part of randomized controlled trials (4).

Hoskovec et al.[5] evaluated pressurized intraperitoneal aerosolized chemotherapy (PIPAC) every 6 weeks in 41 patients with abdominal cancers, focusing on PC extension, criteria for CRS and HIPEC, the effect on the peritoneal cancer index, peritoneal regression score, and ascites volume. A total of 100 PIPAC procedures were performed, ranging from 1 to 6 per patient, with 2 major complications. Five patients transitioned to CRS and HIPEC, one entered a watch-and-wait strategy following total regression, three continued treatment, and the remainder discontinued due to cancer progression or loss of metastases.[5] The authors concluded that PIPAC was a palliative measure that improves quality of life by reducing ascites and, in approximately 10% of cases, decreases disease extent, facilitating further radical treatment.[5]

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Perelló-Trias et al.[6] reviewed the literature on intraperitoneal drug delivery systems for optimal PC management, aiming to bridge the gap between research and clinical implementation. They emphasized that the adoption of novel delivery systems requires understanding peritoneal reactions, retention, distribution, penetration, metabolism, clearance, microenvironment effects, and systemic toxicity, as well as demonstrating clinical efficacy through randomized trials, which require substantial funding.[6]

Footnotes

Authorship Contributions

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