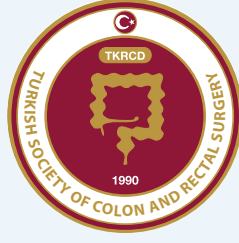


e-ISSN 2536-4898

Volume 34

Issue 3

September 2024



# Turkish Journal of **COLORECTAL DISEASE**

Official Journal of the Turkish Society of Colon and Rectal Surgery



# Turkish Journal of COLORECTAL DISEASE

## EDITORIAL BOARD

### Editor-in-Chief

**Fatma Ayça Gültekin M.D.**

Zonguldak Bülent Ecevit University Faculty of Medicine, Department of General Surgery, Zonguldak, Turkey  
E-mail: aycafgultekin@gmail.com  
ORCID-ID: orcid.org/0000-0002-4148-5871

### Co-Editor

**İlknur Erenler Bayraktar, M.D.**

Memorial Şişli Hospital, Department of General Surgery, İstanbul, Turkey  
E-mail: ilknurerenler@hotmail.com  
ORCID ID: orcid.org/0000-0002-4878-0873

### Section Editors

#### Colorectal Cancer

**Ercan Gedik, M.D.**

Dicle University Faculty of Medicine, Department of General Surgery, Diyarbakır, Turkey  
E-mail: ercan.gedik@yahoo.com.tr  
ORCID-ID: orcid.org/0000-0002-5812-6998

#### Inflammatory Bowel Disease

**Murat Kendirci, M.D.**

Hitit University Faculty of Medicine, Department of General Surgery, Çorum, Turkey  
E-mail: muratkendirci@gmail.com, muratkendirci@hitit.edu.tr  
ORCID-ID: orcid.org/0000 0002 6594 3777

#### Pelvic Floor & Functional Bowel Disorder

**Necdet Fatih Yaşar, M.D.**

Eskişehir Osmangazi University Faculty of Medicine, Department of General Surgery, Eskişehir, Turkey  
E-mail: nfyasar@gmail.com  
ORCID-ID: orcid.org/0000-0002-9751-2912

#### Proctology

**Sevil Işık, M.D.**

Medicana International İzmir Hospital, Department of General Surgery, İzmir, Turkey  
E-mail: isiksevil@hotmail.com  
ORCID-ID: orcid.org/0000-0002-35353-6977

**Murat Urkan, M.D.**

Muğla Sıtkı Koçman University, Muğla Training and Research Hospital, Clinic of General Surgery, Muğla, Turkey  
E-mail: muraturkan@gmail.com  
ORCID-ID: orcid.org/0000-0002-3191-4724

#### Endoscopy-Colorectal Polyps

**Fevzi Cengiz, M.D.**

Tınaztepe University Faculty of Medicine, Department of General Surgery, İzmir, Turkey  
E-mail: drfevzi@gmail.com  
ORCID-ID: orcid.org/0000-0002-1614-5568

#### Miscellaneous (diverticular disease, intestinal stomas, appendical disease, surgical quality, sito-reduction, HIPEC)

**Abdülcabbar Kartal, M.D.**

Anadolu Medical Center Hospital in Affiliation with Johns Hopkins Medicine, Kocaeli, Turkey  
E-mail: abdulcabbar.kartal@anadolusaglik.org, narcabb@gmail.com  
ORCID-ID: orcid.org/0000-0001-7536-3146

### Statistic Editor

**İlker Ercan, PhD.**

### English Language Editor

**Jeremy Jones**

Kocaeli, Turkey

All inquiries should be addressed to

**TURKISH JOURNAL OF COLORECTAL DISEASE**

Address: Mecidiyeköy, Latilokum Sk. Alphan İşhanı No: 3 Kat: 2, Şişli, İstanbul, Turkey

Phone: +90 212 356 01 75-76-77 Gsm: +90 532 300 72 36 Fax: +90 212 356 01 78

Online Manuscript: www.journalagent.com/krhd Web page: www.turkishjcrd.com E-mail: info@turkishjcrd.com

∞ All rights are reserved. Rights to the use and reproduction, including in the electronic media, of all communications, papers, photographs and illustrations appearing in this journal belong to the Turkish Journal of Colorectal Disease. Reproduction without prior written permission of part or all of any material is forbidden. The journal complies with the Professional Principles of the Press. The paper used to print this journal conforms to ISO 9706: 1994 standard (Requirements for Permanence). The National Library of Medicine suggests that biomedical publications be printed on acid-free paper (alkaline paper).

Reviewing the articles' conformity to the publishing standards of the Journal, typesetting, reviewing and editing the manuscripts and abstracts in English and publishing process are realized by Galenos.

**Publisher Contact**  
Galenos Publishing House

Address: Molla Gürani Mah. Kaçamak Sk. No: 21/1 34093 İstanbul, Turkey Phone: +90 530 177 30 97 Fax: E-mail: info@galenos.com.tr/gamze@galenos.com.tr

Web: www.galenos.com.tr Publisher Certificate Number: 14521

Printing at: Son Sürat Daktilo

Gayrettepe Mahallesi Yıldızposta Caddesi Evren Sitesi A Blok No: 3D:1-, 34394 Beşiktaş/İstanbul Phone: 021288 45 75 / 76 Mail: print@sonsuratdaktilo.com

Printing Date: June 2024 ISSN: 2536-4898 E-ISSN: 2536-4901



# Turkish Journal of **COLORECTAL DISEASE**

## ADVISORY BOARD

---

**Audrius Dulskas**

Vilnius University, Center of Abdominal Surgery, Vilnius, Lithuania

**Gonzalo P. Martin**

Quirúrgica Decentralized Private Surgery Service, Barcelona, Spain

**Badma Bashankaev**

Global Medical System Clinics and Hospitals, Department of Surgery, Moscow, Russia

**Joaquim Costa Pereira**

Braga Public Hospital, Clinic of Colorectal Surgeon, Braga, Portugal

**Niranjan Agarwal**

Bombay Hospital & Medical Research Centre, Department of Colorectal Surgery, Mumbai, India

**Richard Fortunato**

Allegheny General Hospital & ACMH Hospital, Clinic of Colon and Rectal Surgery, Pittsburgh, USA

**Narimantas Samalavicius**

Klaipėda University Hospital, Department of Surgery, Klaipėda, Lithuania

**Alaa El-Hussuna**

Aalborg University Hospital, Department of Surgery, Aalborg, Denmark

**Gabrielle van Ramshorst**

Ghent University Hospital, Department of Surgical Oncology, Ghent, Belgium

**Nicolas Luis Avellaneda**

Center for Medical Education and Clinical Research, Department of General Surgery, Buenos Aires, Argentina  
e-mail: n.avellaneda86@gmail.com

**Yutaka Saito**

National Cancer Center Hospital, Chief of Endoscopy Division Director of Endoscopy Center  
e-mail: ytsaito@ncc.go.jp



# Turkish Journal of **COLORECTAL DISEASE**

Please refer to the journal's webpage (<https://www.turkishjcrd.com/home>) for "Ethical Policy" and "Instructions to Authors".

The editorial and publication processes of the journal are shaped in accordance with the guidelines of the ICMJE, WAME, CSE, COPE, EASE, and NISO. Turkish Journal of Colorectal Disease is currently indexed in TÜBİTAK/ULAKBİM, British Library, ProQuest, Ebsco Host: CINAHL, IdealOnline, Embase, Gale/Cengage Learning, Turkish Citation Index, Hinari, GOALI, ARDI, OARE, AGORA J-GATE, CNKI and TürkMedline.

The journal is printed on an acid-free paper and published online.

**Owner:** Feza Yarıbuğ Karakayalı on behalf of the Turkish Society of Colon and Rectal Surgery

**Responsible Manager:** Fatma Ayça Gültekin



# Turkish Journal of **COLORECTAL DISEASE**

## CONTENTS

---

### Research Articles

- 69 **Triangle Excision and Advancement Flap in Pilonidal Disease: A Single-Center Prospective Case Series**  
Nurhilal Kızıltoprak, İlknur Turan, Ahmet Furkan Mazlum, Mahmut Salih Genç, Murat Kalın, Gülçin Ercan, Uğur Kesici; İstanbul, Yalova, Turkey
- 75 **Management and Long-Term Follow-up Outcomes of Appendiceal Neuroendocrine Tumor Patients: Evaluation of Single-Center Data**  
Ömer Akay, Mert Güler, Hüsnü Ozan Şevik, Cihad Tatar, Ufuk Oğuz İdiz; Konya, İstanbul, Turkey
- 81 **Adaptation of the Colostomy Impact Score for Use in the Turkish Population: A Validity and Reliability Study**  
Evrinm Santaş, Zehra Göçmen Baykara, Hatice Karabulut, Aysel Ören Hin, Sezai Leventoğlu; Ankara, Turkey
- 90 **Risk Factors Affecting Surgical Site Infections in Colorectal Cancer Surgery: Analysis of National Multicenter Data**  
Ahmet Ali Aktaş, Barış Gülcü, Özgen Işık, Şırnak, Bursa, Turkey
- 97 **Clinicopathological Characteristics and Population-Level Survival Outcomes of Mucinous Adenocarcinoma Across Different Colon Segments: An Analysis Using the Surveillance Epidemiology and End Result Database**  
Çiğdem Benlice, Metinçan Erkaya, Emre Görgün, Mehmet Ayhan Kuzu, Ankara, İstanbul, Turkey; Ohio, United States

### Case Report

- 105 **Can Electrolyte Imbalance Indicate a Diagnosis? McKittrick-Wheelock Syndrome and Synchronous Colon Tumor**  
Erhan Eröz, Alp Ömer Cantürk, Enise Bacak, Penbe Gül Ergün, Fatih Altuntoprak, Sakarya, Turkey



# Triangle Excision and Advancement Flap in Pilonidal Disease: A Single-Center Prospective Case Series

© Nurhilal Kızıltoprak<sup>1</sup>, © İlknur Turan<sup>2</sup>, © Ahmet Furkan Mazlum<sup>1</sup>, © Mahmut Salih Genç<sup>1</sup>, © Murat Kalın<sup>1</sup>,  
© Gülçin Ercan<sup>1</sup>, © Uğur Kesici<sup>3</sup>

<sup>1</sup>University of Health Sciences Turkey, Sultan 2. Abdülhamid Han Training and Research Hospital, Clinic of General Surgery, İstanbul, Turkey

<sup>2</sup>Yalova Private Aktif Hospital, Clinic of General Surgery, Yalova, Turkey

<sup>3</sup>University of Health Sciences Turkey, Prof. Dr. Cemil Taşcıoğlu City Hospital, Clinic of General Surgery, İstanbul, Turkey

## ABSTRACT

**Aim:** Pilonidal disease (PD) is frequently encountered within the community. There are still ongoing debates regarding its treatment in general surgery clinics. Although minimally invasive methods such as phenol, laser ablation, and endoscopic pilonidal sinus treatment are gaining prominence, flap applications remain the preferred option in patients where these methods fail or the disease is widespread. In this study, we describe the clinical outcomes of patients operated on using the triangle excision and advancement flap technique, which allows for the removal of less tissue near the perianal region.

**Method:** Prospectively collected data were retrospectively analyzed. Age, gender, body mass index (BMI), disease duration, hirsutism score, number of pits, complications, operation time, hospitalization period, and postoperative 3-, 6-, and 9-month follow-up results of the patients were analyzed. The results of the analysis showed that no complications or recurrences were observed in any patient.

**Results:** A total of 46 patients were included in this study. The mean age of the patients was 23.69 ( $\pm 7.06$ ). Of the 46 patients, 41 were men (89.1%), and 5 were women (10.9%). The mean age of the men was 23.3 ( $\pm 7.33$ ), and the mean age of the women was 26.6 ( $\pm 3.5$ ). In terms of hirsutism score, 34 patients (73%) had a score of 2, and 12 patients (27%) had a score of 3. The mean BMI was 23 ( $\pm 2.16$ ). All patients were operated on under spinal anesthesia. The mean operation time was 40 ( $\pm 7.55$ ) minutes, and the mean hospitalization time was 1 ( $\pm 0$ ) day. In terms of early complications, flap dehiscence was observed in 2 patients. Of these, one was a patient for whom a surgical drain was not placed. No bleeding was detected in any patient, and urinary retention was observed in 3 patients.

**Conclusion:** We believe that the triangle excision and advancement flap method can be safely employed in PD.

**Keywords:** Advancement flap, pilonidal disease, triangle excision

## Introduction

Pilonidal disease (PD) is a common condition in young people.<sup>1</sup> The pathophysiology of PD remains controversial; however, it is generally accepted that the disease arises due to hair in the gluteal cleft.<sup>2</sup> Risk factors include white race, male gender, family history, poor hygiene, deep natal cleft, hypertrichosis, obesity, and prolonged sitting.<sup>3</sup> Diagnosis is made clinically, and it is usually simple to perform. If an abscess is present in acute form, the patient's main complaint is pain. In chronic form, the clinical presentation may vary depending on the number of pits and sinuses. The cavity communicates with the skin through one or more sinuses. Whether acute or chronic,

there are typically one or more sinus orifices located in the midline, and epithelialized channels open to these orifices.<sup>4</sup>

The clinical presentation of PD can take many different forms. As a result, there are numerous treatment methods available. The critical aspect is identifying and implementing the most appropriate treatment for each patient; there is no ideal standard technique. However, if there is an abscess present, the abscess must be drained. In treatment, the goal is to ensure that the remaining tissues following the complete excision of diseased tissues are well-vascularized, tension-free, and resilient. Additionally, minimizing postoperative pain and dressing requirements, facilitating the patient's prompt return to daily



Address for Correspondence: Nurhilal Kızıltoprak, MD,

University of Health Sciences Turkey, Sultan 2. Abdülhamid Han Training and Research Hospital, Clinic of General Surgery, İstanbul, Turkey

E-mail: drnurhilalkiziltoprak@gmail.com ORCID ID: orcid.org/0000-0003-4241-5872

Received: 20.04.2024 Accepted: 04.09.2024



Copyright© 2024 The Author. Published by Galenos Publishing House on behalf of Turkish Society of Colon and Rectal Surgery. This is an open access article under the Creative Commons Attribution-NonCommercial 4.0 International (CC BY-NC 4.0) License.

activities or work, and preventing recurrence are crucial objectives. When the wound is left open, the recurrence rate is lower, but the need for care is higher.

In this study, the results of the triangle excision and advancement flap we performed in the treatment of PD are presented. The advantage of this method is that less tissue is excised from the area near the anus, which can reduce anal complications.

## Materials and Methods

Prospectively collected data were retrospectively analyzed. A total of 46 patients who underwent triangle excision advancement flap between October 2020 and October 2022 were included in this study. Age, gender, disease duration, the modified Ferriman-Gallwey visual scoring for hirsutism (1: mild, 2: moderate, and 3: severe), number of pits, complications, body mass index (BMI), operation time, hospitalization period, and postoperative 3-, 6-, and 9-month follow-up results of the patients were analyzed. All patients had chronic PD without abscess. The surgical methods were explained to the patients, and informed consent was obtained from them after choosing this method. This study was approved by the Ethics Committee of University of Health Sciences Turkey, Haydarpaşa Numune Training and Research Hospital (approval number: HNEAH-KAEK/KK/2024/07, date: 29.01.2024). Informed consent was obtained from all patients for the surgical method to be applied. Procedures were performed in accordance with the Declaration of Helsinki. All patients shaved and bathed 1 day before surgery.

At the time of admission, the patients were classified as follows:<sup>5</sup>

1. Mild disease (1-3 pits, no exudate, and no open wound),
2. Moderate disease (>3-5 pits, rare exudate, and <1 cm open wound),
3. Severe disease (multiple pits, continuous drainage, <1 cm open wound, and chronic wounds due to previous surgery).

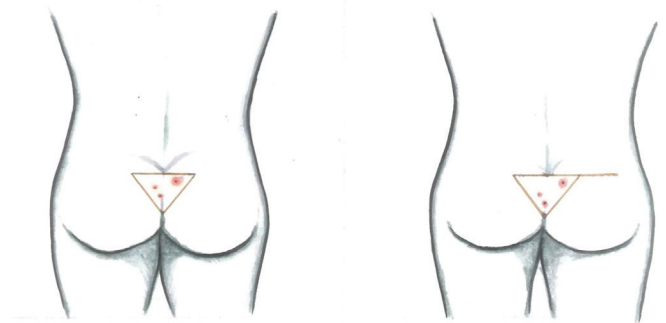
Patients with mild to moderate conditions were included in this study. Additionally, the pits and granulomas needed to conform to the inverted triangle shape to be drawn. The excision and flap method was not performed on all the patients with PD. Local minimally invasive procedures, such as phenol, were performed on patients whose pits were on the natal cleft. The exclusion criteria were as follows: patients with American Society of Anesthesiologists (ASA) scores of 3 and higher, BMI  $\geq 35$ , severe diseases, allergies to anesthetic substances, and contraindications to spinal anesthesia.

The same surgical technique was applied to all patients. The patients were first taken into surgery under spinal anesthesia in the jack-knife position. They were administered first-generation cephalosporin 1 hour prior to treatment. The

gluteal region was fixed to the sides with waterproof tapes, and the area to be operated on was exposed. Figure 1 shows the exposition of the surgical site. Preoperative skin preparation of the surgical area was performed using povidone-iodine. An inverted triangle was drawn to include all of the sinus orifices. A line was drawn extending toward the diseased tissue side, which was equal in length to the upper edge of the triangle (Figure 2). The triangle encompassed all granulomas and orifices, and its lower tip remained outside the midline. The triangle was shifted to the right or left rather than remaining



**Figure 1.** Pilonidal disease; pits in the intergluteal cleft and sinus in the left lateral



**Figure 2.** Drawing an inverted triangle shape to include all orifices and extending the upper edge

exactly on the midline. If the site to be flapped was on the right, the lower tip of the triangle was positioned on the right side; if the site was on the left, the lower tip was positioned on the left side. The triangular area where the diseased tissues were located was fully excised down to the post-sacral region (Figure 3). The flap created by extending the upper edge of the triangle was lifted from the base and transposed to the post-sacral region (Figure 4). Any excess tissue formed in the brought area was then excised. After achieving hemostasis, a Hemovac drain was placed in the lodge, and subcutaneous tissues were sutured in two layers with 2-0 polyglactin sutures (Damacryl, GMD Group Medical, Turkey). The skin was closed using 2-0 polypropylene (Polypropylene, MEDICO, China) sutures in a mattress configuration. Care was taken to ensure that the knots were not located on the flap, and a Hemovac drain was placed in the lodge. The postoperative 1<sup>st</sup>-year follow-up details are shown in Figure 5.

Patients could be mobilized in the postoperative period and were discharged with an analgesic prescription. Antibiotics were not routinely prescribed. Patients were advised to renew the dressing every day for the 1<sup>st</sup> week in the postoperative period, keep the area clean and hair-free, and avoid heavy work and intense contact sports. Patients were discharged on the first postoperative day and were asked to note the amount of fluid accumulated in the drain.

When the patients returned for postoperative follow-up on the 3<sup>rd</sup> day, the drain was removed if the fluid amount had decreased to 25 cc. The patients were scheduled for a follow-up on the 7<sup>th</sup> day and suture removal on the 14<sup>th</sup> day. They were invited to the outpatient clinic for follow-up appointments in the 3<sup>rd</sup>, 6<sup>th</sup>, and 9<sup>th</sup> months. The primary outcome of the treatment was the low rate of complications, and the secondary outcomes were the low rate of early recurrence and rapid healing process.

### Statistical Analysis

Data were reported as percentages and as mean  $\pm$  standard deviation. The Social Science Statistical Package 29 (SPSS Inc., Chicago, IL, USA) was used to analyze all data.

### Results

A total of 46 patients were included in this study. The mean age of the patients was 23.69 ( $\pm 7.06$ ). Among them, 41 were men (89.1%), and 5 were women (10.9%). The mean age was 23.3 for the men and 26.6 for the women. According to the Modified Ferriman-Gallwey visual scoring for hirsutism, 34 patients (73%) had a score of 2, and 12 patients (27%) had a score of 3, and none of the patients had previously undergone PD surgery. All patients were primary cases.

The mean BMI was 23, the mean operation time was 40 minutes, and the mean hospitalization time was 1 day. In terms of early complications, flap dehiscence was observed

in 2 patients, and 1 of these patients did not have a drain inserted. The other 2 patients healed with additional sutures and pressure dressings. There was no bleeding, hematoma, flap necrosis, infection, or need for flap reconstruction in any

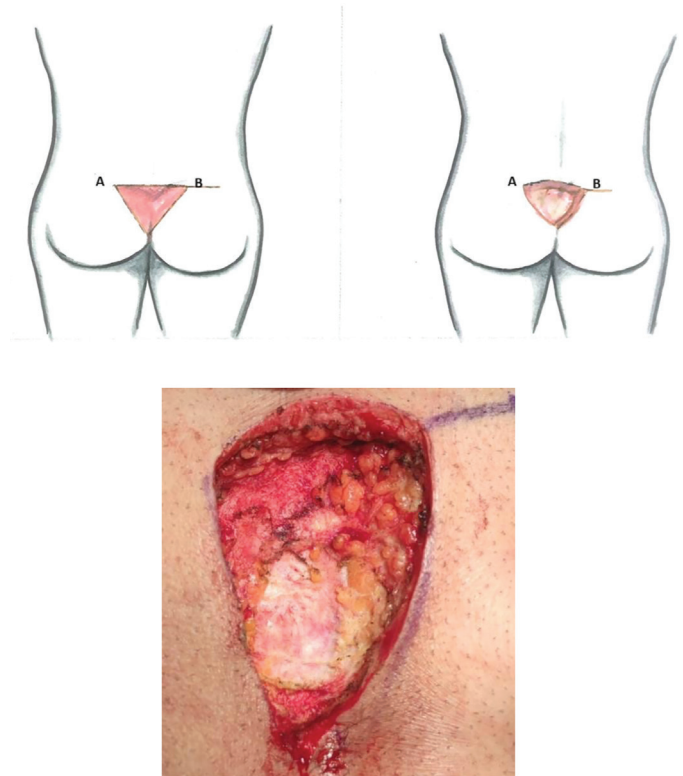


Figure 3. Excision up to the post-sacral region

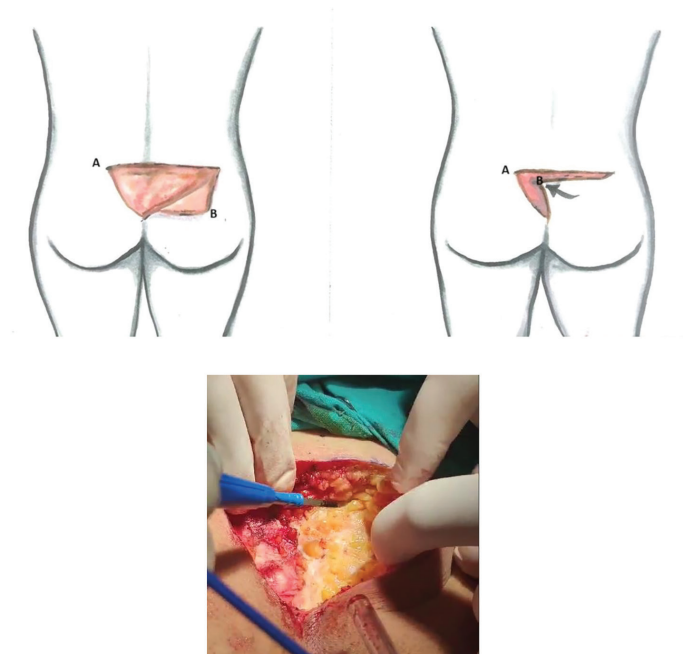


Figure 4. Lifting the flap from the base and the transposition of the flap. "B" is transposing to point "A"



of the patients. All patients were operated on under spinal anesthesia. Urinary retention was observed in 3 patients, and recurrence was not observed in any patient. Demographic data and the surgical outcomes are shown in Table 1.



**Figure 5.** Postoperative year 1

**Table 1.** Demographic data and our surgical results

Gender, n (%)	
Male	41 (89.1%)
Female	5 (10.9%)
Age, mean $\pm$ SD	23.69 ( $\pm$ 8.9) years
Body mass index, mean $\pm$ SD	23 ( $\pm$ 8.3) kg/m <sup>2</sup>
Had previous PD surgery	0
Anesthesia, n (%)	
General	0 (0%)
Spinal	46 (100%)
Operation time, mean $\pm$ SD	40 ( $\pm$ 7.9) minutes
Postoperative complications	
Infection, n (%)	0
Necrosis, n (%)	0
Complete wound opening, n (%)	0
Seroma, n (%)	0
Hematoma, n (%)	0
Recurrence, n (%)	0
Follow-up time, median (min.-max.)	6 (3-9) months

SD: Standard deviation, PD: Pilonidal disease, Min: Minimum, Max: Maximum

## Discussion

PD treatment should be determined according to the characteristics of each patient. Leaving the wound open until granulation tissue forms, partially closing the wound with sutures, and performing secondary closure of the open wound with a skin graft are methods associated with low recurrence rates. However, these methods usually require long-term treatment, and their direct and indirect effects are significant. Furthermore, these treatments lead to high costs<sup>6</sup> and require longer healing times (typically 3-8 weeks). A previous study showed that the mean recovery time of 150 patients who underwent marsupialization was 4 weeks, and the recurrence rate was 6%.<sup>7</sup> The follow-up period in that study was 4 years, whereas that of the present study was 9 months. In addition, poor scar healing is a disadvantage of these treatment methods.<sup>8</sup> In the present study, we investigated the triangle excision and flap method in terms of complications and early recurrence.

Wound closure may be more cosmetically acceptable for some patients and is associated with shorter healing and quicker return to daily activities. Wide local excision and primary closure are advocated by some researchers in the treatment of PD; however, with this method, the scar remains in the midline, which is associated with a high incidence of recurrence.<sup>9</sup> To resolve this problem and reduce the depth of the natal cleft, the Karydakakis technique uses an eccentric elliptical incision for sinus excision. In this method, a flap is moved from the middle side of the wound, and the last suture line is left on both sides of the midline.<sup>10</sup> A portion of the abscess cavity wall opposite the incision is lifted as a flap and used to close the connection between the midline pits and the abscess cavity. Therefore, these techniques have high recurrence rates. In the present study, no bleeding, hematoma, flap necrosis, infection, or need for flap reconstruction was observed in any of the 46 patients.

In patients requiring wide excision, the flap method can be an effective option. Radical excision of the sinus was performed to reshape and flatten the natal cleft to reduce friction, local temperature, humidity, and hair accumulation.

Various flap methods have been used to close the defect following excision. Most flap techniques avoid tension on the wound and midline scar tissue. Although several studies have reported a recurrence rate of 0-3% for excision and flap repair, recurrence rates were 7-42% after conventional primary closure.<sup>11</sup> In the meta-analysis conducted by Berthier et al.<sup>12</sup>, 17 randomized controlled trials were examined, comparing flap techniques with lay open/direct sutures. It was observed that direct suturing led to a higher recurrence rate, whereas rapid wound healing was observed with flap repair.

The use of rhomboid excision and the Limberg transposition flap in complex PD was described around 40 years ago.<sup>13</sup> Low

recurrence rates and short hospital stays were reported using this technique.<sup>14,15</sup> The Limberg flap not only reduces the depth of the natal cleft but also transposes the midline incision scar laterally. However, because all the skin required to resurface the rhomboid defect is removed from a single direction, this technique often causes excessive tension on the suture lines. Moreover, the use of this technique in closing large excisional defects of the sacrococcygeal region is associated with poor scar healing. In the meta-analysis conducted by Gavriilidis and Bota<sup>16</sup>, it was observed that the outcomes of Limberg and Karydakakis flaps were approximately the same.

The V-Y advancement flap technique is reliable and effective in closing large pilonidal wounds, but this technique has limitations in terms of the transposition of the resulting vertical scar from the midline.<sup>17</sup> Berkem et al.<sup>18</sup> reported high recurrence rates when the pilonidal sinus was reconstructed using V-Y advancement flaps, and the vertical suture line remained at the midline. In the case of large tissue defects with repeated infection and recurrence, the use of fasciocutaneous and myocutaneous flaps is indicated. These techniques aim to achieve wide excision of all diseased tissue and closure of the resulting defect with well-vascularized tissue that is similar in volume. Additionally, they provide a tension-free suture line. However, these techniques are more complex and require greater surgical expertise, leading to higher rates of morbidity and wound dehiscence, as well as longer hospital stays.<sup>19</sup> All these flap techniques have certain advantages, such as low recurrence and complication rates, short hospital stays, quick return to daily activities, and satisfactory aesthetic results.<sup>20</sup> In this study, we aimed to introduce the method of triangular closure of the defect remaining following excision.

As noted above, although various surgical procedures have been reported to date, a definitive treatment method for PD has yet to be established. Although the best method is not clear, closing the midline is no longer recommended.<sup>21</sup> To create a surgical alternative, we adapted the Mutaf triangular closure technique, first described in the closure of a large meningomyelocele in 2003, to treat PD. This technique can be utilized for defects following pilonidal sinus excision in different regions that are defined by considering the perforators in the sacrococcygeal region. Predictions can be made regarding scar formation following this technique. Our technique manipulates the tissue from two directions during defect closure. This ensures even distribution of tension and reduces the risk of tissue distortion and displacement of adjacent mobile anatomical landmarks. However, in Limberg flap closure, tissues are harvested in a single direction, which can lead to tension along a single line.

Therefore, in large defects, there is an increased risk of complications due to compromised flap circulation.

Additionally, with this method, a smaller area is excised compared with many other flap techniques. Moreover, excising less tissue from the area near the anal region may help prevent complications in this region.<sup>9</sup> No recurrence or necrosis was observed in any of our patients.

### Study Limitations

This study has certain limitations. For example, the limited sample size and short follow-up period may affect the generalizability of the results. Additionally, the lack of objective assessment tools, such as a satisfaction survey or visual analog scale score, may have limited our ability to fully measure the level of improvement and relief that patients subjectively experienced. Furthermore, we did not use any detailed classification other than the mild/moderate/severe disease classification, and we had no strict indication other than the diseased area conforming to the inverted triangle shape. The short follow-up period was the biggest obstacle to our accurate assessment of recurrence. The exclusion of patients with an ASA score of 3 and those with a BMI >35 is another limitation. Being aware of these limitations is important for future studies to be more comprehensive and detailed.

### Conclusion

In this study, it was observed that the triangle excision and advancement flap method achieved successful results. The overall satisfaction of the patients and the rapid recovery process support the effectiveness of this method. In addition, the low rate of post-surgical complications and recurrence rates show that this method is a safe and effective option for treating PD. The triangle excision and advancement flap method can be safely utilized in the management of PD. Randomized controlled trials with long-term follow-up periods comparing this method with other flap techniques and open surgical techniques are needed.

### Ethics

**Ethics Committee Approval:** This study was approved by the Ethics Committee of University of Health Sciences Turkey, Haydarpaşa Numune Training and Research Hospital (approval number: HNEAH-KAEK/KK/2024/07, date: 29.01.2024).

**Informed Consent:** Informed consent was obtained from all patients for the surgical method to be applied.

### Authorship Contributions

Surgical and Medical Practices: N.K., A.F.M., M.S.G., U.K., Concept: N.K., U.K., Design: N.K., İ.T., A.F.M., M.S.G., Data Collection or Processing: N.K., Analysis or Interpretation: N.K., İ.T., M.K., G.E., Literature Search: N.K., İ.T., M.K., Writing: N.K., G.E.

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

**Financial Disclosure:** The authors declared that this study received no financial support.

## References

- Lund J, Tou S, Doleman B, Williams JP. Fibrin glue for pilonidal sinus disease. *Cochrane Database Syst Rev*. 2017;1:CD011923.
- Karydakis GE. Easy and successful treatment of pilonidal sinus after explanation of its causative process. *Aust N Z J Surg*. 1992;62:385-389.
- Akbulut S, Caliskan A, Yilmaz D, Atay A, Garzali IU, Yagmur Y. Evaluation of the coexistence of pilonidal sinus disease and hirsutism in female patients: a retrospective cross-sectional study. *Ann Med Surg (Lond)*. 2023;85:130-135.
- Hull TL, Wu J. Pilonidal disease. *Surg Clin North Am*. 2002;82:1169-1185.
- Delshad HR, Dawson M, Melvin P, Zotto S, Mooney DP. Pit-picking resolves pilonidal disease in adolescents. *J Pediatr Surg*. 2019;54:174-176.
- McCallum IJ, King PM, Bruce J. Healing by primary closure versus open healing after surgery for pilonidal sinus: systematic review and meta-analysis. *BMJ*. 2008;336:868-871.
- Solla JA, Rothenberger DA. Chronic pilonidal disease. An assessment of 150 cases. *Dis Colon Rectum*. 1990;33:758-761.
- Segre D, Pozzo M, Perinotti R, Roche B; Italian Society of Colorectal Surgery. The treatment of pilonidal disease: guidelines of the Italian Society of Colorectal Surgery (SICCR). *Tech Coloproctol*. 2015;19:607-613.
- Petersen S, Koch R, Stelzner S, Wendlandt TP, Ludwig K. Primary closure techniques in chronic pilonidal sinus: a survey of the results of different surgical approaches. *Dis Colon Rectum*. 2002;45:1458-1467.
- Muzi MG, Milito G, Cadeddu F, Nigro C, Andreoli F, Amabile D, Farinon AM. Randomized comparison of Limberg flap versus modified primary closure for the treatment of pilonidal diseases. *Am J Surg*. 2010;200:9-14.
- Yucel E, Tezcan L, Yilmaz OC, Akin ML. "Flag Excision and Flap" Procedure: a Novel Modification for Off-Midline Closure After Pilonidal Sinus Excision. *Indian J Surg*. 2015;77(Suppl 3):1191-1195.
- Berthier C, Bérard E, Meresse T, Grolleau JL, Herlin C, Chaput B. A comparison of flap reconstruction vs the laying open technique or excision and direct suture for pilonidal sinus disease: A meta-analysis of randomised studies. *Int Wound J*. 2019;16:1119-1135.
- Azab AS, Kamal MS, Saad RA, Abou al Atta KA, Ali NA. Radical cure of pilonidal sinus by a transposition rhomboid flap. *Br J Surg*. 1984;71:154-155.
- Mentes BB, Leventoglu S, Cihan A, Tatlicioglu E, Akin M, Oguz M. Modified Limberg transposition flap for sacrococcygeal pilonidal sinus. *Surg Toda*. 2004;34:419-423.
- Dahmann S, Lebo PB, Meyer-Marcotty MV. Comparison of Treatments for an Infected Pilonidal Sinus: Differences in Scar Quality and Outcome Between Secondary Wound Healing and Limberg Flap in a Prospective Study. *Handchir Mikrochir Plast Chir*. 2016;48:111-119.
- Gavriilidis P, Bota E. Limberg flap versus Karydakis flap for treating pilonidal sinus disease: a systematic review and meta-analysis. *Can J Surg*. 2019;62:131-138.
- Öz B, Akcan A, Emek E, Akyüz M, Sözüer E, Akyıldız H, Aydın H. A comparison of surgical outcome of fasciocutaneous V-Y advancement flap and Limberg transposition flap for recurrent sacrococcygeal pilonidal sinus disease. *Asian J Surg*. 2017;40:197-202.
- Berkem H, Topaloglu S, Ozel H, Avsar FM, Yildiz Y, Yuksel BC, Hengirmen S, Akyurek N. V-Y advancement flap closures for complicated pilonidal sinus disease. *Int J Colorectal Dis*. 2005;20:343-348.
- Elalfy K, Emile S, Lotfy A, Youssef M, Elfeki H. Bilateral gluteal advancement flap for treatment of recurrent sacrococcygeal pilonidal disease: A prospective cohort study. *Int J Surg*. 2016;29:1-8.
- Arpaci E, Altun S, Orhan E, Eyuboglu A, Ertas NM. A New Oval Advancement Flap Design for Reconstruction of Pilonidal Sinus Defect. *World J Surg*. 2018;42:3568-3574.
- Iesalniaks I, Ommer A, Petersen S, Doll D, Herold A. German national guideline on the management of pilonidal disease. *Langenbecks Arch Surg*. 2016;401:599-609.



# Management and Long-Term Follow-up Outcomes of Appendiceal Neuroendocrine Tumor Patients: Evaluation of Single-Center Data

Ömer Akay<sup>1</sup>, Mert Güler<sup>2</sup>, Hüsnü Ozan Şevik<sup>3</sup>, Cihad Tatar<sup>4</sup>, Ufuk Oğuz İdiz<sup>5</sup>

<sup>1</sup>Ilgın Dr. Vefa Tanır State Hospital, Clinic of General Surgery, Konya, Turkey

<sup>2</sup>University of Health Sciences Turkey, İstanbul Gaziosmanpaşa Training and Research Hospital, Clinic of General Surgery, İstanbul, Turkey

<sup>3</sup>University of Health Sciences Turkey, Başakşehir Çam and Sakura City Hospital, Clinic of General Surgery, İstanbul, Turkey

<sup>4</sup>Acıbadem Taksim Hospital, Clinic of General Surgery, İstanbul, Turkey

<sup>5</sup>University of Health Sciences Turkey, İstanbul Training and Research Hospital, Clinic of General Surgery, İstanbul, Turkey

## ABSTRACT

**Aim:** Appendiceal neuroendocrine tumors (NETs) are rare NET that are often incidentally discovered following appendectomy performed for acute appendicitis. Herein, we report our institution's experience regarding the management and long-term follow-up of appendiceal NETs.

**Method:** This study included patients who underwent appendectomy for acute appendicitis and were diagnosed with appendiceal NETs between 2011 and 2020. Patient data were retrospectively retrieved from the hospital computer system. Clinical information, demographic details, tumor size, localization within the appendix, histopathological findings, and surgical procedures were evaluated.

**Results:** The study included data from 44 patients, with 22 men and 22 women, and a mean age of 31.1±12.7 years. All patients presented with symptoms consistent with acute appendicitis upon admission to the hospital. Tumors were distally located in 33 patients, centrally located in seven patients, and proximally located in four patients. Among the 44 patients included in the study, 42 underwent appendectomy, whereas two underwent primary right hemicolectomy during the initial surgery. One patient who underwent appendectomy required subsequent right hemicolectomy 3 weeks later. The mean follow-up duration was 5.4±2.5 years. During the follow-up period, metastasis was detected in only one patient with a tumor size larger than 2 cm located proximally. No recurrence or evidence of metastasis was observed in the remaining patients during long-term follow-up.

**Conclusion:** According to the results of this study, appendectomy may be sufficient for appendiceal NETs measuring <1 cm, and routine follow-up may not be necessary. For appendiceal NETs measuring 1-2 cm in diameter, further studies are needed to establish treatment protocols.

**Keywords:** Appendiceal neuroendocrine tumors, appendectomy, surveillance

## Introduction

Appendiceal tumors are rare occurrences, found in approximately 1% of appendectomy specimens.<sup>1,2</sup> Appendiceal neuroendocrine tumors (NETs) are relatively uncommon tumors. The reported incidence of appendiceal NETs is 3-9 per 1,000 appendectomies, equating to approximately one NET per 150-300 appendectomies.<sup>3,4</sup>

Most appendiceal NETs are incidentally found during appendectomy. They are mostly submucosal and located in the distal third of the appendix, where they do not typically cause

obstruction.<sup>1,5</sup> Symptoms are more likely in larger tumors and in the presence of metastases beyond regional lymph nodes. Approximately 10% of appendiceal NETs are located at the base of the appendix, where they may cause obstruction leading to appendicitis.<sup>6</sup>

When it comes to treatment, simple appendectomy is generally considered sufficient and curative for appendiceal NETs smaller than 1 cm, whereas tumors larger than 2 cm may require right hemicolectomy if relevant criteria are met.<sup>7</sup> The debate continues regarding the optimal treatment for tumors measuring 1-2 cm.



Address for Correspondence: Ömer Akay, MD,

Ilgın Dr. Vefa Tanır State Hospital, Clinic of General Surgery, Konya, Turkey

E-mail: omer\_akay\_38@hotmail.com ORCID ID: orcid.org/0000-0002-0824-2077

Received: 08.06.2024 Accepted: 04.09.2024



Copyright© 2024 The Author. Published by Galenos Publishing House on behalf of Turkish Society of Colon and Rectal Surgery. This is an open access article under the Creative Commons Attribution-NonCommercial 4.0 International (CC BY-NC 4.0) License.

Neuroendocrine neoplasms have the highest survival rates (>95%) compared with other tumor types found in the appendix.<sup>8,9</sup> The excellent prognosis may be attributed to factors such as localization, prompt identification, diagnosis, and excision, as well as the biopathology of the tumor itself or the size of the appendiceal NETs at the time of appendectomy.<sup>9-12</sup> Distant metastases primarily affect the liver, and extrahepatic metastases are extremely rare.<sup>13-15</sup>

In this paper, we report the management and long-term follow-up of patients diagnosed with appendiceal NETs at our center.

## Materials and Methods

The study commenced following approval from the University of Health Sciences Turkey, İstanbul Training and Research Hospital Ethics Committee (approval number: 170, date: 07.07.2023). Data of 6,823 patients who underwent appendectomy at our institution between January 1, 2011, and January 1, 2020, were retrospectively reviewed. Among them, 56 patients diagnosed with appendiceal NETs were included as the main study group. Patients with a history of additional malignancies, lack of follow-up continuity, death due to reasons unrelated to the study, or incomplete data were excluded, resulting in a total of 44 included patients. Pathologically measured tumor sizes, tumor locations, tumor differentiation, types of operations performed, tumor stages, metastatic status, Ki-67 indices, and mitotic rates were examined. A standard method to classify the location of appendiceal tumors is to measure their distance from the base of the appendix (where it joins the cecum). A tumor located within the first third from the base is considered proximal, whereas one in the middle third is considered middle and one in the last third distal. Additionally, imaging methods applied during patient follow-ups and assessments of recurrence and mortality were also investigated.

## Statistical Analysis

Statistical analysis was conducted using SPSS 26.0 for Windows. Descriptive statistics, including numbers and percentages for categorical variables, and mean, standard deviation (SD), median, minimum, and maximum for numerical variables, were provided. For comparisons of numerical variables between two independent groups, a Student's t-test was employed for variables meeting the normal distribution assumption, whereas the Mann-Whitney U test was used when the normal distribution assumption was not met. The chi-square test was utilized to analyze ratios between groups. A p-value of <0.05 was considered to indicate statistical significance.

## Results

This study includes data from 44 patients. Of these patients, 22 were men and 22 were women, with a mean age ( $\pm$  SD) of  $31.1 \pm 12.7$ . All patients were operated on due to acute appendicitis. The mean follow-up period was 5.4 years. Tumors were distally located in 33 patients, centrally located in seven patients, and proximally located in four patients. Among the patients, 37 had tumors measuring <1 cm, three had tumors measuring 1-2 cm in diameter, and four had tumors of >2 cm. Among the four patients with tumors >2 cm, only open appendectomy was performed in two patients with distally located tumors; right hemicolectomy was performed in two patients with proximally located tumors. Three of these four patients did not develop recurrence or metastasis during long-term follow-up, whereas one patient had a NET >2 cm with metastasis at the time of diagnosis. This patient received chemotherapy during the 3-year follow-up period without mortality. Among the patients with proximally located NETs, two had tumors measuring >2 cm and two had tumors of <1 cm. Three of these patients underwent right hemicolectomy, whereas one underwent laparoscopic appendectomy. Six patients (13.6%) had a Ki-67 index above 2, with two of these patients undergoing right hemicolectomy and four undergoing simple appendectomy. Patient and tumor characteristics are presented in Table 1.

Open appendectomy was performed in 29 patients, laparoscopic appendectomy in 12 patients, and right hemicolectomy in three patients. One of these three patients was proximal and metastatic at the time of diagnosis. One patient initially underwent a simple appendectomy, but since the tumor was proximally located and >2 cm, a right hemicolectomy was performed 1 month later. In the third patient, the tumor was located proximally and was <1 cm. Treatment strategies are presented in Table 2.

Patient follow-up was performed using computed tomography (CT) and clinical findings in the first 6 months, and the patients were subsequently followed up with annual tomography scans. The long-term follow-up involved symptoms and clinical follow-up. Aside from one patient who presented with the condition at admission, no patients in our series developed metastasis.

## Discussion

Appendiceal NETs are rare neoplasms with a favorable prognosis. The preferred treatment options are either simple appendectomy or right hemicolectomy. Right hemicolectomy is considered the preferred treatment, especially for tumors measuring >2 cm or 1-2 cm with mesoappendiceal invasion. There is insufficient evidence to predict which patients require comprehensive surgical intervention for disease control.

Better patient selection for more extensive surgery may be achieved through multifactorial tumor assessment combining morphological and molecular analyses.

Appendiceal NETs are reported to have an incidence of 3-9 per 1,000 appendectomies, equating to approximately one NET per 150-300 appendectomies.<sup>3,4</sup> Our series showed a similar incidence rate of appendiceal NETs (7.9 per 1,000 cases), consistent with the literature. Histology is crucial in the diagnosis of appendiceal NETs, and most lesions are incidentally found following appendectomy. Endoscopy does not provide significant benefit in the diagnosis of appendiceal NETs since it only detects large tumors infiltrating the cecum.<sup>7</sup> Furthermore, colonoscopy is necessary for colorectal

cancer screening in appendiceal NET patients, as up to 18% of cases may have concomitant neoplasms in the gastrointestinal system.<sup>16</sup>

The European Neuroendocrine Tumor Society guidelines do not recommend follow-up for patients with small tumors (<1 cm) that have been treated with appendectomy and excised with clear margins.<sup>7,17</sup> Additionally, follow-up is not mandatory for appendiceal NETs >1 cm that have undergone right hemicolectomy, provided there are no additional risk factors and histological examination reveals no lymphovascular invasion or residual disease.<sup>17</sup> Conversely, according to recent guidelines, long-term follow-up is required in cases of lymph node involvement, detection of locoregional disease post-surgery, and when the tumor is of high grade.<sup>7,17</sup> Regular follow-up is necessary for patients with tumors measuring 1-2 cm that exhibit features indicating a higher risk of lymph node spread, such as mesoappendiceal invasion of >3 mm, localization at the base of the appendix, vascular infiltration, or intermediate differentiation.<sup>17</sup> In the present study, the majority of patients had tumors smaller than 1 cm, and apart from one patient who was metastatic at the time of surgery, no metastasis or recurrence was observed during long-term follow-up in any patient.

Although appendiceal NETs appear to have a slight female predominance, small intestine NETs are more common in men. Unlike other appendiceal tumors and NETs, which tend to occur in older patients, appendiceal NETs exhibit the highest incidence rates in women aged 15-19 years and in men aged 20-29 years.<sup>18</sup> In the recent study by Pawa et al.<sup>19</sup>, the average age of the patients was 33.2 years, with the majority being women (60.5%). In the present study, the average age was 31.1 years, and the incidence was equal in the men and the women.

Appendiceal NETs are typically located at the tip of the appendix, and only in some cases do those located in other parts cause appendiceal symptoms. Carcinoid syndrome is a rare condition and is usually associated with advanced forms of the disease.<sup>20</sup> In our series, only four patients (9.1%) had proximally located appendiceal NETs, and metastasis was detected in one of these cases; however, none of our patients developed carcinoid syndrome.

At presentation, the likelihood of regional and distant metastasis is related to tumor size. In a series of 902 well-differentiated NETs derived from the National Cancer Data Base, which examined the relationship between tumor size and metastasis risk, 12% of patients with tumors <2 cm had nodal metastases at diagnosis, and 43% of those with larger tumors had distant metastases.<sup>21</sup> Higher rates of nodal involvement have been reported in various studies for patients with tumors measuring 1-2 cm.<sup>22,23</sup> In a series from the Mayo clinic consisting of 150 patients with appendiceal NETs, none of the

**Table 1.** Patient and tumor characteristics

Age (mean ± SD) (years)		31.1±12.7
Gender (n, %)	Male (n, %)	22 (50%)
	Female (n, %)	22 (50%)
Tumor localization (n, %)	Distal (n, %)	33 (75%)
	Middle (n, %)	7 (15.9%)
	Proximal-root (n, %)	4 (9.1%)
Tumor size (n, %)	<1 cm	37 (84.1%)
	1-2 cm	3 (6.8%)
	>2 cm	4 (9.1%)
Tumor type (n, %)	Well-differentiated (n, %)	41 (93.2%)
	Middle-differentiated (n, %)	3 (6.8%)
Ki-67 status	<2%	38 (86.4%)
	2-20%	6 (13.6%)
Tumor grade	Grade 1	38 (86.4%)
	Grade 2	6 (13.6%)
Stage	Stage 1 (n, %)	31 (70.5%)
	Stage 2 (n, %)	11 (25.0%)
	Stage 3 (n, %)	1 (2.3%)
	Stage 4 (n, %)	1 (2.3%)
Follow-up time (mean ± SD) (years)	5.4±2.5	

SD: Standard deviation

**Table 2.** Treatment strategies

Treatment (n, %)	Open appendectomy (n, %)	29 (65.9%)
	Lap appendectomy (n, %)	12 (27.3%)
	Right hemicolectomy (n, %)	2 (4.5%)
	Open appendectomy + right hemicolectomy (n, %)	1 (2.3%)

127 patients with tumors <2 cm developed metastasis, while 3 out of 14 patients with tumors measuring 2-3 cm and four out of nine patients with tumors >4 cm developed metastasis.<sup>24</sup> In a multicenter study, the survival rate for appendiceal NETs was reported as 99.05% at 5 and 10 years of follow-up, with no reported recurrences.<sup>19</sup> Reports of recurrence of the disease have been found in patients with long-term follow-up. In a series of 64 patients diagnosed with appendiceal NETs under the age of 40 and followed up for 10-33 years after surgery, only one recurrence was recorded in a patient with a regional tumor >2 cm.<sup>25</sup> In a study reporting a patient treated with right hemicolectomy for a tumor >2 cm with mesoappendiceal invasion and lymph node metastasis, it was noted that liver metastasis developed 6 years after the surgery.<sup>26</sup> Another report from Duke Hospital showed that for appendiceal carcinoids measuring 1-2 cm, right colon partial resection did not improve survival rates, even in those with higher-grade tumors. Collectively, these findings suggest that resection of the primary tumor alone is likely sufficient for carcinoids <2 cm.<sup>27</sup> In the present study, none of the patients with tumors <2 cm had metastasis or recurrence detected during long-term follow-up, whereas one out of four patients with tumors >2 cm had metastasis. Based on these findings, we believe that simple appendectomy can be safely performed in appendiceal NETs of <2 cm. The metastatic potential of appendiceal NETs is associated with their proliferative rate. A high Ki-67 index is indicative of an aggressive tumor and is often accompanied by a worse prognosis.<sup>28</sup> Therefore, it is recommended that tumors with excessive mitotic counts or significantly elevated Ki-67 indices are treated with right hemicolectomy.<sup>7,24</sup> In a recent multicenter study on appendiceal NETs treated via right hemicolectomy, it was noted that 17% of the study population expressed Ki-67 at a rate of more than 2%, and 50% of these cases (2 out of 4) had metastatic lymph node disease.<sup>29</sup> Well-differentiated G1 or G2 NETs have an overall indolent clinical behavior. All poorly differentiated neuroendocrine neoplasms are G3 neuroendocrine carcinomas with an aggressive clinical course.<sup>30</sup> Poorly differentiated NETs are usually widely metastatic and rarely produce symptoms related to the secretion of bioactive substances. Some poorly differentiated NETs lack morphological features of neuroendocrine differentiation.<sup>31</sup> In the present study, there were only six patients with grade 2 pathology results, and none with grade 3. In addition, there were six patients with a Ki-67 index between 2% and 20%, and none with a Ki-67 index above 20%. The fact that we did not have a high-grade patient and the small number of patients with a high Ki-67 index limits our ability to comment on this issue.

Data supporting the use of imaging in detecting residual disease are inadequate. The most effective imaging method

[CT, magnetic resonance imaging (MRI), or ultrasound] has not yet been determined, and there remain issues regarding the appropriate number of tests during the follow-up period and the duration of the follow-up. Concerns about radiation exposure arise with CT imaging in these patients. As noted, appendiceal NETs are generally in early stages and are small in size, making the likelihood of detection with ultrasound quite low. Positron emission tomography (PET) imaging could be considered as an option, but further studies are needed in this regard.<sup>32</sup> Additionally, the role of colonoscopy is unconfirmed. In this context, MRI emerges as the most effective imaging modality for patients requiring long-term follow-up. Although not yet proven, a reasonable strategy would involve follow-up at 6 and 12-months post-surgery, followed by annual follow-ups thereafter.<sup>17</sup> Despite their indolent course, appendiceal NETs can recur. Therefore, tumors >2 cm or >1 cm with additional risk factors should undergo lifelong surveillance.<sup>7,33</sup> In our practice, we utilized CT or PET imaging for long-term follow-up of our patients, and since we did not have any cases of recurrence or new metastasis development, the effectiveness of the imaging modalities could not be evaluated.

### Study Limitations

One of the most significant limitations of this study is its retrospective nature. Another limitation is that all patients were not followed up at the same frequency and using the same imaging method. Additionally, the number of tumors with a diameter of 1-2 cm was limited to only three. This situation makes it difficult for us to make interpretations regarding this group. Due to these limitations, this study can be seen as a preliminary study for further research.

### Conclusion

Despite being rare, the evaluation of pathology examinations of appendectomy materials should not be overlooked due to appendiceal NETs mimicking acute appendicitis. Based on this study, we believe that simple appendectomy would suffice in patients with distal and mid-settled appendiceal NETs measuring <1 cm, consistent with the literature data. However, for tumors >2 cm and particularly those measuring 1-2 cm, right hemicolectomy should be considered the preferred treatment. The follow-up strategy for these patients remains debatable; however, based on this study's findings of no recurrence or metastasis during long-term follow-up in patients who underwent appendectomy for tumors <1 cm, routine follow-up may not be necessary in such cases.

**Acknowledgments:** No organization or person funded this study. All of the authors report no biomedical financial interests or potential conflicts of interest.

## Ethics

**Ethics Committee Approval:** The study commenced following approval from the University of Health Sciences Turkey, İstanbul Training and Research Hospital Ethics Committee (approval number: 170, date: 07.07.2023).

**Informed Consent:** Retrospective study.

## Authorship Contributions

Surgical and Medical Practices: Ö.A., M.G., H.O.Ş., U.O.İ., Concept: Ö.A., U.O.İ., Design: Ö.A., U.O.İ., Data Collection or Processing: Ö.A., M.G., C.T., Analysis or Interpretation: Ö.A., M.G., H.O.Ş. C.T., Literature Search: Ö.A., H.O.Ş., Writing: Ö.A., C.T., Critical Review: C.T., U.O.İ.

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

**Financial Disclosure:** The authors declared that this study received no financial support.

## References

1. Connor SJ, Hanna GB, Frizelle FA. Appendiceal tumors: retrospective clinicopathologic analysis of appendiceal tumors from 7,970 appendectomies. *Dis Colon Rectum*. 1998;41:75-80.
2. Unver N, Coban G, Arıcı DS, Buyukpınarbasılı N, Gucin Z, Malya FÜ, Onaran OI, Topalan K. Unusual Histopathological Findings in Appendectomy Specimens: A Retrospective Analysis of 2047 Cases. *Int J Surg Pathol*. 2019;27:142-146.
3. Sandor A, Modlin IM. A retrospective analysis of 1570 appendiceal carcinoids. *Am J Gastroenterol*. 1998;93:422-428.
4. Goede AC, Caplin ME, Winslet MC. Carcinoid tumour of the appendix. *Br J Surg*. 2003;90:1317-1322.
5. Roggo A, Wood WC, Ottinger LW. Carcinoid tumors of the appendix. *Ann Surg*. 1993;217:385-390.
6. Moertel CG, Dockerty MB, Judd ES. Carcinoid tumors of the vermiform appendix. *Cancer*. 1968;21:270-278.
7. Pape UF, Perren A, Niederle B, Gross D, Gress T, Costa F, Arnold R, Denecke T, Plöckinger U, Salazar R, Grossman A; Barcelona Consensus Conference participants. ENETS Consensus Guidelines for the management of patients with neuroendocrine neoplasms from the jejunum-ileum and the appendix including goblet cell carcinoma. *Neuroendocrinology*. 2012;95:135-156.
8. McGory ML, Maggard MA, Kang H, O'Connell JB, Ko CY. Malignancies of the appendix: beyond case series reports. *Dis Colon Rectum*. 2005;48:2264-2271.
9. Steffen T, Ebinger SM, Warschkow R, Lüthi C, Schmied BM, Clerici T. Long-Term Survival is not Impaired After the Complete Resection of Neuroendocrine Tumors of the Appendix. *World J Surg*. 2015;39:2670-2676.
10. O'Donnell ME, Carson J, Garstin WI. Surgical treatment of malignant carcinoid tumours of the appendix. *Int J Clin Pract*. 2007;61:431-437.
11. Modlin IM, Kidd M, Latich I, Zikusoka MN, Shapiro MD. Current status of gastrointestinal carcinoids. *Gastroenterology*. 2005;128:1717-1751.
12. Benedix F, Reimer A, Gasteringer I, Mroczkowski P, Lippert H, Kube R; Study Group Colon/Rectum Carcinoma Primary Tumor. Primary appendiceal carcinoma--epidemiology, surgery and survival: results of a German multi-center study. *Eur J Surg Oncol*. 2010;36:763-771.
13. Cai W, Tan Y, Ge W, Ding K, Hu H. Pattern and risk factors for distant metastases in gastrointestinal neuroendocrine neoplasms: a population-based study. *Cancer Med*. 2018;7:2699-2709.
14. Madani A, Thomassen I, van Gestel YRBM, van der Bilt JDW, Haak HR, de Hingh IHJT, Lemmens VEPP. Peritoneal Metastases from Gastroenteropancreatic Neuroendocrine Tumors: Incidence, Risk Factors and Prognosis. *Ann Surg Oncol*. 2017;24:2199-2205.
15. Alexandraki KI, Kaltsas GA, Grozinsky-Glasberg S, Chatzellis E, Grossman AB. Appendiceal neuroendocrine neoplasms: diagnosis and management. *Endocr Relat Cancer*. 2016;23:R27-41.
16. Scott A, Upadhyay V. Carcinoid tumours of the appendix in children in Auckland, New Zealand: 1965-2008. *N Z Med J*. 2011;124:56-60.
17. Pape UF, Niederle B, Costa F, Gross D, Kelestimur F, Kianmanesh R, Knigge U, Öberg K, Pavel M, Perren A, Toumpanakis C, O'Connor J, Krenning E, Reed N, O'Toole D; Vienna Consensus Conference participants. ENETS Consensus Guidelines for Neuroendocrine Neoplasms of the Appendix (Excluding Goblet Cell Carcinomas). *Neuroendocrinology*. 2016;103:144-152.
18. Hemminki K, Li X. Incidence trends and risk factors of carcinoid tumors: a nationwide epidemiologic study from Sweden. *Cancer*. 2001;92:2204-2210.
19. Pawa N, Clift AK, Osmani H, Drymoussis P, Cichocki A, Flora R, Goldin R, Patsouras D, Baird A, Malczewska A, Kinross J, Faiz O, Antoniou A, Wasan H, Kaltsas GA, Darzi A, Cwikla JB, Frilling A. Surgical Management of Patients with Neuroendocrine Neoplasms of the Appendix: Appendectomy or More. *Neuroendocrinology*. 2018;106:242-251.
20. Astudillo A. Classification and biological characterization of neuroendocrine tumors of the gastrointestinal tract. *Oncologia Barc*. 2004;27:51-56.
21. Hsu C, Rashid A, Xing Y, Chiang YJ, Chagpar RB, Fournier KF, Chang GJ, You YN, Feig BW, Cormier JN. Varying malignant potential of appendiceal neuroendocrine tumors: importance of histologic subtype. *J Surg Oncol*. 2013;107:136-143.
22. Mullen JT, Savarese DM. Carcinoid tumors of the appendix: a population-based study. *J Surg Oncol*. 2011;104:41-44.
23. Rault-Petit B, Do Cao C, Guyétant S, Guimbaud R, Rohmer V, Julié C, Baudin E, Goichot B, Coriat R, Tabarin A, Ramos J, Goudet P, Hervieu V, Scoazec JY, Walter T. Current Management and Predictive Factors of Lymph Node Metastasis of Appendix Neuroendocrine Tumors: A National Study from the French Group of Endocrine Tumors (GTE). *Ann Surg*. 2019;270:165-171.
24. Moertel CG, Weiland LH, Nagorney DM, Dockerty MB. Carcinoid tumor of the appendix: treatment and prognosis. *N Engl J Med*. 1987;317:1699-1701.
25. Svendsen LB, Bülow S. Carcinoid tumours of the appendix in young patients. *Acta Chir Scand*. 1980;146:137-139.
26. Fornaro R, Frascio M, Sticchi C, De Salvo L, Stabilini C, Mandolino F, Ricci B, Gianetta E. Appendectomy or right hemicolectomy in the treatment of appendiceal carcinoid tumors? *Tumori*. 2007;93:587-590.
27. Nussbaum DP, Speicher PJ, Gulack BC, Keenan JE, Ganapathi AM, Englum BR, Tyler DS, Blazer DG 3rd. Management of 1- to 2-cm Carcinoid Tumors of the Appendix: Using the National Cancer Data Base to Address Controversies in General Surgery. *J Am Coll Surg*. 2015;220:894-903.
28. Liu E, Telem DA, Hwang J, Warner RR, Dikman A, Divino CM. The clinical utility of Ki-67 in assessing tumor biology and aggressiveness in patients with appendiceal carcinoids. *J Surg Oncol*. 2010;102:338-341.
29. Grozinsky-Glasberg S, Alexandraki KI, Barak D, Doviner V, Reissman P, Kaltsas GA, Gross DJ. Current size criteria for the management of neuroendocrine tumors of the appendix: are they valid? Clinical experience and review of the literature. *Neuroendocrinology*. 2013;98:31-37.
30. Nagtegaal ID, Odze RD, Klimstra D, Paradis V, Rugge M, Schirmacher P, Washington KM, Carneiro F, Cree IA; WHO Classification of Tumours Editorial Board. The 2019 WHO classification of tumours of the digestive system. *Histopathology*. 2020;76:182-188.
31. Hainsworth JD, Johnson DH, Greco FA. Poorly differentiated neuroendocrine carcinoma of unknown primary site. A newly recognized clinicopathologic entity. *Ann Intern Med*. 1988;109:364-371.



32. Perez MA, Saul SH, Trojanowski JQ. Neurofilament and chromogranin expression in normal and neoplastic neuroendocrine cells of the human gastrointestinal tract and pancreas. *Cancer*. 1990;65:1219-1227.
33. Arnold R, Chen YJ, Costa F, Falconi M, Gross D, Grossman AB, Hyrdel R, Kos-Kudła B, Salazar R, Plöckinger U; Mallorca Consensus Conference participants; European Neuroendocrine Tumor Society. ENETS Consensus Guidelines for the Standards of Care in Neuroendocrine Tumors: follow-up and documentation. *Neuroendocrinology*. 2009;90:227-233.



# Adaptation of the Colostomy Impact Score for Use in the Turkish Population: A Validity and Reliability Study

© Evrim Sarıtaş<sup>1</sup>, © Zehra Göçmen Baykara<sup>1</sup>, © Hatice Karabulut<sup>2</sup>, © Aysel Ören Hin<sup>3</sup>, © Sezai Leventoğlu<sup>4</sup>

<sup>1</sup>Gazi University Faculty of Nursing, Department of Nursing, Ankara, Turkey

<sup>2</sup>Ankara University Faculty of Nursing, Department of Nursing, Ankara, Turkey

<sup>3</sup>Gazi University Health Application and Research Center Hospital, Department of Nursing, Ankara, Turkey

<sup>4</sup>Gazi University Health Application and Research Center Hospital, Clinic of General Surgery, Ankara, Turkey

## ABSTRACT

**Aim:** This study was conducted to adapt the colostomy impact (CI) score for use in the Turkish population and evaluate its validity and reliability.

**Method:** For data collection, the Descriptive Characteristics Form, CI score, and Stoma Quality-of-Life Scale were used. The CI score, designed to assess stoma dysfunction impacting health-related quality of life in patients with a colostomy, comprises one dimension and seven question items. Data were collected from individuals with colostomies who met the inclusion criteria between January 2022 and March 2023. The test-retest procedure was administered to 20 participants in the sample group.

**Results:** The research involved 202 participants with colostomies. The mean CI score was 15.40±8.13. All CI score items significantly contributed to the total score. The test-retest assessments exhibited statistically significant similarity ( $p=0.119$ ). The intraclass correlation coefficient was 0.45, which is statistically significant ( $p=0.001$ ). Confirmatory factor analysis indicated acceptable moderate fit within the limits. The mean score derived from the CI score demonstrated a statistically significant negative relationship with the Stoma Quality-of-Life Scale ( $r=-0.711$ ,  $p=0.001$ ).

**Conclusion:** Methodologically conducted, this study determined that the CI score is a valid and reliable measurement tool for use in the Turkish population. It is recommended that the CI score be utilized in various studies and with larger sample groups in future research.

**Keywords:** Colostomy, quality of life, stoma dysfunction, colostomy impact score

## Introduction

A colostomy may be required temporarily or permanently for the management of various pathological conditions, such as congenital anomalies, colonic obstruction, inflammatory bowel disease, intestinal trauma, or gastrointestinal malignancy.<sup>1,2</sup> Although colostomy is considered a therapeutic approach, it results in the loss of voluntary bowel control and the transition from previously discreet bowel elimination functions to a more visible state. Colostomy, which alters voiding habits and causes functional loss or changes, exposes individuals to diverse life experiences in physiological, psychological, social, and other

aspects. These experiences significantly impact the adaptation process to colostomy and overall quality of life.<sup>1,3,4</sup>

In the literature, studies show that the lives of individuals with ostomy/colostomy are affected at different levels. In the study by Krogsgaard et al.<sup>5</sup> ( $n=2,262$ ), 19% of patients reported “a lot of” or “some” restrictions on daily activities because of the stoma, with 44% reporting no restrictions. The study conducted by Baykara et al.<sup>6</sup> ( $n=30$ ) reported that ostomy negatively impacted the biopsychosocial quality of life of both individuals and their spouses. In a study by Colbran et al.<sup>3</sup> with a sample size of 23, 65.2% of patients with permanent colostomy believed their colostomy caused some degree of restriction in their



Address for Correspondence: Evrim Sarıtaş, MD,

Gazi University Faculty of Nursing, Department of Nursing, Ankara, Turkey

E-mail: evrimeyikara@gazi.edu.tr/evrimeyikara@gmail.com ORCID ID: orcid.org/0000-0003-1334-4243

Received: 11.07.2024 Accepted: 04.09.2024



Copyright© 2024 The Author. Published by Galenos Publishing House on behalf of Turkish Society of Colon and Rectal Surgery. This is an open access article under the Creative Commons Attribution-NonCommercial 4.0 International (CC BY-NC 4.0) License.

daily activities or chores. In research studies, although ostomy generally has a negative impact on individuals' lives, patients who receive sufficient information and counseling about the process tend to exhibit improved quality of life and adaptation to ostomy.<sup>5-7</sup>

The methods and measurement tools used to evaluate the objective and subjective effects of ostomy are gaining value daily. Evaluating health-related quality of life in individuals with colostomy, one type of ostomy, is an essential source of data on the individual's life, health, disease, diagnosis, and treatment processes.<sup>8</sup> Valid and reliable measurement tools facilitate the presentation of quantitative data and consider individual differences. Several measurement instruments have been developed to examine the impact of stoma on quality of life.<sup>9,10</sup> One of these measurement tools is the colostomy impact (CI) score. The CI score, developed by Thyø et al.<sup>11</sup>, has one dimension consisting of seven question items.<sup>4</sup> The CI score is a tool related to stoma dysfunction that influences health-related quality of life. It assists healthcare professionals in identifying patients with stoma dysfunction effectively and systematically, enabling targeted interventions.<sup>8</sup>

The CI score was developed based on a study involving individuals who underwent permanent colostomy as a result of rectal cancer (n=610). It has been established as a valid measurement tool within the Danish community.<sup>11</sup> In a study conducted by Kristensen et al.<sup>4</sup> (n=244), it was determined that the CI score is a valid measurement tool that can also be used in individuals who undergo colostomy following surgery for other benign conditions such as ileus and Crohn's disease in addition to rectal cancer. In the study by Kristensen et al.<sup>8</sup>, the CI score was administered to 2,470 patients across communities in Australia, China, Denmark, Portugal, the Netherlands, Spain, and Sweden. The structure of the CI score, along with its discriminative validity, sensitivity, and specificity, was evaluated, confirming its validity and reliability.<sup>8</sup>

The CI score's unidimensional nature, consisting of seven items, and ability to provide quick responses are essential factors supporting its use. It is crucial to adapt the CI score, which has been adapted for many societies, into a format usable within the Turkish community. The results from this research are expected to offer a quantitative understanding of the current situation among individuals with colostomies, enabling the planning of preventive and therapeutic interventions. Furthermore, these findings are believed to guide the conduct of new studies contributing to the field.

### Aim

The research was conducted to adapt the CI score for use in the Turkish population and evaluate its validity and reliability.

## Materials and Methods

### Design and Setting

This study had a methodological design. The research was conducted with 202 individuals with colostomies who visited the stomatherapy units of hospitals that granted institutional permission. Data were collected between January 2022 and March 2023.

### Procedures

To adapt the CI score for use in the Turkish population and conduct validity and reliability studies, permission was obtained through e-mail from the authors who developed the CI score. The adaptation process followed the recommendations of the International Test Commission<sup>12</sup> and the World Health Organization.<sup>13</sup> The steps followed in the adaptation process are outlined below.

**1. Translation:** The CI score was translated from English to Turkish by three native Turkish speakers with a strong command of both languages.

**2. Semantic explanations:** The researchers meticulously analyzed the Turkish translations provided by the three experts. A single draft form that best represented the items was then created.

**3. Expert committee assessment:** The draft of the CI score translated into Turkish was sent to seven experts who are knowledgeable about stoma-related concepts and have experience in this field. The experts independently evaluated whether the words had equivalent meanings in both languages, whether the sentences were ambiguous, whether the items had culturally altered meanings, and whether they were appropriate for the target group. Feedback was obtained from a Turkish language expert to assess the appropriateness of the items for Turkish culture and grammar. The content validity indices of the items were calculated using the Davis technique, where each item was rated from "a" to "d" (a: appropriate, b: needs some revision, c: needs major revision, d: inappropriate). The proportion of experts selecting "a" and "b" was then divided by the total number of experts, resulting in a content validity index for each item.<sup>14</sup> Items achieving a content validity index value of 0.80 and above were included in the Turkish draft version. The content validity index and the content validity ratio were both calculated as 1 (100%).

**4. Back translation:** The CI score was back translated into English by a language expert proficient in advanced English and not involved in the initial translation. The English back translation was synthesized by the researchers and compared with the original version.

**5. Pilot application:** A preliminary study involving 30 participants was conducted to assess the comprehensibility of

the items. Participants were instructed to read the items and briefly explain their understanding of each item's meaning. Following the pilot application, no changes were necessary for the Turkish draft form.

**6. Final version:** The back translation into English was sent to the author who developed the original CI score via e-mail. Based on the positive feedback received from the author, the final Turkish version of the CI score was obtained.

**7. Documentation:** The adaptation stages were meticulously documented, with careful attention paid to each phase of the adaptation process.<sup>15</sup>

### Participants

The inclusion criteria for the research were individuals aged 18 years or older who had a permanent colostomy or had been living with a colostomy for at least 12 months, understood and spoke Turkish, and consented to participate in the study. Exclusion criteria for the research comprised individuals who had physical or mental health issues that would prevent them from completing or understanding the data collection forms or who were unwilling to participate voluntarily. The criterion for withdrawal from the study was incomplete or inaccurate completion of the data collection forms.

In cross-cultural adaptation studies, Kline<sup>16</sup> recommends a minimum sample size of 200, whereas Hair et al.<sup>17</sup> indicate that each parameter of the measurement tool should be responded to by at least 10 participants, with a total dataset size of at least 100 or more.<sup>18</sup> Based on the inclusion, exclusion, and withdrawal criteria, a total of 206 individuals were initially included in this study. However, four individuals who completed the form incompletely were excluded from the sample group. Accordingly, the final sample group consisted of 202 individuals with colostomies. The sample size for this research meets the criteria mentioned above.

### Data Collection Forms

The data collection utilized the Descriptive Characteristics Form, the CI score, and the Stoma Quality-of-Life Scale.

The researchers developed the Descriptive Characteristics Form. The formulation of these questions drew upon both existing literature<sup>2,6,19</sup> and the researchers' academic expertise. The CI score was developed by Thyø et al.<sup>11</sup> for individuals who underwent permanent colostomy as a result of rectal cancer. It determines health-related quality of life affected by stoma dysfunction with a sensitivity of 85.7% and specificity of 59.5%.<sup>11</sup> Subsequent studies have determined that the CI score can also be utilized in individuals with colostomies for reasons other than rectal cancer, including those with permanent colostomies or individuals who have had a colostomy for at least 12 months.<sup>4,8</sup> The CI score is unidimensional and consists

of seven items. Each item has different response options: three response options for items 1, 2, and 6; five response options for item 3; and two response options for items 4, 5, and 7. Each response option corresponds to a different score. The CI score ranges from 0 to 38, reflecting the impact of colostomy on an individual's life. Higher scores indicate a major impact of colostomy, whereas lower scores indicate a minor impact. Scores of 0-9 indicate a minor CI score, whereas scores of 10-38 indicate a major CI score.

The Stoma Quality-of-Life Scale was developed by Baxter et al.<sup>10</sup> and consists of two sections, twenty-one items, and four subscales. The first two items of the scale relate to overall satisfaction with life and are scored on a scale of 0 to 100. A score of 0 indicates complete dissatisfaction, whereas a score of 100 indicates complete satisfaction. The remaining nineteen scale items are grouped into three subscales and utilize a 5-point Likert scale (1: never, 2: rarely, 3: sometimes, 4: often, and 5: always). These subscales include work/social life (6 items), sexuality/body image (5 items), and stoma function (6 items). The Turkish scale, validated by Karadağ et al.<sup>19</sup>, consists of nineteen items. The overall reliability coefficient for the Turkish version of the scale is 0.87.

### Data Collection

Researchers visited stomatherapy units to obtain written permission. Individuals who met the inclusion criteria were provided detailed explanations about the purpose and methods of the study. Participants were instructed to carefully read all questions and mark the option that best suited their response.

Twenty participants were asked to complete the instruments again after 2 weeks. The consistency between the test-retest score averages of the participants was evaluated.

### Ethical Considerations

Written permission was obtained from the Ethics Committee of a Gazi University (approval number: E-77082166-604.01.02-224999, date: 01.12.2021). Written permissions were also obtained from two separate hospitals where the study would be conducted (institution 1/date and number: 29.12.2021, E.251154; institution 2/date and number: 13.01.2022, E.263831). Permissions were obtained from the researchers who developed the CI score and adapted the Stoma Quality-of-Life Scale for the Turkish population.

### Statistical Analysis

In the statistical evaluation, SPSS for Windows (Chicago, IL, USA) was utilized. A paired t-test was employed to examine the difference between the total impact score in the test and retest assessments, while intraclass correlation (ICC) analysis was used to assess internal consistency. The influence of the

seven questionnaire items constituting the CI score on the total score and their relationship with the Stoma Quality-of-Life Scale were evaluated using Pearson correlation analysis. Confirmatory factor analysis (CFA) was conducted to assess the fit of the CI score's item questions to the sample. The chi-square test and independent samples t-test were used to group the CI score. Independent samples t-test and One-Way analysis of variance with the Bonferroni post-hoc test were applied to analyze the mean scores obtained from the CI score. A p-value of 0.050 was considered to represent statistical significance.

## Results

### Descriptive Characteristics

Table 1 summarizes the descriptive characteristics of the participants (n=202). The mean age of the participants was 58.86±11.99 years, 51.5% (n=104) were male, 45.1% (n=91) were either illiterate or had only completed primary school, 82.7% (n=167) were married, and 48.5% (n=98) were retired. A total of 88.6% (n=179) of individuals lived with their families, 54% (n=109) had no comorbidities, and 80.7% (n=163) did not receive chemotherapy or radiotherapy. Moreover, 83.7% (n=169) had undergone planned stoma surgery, 85.1% (n=172) reported receiving information before surgery, and 53.5% (n=108) indicated that stoma marking was completed before surgery. In addition, 70.3% (n=142) had a permanent stoma, 83.2% (n=168) had undergone stoma creation as a result of cancer, 44.6% (n=90) performed stoma care themselves, and 65.8% (n=133) reported currently experiencing no complications related to their stoma. The average duration of living with a stoma was 4.30±4.62 years.

Table 2 presents the impact scores for minor, major, and total CI scores. Accordingly, 22.8% (n=46) of individuals had a minor impact score, and 77.2% (n=156) had a major impact score.

Table 3 presents the relationship between descriptive characteristics and mean CI score. It was found that individuals with a middle school education exhibited a statistically significantly lower mean CI score compared with others (p=0.026), and individuals with comorbidities had statistically significantly higher CI scores than those without (p=0.002). Patients with temporary stoma exhibited a statistically significantly higher CI score than patients with permanent stoma (p=0.003), and those reporting stoma-related complications had a statistically significantly higher CI score than those reporting no complications (p=0.001). Although not presented in the table, there is no statistically significant relationship between age and CI score (p=0.144).

Table 4 displays the distribution of responses across the seven items comprising the CI score. In total, 38.6% (n=78)

**Table 1.** Participant characteristics

Characteristics	n	%
Age (years) (mean ± SD)	58.86±11.99	
<b>Gender</b>		
Male	104	51.5
Female	98	48.5
<b>Education status</b>		
Illiterate, primary school graduate	91	45.1
Middle school	37	18.3
High school	41	20.3
University	33	16.3
<b>Marital status</b>		
Married	167	82.7
Single	35	17.3
<b>Profession</b>		
Not working	79	39.1
Retired	98	48.5
Working	25	12.4
<b>Living with the person</b>		
Alone	23	11.4
With his/her family	179	88.6
<b>Comorbidities</b>		
Yes	93	46.0
No	109	54.0
<b>Chemotherapy, radiotherapy</b>		
Yes	39	19.3
No	163	80.7
<b>Operation setting</b>		
Emergency	33	16.3
Planned	169	83.7
<b>Receiving information before surgery</b>		
Informed	172	85.1
Not informed	30	14.9
<b>Stoma marking before surgery</b>		
Done	108	53.5
Not done	94	46.5
<b>Stoma</b>		
Temporary	60	29.7
Permanent	142	70.3
<b>Indication for surgery</b>		
Cancer	168	83.2
Other	34	16.8
<b>Need assistance for stoma care</b>		
Self-care	90	44.6
Other	56	27.7
Assistance when needed	56	27.7
<b>Stoma complications</b>		
Yes	69	34.2
No	133	65.8
Time since stoma creation (years) (mean ± SD)	4.30±4.62	

SD: Standard deviation

of participants experienced embarrassing smells from their stoma bag less than once a week, 43.6% (n=88) did not experience stool leakage under the adapter, 38.1% (n=77) had variable feces consistency, 53% (n=107) did not experience pain around the stoma and its surroundings, 51% (n=103) did not encounter any skin problems around the stoma, 69.3% (n=140) had not noticed a bulge around the stoma, and 50.5% (n=102) managed stoma care themselves.

### Evaluation of Reliability and Validity of the Colostomy Impact Score

In Table 5, the item-total correlations for the CI scores are presented. Accordingly, all seven question items have significantly affected the total CI score (p=0.001).

When analyzing the difference in CI scores between the test and retest measurements, no statistically significant difference was found between the mean scores (test: 12.90±7.21, retest: 12.45±6.97; p=0.119). The ICC calculated to assess the internal consistency of the CI score was found to be 0.45, which is statistically significant (p=0.001). This analysis determined that the items within the CI score are moderately consistent with each other.

To test the suitability of the one-dimensional CI score, CFA was applied. The fit indices such as the chi-square ( $\chi^2$ ) degrees of freedom (df), root mean square error of approximation (RMSEA), comparative fit index (CFI), and normed fit index (NFI) were used. The fit indices were  $\chi^2/df=3.54$ , RMSEA=0.11, CFI=0.83, and NFI=0.78 (Figure 1).

The relationship between the scores obtained from the Stoma Quality-of-Life Scale and the CI score is provided in Table 6. Accordingly, the mean score obtained from the CI score exhibited a significantly negative relationship with the work/social life subdimension (r=-0.575, p=0.008), the sexuality/body image subdimension (r=-0.484, p=0.026), and the overall Stoma Quality-of-Life Scale (r=-0.711, p=0.001). Graphic 1 illustrates the relationship between the CI score and the overall Stoma Quality-of-Life Scale and its subdimensions.

**Table 2.** Participants' minor, major, and total colostomy impact scores

CI score	n	%
Minor CI score	46	22.8
Major CI score	156	77.2
CI score ( $\bar{X} \pm SD$ )	15.40±8.13 (min.: 0, max.: 36)	

CI: Colostomy impact,  $\bar{X}$ : Mean, SD: Standard deviation, min.: Minimum, max.: Maximum

**Table 3.** Relationship between descriptive characteristics and mean colostomy impact scores

Characteristics	CI score, ( $\bar{X} \pm SD$ )	p
<b>Gender</b>		
Male	14.70±8.18	0.206
Female	16.15±8.06	
<b>Education status</b>		
Illiterate, primary school graduate	16.80±8.07	0.026
Middle school	12.03±6.97	
High school	15.68±9.17	
University	15.00±7.33	
<b>Marital status</b>		
Married	15.70±8.26	0.322
Single	15.67±7.09	
<b>Profession</b>		
Not working	16.75±8.34	0.140
Retired	14.31±7.91	
Working	15.48±8.04	
<b>Living with the person</b>		
Alone	14.52±8.26	0.558
With his/her family	15.52±8.14	
<b>Comorbidities</b>		
Yes	17.27±8.18	0.002
No	13.82±7.78	
<b>Chemotherapy, radiotherapy</b>		
Yes	16.87±8.46	0.211
No	15.06±8.04	
<b>Operation setting</b>		
Emergency	16.09±8.69	0.598
Planned	15.27±8.04	
<b>Receiving information before surgery</b>		
Informed	15.68±8.20	0.252
Not informed	13.83±7.67	
<b>Stoma marking before surgery</b>		
Done	15.44±8.05	0.943
Not done	15.36±8.27	
<b>Stoma</b>		
Temporary	17.98±8.12	0.003
Permanent	14.32±7.92	
<b>Indication for surgery</b>		
Cancer	15.72±8.20	0.223
Other	13.85±7.75	
<b>Need assistance for stoma care</b>		
Self-care	11.30±6.22	0.001
Other	20.48±7.19	
Assistance when needed	16.93±8.44	
<b>Stoma complications</b>		
Yes	21.03±7.40	0.001
No	12.49±6.89	

CI: Colostomy impact,  $\bar{X}$ : Mean, SD: Standard deviation

**Table 4.** Participants' responses to the colostomy impact score items

CI score items	n	%
<b>Do you experience embarrassing smells from your stoma bag?</b>		
No, never	77	38.1
Yes, less than once a week	78	38.6
Yes, at least once a week	47	23.3
<b>Do you experience seepage of feces under the sticking plaster?</b>		
No, never	88	43.6
Yes, less than once a week	81	40.1
Yes, at least once a week	33	16.3
<b>What is the consistency of your feces?</b>		
Hard and lumpy	22	10.9
Formed and soft	51	25.2
Mushy	32	15.8
Watery	20	9.9
Variable	77	38.1
<b>Do you ever experience pain in and around the stoma?</b>		
No, never	107	53.0
Yes	95	47.0
<b>Do you experience any skin problems around your stoma?</b>		
No, never	103	51.0
Yes	99	49.0
<b>Have you noticed a bulge around the stoma?</b>		
No	140	69.3
Yes, I have a small bulge (under 10 cm)	47	23.3
Yes, I have a large bulge (over 10 cm)	15	7.4
<b>Who manages your stoma care?</b>		
I do it all myself	102	50.5
I need support and instruction	100	49.5

CI: Colostomy impact

**Table 5.** Item-total correlations of colostomy impact scores

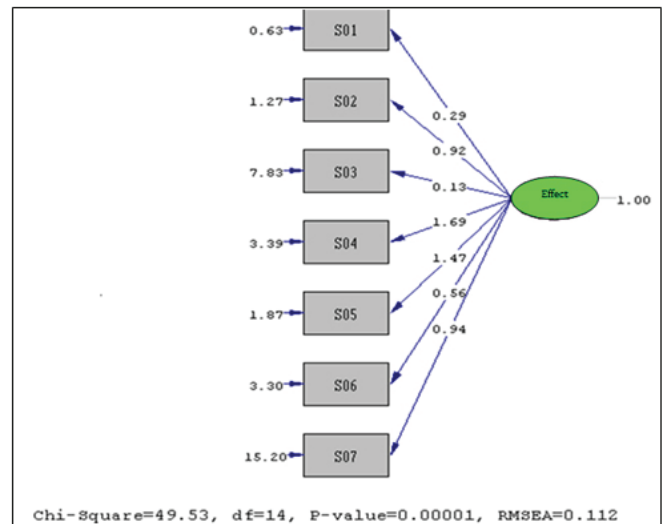
CI score items	Total point	
	r	p
Item 1	0.420	0.001
Item 2	0.551	0.001
Item 3	0.319	0.001
Item 4	0.650	0.001
Item 5	0.676	0.001
Item 6	0.426	0.001
Item 7	0.573	0.001

r: Pearson correlation coefficient, CI: colostomy impact

**Table 6.** Relationship between colostomy impact score and Stoma Quality-of-Life Scale

Stoma Quality-of-Life Scale and its subdimensions	CI score	r	p
Work/social life (6 items)		-0.575	0.008
Sexuality/body image (5 items)		-0.484	0.026
Stoma function (6 items)		-0.299	0.188
Total		-0.711	0.001

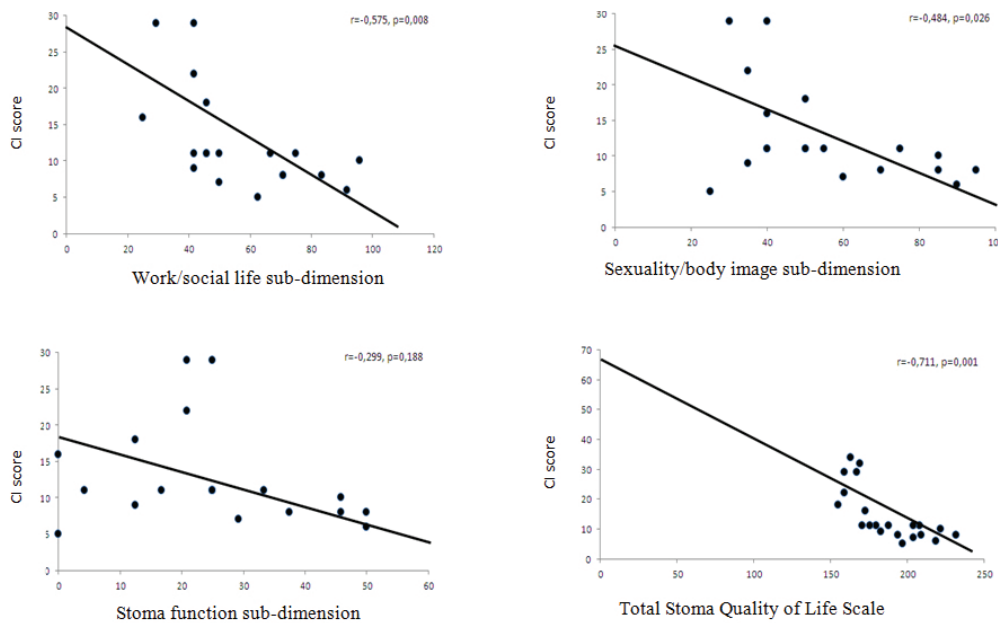
r: Pearson correlation coefficient, CI: colostomy impact

**Figure 1.** Confirmatory factor analysis for the colostomy impact score

## Discussion

This study was conducted to adapt the CI score for use in the Turkish population and evaluate its validity and reliability (n=202). In this study, the mean CI score was  $15.40 \pm 8.13$ , with 77.2% identified as having a major CI score (Table 2). Similar findings have been reported previously. In a study conducted by Kristensen et al.<sup>20</sup>, 51.9% (n=1244) of individuals with colostomy had a minor CI score, whereas 48.1% (n=1154) had a major CI score. In a study conducted by Colbran et al.<sup>3</sup>, the mean CI score was  $13.4 \pm 2.5$ , and 91.4% of patients (n=21) had a CI score greater than 10.

In our study, participants with different chronic diseases, those who underwent temporary stoma placement, and those reporting any stoma-related complications had statistically significantly higher CI scores (Table 3). In a study conducted by Kristensen et al.<sup>20</sup>, stoma dysfunction measured by the CI score was significantly associated with unemployment, financial burden of the stoma, young age, being unmarried, and decreased health-related quality of life. In our research, the results indicated that participants experienced skin



**Graphic 1.** Relationship between the Stoma Quality-of-Life Scale and colostomy impact score  
RMSEA: Root mean square error of approximation, CI: colostomy impact

problems around the stoma (49%, n=99), pain (47%, n=95), and expressed a need for support and information on stoma care (49.5%, n=100) (Table 4). In other studies, similarly determined by CI scores, the number of participants with skin problems ranged from 27% to 44.5%, stoma site pain from 17.4% to 31%, and the need for support and information in stoma care from 15% to 46.8%.<sup>4,5,21</sup> Our study and other research findings reveal that individuals' adaptation to colostomy and their specific challenges vary.

The test-retest evaluation determined that individuals' mean CI score ratings were similar ( $p=0.119$ ). The proximity of the mean ratings indicates a similarity between the two measurements. In a study by Kristensen et al.<sup>8</sup>, no differences were found in the item-level score or sum score between the test and the retest of the CI score. However, the scoring of CI score items differed and was not a continuous measurement. In our study, an ICC value of 0.45 was determined to be statistically significant ( $p=0.001$ ), indicating that the CI score item questions were moderately consistent. In the study by Kristensen et al.<sup>8</sup>, ICC scores indicated moderate reliability in Sweden and the Netherlands for both the sum score (0.663 and 0.701, respectively) and item-level scores (0.640 and 0.749, respectively).

The CFA examines the fit of the constructed model based on the proposed factor structure of the measurement instrument with the data. The CFA fit indices for the CI score are presented in Figure 1. Accordingly,  $\chi^2/df=3.54$ , and since the index ranges between 3 and 5, this result indicates a moderate fit.<sup>22</sup> In this study, RMSEA=0.11, which is considered acceptable, as values  $\leq 0.08$  are acceptable.<sup>22</sup> The CFI was determined as 0.83 and

NFI as 0.78; CFI and NFI indices approaching 1 indicate excellent fit, whereas those approaching 0 indicate model misfit.<sup>22,23</sup> The findings obtained from the analysis indicate that the factor structure of the CI score generally aligns with acceptable moderate fit within the limits.

In this study, individuals' CI scores were correlated with the Stoma Quality-of-Life Scale. The scale's work/social life and sexuality/body image subdimensions and the total score demonstrated significant negative correlations with the CI score (Table 6). In a study conducted by Khomyakov et al.<sup>24</sup>, the Stoma Impact on Quality-of-Life Questionnaire revealed an inverse negative relationship with the European Organization for Research and Treatment of Cancer (EORTC) Core Quality-of-Life Questionnaire (QLQ-C30) global quality-of-life scale, including physical, emotional, role, and social functioning ( $p<0.05$ ). In another study, patients reporting that colostomy "never" or "slightly" affected their quality of life (n=1850, 74.2%) had significantly higher EORTC QLQ-C30 functional scale scores compared with patients reporting that colostomy "slightly" or "very much" affected their quality of life (n=642, 25.8%).<sup>20</sup> Thus, the CI score is useful in evaluating health-related quality of life, and negative experiences related to stoma negatively affect quality of life.

Patients with colostomy face significant life changes.<sup>3</sup> Adequate education on diagnosis, treatment procedures, colostomy care, and complication prevention is crucial to improve individuals' adjustment to the stoma and enhance their quality of life. Stoma care nurses and physicians bear significant responsibility during the preoperative and postoperative periods.<sup>6</sup> In this regard, the CI score is considered a valuable



measurement tool for assessing current status and identifying areas for improvement.

### Study Limitations

The researchers conducted the study in institutions where written consent was obtained; therefore, the study was limited to individuals in the stomatherapy units of two institutions. Another limitation was that the results of the measurement tools were evaluated based on self-reports provided by individuals with colostomy. Data were collected through participants' self-reports, potentially introducing a subjective aspect to the results. Furthermore, there could be information bias, as participants might over- or under-report their behaviors.

### Conclusion

The results of this research indicate that the seven-item CI score is a valid and reliable measurement tool for individuals with colostomy in the Turkish population. Although describing and quantifying experiences is sometimes difficult, measurement tools provide reliable data. Therefore, the Turkish version of the CI score can be used to evaluate the impact of a stoma on patients who undergo a colostomy. It is recommended that research be conducted on stoma function and the quality of life of patients with a colostomy using the CI score. Precautions should be taken when interpreting the results, remedial interventions should be implemented, and the outcomes should be evaluated.

### Ethics

**Ethics Committee Approval:** Written permission was obtained from the Ethics Committee of a Gazi University (approval number: E-77082166-604.01.02-224999, date: 01.12.2021).

**Informed Consent:** Informed consent was obtained.

### Authorship Contributions

Surgical and Medical Practices: E.S., Z.G.B., H.K., A.Ö.H., S.L., Concept: E.S., Z.G.B., H.K., A.Ö.H., S.L., Design: E.S., Z.G.B., H.K., A.Ö.H., S.L., Data Collection or Processing: E.S., Z.G.B., H.K., Analysis or Interpretation: E.S., Z.G.B., Literature Search: E.S., Z.G.B., Writing: E.S., Z.G.B., H.K., A.Ö.H., S.L.

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

**Financial Disclosure:** The authors declared that this study received no financial support.

### References

- Duluklu B, Şenol Çelik S. Quality of Life of Persons with Colostomy: Problems and Nursing Interventions. *HUHEMFAD*. 2019;6:111-119 (Turkish).
- Türkmenoglu G, Karadağ A. Problems Experienced by Spouses of Turkish Patients With a Stoma: A Descriptive, Cross-Sectional Study. *Wound Manag Prev*. 2019;65:33-41.
- Colbran R, Gillespie C, Christensen P, Kristensen HØ, Warwick A. Quality of life and financial impacts of permanent colostomy for rectal cancer. *J Coloproctol* 2024;44:e47-e52.
- Kristensen HØ, Krogsgaard M, Christensen P, Thomsen T. Validation of the colostomy impact score in patients ostomized for a benign condition. *Colorectal Dis*. 2020;22:2270-2277.
- Krogsgaard M, Kristensen HØ, Furnée EJB, Verkuijl SJ, Rama NJ, Domingos H, Maciel J, Solis-Peña A, Espín-Basany E, Hidalgo-Pujol M, Biondo S, Sjövall A, Emmertsen KJ, Thyø A, Christensen P. Life with a stoma across five European countries—a cross-sectional study on long-term rectal cancer survivors. *Support Care Cancer*. 2022;30:8969-8979.
- Baykara ZG, Eyikara E, Hin AÖ, Acarlar H, Leventoglu S. Changes in the Lives of Individuals with a Stoma and Their Spouses: A Qualitative Study. *Adv Skin Wound Care*. *Adv Skin Wound Care*. 2022;35:281-288.
- Ongün P, Yılmaz NB, Kırıl Yİ. Anxiety, Sexuality and Quality of Life of Individuals with Stoma: A Systematic Review. *THDD*. 2021;2:41-52 (Turkish).
- Kristensen HØ, Thyø A, Jøssing Emmertsen K, Smart NJ, Pinkney T, Warwick AM, Pang D, Furnée EJB, Verkuijl SJ, José Rama N, Domingos H, Maciel J, Solis-Peña A, Espín Basany E, Hidalgo-Pujol M, Biondo S, Sjövall A, Christensen P. Translation and international validation of the Colostomy Impact score. *Colorectal Dis*. 2021;23:1866-1877.
- Prieto L, Thorsen H, Juul K. Development and validation of a quality of life questionnaire for patients with colostomy or ileostomy. *Health Qual Life Outcomes*. 2005;3:62.
- Baxter NN, Novotny PJ, Jacobson T, Maidl LJ, Sloan J, Young-Fadok TM. A stoma quality of life scale. *Dis Colon Rectum*. 2006;49:205-212.
- Thyø A, Emmertsen KJ, Pinkney T, Christensen P, Laurberg S. The colostomy impact score: development and validation of a patient reported outcome measure for rectal cancer patients with a permanent colostomy. A population-based study. *Colorectal Dis*. 2017;19:25-33.
- International Test Commission (ITN). Guidelines for translating and adapting tests. *International Journal of Testing*. 2018;18:101-134.
- World Health Organization (WHO). (2017). Process of translation and adaptation of instruments. Available from: [http://www.who.int/substance\\_abuse/research\\_tools/translation/en/](http://www.who.int/substance_abuse/research_tools/translation/en/)
- Davis LL. Instrument review: Getting the most from a panel of experts. *App Nurs Res*. 1992;5:194-197.
- Çapık C, Gözüm S, Aksayan S. Intercultural Scale Adaptation Stages, Language and Culture Adaptation: Updated Guideline. *Florence Nightingale J Nurs*. 2018;26:199-210 (Turkish).
- Kline RB. *An Easy Guide to Factor Analysis*. New York: The Guilford Press; 2011.
- Hair JF, Anderson RE, Babin BJ, Black WC. *Multivariate data analysis: A global perspective*. Upper Saddle River, NJ: Pearson; 2010; p. 7.
- Yücel E, Çizel B. Adaptation of the Cognitive Dissonance Scale into Turkish: The Validity and Reliability Study. *Journal of Travel and Hospitality Management*. 2019;16:106-120 (Turkish).
- Karadağ A, Öztürk D, Çelik B. Adaptation of Quality Life Scale for The Ostomy Patients into Turkish. *Journal of Disease of the Colon and Rectum*. 2011;21:173-181 (Turkish).
- Kristensen HØ, Thyø A, Emmertsen KJ, Smart NJ, Pinkney T, Warwick AM, Pang D, Elfeki H, Shalaby M, Emile SH, Abdelkhalek M, Zuhdy M, Poskus T, Dulskas A, Horesh N, Furnée EJB, Verkuijl SJ, Rama NJ, Domingos H, Maciel J, Solis-Peña A, Espín-Basany E, Hidalgo-Pujol M, Biondo S, Sjövall A, Christensen P. Surviving rectal cancer at the cost of a colostomy: global survey of long-term health-related quality of life in 10 countries. *BJS Open*. 2022;6:zrac085.
- Wang J, Zhong C, Kristensen HØ, Christensen P, Liu J, Pang D. Validation of the Chinese version of the colostomy impact score in rectal cancer patients with permanent colostomy. *Colorectal Dis*. 2022;24:773-781.

22. Çokluk Ö, Şekercioğlu G, Büyüköztürk Ş. Sosyal bilimler için çok değişkenli istatistik SPSS ve LISREL uygulamaları. Pegem akademi, 6. Baskı, Ankara; 2021; p. 268-272.
23. Schermelleh-Engel K, Moosbrugger H, Müller H. Evaluating the fit of structural equation models: tests of significance and descriptive goodness-of-fit measures. MPR-online. 2003;8:23-74.
24. Khomyakov EA, Pikunov DY, Mamedli ZZ, Karachun AM, Kostenko NV, Zhilin IV, Ignatov IS, Medvednikov AA, Moskalev AI, Khakamov TS, Skopintsev VB, Lukmonov SN, Samsonov DV, Razuvailova AG, Lee YB, Radostev SI, Ayupov RT, Malgina NV, Achkasov SI, Rybakov EG. Validation and adaptation of the Russian version colostomy impact score (CIS). Koloproktologia. 2023;22:112-120.



# Risk Factors Affecting Surgical Site Infections in Colorectal Cancer Surgery: Analysis of National Multicenter Data

© Ahmet Ali Aktaş<sup>1</sup>, © Barış Gülcü<sup>2</sup>, © Özgen Işık<sup>1,2</sup>, Turkish Colorectal Cancer Database Study Group\*

<sup>1</sup>Bursa Uludağ University Faculty of Medicine, Department of Surgery, Bursa, Turkey

<sup>2</sup>Medicana Bursa Hospital, Department of Surgery, Bursa, Turkey

## ABSTRACT

**Aim:** Surgical site infections (SSIs) are a significant complication in colorectal cancer (CRC) surgery. This study investigates the risk factors affecting SSI in CRC using national data.

**Method:** Prospective data collected from the Turkish Colon and Rectum Surgery Association Colorectal Cancer Database were retrospectively analyzed. A total of 1,216 patients who underwent surgery between July 2018 and March 2022 were included in the study. Factors affecting SSI were evaluated using multivariate analysis.

**Results:** The total SSI rate was 13.98% (9.29% superficial, 2.06% deep, and 2.63% organ/space). In univariate analyses, the presence of SSI was associated with several factors, including high body mass index (BMI), advanced TNM stage, presence of coronary artery disease (CAD), presence of concurrent malignancy, high American Society of Anesthesiologists score, receiving neoadjuvant therapy, emergency operation, open surgery, hand anastomosis, anastomosis configuration, iatrogenic ureter injury, simultaneous prostate resection, postoperative blood transfusion, evisceration, prolonged ileus, anastomotic leak, urinary fistula, urinary retention, postoperative bleeding, postoperative pneumonia, postoperative renal failure, reoperation and need for readmission. In multivariate analysis, high BMI [odds ratio (OR): 1.51, 95% confidence interval (CI): 1.02-2.21, p=0.0354], advanced stage disease (OR: 2.06, 95% CI: 1.38-3.07, p=0.0004), CAD (OR: 1.85, 95% CI: 1.14-3.01, p=0.0120), concurrent malignancy (OR: 3.35, 95% CI: 1.64-6.84, p=0.0009), receiving neoadjuvant therapy (OR: 1.76, 95% CI: 1.18-2.61, p=0.0048), emergency operation (OR: 3.26, 95% CI: 1.84-5.78, p<0.0001), postoperative blood transfusion (OR: 2.44, 95% CI: 1.67-3.56, p<0.0001) were identified as independent risk factors.

**Conclusion:** SSI following CRC is still a problem in our country. In this study, risk factors similar to those reported in the literature were detected.

**Keywords:** Surgical site infection, colorectal cancer, prevention

## Introduction

Infection, bleeding, and even death were seen as common complications of surgery before the mid-19<sup>th</sup> century. Thanks to pioneers such as Ignaz Semmelweis and Joseph Lister, a breakthrough has been made in surgical site infections (SSIs) and the associated problems. The positive momentum of the development of disinfection and sterilization has been maintained with the technical developments that enable it and the increase in antibiotic therapy options.<sup>1</sup> Despite this

progress, SSIs continue to constitute more than a third of healthcare-associated infections today and continue to be a significant health problem.<sup>2</sup>

When all types of operations are considered, the overall pooled incidence of SSI is estimated to be 2.5%.<sup>3</sup> However, when looking specifically at digestive system surgery, this rate can rise above 11%.<sup>4</sup> Therefore, SSI is of particular importance in colorectal surgery. Furthermore, SSI brings a significant additional cost burden for health systems. In the United



Address for Correspondence: Özgen Işık, MD,  
Bursa Uludağ University Faculty of Medicine, Clinic of General Surgery, Bursa, Turkey  
E-mail: drozgen006@gmail.com ORCID ID: orcid.org/0000-0002-9541-5035  
Received: 29.07.2024 Accepted: 04.09.2024



Copyright© 2024 The Author. Published by Galenos Publishing House on behalf of Turkish Society of Colon and Rectal Surgery. This is an open access article under the Creative Commons AttributionNonCommercial 4.0 International (CC BY-NC 4.0) License.

States, the annual cost of SSI is estimated to be between 3.5 and 10 billion dollars.<sup>5</sup> It has been reported that cases of SSI developing following colorectal operations can double the costs of index hospitalization and increase the 30-day costs by six times due to increased hospital stay.<sup>6</sup> A study conducted in Turkey showed that the index hospitalization cost increases by 1.6 times in patients who develop an SSI.<sup>7</sup>

In addition to all these negative effects, there are studies reporting that SSI developed following colorectal cancer (CRC) surgery also negatively affects oncological outcomes.<sup>8,9</sup> The Centers for Disease Control and Prevention (CDC) declared that no positive improvement was recorded in the rate of SSI following colon surgery in its last two reports, the 2021 and 2022 National and State Healthcare-Associated Infections Progress Reports.<sup>10,11</sup> Thus, factors affecting SSI following colorectal surgery continue to be an important topic of research today in view of improving outcomes. This study aims to identify the factors affecting SSI in CRC surgery using a national database.

## Materials and Methods

### Patient Selection

The study protocol was approved by a Uludağ University Faculty of Medicine Clinical Research Ethics Committee (approval no: 2023-17/44, date: 19.09.2023).

Data were obtained from the national Colorectal Cancer Database (CCD) of the Turkish Society of Colon and Rectal Surgery (TSCRS). Preoperative, operative and short-term (30 days) postoperative data of patients who underwent curative colon or rectal resection due to CRC are prospectively entered into this database. In total, 1,216 consecutive cases from 18 centers involving surgery due to colon or rectal cancer between July 2018 and March 2022 were included in the study.

### Variables Examined

In the TSCRS-CCD, the data entry process is performed by the responsible colorectal surgeons from each data-providing center, and the entered data are then verified by the CCD working study group. Here, SSIs are defined according to the CDC classification.<sup>12</sup> The factors examined for their effect on SSI were grouped as patient- or disease-related, operation-related, and postoperative factors. Patients were divided into two groups: those who developed SSI and those who did not. The main patient-related factors examined were age, gender, body mass index (BMI), hypertension (HT), diabetes mellitus (DM), coronary artery disease (CAD), chronic obstructive pulmonary disease (COPD), chronic kidney failure (CKF), smoking, accompanying malignancy status, past surgical history, and American Society of Anesthesiologists (ASA) score.

The main disease-related factors were tumor localization, TNM stage, and neoadjuvant treatment status. The American Joint Committee on Cancer staging manual (8<sup>th</sup> edition)<sup>13</sup> was used for TNM staging.

Operative setting (emergency/elective), operation time, operator, open or minimally invasive operation, anastomosis type (hand/stapler), anastomosis configuration (end-to-end, end-to-side, side-to-end, side-to side, j pouch), stoma formation, perioperative blood transfusion, iatrogenic organ injury, and simultaneous organ resections were the operation-related factors.

Postoperative factors examined for their effect on SSI were postoperative blood transfusion, wound evisceration, prolonged ileus, anastomotic leak, urinary retention, urinary fistula, postoperative bleeding, postoperative acute kidney failure, reoperation, and readmission.

### Statistical Analysis

Continuous variables are expressed as mean  $\pm$  standard deviation, time variables as percentile, and categorical variables as number (%). The significance between categorical variables was analyzed using Fisher's exact test or the chi-square test, and the significance between continuous variables was analyzed using the t-test or Wilcoxon rank-sum test. Independent risk factors were determined using logistic regression analysis and expressed by odds ratio (OR). Data were transferred to the JMP® (version 17.0. SAS Institute Inc., Cary, NC, 1989-2023) statistical package program, and statistical analyses were performed.

## Results

The overall SSI rate was 13.98% (9.29% superficial incisional, 2.06% deep incisional, and 2.63% organ/space). Patient and disease-related factors, such as age, gender, DM, HT, COPD, CKF, smoking, past surgical history, and tumor localization, did not show a significant relationship with the presence of SSI in univariate analyses. The presence of SSI was found to be associated with factors such as high BMI, presence of CAD, presence of accompanying malignancy, high ASA score, receiving neoadjuvant treatment, and locally advanced clinical TNM stage. The patient-related factors are summarized in Table 1.

When the relationship between operation-related factors and the presence of SSI was examined, operation time (being above the 75<sup>th</sup> percentile), the operator being an assistant/specialist, stoma formation status, and preoperative blood transfusion did not show a significant relationship. Emergency operation, open surgery, anastomotic technique, anastomosis configuration, iatrogenic ureter injury, simultaneous partial prostatectomy, and postoperative blood transfusion were found to be associated with the presence of SSI. The operation-related factors are presented in Table 2.

Among postoperative factors, evisceration, prolonged ileus, anastomotic leak, urinary fistula, urinary retention, postoperative bleeding, postoperative pneumonia, postoperative kidney failure, increased reoperation, and need for readmission were associated with the presence of SSI. The postoperative factors are detailed in Table 3.

Factors showing a significant relationship with the presence of SSI were included in the multivariate analysis. Accordingly, BMI, advanced stage disease, CAD, accompanying malignancy, receiving neoadjuvant treatment, emergency operation, and postoperative blood transfusion were determined to be independent risk factors. The results of the multivariate analysis are summarized in Table 4.

**Table 1.** Patient-related factors

Variable		SSI (+), n (%)	SSI (-), n (%)	p value
Age		63.69±0.95	62.68±0.38	0.32
Gender	Female	56 (11.76)	420 (88.24)	0.07
	Male	114 (15.41)	626 (84.59)	
BMI		27.46±0.34	26.28±0.13	<b>0.0015</b>
HT	Yes	67 (14.47)	396 (85.53)	0.69
	No	103 (13.68)	650 (86.32)	
DM	Yes	42 (16.54)	212 (83.46)	0.18
	No	128 (13.31)	834 (86.69)	
CAD	Yes	32 (20.25)	126 (79.75)	<b>0.0148</b>
	No	138 (13.04)	920 (86.96)	
COPD	Yes	8 (15.38)	44 (84.62)	0.76
	No	162 (13.92)	1,002 (86.08)	
CKF	Yes	5 (27.78)	13 (72.22)	0.08
	No	165 (13.77)	1,033 (86.23)	
Malignancy	Yes	13 (24.53)	40 (75.47)	<b>0.0236</b>
	No	157 (13.5)	1,006 (86.5)	
Smoking	Yes	21 (13.91)	130 (86.09)	0.97
	No	149 (13.99)	916 (86.01)	
Tumor localization	Colon	100 (12.71)	687 (87.29)	0.07
	Rectum	70 (16.36)	358 (83.64)	
TNM stage	1	14 (7.87)	164 (92.13)	<b>&lt;0.0001</b>
	2	31 (10.51)	264 (89.49)	
	3	83 (20.34)	325 (79.66)	
	4	26 (19.7)	106 (80.3)	
ASA score	1	28 (9.86)	256 (90.14)	<b>0.0369</b>
	2	97 (14.1)	591 (85.9)	
	3	41 (17.83)	189 (82.17)	
	4	3 (25)	9 (75)	
	5	1 (50)	1 (50)	
Neoadjuvant therapy	Yes	72 (19.2)	303 (80.8)	<b>0.0005</b>
	No	98 (11.68)	741 (88.32)	
Previous surgery	Yes	47 (16.49)	238 (83.51)	0.15
	No	122 (13.15)	806 (86.85)	

Variables reported in \*median (minimum-maximum) or \*mean ± standard deviation. N: Number of studies reporting the variable, SSI: Surgical site infection, BMI: Body mass index, HT: Hypertension, DM: Diabetes mellitus, CAD: Coronary artery disease, COPD: Chronic obstructive pulmonary disease, CKF: Chronic kidney failure, ASA: American Society of Anesthesiologists

## Discussion

SSI is a significant clinical problem that negatively affects morbidity, mortality, and cost, and potentially worsens oncological outcomes. There are complex and numerous factors related to the patient, surgeon, operation, and postoperative care that affect the risk of SSI. The CDC reports that around half of SSIs can be reduced if a focus is placed on correctable factors. In the present study, points that could be effective in reducing SSI are highlighted beyond the commonly reported measures.

In addition to providing an idea about the general medical condition of the patients, the ASA score can show a significant relationship with the presence of SSI. In fact, SSI is significantly common in patients with a high ASA score (>2).<sup>14</sup> In previously conducted studies, a high ASA score is reported as a risk factor for SSI following CRC surgery.<sup>15,16</sup> In a study examining the risk factors for SSI following laparoscopic colon cancer surgery, Nakamura et al.<sup>17</sup> did not find the ASA score to be a significant variable. However, in the present study, patients with an ASA score of >1 were evaluated as high ASA

score. In the literature, when a high ASA score is taken as >2, it is mostly considered as a significant variable in terms of SSI. However, although a significant relationship was found in univariate analyses in the present study, the ASA score was not determined to be an independent variable.

In this study, obesity and the presence of CAD were determined to be independent risk factors for the development of SSI. On the contrary, the presence of HT, DM, and COPD were found not to be independent risk factors for the development of SSI. Studies on the risk posed by the presence of DM and HT in terms of SSI present complex results. While some publications emphasize that DM is an independent risk factor,<sup>18,19</sup> in a prospective study examining risk factors for SSI following colorectal resection, it was stated that DM and HT were not independent variables.<sup>20</sup> When combined with the results of the present study, it becomes important whether factors such as DM and HT cause microcirculatory damage that can result in SSI development in the patient beyond their presence. When CAD is considered as vasculopathy developing in the organism with the effect of DM, HT, hyperlipidemia, smoking,

**Table 2.** Operation-related factors

Variable		SSI (+), n (%)	SSI (-), n (%)	p-value
Operative condition	Emergent	23 (26.14)	65 (73.86)	<b>0.0006</b>
	Elective	147 (13.03)	981 (86.97)	
<b>Operation time (&gt;75 percentile)</b>				<b>0.56</b>
Operator	Specialist	161 (14.07)	983 (85.93)	0.7
	Resident	9 (12.5)	63 (87.5)	
Operative approach	Open	120 (19.11)	508 (80.89)	<b>&lt;0.0001</b>
	Minimally invasive	50 (8.5)	538 (91.5)	
Anastomosis	Hand sewn	12 (13.33)	78 (86.67)	<b>0.0036</b>
	Staple	119 (12.04)	869 (87.96)	
	None	17 (26.56)	47 (73.44)	
Anastomosis configuration	J pouch	2 (28.57)	5 (71.43)	<b>0.0132</b>
	End-end	56 (9.33)	544 (90.67)	
	End-side	5 (10.2)	44 (89.8)	
	Side-end	25 (16.45)	127 (83.55)	
	Side-side	43 (15.93)	227 (84.07)	
Stoma	+	56 (14.78)	323 (85.22)	0.21
	-	93 (12.14)	673 (87.86)	
Peri-operative blood tx	+	8 (12.5)	56 (87.5)	0.71
	-	162 (14.1)	987 (85.9)	
Iatrogenic ureter injury	+	3 (50)	3 (50)	<b>0.0389</b>
	-	167 (13.8)	1,043 (86.2)	
Simultaneous prostate resection	+	3 (75)	1 (25)	<b>0.0097</b>
	-	167 (13.78)	1,045 (86.22)	

Variables reported in \*median (minimum-maximum) or #mean ± standard deviation. SSI: Surgical site infection, N: number of studies reporting the variable

and many other factors, the fact that, unlike DM and HT, the disease was found to be an independent risk factor for SSI in the present study provides some resolution to the contradictory results in the literature.

Similarly, obesity (BMI >30) was found to be an independent variable in terms of SSI. Obesity is a commonly reported

risk factor for SSI.<sup>21</sup> In a study conducted on a large-scale CRC surgery series, Shariq et al.<sup>22</sup> reported that there was a significant risk increase for SSI and other wound complications in patients exhibiting metabolic syndrome criteria. Taking a holistic view in terms of CAD and obesity, these results are consistent with those obtained in the present study.

**Table 3.** Postoperative factors

Variable		SSI (+), n (%)	SSI (-), n (%)	p value
Postoperative blood tx	Yes	69 (22.19)	242 (77.81)	<0.0001
	No	101 (11.17)	803 (88.83)	
Evisceration	Yes	12 (60)	8 (40)	<0.0001
	No	158 (13.21)	1,038 (86.79)	
Prolonged ileus	Yes	21 (22.83)	71 (77.17)	0.0109
	No	149 (13.26)	975 (86.74)	
Anastomotic leak	Yes	20 (33.9)	39 (66.1)	<0.0001
	No	111 (10.89)	908 (89.11)	
Urinary retention	Yes	8 (30.77)	18 (69.23)	0.126
	No	162 (13.61)	1,028 (86.39)	
Urinary fistula	Yes	3 (60)	2 (40)	0.0217
	No	167 (13.79)	1,044 (86.21)	
Postoperative bleeding	Yes	5 (38.46)	165 (13.72)	0.0252
	No	8 (61.54)	1,038 (86.28)	
Postoperative pneumonia	Yes	4 (44.44)	5 (55.56)	0.0263
	No	166 (13.75)	1,041 (86.25)	
Postoperative AKF	Yes	5 (33.33)	10 (66.67)	0.0465
	No	165 (13.74)	1,036 (86.26)	
Reoperation	Yes	34 (42.5)	46 (57.5)	<0.00001
	No	136 (11.98)	999 (88.02)	
Readmission	Yes	40 (37.38)	67 (62.62)	<0.0001
	No	130 (11.72)	979 (88.28)	

Variables reported in \*median (minimum-maximum) or #mean ± standard deviation. N: number of studies reporting the variable, SSI: Surgical site infection, AKF: Acute kidney failure

**Table 4.** Multivariate analysis

Variable	OR	CI (95%)	p value
High BMI (>30)	1.51	1.02-2.21	0.0354
Advanced stage disease (TNM 3 and 4)	2.06	1.38-3.07	0.0004
CAD	1.85	1.14-3.01	0.0120
Accompanying malignancy	3.35	1.64-6.84	0.0009
Received neoadjuvant treatment	1.76	1.18-2.61	0.0048
Emergency operation	3.26	1.84-5.78	<0.0001
Postoperative blood transfusion	2.44	1.67-3.56	<0.0001

Variables reported in median (minimum-maximum) or mean ± standard deviation. N: number of studies reporting the variable. OR: Odds ratio, CI: Confidence interval, BMI: Body mass index, CAD: Coronary artery disease

It is known that malignancies weaken immunity by disrupting the balances of cellular and humoral immune responses and weaken defense against infectious complications.<sup>23</sup> This effect arises from cytokine release resulting from a warning mechanism caused by tumor cells, and in studies based on the fact that this mechanism may be more pronounced in advanced stage tumors, it is reported that the presence of advanced stage and metastatic tumors is a risk factor for SSI.<sup>24-26</sup> In the present study, both advanced stage disease (TNM stage 3 and 4) and the presence of accompanying malignancy were determined to be independent risk factors for SSI.

Neoadjuvant chemoradiotherapy (NCRT) has been reported to cause an increase in SSI and other complications due to its negative effects on local microvascular structure in the pelvic region in rectum surgery and systemic effects in colon surgery.<sup>27,28</sup> In the present study, having received NCRT was found to be a significant risk factor for SSI. This result may be significant in terms of tumor stage and localization and multivariate analysis.

Emergency operative setting potentiates many factors related to the patient, operation, and operator, posing an additional risk of mortality and morbidity. In a previous study, it was stated that emergency resections in CRC surgery could be associated with high morbidity, mortality, and even poor oncological outcomes.<sup>29</sup> In the present study, the risk of developing SSI following CRC surgery performed under emergency conditions was found to be 3.26 times higher compared with elective cases.

It is well known that allogeneic blood transfusion leads to an increase in pro-inflammatory cytokines, causing an immunocompromised picture. In this regard, many studies examining the relationship between perioperative blood transfusion and SSI have reported significant results.<sup>30</sup> Some studies aimed to specify a threshold value for the amount of transfusion that causes a significant risk increase, whereas others examined the direct effect of the presence of transfusion.<sup>31</sup> Even meta-analyses report conflicting results on blood transfusion as a risk factor for SSI.<sup>32,33</sup> In the present study, the relationship between preoperative blood transfusion and postoperative blood transfusion with the presence of SSI was examined separately, and the latter was determined to be an independent risk factor. The significance of blood transfusion in the postoperative period in this regard may be associated with the addition of factors such as transfusion-related immune modulation, transfusion reactions, and agents coming through the transfused blood product to induce immune weakness brought about by surgical stress.

### Study Limitations

The major limitation of this study is its retrospective design. As such, data entry errors may be present, despite all patient

data entered into the TSCRS-CCD being cross-checked by CCD study group members. Data were obtained from a database including certain variables, and investigating other potential risk factors was not possible since patient chart review was not feasible. However, studying prospectively maintained, multicentric, and national data gives this study its clinical value.

### Conclusion

The SSI rate determined in the present study is consistent with the data in the existing literature. According to our results, selective postoperative blood transfusion, avoiding unnecessary neoadjuvant therapy, optimizing prehabilitation, and expanding CRC screening may help reducing SSI rate following CRC surgery. SSI will continue to be a significant issue in surgical practice, and there is a need for the continuity of more extensive studies on this subject.

**Acknowledgements:** The authors wish to thank Dr. Cihangir Akyol, Dr. Ayhan Kuzu (Ankara University Hospital) Dr. Emre Balık, Dr. Dursun Buğra (Koç University Hospital), Dr. Tahsin Çolak (Mersin University Hospital), Dr. Feza Karakayalı (Başkent University, İstanbul Hospital), Dr. Sezai Leventoğlu (Gazi University Hospital), Dr. Mustafa Öncel (Medipol University Hospital), Dr. Ersin Öztürk (Bursa Medica Hospital), Dr. Selman Sökmen (Dokuz Eylül University Hospital), Dr. İlker Sücüllü (Sultan Abdulhamid Han Training and Research Hospital), Dr. Uğur Sungurtekin (Pamukkale University Hospital), Dr. Aras Emre Canda and Dr. Cem Terzi (private practice), Dr. Tuncay Yılmazlar (Uludağ University Hospital) for data contribution to this database.

**\*Turkish Colorectal Cancer Database Study Group:** Erman Aytacı, Prof. Dr. (Department of General Surgery, Acıbadem Mehmet Ali Aydınlar University Faculty of Medicine; Acıbadem Atakent Hospital, İstanbul, Turkey); Tayfun Bişgin, Assoc. Prof. Dr. (Department of General Surgery, Dokuz Eylül University Faculty of Medicine, İzmir, Turkey); Osman Bozbıyık, Assoc. Prof. Dr. (Department of General Surgery, Ege University Faculty of Medicine, İzmir, Turkey); İsmail Cem Eray, Assoc. Prof. Dr. (Department of General Surgery, Çukurova University Faculty of Medicine, Adana, Turkey); Barış Gülcü, Assoc. Prof. Dr. (Bursa Medica Hospital, Bursa, Turkey); Özgen Işık, Prof. Dr. (Department of General Surgery, Uludağ University Faculty of Medicine, Bursa, Turkey); Mehmet Ali Koç, Assoc. Prof. Dr. (Department of General Surgery, Ankara University Faculty of Medicine, Ankara, Turkey); Nuri Okkabaz, Assoc. Prof. Dr. (Department of General Surgery, Atlas University Faculty of Medicine, İstanbul, Turkey); Dr. Volkan Özben, Assoc. Prof. Dr. (Department of General Surgery, Acıbadem Mehmet Ali Aydınlar University Faculty of Medicine, İstanbul, Turkey); Ahmet Rencüzoğulları, Assoc. Prof. Dr. (Department of General Surgery, Koç University Faculty of Medicine, İstanbul, Turkey).



## Ethics

**Ethics Committee Approval:** The study protocol was approved by a Uludağ University Faculty of Medicine Clinical Research Ethics Committee (approval no: 2023-17/44, date: 19.09.2023).

**Informed Consent:** Retrospective study.

## Authorship Contributions

Surgical and Medical Practices: A.A.A., B.G., Ö.I., Concept: B.G., Ö.I., Design: B.G., Ö.I., Data Collection or Processing: Ö.I., Analysis or Interpretation: Ö.I., Literature Search: A.A.A., B.G., Ö.I., Writing: A.A.A., B.G., Ö.I.

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

**Financial Disclosure:** The authors declared that this study received no financial support.

## References

- Sartelli M, Coimbra R, Pagani L, Rasa K, (eds). *Infections in Surgery*. Springer International Publishing; 2021; p. 51-54.
- Suetens C, Hopkins S, Kolman J, Högberg LD. European Centre for Disease Prevention and Control. Point Prevalence Survey of Healthcare-associated Infections and Antimicrobial Use in European Acute Care Hospitals; Stockholm: ECDC; 2013.
- Mengistu DA, Alemu A, Abdulkadir AA, Mohammed Husen A, Ahmed F, Mohammed B, Musa I. Global Incidence of Surgical Site Infection Among Patients: Systematic Review and Meta-Analysis. *Inquiry*. 2023;60:469580231162549.
- Ouedraogo S, Kambire JL, Ouedraogo S, Ouangre E, Diallo I, Zida M, Bandre E. Surgical Site Infection after Digestive Surgery: Diagnosis and Treatment in a Context of Limited Resources. *Surg Infect (Larchmt)*. 2020;21:547-551.
- Scott RD. The Direct Medical Costs of Healthcare-Associated Infections in U.S. Hospitals and the Benefits of Prevention. United States, Stephen B. Thacker CDC Library collection; 2009.
- Levy BE, Wilt WS, Castle JT, McAtee E, Walling SC, Davenport DL, Bhakta A, Patel JA. Surgical Site Infections in Colorectal Resections: What is the Cost? *J Surg Res*. 2023;283:336-343.
- Kaya E, Yetim I, Dervisoglu A, Sunbul M, Bek Y. Risk factors for and effect of a one-year surveillance program on surgical site infection at a university hospital in Turkey. *Surg Infect (Larchmt)*. 2006;7:519-526.
- Akabane S, Egi H, Takakura Y, Sada H, Kochi M, Taguchi K, Nakashima I, Sumi Y, Sato K, Yoshinaka H, Hattori M, Ohdan H. The prognostic value of organ/space surgical site infection in stage I colorectal cancer recurrence. *Int J Colorectal Dis*. 2020;35:1689-1694.
- Tang Y, Zhang R, Yang W, Li W, Tao K. Prognostic Value of Surgical Site Infection in Patients After Radical Colorectal Cancer Resection. *Med Sci Monit*. 2020;26:e928054.
- 2021 National and State Healthcare-Associated Infections Progress Report; 2023.
- 2022 National and State Healthcare-Associated Infections Progress Report; 2023.
- Horan TC, Gaynes RP, Martone WJ, Jarvis WR, Emori TG. CDC definitions of nosocomial surgical site infections, 1992: a modification of CDC definitions of surgical wound infections. *Infect Control Hosp Epidemiol*. 1992;13:606-608.
- Amin MB, Edge SB, Greene FL, Byrd DR, Brookland RK, Washington MK, Gershenwald JE, Compton CC, Hess KR, Sullivan DC, Jessup JM, Brierley JD, Gaspar LE, Schilsky RL, Balch CM, Winchester DP, Asare EA, Madera M, Gress DM, Meyer LR. *AJCC Cancer Staging Manual*. 8th ed. Springer International Publishing; AG Switzerland; 2017.
- Isik O, Kaya E, Dundar HZ, Sarkut P. Surgical Site Infection: Re-assessment of the Risk Factors. *Chirurgia (Bucur)*. 2015;110:457-461.
- Silvestri M, Dobrinja C, Scomersi S, Giudici F, Turoldo A, Princic E, Luzzati R, de Manzini N, Bortul M. Modifiable and non-modifiable risk factors for surgical site infection after colorectal surgery: a single-center experience. *Surg Today*. 2018;48:338-345.
- Watanabe M, Suzuki H, Nomura S, Hanawa H, Chihara N, Mizutani S, Yoshino M, Uchida E. Performance assessment of the risk index category for surgical site infection after colorectal surgery. *Surg Infect (Larchmt)*. 2015;16:84-89.
- Nakamura T, Takayama Y, Sato T, Watanabe M. Risk Factors for Wound Infection After Laparoscopic Surgery for Colon Cancer. *Surg Laparosc Endosc Percutan Tech*. 2020;30:45-48.
- Han C, Chen W, Ye XL, Cheng F, Wang XY, Liu AB, Mu ZH, Jin XJ, Weng YH. Risk factors analysis of surgical site infections in postoperative colorectal cancer: a nine-year retrospective study. *BMC Surg*. 2023;23:320.
- Martin ET, Kaye KS, Knott C, Nguyen H, Santarossa M, Evans R, Bertran E, Jaber L. Diabetes and Risk of Surgical Site Infection: A Systematic Review and Meta-analysis. *Infect Control Hosp Epidemiol*. 2016;37:88-99.
- Bislenghi G, Vanhaverbeke A, Fieuws S, de Buck van Overstraeten A, D'Hoore A, Schuermans A, Wolthuis AM. Risk factors for surgical site infection after colorectal resection: a prospective single centre study. An analysis on 287 consecutive elective and urgent procedures within an institutional quality improvement project. *Acta Chir Belg*. 2021;121:86-93.
- Gurunathan U, Ramsay S, Mitrić G, Way M, Wockner L, Myles P. Association Between Obesity and Wound Infection Following Colorectal Surgery: Systematic Review and Meta-Analysis. *J Gastrointest Surg*. 2017;21:1700-1712.
- Shariq OA, Hanson KT, McKenna NP, Kelley SR, Dozois EJ, Lightner AL, Mathis KL, Habermann EB. Does Metabolic Syndrome Increase the Risk of Postoperative Complications in Patients Undergoing Colorectal Cancer Surgery? *Dis Colon Rectum*. 2019;62:849-858.
- Sato M, Goto S, Kaneko R, Ito M, Sato S, Takeuchi S. Impaired production of Th1 cytokines and increased frequency of Th2 subsets in PBMC from advanced cancer patients. *Anticancer Res*. 1998;18:3951-3955.
- Bot J, Piessen G, Robb WB, Roger V, Mariette C. Advanced tumor stage is an independent risk factor of postoperative infectious complications after colorectal surgery: arguments from a case-matched series. *Dis Colon Rectum*. 2013;56:568-576.
- Ishikawa M, Nishioka M, Hanaki N, Miyauchi T, Kashiwagi Y, Ioki H, Kagawa A, Nakamura Y. Perioperative immune responses in cancer patients undergoing digestive surgeries. *World J Surg Oncol*. 2009;7:7.
- Biondo S, Kreisler E, Fraccalvieri D, Basany EE, Codina-Cazador A, Ortiz H. Risk factors for surgical site infection after elective resection for rectal cancer. A multivariate analysis on 2131 patients. *Colorectal Dis*. 2012;14:e95-e102.
- Thorgersen EB, Goscinski MA, Spasojevic M, Solbakken AM, Mariathanas AB, Boye K, Larsen SG, Flatmark K. Deep Pelvic Surgical Site Infection After Radiotherapy and Surgery for Locally Advanced Rectal Cancer. *Ann Surg Oncol*. 2017;24:721-728.
- Sutton E, Miyagaki H, Bellini G, Shantha Kumara HM, Yan X, Howe B, Feigel A, Whelan RL. Risk factors for superficial surgical site infection after elective rectal cancer resection: a multivariate analysis of 8880 patients from the American College of Surgeons National Surgical Quality Improvement Program database. *J Surg Res*. 2017;207:205-214.
- Esswein K, Ninkovic M, Gasser E, Barenberg L, Perathoner A, Kafka-Ritsch R. Emergency resection is an independent risk factor for decreased long-term overall survival in colorectal cancer: a matched-pair analysis. *World J Surg Oncol*. 2023;21:310.
- Miki C, Inoue Y, Mohri Y, Kobayashi M, Kusunoki M. Site-Specific Patterns of Surgical Site Infections and Their Early Indicators After Elective Colorectal Cancer Surgery. *Dis Colon Rectum*. 2006;49:S45-S52.
- Shaffer VO, Baptiste CD, Liu Y, Srinivasan JK, Galloway JR, Sullivan PS, Staley CA, Sweeney JF, Sharma J, Gillespie TW. Improving quality of surgical care and outcomes: factors impacting surgical site infection after colorectal resection. *Am Surg*. 2014;80:759-763.
- Chen Y, Guo H, Gao T, Yu J, Wang Y, Yu H. A meta-analysis of the risk factors for surgical site infection in patients with colorectal cancer. *Int Wound J*. 2023;21:e14459.
- Xu Z, Qu H, Kanani G, Guo Z, Ren Y, Chen X. Update on risk factors of surgical site infection in colorectal cancer: a systematic review and meta-analysis. *Int J Colorectal Dis*. 2020;35:2147-2156.



# Clinicopathological Characteristics and Population-Level Survival Outcomes of Mucinous Adenocarcinoma Across Different Colon Segments: An Analysis Using the Surveillance Epidemiology and End Result Database

Çiğdem Benlice<sup>1</sup>, Metincan Erkaya<sup>2</sup>, Emre Görgün<sup>3</sup>, Mehmet Ayhan Kuzu<sup>1</sup>

<sup>1</sup>Ankara University Faculty of Medicine, Department of General Surgery, Ankara, Turkey

<sup>2</sup>Acıbadem Mehmet Ali Aydınlar University Faculty of Medicine, Department of General Surgery, İstanbul, Turkey

<sup>3</sup>Cleveland Clinic, Department of Colorectal Surgery, Ohio, United States

## ABSTRACT

**Aim:** To determine population-level survival differences for patients undergoing curative resection for mucinous adenocarcinoma (MAC) based on specific anatomical colon segment and stage over the last two decades.

**Method:** The study was conducted using the Surveillance Epidemiology and End Result program. Patients who underwent curative colectomy for MAC between 2004 and 2019 were identified. Demographics and clinical and histopathologic factors were compared for different colon segments, stages, and time periods. Kaplan-Meier survival analysis was conducted for each colon subsite location and stage, and curves were compared using the log-rank test.

**Results:** A total of 19,427 patients met the inclusion criteria. Patients with proximal colon cancers were significantly older (70.6±12.6 years) and more likely to be female (56.5%) than those with distally located tumor sites (p<0.001). The incidence of MAC was higher in the cecum (30.8%) and ascending colon (27.9%) than at distal sites (3.4-14.6%). The 3-year and 5-year overall survival rates were similar among the different colon sites (3-year survival rate: 66.7-69.9%, 5-year overall survival rate: 54.7-58.7%) for patients at stage 2, 3, and 4. Only patients at stage 1 exhibited significantly different outcomes among colon sites (p=0.018). Patients at stage 1 with MAC in the sigmoid colon exhibited a significantly improved overall survival rate compared with other colon sites (p<0.001). Multivariable Cox regression analysis revealed that age [hazard ratio (HR): 2.2, p<0.001], stage (p<0.001), degree of differentiation (p<0.001), and greater tumor diameter (HR: 1.05, p=0.007) were independently associated with less favorable survival.

**Conclusion:** In contrast to previous literature, our study revealed that the results of long-term population-level stage-by-stage survival analysis for MAC were similar across seven different colon sites, except for patients at stage 1, who exhibited significantly improved survival for MAC in the sigmoid colon.

**Keywords:** Surveillance Epidemiology and End Result data, colon cancer, mucinous adenocarcinoma

## Introduction

Mucinous adenocarcinoma (MAC) is a less common subtype of colorectal adenocarcinoma that accounts for 5-15% of all cases and is defined by the World Health Organization (WHO) as the presence of extracellular mucin in >50% of the tumor area.<sup>1,2</sup> Many studies have highlighted the distinct clinical and

pathological features of MAC, which is regarded as being more advanced at diagnosis and has a less favorable prognosis than non-MAC.<sup>3</sup>

Colorectal cancer encompasses a heterogeneous group of tumors, characterized by significant variations in clinical presentation, genetic configuration, and, ultimately, survival



**Address for Correspondence:** Çiğdem Benlice, MD,  
Ankara University Faculty of Medicine, Department of General Surgery, Ankara, Turkey  
E-mail: cigdembenlice@gmail.com ORCID ID: orcid.org/0000-0002-5211-1779  
Received: 05.08.2024 Accepted: 04.09.2024



Copyright© 2024 The Author. Published by Galenos Publishing House on behalf of Turkish Society of Colon and Rectal Surgery. This is an open access article under the Creative Commons Attribution-NonCommercial 4.0 International (CC BY-NC 4.0) License.

rates.<sup>4</sup> Among the numerous factors that contribute to this diversity, the specific localization of the primary colon tumor plays a particularly crucial role. Given the intricate nature of tumor anatomy and location, selecting the appropriate surgical technique and oncological approach is of the utmost importance, as both can profoundly influence disease progression, treatment decision-making, and overall patient care.<sup>5,6</sup> Consequently, contemporary research efforts have increasingly focused on unraveling the molecular, histological, and prognostic implications associated with the precise segments of the colon affected by cancer.<sup>7</sup>

Considering the relatively low prevalence rates of MAC in the setting of colorectal surgery, comprehensive population-level cancer data are essential for generating meaningful insights into the impact of clinical and epidemiological factors, including tumor location, age, sex, and disease stage, on disease outcomes. To the best of our knowledge, there is currently no study that compares the stage-by-stage progression of each colon segment over time. The main objective of this research is, therefore, to comprehensively evaluate population-level survival differences for patients undergoing curative surgery for MAC based on specific anatomical colon segment and stage over the last two decades.

## Materials and Methods

Patients who underwent curative colonic resection for stage 1-4 colon MAC between 2004 and 2019 were identified using the Surveillance Epidemiology and End Result (SEER) database and reviewed. Patients who were diagnosed with primary colon MAC were identified according to the 3<sup>rd</sup> edition of the International Classification of Diseases for Oncology (ICD-O-3) topography codes (ICD-O-3 codes: 8480 and 8481) and categorized into seven colon anatomical subsegments. The ICD-O-3 topography codes for the anatomical subsegments of the colon, from proximal to distal, were as follows: cecum (C18.0), ascending colon (C18.2), hepatic flexure (C18.3), transverse colon (C18.4), splenic flexure (C18.5), descending colon (C18.6), and sigmoid colon (C18.7). Patients who were initially diagnosed with a second primary cancer in addition to colon cancer, unknown tumor site and stage (T, N), and/or with recurrent/synchronous cancer were excluded from the study. Data were extracted from the SEER database and approved by the Ankara University Institutional Ethics Review Board (approval number: İ07-450-22, date: 15.08.2022).

The present study utilized data sourced from the National Cancer Institute SEER program database, renowned for its comprehensive and diverse compilation of cancer-related data spanning multiple regions across the United States. The SEER database, accessible at <https://seer.cancer.gov/>, is an integral component of the SEER program at the National Cancer

Institute, dedicated to gathering both incidence and survival data from all participating areas.<sup>8</sup>

Demographics, histopathological outcomes, and long-term overall survival rates were assessed and compared among different colon segments over different time intervals. Survival analysis was conducted for each colon location and stage. The primary endpoint of this study is to reveal the impact of tumor localization on overall survival.

## Parameters

The location of primary colon MAC and its histology were defined according to the criteria in ICD-O-3 (8480, 8481). Each colon segment was localized and coded based on the location indicated in a priority order of preoperative imaging, surgery report, and pathology report. The following variables were included in our study: age, gender, year of diagnosis, American Joint Committee on Cancer stage (T, N), histologic grade (well differentiated, moderately differentiated, poorly differentiated/undifferentiated/anaplastic), number of lymph nodes retrieved, metastatic lymph nodes, and chemotherapy status. The negative lymph node number was calculated as the difference between the total lymph node number and metastatic lymph node number. The study time period was categorized into four subgroups (2004-2007, 2008-2011, 2012-2015, and 2016-2019), and changes over the years were evaluated.

## Statistical Analysis

Statistical analysis was performed using descriptive statistics, including mean, standard deviation, median, minimum, and maximum values. The chi-square test or Fisher's exact test was used to compare categorical variables among the groups, the Student's t-test was used for continuous variables, and the Mann-Whitney U test was used for non-normally distributed continuous or ordinal variables. Kaplan-Meier survival analysis and the log-rank test were used for univariate analysis, and Cox proportional hazards regression was used for multivariate analysis. Variables with a p value <0.25 in the univariate Cox proportional hazards regression were selected as candidates for the multivariate model along with all variables of known clinical importance. The final model was constructed using variables with a p value <0.05, which was considered statistically significant. Statistical analysis was performed using Jamovi statistical software (version: 2.3.1) and R version 4.3.1.

## Results

A total of 33,497 patients were initially identified from the 2004-2019 SEER dataset. After applying the exclusion criteria, which included cases with unknown stage (n=8,480), appendix involvement (n=3,440), colon not otherwise specified (n=770), overlapping lesions of the colon (n=515),

and patients with signet-ring cell histology (n=75,456), 28,772 patients remained. Among them 24,922 patients had undergone surgery. After further refining the dataset to include only cases with complete dates and a minimum survival duration greater than 0 days, as well as excluding patients with missing TNM stages and those with follow-up periods greater than 0 months, a final cohort of 19,427 patients met the inclusion criteria for analysis.

The comparison of demographics and pathological characteristics among different colon segments is presented in Table 1. Patients with proximal colon cancer exhibited a significantly higher average age of 70.6 years ( $\pm 12.6$ ) and a greater likelihood of being female (56.5%) than those with distally located tumors ( $p < 0.001$ ). The incidence of MAC was notably elevated in the cecum (30.8%) and ascending colon (27.9%) in contrast to the lower rates observed at distal sites (ranging from; 3.4% to 14.6%) (Figure 1). Histopathological tumor stage, T-stage, N-stage, and grade of differentiation were statistically different among the study groups ( $p < 0.001$ ). Chemotherapy rates were significantly higher in more proximally located MAC (cecum: 66.3%, ascending colon: 70.9%) compared with more distal sites (sigmoid colon: 58.9%, descending colon: 62.5%) ( $p < 0.001$ ).

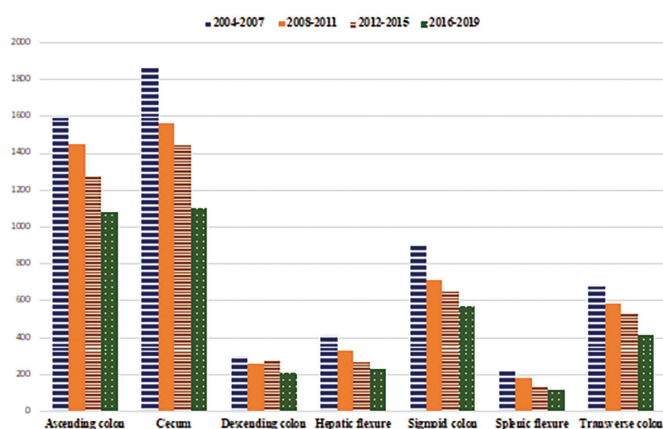
Regarding overall survival rates, this study found remarkable similarity among different colon sites. For different colon segments, the 3-year survival rates ranged from 66.7% to 69.9%, and the 5-year survival rates ranged from 54.7% to 58.7% (Figure 2). The Kaplan-Meier survival curves comparing different colon segments at each stage are presented in Figure 3. The overall survival rates were comparable among different colon segments in patients at stage 2, 3, and 4. Notably, significant differences in outcomes were observed only among patients at stage 1 across the different colon sites ( $p = 0.018$ ). In patients at stage 1, the sigmoid colon was associated with significantly improved overall survival rate compared with the

other colon sites ( $p < 0.001$ ). To delve deeper into the factors influencing long-term survival, we conducted a comprehensive multivariable Cox regression analysis across the entire cohort (Table 2). This analysis revealed several independent factors that were associated with poorer survival outcomes, including age [hazard ratio (HR): 2.2,  $p < 0.001$ ], cancer stage ( $p < 0.001$ ), degree of differentiation ( $p < 0.001$ ), and greater tumor diameter (HR: 1.05,  $p = 0.007$ ).

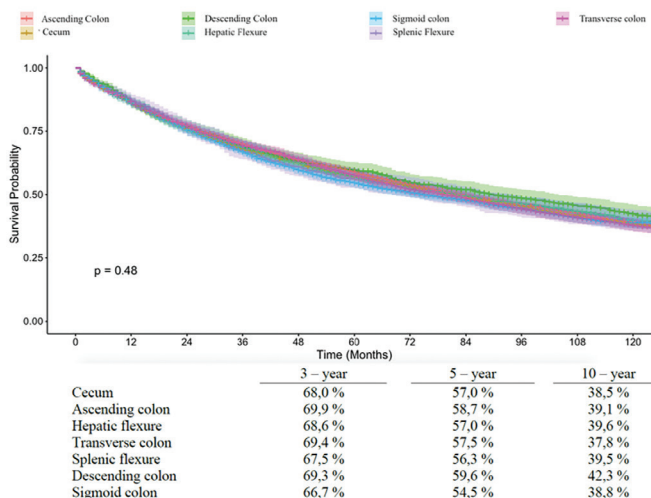
## Discussion

This study represents one of the most extensive investigations to date on the demographics and histopathological characteristics of colon MAC based on anatomical colon segment locations. Our research provides a novel perspective by performing a detailed long-term survival analysis, conducted at a population level and evaluated stage by stage, across seven distinct anatomical sites within the colon. The findings revealed that survival outcomes for MAC were largely consistent across the different locations. However, a significant exception was identified among patients at stage 1 - those with tumors located in the sigmoid colon exhibited markedly high survival rates. The reason for significant survival differences among each colon location for patients at stage 1 could be molecular and biological differences. This unique finding underscores the value of considering the anatomical site of the tumor, particularly for early-stage MAC, in understanding prognosis and guiding treatment strategies.

Consistent with our results, MAC was more frequently documented in women, located in the proximal right colon, and presented with advanced stages;<sup>9,10</sup> MAC located at more proximal colon segments generally present with more advanced tumor stages and poorer differentiation, consistent with findings from several other studies.<sup>11</sup> The underlying reasons for this pattern are not yet fully understood, but



**Figure 1.** Prevalence of mucinous adenocarcinoma by years and different colon locations. Rate of mucinous adenocarcinoma by tumor locations (in blue rectangles)



**Figure 2.** Kaplan-Meier survival curve by different colonic location

Table 1. Demographics and pathological characteristics of mucinous adenocarcinoma by different colon locations

Characteristics	Right-sided colon cancer				Left-sided colon cancer				p value
	Cecum, (n=5,975)	Ascending colon, (n=5,414)	Hepatic flexure, (n=1,248)	Transverse colon, (n=2,218)	Splenic flexure, (n=669)	Descending colon, (n=1,059)	Sigmoid colon, (n=2,844)		
Age (years), mean (SD)	70.6 (12.6)	71.0 (12.5)	70.0 (13.3)	69.8 (13.4)	67.9 (13.4)	65.4 (14.4)	66.0 (13.7)	<0.001	
Age (years), median (interquartile range)	73 (19)	74 (19)	72 (19)	73 (19)	70 (20)	67 (22)	67 (22)		
<b>Gender, n (%)</b>									
Male, (%)	2,598 (43.5)	2,367 (43.7)	624 (50.0)	1,021 (46.0)	349 (52.2)	593 (56.0)	1,569 (55.2)	<0.001	
Female, (%)	3,377 (56.5)	3,047 (56.3)	624 (50.0)	1,197 (54.0)	320 (47.8)	466 (44.0)	1,275 (44.8)		
<b>Year of diagnosis, n (%)</b>									
2004-2007	1,867 (31.2)	1,603 (29.6)	418 (33.5)	680 (30.7)	226 (33.8)	305 (28.8)	906 (31.9)		
2008-2011	1,565 (26.2)	1,451 (26.8)	334 (26.8)	587 (26.4)	185 (27.6)	260 (24.6)	713 (25.1)	0.026	
2012-2015	1,443 (24.2)	1,276 (23.6)	267 (21.4)	534 (24.1)	139 (20.8)	282 (26.6)	652 (22.9)		
2016-2019	1,100 (18.4)	1,084 (20.0)	229 (18.3)	417 (18.8)	119 (17.8)	212 (20.0)	573 (20.1)		
<b>Tumor stage, n (%)</b>									
Stage 1	820 (13.7)	857 (15.8)	181 (14.5)	276 (12.4)	76 (11.4)	131 (12.4)	360 (12.7)		
Stage 2	2,354 (39.4)	2,288 (42.3)	533 (42.7)	1,003 (45.2)	281 (42.0)	455 (43.0)	1,024 (36.0)	<0.001	
Stage 3	2,137 (35.8)	1,844 (33.1)	424 (34.0)	722 (32.6)	247 (36.9)	348 (32.8)	1,118 (39.3)		
Stage 4	664 (11.1)	425 (7.8)	110 (8.8)	217 (9.8)	65 (9.7)	125 (11.8)	342 (12.0)		
<b>Grade, n (%)</b>									
Well differentiated	561 (9.4)	547 (10.1)	133 (10.7)	214 (9.7)	66 (9.9)	151 (14.3)	412 (14.5)		
Moderately differentiated	4,083 (68.3)	3,646 (67.3)	829 (66.4)	1,500 (67.6)	472 (70.6)	721 (68.1)	1,896 (66.7)	<0.001	
Poorly differentiated	1,128 (18.9)	1,050 (19.4)	248 (19.9)	426 (19.2)	115 (17.2)	163 (15.4)	478 (16.8)		
Undifferentiated	203 (3.4)	171 (3.2)	38 (3.0)	78 (3.5)	16 (2.3)	24 (2.2)	58 (2.0)		
<b>T-stage, n (%)</b>									
T1	178 (3.0)	231 (4.3)	34 (2.7)	80 (3.6)	22 (3.3)	37 (3.5)	144 (5.1)		
T2	904 (15.1)	818 (15.1)	186 (14.9)	255 (11.5)	72 (10.7)	120 (11.3)	340 (12.0)	<0.001	
T3	3,594 (60.2)	3,573 (66.0)	857 (68.7)	1,508 (68.0)	457 (68.3)	693 (65.5)	1,705 (59.9)		
T4	1,299 (21.7)	792 (14.6)	171 (13.7)	375 (16.9)	118 (17.7)	209 (19.7)	655 (23.0)		
<b>N-stage, n (%)</b>									
N0	3,259 (54.5)	3,218 (59.4)	733 (58.7)	1,322 (59.6)	368 (55.0)	611 (57.7)	1,449 (50.9)		
N1	1,519 (25.4)	1,281 (23.7)	298 (23.9)	520 (23.9)	186 (27.8)	273 (25.8)	798 (28.1)	<0.001	
N2	1,197 (20.1)	915 (16.9)	217 (17.4)	366 (16.5)	115 (17.2)	175 (16.5)	597 (21.0)		

Table 1. Continued

Characteristics	Right-sided colon cancer			Left-sided colon cancer			p value
	Cecum, (n=5,975)	Ascending colon, (n=5,414)	Hepatic flexure, (n=1,248)	Transverse colon, (n=2,218)	Splenic flexure, (n=669)	Descending colon, (n=1,059)	
<b>M stage, n (%)</b>							
M0	5,311 (88.9)	4,989 (92.1)	1,138 (91.2)	2,001 (90.2)	604 (90.3)	934 (88.2)	2,502 (88.0)
M1	664 (11.1)	425 (7.9)	110 (8.8)	217 (9.8)	65 (9.7)	125 (11.8)	342 (12.0)
<b>Number of retrieved regional lymph nodes, n (%)</b>							
<12 lymph nodes	381 (6.4)	263 (4.9)	77 (6.2)	179 (8.1)	61 (9.1)	71 (6.7)	247 (8.7)
>12 lymph nodes	5,594 (93.6)	5,151 (95.1)	1,171 (93.8)	2,039 (91.9)	608 (90.9)	988 (93.3)	2,597 (91.3)
Number of positive regional lymph nodes, mean (SD)	2.2 (4.2)	1.8 (3.8)	1.8 (4.0)	1.8 (3.9)	2.3 (4.2)	1.81 (3.6)	2.3 (4.4)
Tumor size (mm), mean (SD)	60.0 (40.6)	57.8 (40.5)	55.5 (27.0)	55.0 (36.1)	57.5 (33.8)	54.6 (29.2)	53.2 (41.9)
<b>Chemotherapy, n (%)</b>							
Yes	2,016 (66.3)	1,575 (70.9)	377 (69.8)	698 (68.5)	233 (65.2)	397 (62.5)	1169 (58.9)
No/unknown	3,959 (33.7)	3,839 (29.1)	871 (30.2)	1,520 (31.5)	436 (34.8)	662 (37.5)	1,675 (41.1)

CI, confidence interval; SD, standard deviation

molecular and genetic factors such as microsatellite instability and mismatch repair deficiency, which are linked to MAC, might play a role. Microsatellite instability has been associated with poor differentiation and advanced tumor stages in multiple reports. Due to the lack of detailed molecular data in the SEER database, microsatellite instability could not be accounted for in this analysis, which is a limitation of the study.<sup>12,13</sup> The rate of MAC decreased over the study period, potentially due to colorectal cancer screening programs implemented in the United States. It is widely accepted that cancer screening, including colonoscopy and polypectomy, reduces mortality by detecting tumors at an earlier stage.<sup>14</sup> Because MAC is typically detected at a more advanced stage, the effective screening and removal of polyps might result in fewer MAC cases being identified in later study periods. Additionally, the widespread adoption of the histologic criteria for MAC defined by the WHO could have contributed to the reduction in MAC diagnoses over time.

Despite the distinct clinicopathologic characteristics of right-sided MAC compared with that of the left colon, our long-term population-level survival analysis in this study revealed similar outcomes across different colon locations. The complex interplay between clinicopathologic features and tumor location in colon cancer may partly account for the contradictory findings in the literature regarding survival comparisons.<sup>6,9,15-17</sup> Some studies have reported higher survival rates on the left side compared with the right, whereas others have found no significant relationship between colon location and survival. Considering these conflicting results in the literature, we hypothesized that survival comparisons between the right and left colon may vary depending on specific contexts characterized by different mutation profiles despite having the same histological type. This variability underscores the need for further research to elucidate the molecular underpinnings that contribute to survival disparities observed across different anatomical locations within the colon.

In the multivariate analysis, we found that location was not an independent prognostic factor in the whole population. Other studies have used the SEER database or SEER-Medicare database to explore the role of location on survival, with numerous studies investigating the impact of primary colon cancer location on long-term overall survival.<sup>5,7-11</sup> For instance, Benesch et al.<sup>9</sup> conducted a rigorous 10-year overall survival analysis focusing on all histopathological types of colon cancer, examining the influence of tumor location on survival outcomes, and revealed similar results. Moreover, a comprehensive analysis by Wu et al.<sup>18</sup> encompassing a cohort of patients with colon cancer across various demographics, cancer stages, study durations, and chemotherapy protocols, highlighted a significant association between tumor location and mortality. These collective findings underscore the

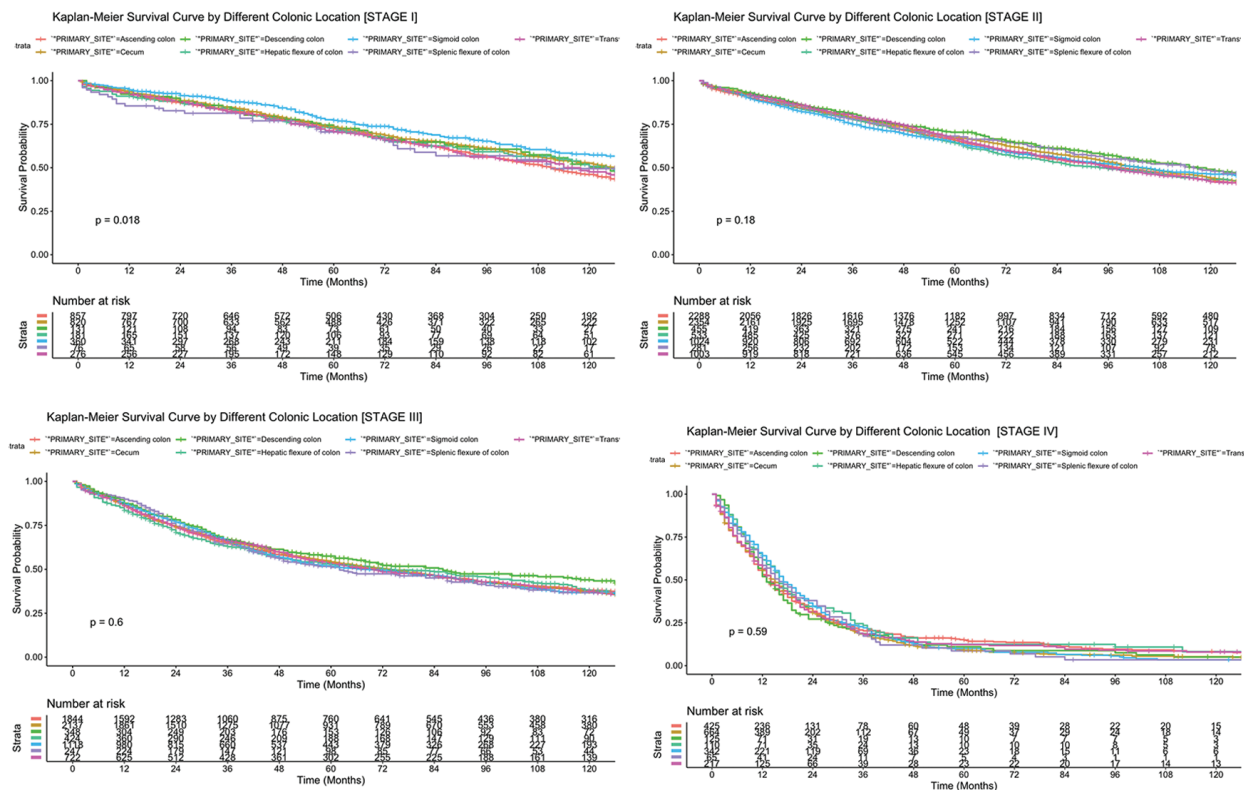


Figure 3. Kaplan-Meier survival curves for stage 1, 2, 3, and 4

complexity of how tumor location within the colon impacts survival outcomes, warranting further exploration into the underlying mechanisms driving these disparities.

### Study Limitations

Our study has some limitations that should be considered before interpreting the findings. First, the SEER database lacks detailed information on certain pathological parameters, such as neural or vascular invasion, and treatment-related data, including the quality of surgery and whether a case was elective or an emergency. These factors are known to be closely linked to survival outcomes and could have influenced our results. Second, the absence of molecular cancer profiles prevented us from exploring the intrinsic mechanisms underlying survival differences among various subgroups.<sup>7,19</sup> Such molecular data could have provided valuable insights into the underlying biology driving survival disparities. Additionally, the inclusion of new centers in the SEER database throughout the study period could have introduced variability in treatment modalities and approaches, potentially impacting outcomes. Changes in staging systems also need to be considered. Moreover, because our study relied on a database, some patients were excluded from the statistical analysis due to missing or incomplete data, which could have introduced bias. Certain demographic data, symptoms, treatments, and disease-related information were

not available, limiting the depth of our analysis. Furthermore, due to the general nature of some data, we were unable to conduct more in-depth analyses on certain aspects. Finally, the lack of a definitive definition for each colon segment, coded according to the ICD coding system, makes it challenging to assess and compare results from each center. Despite these limitations, we believe that the substantial size of our study cohort and the extended follow-up period compensate to some extent for these drawbacks. This study represents one of the largest and most comprehensive investigations to date, providing a valuable epidemiological overview of colon cancer. While acknowledging these limitations, we trust that our findings contribute key insights to the field of colon cancer research and further understanding of this complex disease.

### Conclusion

Our study offers new insights that contrast with the existing literature on colon MAC. Specifically, our comprehensive long-term population-level analysis examined survival rates stage by stage across seven distinct colon sites. Unlike previous findings, our results demonstrated that survival outcomes were remarkably consistent across these different sites for most stages of MAC. However, a notable exception was observed for patients at stage I, who exhibited significantly better survival

**Table 2.** Univariate and multivariate analysis

Mucinous adenocarcinoma	Univariate analysis			Multivariate analysis		
	HR	95% CI	p-value	HR	95% CI	p-value
<b>Age (ref = ≤65 years old)</b>						
>65 years old	2,285	(2,185, 2,391)	<0.001	2,270	(2,167, 2,378)	<0.001
<b>Gender (ref = Female)</b>						
Male	1,002	(0.965, 1,041)	0.91			
<b>Year of diagnosis (ref = 2004-2007)</b>						
2016-2019	0.87	(0.981, 1,076)	<0.001			
2012-2015	0.99	(0.936, 1.04)	0.61			
2008-2011	1.02	(0.98, 1,076)	0.26			
<b>Primary location (ref = descending colon)</b>						
Cecum	1,092	(0.998, 1,195)	0.054			
Ascending colon	1,059	(0.967, 1,159)	0.22			
Hepatic flexure	1,051	(0.94, 1,175)	0.38			
Transverse colon	1,075	(0.972, 1,188)	0.158			
Splenic flexure	1,050	(0.921, 1,197)	0.46			
Sigmoid colon	1,095	(0.994, 1,206)	0.067			
<b>Primary side (ref = left-sided colon cancer)</b>						
Right-sided colon cancer	1,008	(0.964, 1,053)	0.74			
<b>Tumor stage (ref = stage 1)</b>						
Stage 2	1,174	(1,101, 1,251)	<0.001	1,244	(1,164, 1,328)	<0.001
Stage 3	1,528	(1,433, 1,629)	<0.001	2,121	(1,978, 2,275)	<0.001
Stage 4	5,718	(5,310, 6,157)	<0.001	8,452	(7,790, 9,168)	<0.001
<b>Grade (ref = well differentiated)</b>						
Moderately differentiated	1,136	(1,065, 1,212)	<0.001	1,087	(0.920, 1,019)	0.012
Poorly differentiated	1,481	(1,377, 1,593)	<0.001	1,246	(0.803, 1,157)	<0.001
Undifferentiated	1,677	(1,492, 1,885)	<0.001	1,468	(0.681, 1,652)	<0.001
<b>Tumor size (ref = 50 mm)</b>						
≥50 mm	1,141	(1,098, 1,185)	<0.001	1,056	(1,015, 1,099)	0.007
<b>Chemotherapy (ref = no)</b>						
Yes	0.85	(0.818, 0.887)	<0.001	0.609	(0.580, 0.639)	0.987

HR: Hazard Ratio, CI, confidence interval

rates for MAC in the sigmoid colon. This finding highlights the unique behavior of stage 1 MAC in the sigmoid colon and underscores the importance of site-specific considerations in the management and prognosis of colon cancer. This manuscript underscores the critical need for future studies aimed at deepening our understanding of the behavior of colon cancers. Such research is essential for refining treatment strategies and improving patient outcomes across different tumor stages and locations.

### Ethics

**Ethics Committee Approval:** This study was approved by the Ankara University Ethics Committee (approval number: İ07-450-22, date: 15.08.2022).

**Informed Consent:** It wasn't obtained.

### Authorship Contributions

Surgical and Medical Practices: Ç.B., E.G., M.A.K., Concept: Ç.B., M.E., E.G., M.A.K., Design: Ç.B., M.E., Data Collection



or Processing: Ç.B., M.E., Analysis or Interpretation: Ç.B., M.E., Literature Search: Ç.B., M.E., Writing: Ç.B., M.E., E.G., M.A.K.

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

**Financial Disclosure:** The authors declared that this study received no financial support.

## References

- Chen JX, Tang XD, Xiang DB, Dong XL, Peng FY, Sun GY. TNM stages and prognostic features of colorectal mucinous adenocarcinomas: a meta analysis. *Asian Pac J Cancer Prev.* 2012;13:3427-3430.
- Tarantino I, Hüttner FJ, Warschkow R, Schmied BM, Diener MK, Ulrich A. Prognostic relevance of mucinous subtype in a population-based propensity score analysis of 40,083 rectal cancer patients. *Ann Surg Oncol.* 2016;23:1576-1586.
- Xie L, Villeneuve PJ, Shaw A. Survival of patients diagnosed with either colorectal mucinous or non-mucinous adenocarcinoma: a population-based study in Canada. *Int J Oncol.* 2009;34:1109-1115.
- Azzoni C, Bottarelli L, Campanini N, Di Cola G, Bader G, Mazzeo A, Salvemini C, Morari S, Di Mauro D, Donadei E, Roncoroni L, Bordi C, Sarli L. Distinct molecular patterns based on proximal and distal sporadic colorectal cancer: arguments for different mechanisms in the tumorigenesis. *Int J Colorectal Dis.* 2007;22:115-126.
- Karim S, Brennan K, Nanji S, Berry SR, Booth CM. Association Between Prognosis and Tumor Laterality in Early-Stage Colon Cancer. *JAMA Oncol.* 2017;3:1386-1392.
- Wray CM, Ziogas A, Hinojosa MW, Le H, Stamos MJ, Zell JA. Tumor subsite location within the colon is prognostic for survival after colon cancer diagnosis. *Dis Colon Rectum.* 2009;52:1359-1366.
- Ugai T, Haruki K, Harrison TA, Cao Y, Qu C, Chan AT, Campbell PT, Akimoto N, Berndt S, Brenner H, Buchanan DD, Chang-Claude J, Fujiyoshi K, Gallinger SJ, Gunter MJ, Hidaka A, Hoffmeister M, Hsu L, Jenkins MA, Milne RL, Moreno V, Newcomb PA, Nishihara R, Pai RK, Sakoda LC, Slattery ML, Sun W, Amitay EL, Alwers E, Thibodeau SN, Toland AE, Van Guelpen B, Woods MO, Zaidi SH, Potter JD, Giannakis M, Song M, Nowak JA, Phipps AI, Peters U, Ogino S. Molecular Characteristics of Early-Onset Colorectal Cancer According to Detailed Anatomical Locations: Comparison With Later-Onset Cases. *Am J Gastroenterol.* 2023;118:712-726.
- Surveillance, Epidemiology, and End Results Program. SEER Incidence Data, 1975- 2020. National Cancer Institute, National Institutes of Health. Mar 1 2022. (accessed: June 11, 2023). Available from: <https://seer.cancer.gov/data>
- Benesch MGK, Nelson ED, O'Brien SBL. Location has prognostic impact on the outcome of colorectal mucinous adenocarcinomas. *Cancers (Basel).* 2023;16:147.
- Wang P, Song Q, Lu M, Xia Q, Wang Z, Zhao Q, Ma X. Establishment and validation of a postoperative predictive model for patients with colorectal mucinous adenocarcinoma. *World J Surg Oncol.* 2022;20:330.
- Debunne H, Ceelen W. Mucinous differentiation in colorectal cancer: molecular, histological and clinical aspects. *Acta Chir Belg.* 2013;113:385-390.
- Sun Z, Yu X, Wang H, Zhang S, Zhao Z, Xu R. Clinical significance of mismatch repair gene expression in sporadic colorectal cancer. *Exp Ther Med.* 2014;8:1416-1422.
- Lin CC, Lai YL, Lin TC, Chen WS, Jiang JK, Yang SH, Wang HS, Lan YT, Liang WY, Hsu HM, Lin JK, Chang SC. Clinicopathologic features and prognostic analysis of MSI-high colon cancer. *Int J Colorectal Dis.* 2012;27:277-286.
- US Preventive Services Task Force; Bibbins-Domingo K, Grossman DC, Curry SJ, Davidson KW, Epling JW Jr, Garcia FAR, Gillman MW, Harper DM, Kemper AR, Krist AH, Kurth AE, Landefeld CS, Mangione CM, Owens DK, Phillips WR, Phipps MG, Pignone MP, Siu AL. Screening for Colorectal Cancer: US Preventive Services Task Force Recommendation Statement. *JAMA.* 2016;315:2564-2575.
- Weiss JM, Pfau PR, O'Connor ES, King J, LoConte N, Kennedy G, Smith MA. Mortality by stage for right- versus left-sided colon cancer: analysis of surveillance, epidemiology, and end results--Medicare data. *J Clin Oncol.* 2011;29:4401-4409.
- Christodoulidis G, Spyridakis M, Symeonidis D, Kapatou K, Manolakis A, Tepetes K. Clinicopathological differences between right- and left-sided colonic tumors and impact upon survival. 2010;14(Suppl 1):S45-47.
- Meguid RA, Slidell MB, Wolfgang CL, Chang DC, Ahuja N. Is there a difference in survival between right- versus left-sided colon cancers? *Ann Surg Oncol.* 2008;15:2388-2394.
- Wu Q, Zhang S, Wang H, Zeng Y, Yang W, Pan W, Hong G, Gao W. A prognostic nomogram for predicting overall survival in colorectal mucinous adenocarcinoma patients based on the SEER database. *Biomol Biomed.* 2023;23:517-526.
- Taieb J, Kourie HR, Emile JF, Le Malicot K, Balogoun R, Tabernero J, Mini E, Folprecht G, Van Laethem JL, Mulot C, Bouché O, Aparicio T, Michel P, Thaler J, Bridgewater J, Van Cutsem E, Perkins G, Lepage C, Salazar R, Laurent-Puig P; Pan-European Trials in Alimentary Tract Cancer (PETACC)-8 Investigators. Association of Prognostic Value of Primary Tumor Location in Stage III Colon Cancer with RAS and BRAF Mutational Status. *JAMA Oncol.* 2018;4:e173695.



# Can Electrolyte Imbalance Indicate a Diagnosis? McKittrick-Wheelock Syndrome and Synchronous Colon Tumor

Erhan Eröz<sup>1</sup>, Alp Ömer Cantürk<sup>1</sup>, Enise Bacak<sup>1</sup>, Penbe Gül Ergün<sup>2</sup>, Fatih Altıntoprak<sup>3</sup>

<sup>1</sup>Sakarya University Training and Research Hospital, Clinic of General Surgery, Sakarya, Turkey

<sup>2</sup>Sakarya University Training and Research Hospital, Clinic of Pathology, Sakarya, Turkey

<sup>3</sup>Sakarya University Faculty of Medicine, Department of General Surgery, Sakarya, Turkey

## ABSTRACT

Colorectal polyps are noteworthy because of their role in the development of various clinical conditions and their malignant potential. McKittrick-Wheelock syndrome, one of these clinical conditions, is characterized by dehydration, tenesmus, secretory diarrhea, fluid-electrolyte disturbance (hyponatremia, hypokalemia, hypochloremia, metabolic acidosis), and prerenal acute renal failure accompanied by large colorectal villous adenomas. Large villous adenomas, which cause the syndrome due to the hormones and secretions they produce, carry a high risk of invasive cancer because of their size and histological type. Definitive surgery or endoscopic resection following supportive treatment for fluid-electrolyte disorders is essential in the syndrome's treatment and leads to an increase in survival rate and quality of life. In this case report, we aim to present this rare syndrome and the synchronous tumor accompanying it for the first time in the literature.

**Keywords:** Colorectal polyps, colorectal carcinoma, electrolyte imbalance, McKittrick-Wheelock syndrome, synchronous colon tumor

## Introduction

One of the well-known features of colorectal adenomas is their ability to become malignant. The more the villous component increases, the higher the risk of malignant transformation.<sup>1</sup> In some rare clinical features, such as McKittrick-Wheelock syndrome, polyps have clinical significance beyond the potential for malignancy. McKittrick-Wheelock syndrome is a rare clinical feature characterized by large colorectal villous adenomas leading to dehydration, tenesmus, secretory diarrhea, fluid-electrolyte disturbance (hyponatremia, hypokalemia, hypochloremia, metabolic acidosis), and acute renal failure.<sup>2,3</sup> Giant villous adenomas have been reported to be the source of these symptoms in the syndrome, but detailed histopathological examinations have also reported that the villous polyp is sometimes a malignant component.<sup>4</sup> This case report details the association of McKittrick-Wheelock syndrome caused by a giant villous adenoma in the rectum and synchronous sigmoid colon adenocarcinoma.

## Case Report

A 67-year-old male patient was admitted to the emergency department with complaints of weakness and bloody diarrhea with mucus lasting longer than a week. In addition, the patient exhibited symptoms of tenesmus; however, due to the prominence of other clinical conditions, the patient did not initially report this complaint. Upon rectal examination, an irregular mass was palpated. Laboratory tests showed hypopotassemia [potassium: 2.9 millimoles/liter (mmol/L)], hyponatremia (sodium: 111 mmol/L), hypochloremia (chloride: 69 mmol/L), creatinine and urea elevation [5.81 milligrams/deciliter (mg/dL) and 290 mg/dL], and metabolic acidosis [pH: 7.30/bicarbonate (HCO<sub>3</sub>): 15 mmol/L]. The patient's hemoglobin and other parameters were within the normal range. Urinary ultrasonography revealed no pathological findings. The patient was interned by nephrology for the treatment of acute renal failure and electrolyte imbalance.



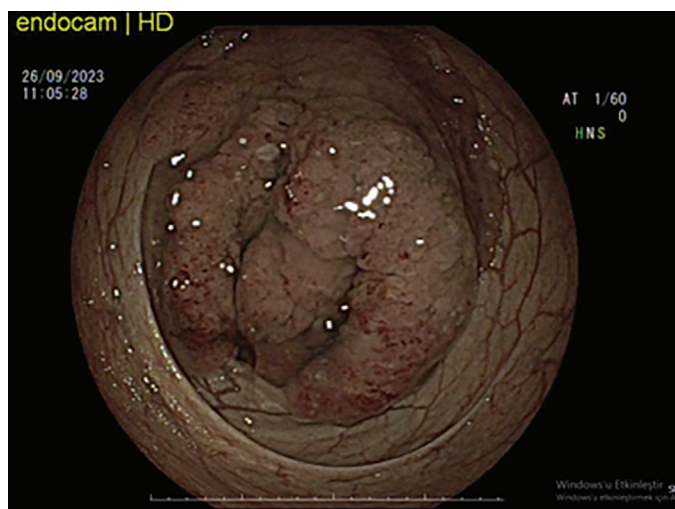
**Address for Correspondence:** Alp Ömer Cantürk, MD  
Sakarya University Training and Research Hospital, Clinic of General Surgery, Sakarya, Turkey  
E-mail: dr.omercanturk@gmail.com ORCID ID: orcid.org/0000-0003-3641-7628  
Received: 23.05.2024 Accepted: 27.08.2024



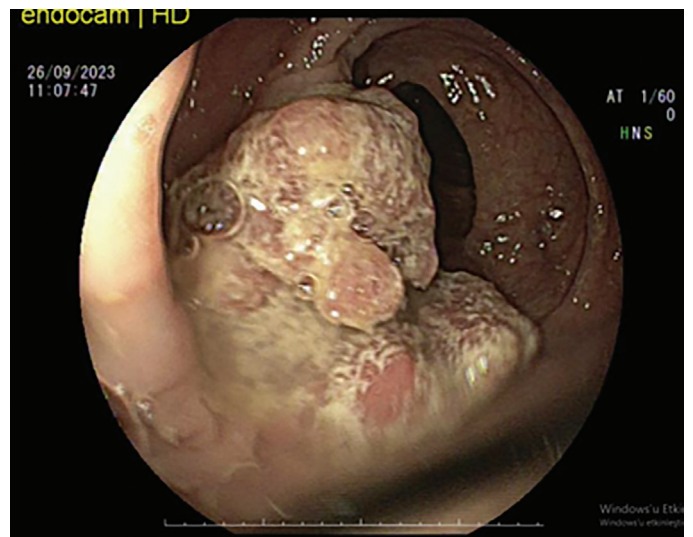
Copyright© 2024 The Author. Published by Galenos Publishing House on behalf of Turkish Society of Colon and Rectal Surgery. This is an open access article under the Creative Commons Attribution-NonCommercial 4.0 International (CC BY-NC 4.0) License.

As a result of progressive creatinine, uremia, and deep metabolic acidosis (creatinine: 7.35 mg/dL, urea: 246 mg/dL, pH: 7.26,  $\text{HCO}_3^-$ : 10 mmol/L), which did not improve, hemodialysis treatment was initiated.

In the clinical follow-up after hemodialysis, kidney function tests and electrolyte values were evaluated as normal, and the patient was discharged. This clinical presentation recurred three times in the following three months and was treated similarly. A colonoscopy was planned for a rectal mass but was delayed due to these clinical conditions. In colonoscopic evaluation, a lobule-contoured, soft-textured vegetative mass was detected, starting from the 3<sup>rd</sup> cm of the rectum and continuing toward the 13 cm proximal, filling most of the lumen but not preventing the endoscope from progressing to the proximal (Figure 1). In addition, a second lesion was detected in the sigmoid colon (28 cm), occupying 40% of the lumen, not obstructing the proximal progression of the endoscope, with irregular borders, hard consistency, vegetative, and bleeding to the touch (Figure 2). There were no other pathological findings in the colonoscopy; biopsies were taken from both lesions. Abdominal computed tomography (CT) revealed increased wall thickness in the rectum and sigmoid colon at two different localizations, which suggested malignancy (Figure 3). Histopathological examination of the lesion in the rectum revealed a villous adenoma and the lesion in the sigmoid colon as adenocarcinoma. On positron emission tomography-CT examination, a hypermetabolic mass lesion localized in the rectosigmoid region was evaluated as primary malignancy [maximum standardized uptake value ( $\text{SUV}_{\text{max}}$ ): 23.3], and hypermetabolic wall thickness increase in the sigmoid colon was evaluated as synchronous malignancy ( $\text{SUV}_{\text{max}}$ : 43.3) (Figure 4). The patient underwent laparoscopic low anterior resection and loop ileostomy (Figure 5), and the postoperative



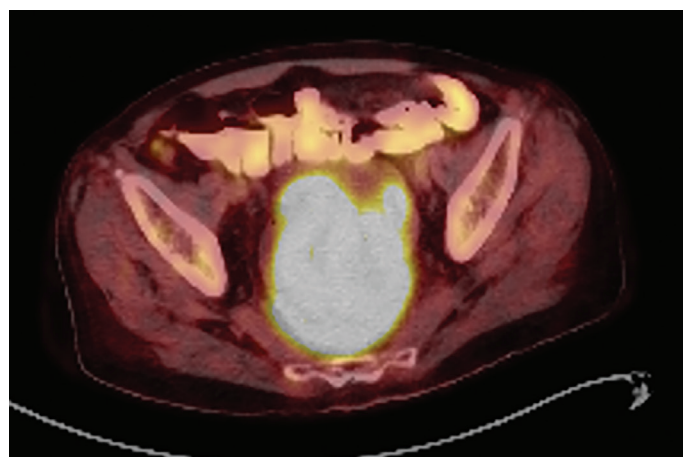
**Figure 1.** Endoscopic image of a soft, vegetative mass in the rectum



**Figure 2.** Endoscopic image of an ulcero-vegetative mass in the sigmoid colon



**Figure 3.** Computed tomography image of the mass



**Figure 4.** Positron emission tomography-computed tomography view of the hypermetabolic mass in the rectosigmoid

follow-up was uneventful. In the postoperative follow-up, it was observed that the patient's creatinine values, which had previously been partially improved despite hemodialysis, and electrolyte imbalance were almost completely restored. The patient's laboratory results in the postoperative period are shown in the Table 1 below. In the final histopathologic examination of the patient, a low anterior and sigmoid resection material was examined. Two different low-grade tumor foci were reported in the upper middle rectum and sigmoid colon. Histopathological features of the vegetative tumor adenocarcinoma were 60% cribriform and a 40% tubular pattern. A total of 25 lymph nodes were dissected, and one lymph node had tumoral invasion (histopathologic tumor grade was pT2N1aM0). Surgical margins were tumor-free and consistent with the oncologic resection margin.

After these pathologic results, the patient was referred for adjuvant treatment through the oncology outpatient clinic, and 12 cycles of m6 FOLFOX chemotherapy protocol were administered. The patient remains tumor-free in postoperative follow-up.

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

## Discussion

McKittrick-Wheelock syndrome has been defined as excessive secretory diarrhea caused by a villous adenoma and complicated by dehydration, a severe electrolyte imbalance, and acute prerenal failure.<sup>2</sup> There have been many assessments of the pathophysiology of the disease; the basic accepted theory is as follows: Small adenomas are usually asymptomatic; large

villous adenomas sometimes produce sizeable amounts of mucin-containing electrolytes and can become symptomatic by causing mucus diarrhea, in which case it has been suggested that high levels of prostaglandin E2 (PGE2) in the blood may be the cause of the diarrhea. In the literature, PGE2 levels 3-6 times higher than normal have been shown in the presence of secretory diarrhea.<sup>5</sup> When mucin is produced, sodium and potassium pass to the intraluminal region, carrying the fluid together, and diarrhea occurs. In this syndrome, the large area covered by the adenoma with mucin production reduces the normal mucosal area required for absorption and disrupts the mechanism in two ways.<sup>6</sup> Electrolyte disturbances seen in large villous adenomas can reach remarkable dimensions. These adenomas can secrete approximately 4 L of fluid per day with an average sodium concentration of 120 mmol/L, potassium concentration of 4.4 mmol/L, and chlorine concentration of 123 mmol/L.<sup>7</sup> Increasing oral intake and other mechanisms can compensate for this fluid-electrolyte disorder and volume loss for a long time. However, if diagnosis and treatment are delayed, serious consequences, including cancer, may occur.<sup>8</sup> There may be recurrent hospital admissions for years due to compensatory mechanisms before deep metabolic acidosis, severe neurological symptoms, or severe acute renal failure that require intensive care unit hospitalization. In one case series, the mean time from the onset of symptoms to the development of severe circulatory disorders was reported as 5.5 years.<sup>9</sup> In our case, the patient had long-standing complaints of intermittent diarrhea. These symptoms, which were compensated for a while, eventually led to many consequences, including kidney failure, when they became unbearable. Fortunately, the patient received the necessary interventions before the results could cause irreversible damage.

Although a villous adenoma is mentioned in most of the cases with McKittrick-Wheelock syndrome in the literature, it should not be forgotten that an adenoma may turn into malignancy in the time until diagnosis and surgical resection, or an adenoma may accompany a synchronous malignancy. Cases with neuroendocrine tumors are also known in the pathology of patients who underwent surgical resection after diagnosis.<sup>4</sup> In 2016, Malik et al.<sup>10</sup> published the characteristics of 35 cases with McKittrick-Wheelock syndrome and reported that 22 patients had a villous adenoma, eight patients had

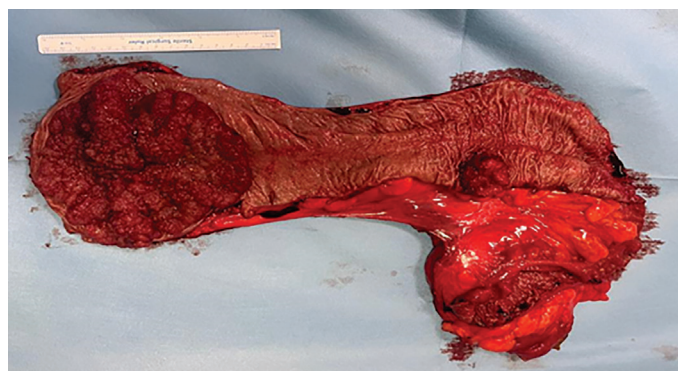


Figure 5. Surgical resection material

Table 1. Analysis of electrolyte and biochemical parameters of the patient in the perioperative period

	Preop	1-day postop	1-week postop	2-months postop
Urea (mg/dL)	182	190	68	35
Creatinine (mg/dL)	4.66	4.61	1.67	1.66
Sodium (mmol/L)	125.7	130.1	133	138
Potassium (mmol/L)	2.8	3	3.1	4.5

adenocarcinoma, one patient had hyperplastic polyps, and one patient had liver metastatic neuroendocrine tumor pathology. In our patient, the final pathology report after surgical resection indicated that low-grade infiltrative adenocarcinoma developed in two different foci in both the upper-middle rectum and the sigmoid colon. The development of adenocarcinoma on the background of both synchronous tumor and villous polyp makes our case unique in the literature.

In the literature, various modalities have been described in the treatment of McKittrick-Wheelock syndrome, ranging from medical support to minimally invasive to open surgery. It has also been shown that symptoms begin to regress 48 hours after the initiation of indomethacin treatment.<sup>11</sup> Endoscopic submucosal dissection can be applied successfully and beneficially in this case.<sup>12</sup> Transanal minimally invasive surgical techniques can similarly be applied in appropriate cases. Apart from these, the most used surgical method in the literature is minimally invasive laparoscopic surgery,<sup>13</sup> which, due to the characteristics of our case, is what we preferred.

McKittrick-Wheelock syndrome is a rare syndrome in which there are giant villous polyps and related clinical consequences. If the underlying clinical findings do not improve with treatment, it is important to investigate this in detail. Although villous polyp histopathology is usually evident in this syndrome, sometimes malignant potential can be seen.<sup>8</sup> Occasionally, a synchronous tumor may be present, although rare, and tumor development on the background of a villous polyp has never been reported in the literature. We aimed to contribute to the literature by presenting this phenomenon.

### Ethics

**Informed Consent:** Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

### Authorship Contributions

Concept: F.A., Design: E.E., Data Collection or Processing: E.B., Analysis or Interpretation: E.E., A.Ö.C., E.B., P.G.E., F.A., Literature Search: E.E., A.Ö.C., E.B., P.G.E., F.A., Writing: E.E., A.Ö.C., E.B., P.G.E., F.A.

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

**Financial Disclosure:** The authors declared that this study received no financial support.

### References

- O'Brien MJ, Winawer SJ, Zauber AG, Gottlieb LS, Sternberg SS, Diaz B, Dickersin GR, Ewing S, Geller S, Kasimian D, et al. The National Polyp Study. Patient and polyp characteristics associated with high-grade dysplasia in colorectal adenomas. *Gastroenterology*. 1990;98:371-379.
- McKittrick LS, Wheelock FC. *Carcinoma of the colon*. Springfield (IL): Charles C Thomas; 1954:61.
- Popescu A, Orban-Schiopu AM, Becheanu G, Diculescu M. McKittrick-Wheelock syndrome - a rare cause of acute renal failure. *Rom J Gastroenterol*. 2005;14:63-66.
- Nakhla SG, Murakami TT, Sundararajan S. Poorly differentiated neuroendocrine tumor of the rectum coexistent with giant rectal villous adenoma presenting as McKittrick-Wheelock syndrome. *Case Rep Oncol Med*. 2015;2015:242760.
- Jacob H, Schlondorff D, St Onge G, Bernstein LH. Villous adenoma depletion syndrome. Evidence for a cyclic nucleotide-mediated diarrhea. *Dig Dis Sci*. 1985;30:637-641.
- Older J, Older P, Colker J, Brown R. Secretory villous adenomas that cause depletion syndrome. *Arch Intern Med*. 1999;159:879-880.
- Blight WJ, Pan A. Functioning villous adenoma of the rectum. *Can Med Assoc J*. 1971;104:65.
- Emrich J, Niemeyer C. The secreting villous adenoma as a rare cause of acute renal failure. *Med Klin (Munich)*. 2002;15:97:619-623.
- Shnitka TK, Friedman MHW, Kidd EG, MacKenzie WC. Villous tumors of the rectum and colon characterized by severe fluid and electrolyte loss. *Surg Gynecol Obstet*. 1961;112:609-621.
- Malik S, Mallick B, Makkar K, Kumar V, Sharma V, Rana SS. Malignant McKittrick-Wheelock syndrome as a cause of acute kidney injury and hypokalemia: Report of a case and review of literature. *Intractable Rare Dis Res*. 2016;5:218-221.
- Kagan MD, Schmidt K, Sangha G. Indomethacin therapy effective in a patient with depletion syndrome from secretory villous adenoma. *BMJ Case Rep*. 2017;2017:bcr2016217211.
- Ohara Y, Toyonaga T, Watanabe D, Hoshi N, Adachi S, Yoshizaki T, Kawara F, Tanaka S, Ishida T, Okuno T, Ikehara N, Morita Y, Umegaki E, Yokozaki H, Azuma T. Electrolyte depletion syndrome (McKittrick-Wheelock syndrome) successfully treated by endoscopic submucosal dissection. *Clin J Gastroenterol*. 2015;8:280-284.
- van der Pool AEM, de Graaf EJR, Vermaas M, Barendse RM, Doornebosch PG. McKittrick Wheelock Syndrome Treated by Transanal Minimally Invasive Surgery: A Single-Center Experience and Review of the Literature. *J Laparoendosc Adv Surg Tech A*. 2018;28:204-208.