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Low Level of Albumin and Longer Interval to Closure Time Increase the Morbidities in Ileostomy Closure; A Cohort Study of 354 Consecutive Patients

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Abstract

Introduction: Temporary diverting ileostomy has an important role of mitigating the serious effects of anastomotic leakage in colorectal surgery. However, morbidity and mortality of ileostomy reversal cannot be overlooked. We investigated the possible risk factors for complications following ileostomy reversal.

Methods: All the patients who underwent loop ileostomy closure between 2008 and 2017 at Inje University Busan Paik Hospital were identified. Medical records on patient characteristics, preoperative managements, surgical techniques, postoperative managements, chemotherapy/radiotherapy and complications were retrospectively analyzed in the prospectively collected database.

Results: Three hundred fifty-four underwent loop ileostomy closure. The overall complication rate was 23.7% with Clavien-Dindo grade I being the most common (15.8%), 5.6% in grade II, 2.2% in grade III-V, and three patients died. The two most common complications were wound infection (11.6%) and small bowel obstruction (4.8%). In univariable and multivariable analysis, closure technique or chemotherapy did not affect the outcome, but low serum albumin <3.5 g/dL (OR 7.248, CI 2.416–22.838, p<0.001) and longer interval to ileostomy closure (OR 1.977, CI 1.167–3.350, p=0.0113) were independent contributing factors for morbidities of ileostomy closure.

Conclusions: Closure technique or chemotherapy did not affect the complication of ileostomy closure. However, serum albumin <3.5 g/dL and longer interval to ileostomy closure were identified as the risk factor for morbidity of ileostomy closure. These two factors should be corrected and planned before ileostomy closure.

Keywords: Colorectal surgery; Ileostomy closure; Risk factors

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Introduction

A temporary diverting ileostomy is made to proximally divert bowel contents in colorectal surgery, most often after a low anterior resection of colorectal cancer, thereby preventing the detrimental consequences of distal anastomosis leakage [1]. The morbidities of ileostomy closure (IC) range from 3% to 30%, and its mortality range from 0% to 4% in various reports [2-6].

It has been reported that chemotherapy is an important factor affecting both the timing of IC and postoperative complications in colorectal cancer patients. Tulchinsky et al. [7] suggest that chemotherapy does not increase postoperative complications and therefore it is safe to perform IC during chemotherapy. Others argue that IC during chemotherapy may result in severe complications, and this notion causes a delay or halt of chemotherapy and therefore worse oncologic outcomes, too [8,9].

Stoma-related complications such as dehydration, electrolyte imbalance, parastomal hernia, and cellulitis caused by peristomal infection have detrimental effects on patients' health and quality of life (QoL) [10]. In line with such concerns, recent findings suggest that early closure of ileostomy from the index operation is beneficial to patients, with comparable postoperative and lower stoma-related complication rates [11,12]. On the other hand, studies indicate that early ileostomy closure is significantly associated with complications [5,13].

To date, no general consensus has been reached regarding the optimal timing of ileostomy closure. Furthermore, there is no uniform consensus on the technique of IC in terms of complications. Although most literatures favor stapled closure over handsewn closure with lower rates of early postoperative small bowel obstruction, it is still under debate that there is definite benefit of stapled closure. Thus, the authors would like to investigate whether chemotherapy, operation interval, types of IC, and other clinicopathologic parameters are risk factors of postoperative complications of IC using multiple regression analysis.

Materials and Methods

A total of 611 patients who underwent enterostomy closure between 2008 and 2017 were reviewed. The patients' preoperative diagnoses varied from rectal cancer to ovarian cancer and inflammatory diseases such as Crohn's disease and diverticular diseases, and all of the patients were included in the study. Of these patients, 354 underwent IC were enrolled in this study with exclusion of transverse loop colostomy, Hartmann's end colostomy or ileal end enterostomy. Patient demographics and clinicopathological variables were retrospectively analyzed in the prospectively collected database. The institutional review board of Busan Paik Hospital, Inje University, approved this study (No. 18-0174). Prior to ileostomy closure, all the patients underwent a water-soluble contrast enema study to ensure the integrity and patency of colorectal anastomosis. They were given prophylactic antibiotics per oral (p.o.) metronidazole plus intravenous (IV) antibiotics or IV antibiotics alone, with bowel preparation. All the operations were either performed or supervised by one of three colorectal surgeons. Postoperative antibiotics were prescribed as needed. The timing of IC was decided by the surgeon depending on the patient's ongoing chemotherapy status, nutrition status, or if the patient has complication. If patients demanded early closure than anticipated and had no absolute contraindication, some would receive IC even during chemotherapy; however, most adjuvant chemotherapy patients received their IC after the completion of chemotherapy.

An elliptical incision was made around the mucocutaneous junction of the stoma, followed by dissection from the rectus sheath and peritoneum. Stoma closure was performed in one of the following three methods depending on the surgeon's preference: Handsewn anastomosis with stoma resection, handsewn anastomosis without stoma resection, or stapled closure. For handsewn closure, Gambi and Lembert sutures were performed with black silk NS2117 (braided non-absorbable suture; WooRhi Medical, Gyeonggido, South Korea). For stapled closure, functional end-to-end closure using linear staples (Covidien GIA Auto Suture or Ethicon NTLC75) was performed, followed by Lembert sutures of the staple lines (Figure 1). The rectus sheath was closed with interrupted sutures, and the skin was closed using either interrupted sutures or skin staples.

We have gathered patient data regarding known relevant variables of IC. Age, sex, initial diagnosis and operation, Body Mass Index (BMI), American Society of Anesthesiologists (ASA) class, social history such as smoking history, preoperative comorbidity variables grouped by organ systems, chemotherapy/radiotherapy before stoma closure, closure technique, preoperative serum albumin level, duration from ileostomy creation to closure, operation time, and length of hospital stay were analyzed. The BMI values were grouped according to the World Health Organization (WHO) Asian guideline as follows: Underweight, <18.5 kg/m^2; normal, 18.5 kg/m^2 to 23 kg/m^2; overweight, 23 kg/m^2 to 25 kg/m^2; and obese, ≥ 25 kg/m^2. Postoperative complications were analyzed with the Clavien-Dindo classification.

Statistical analysis

We conducted chi-square test for categorical variables, student t-test for continuous variables, and logistic regression with stepwise selection for multivariable analysis to find risk factors associated with complication. Those variables with a p-value <0.1 in the univariate model were selected for inclusion in the multivariate logistic regression. A p-value less than 0.05 was deemed statistically significant. The analyses were performed using SAS 9.4 (SAS Institute, Cary, NC, USA). For time to IC, we have used the Receiver Operating Characteristic (ROC) curve to evaluate the cutoff time value (Figure 2).

Definitions

-Wound infection: Signs of inflammation, such as erythema, swelling, and discharge as a result of opening the wound and either secondary or delayed primary closure

-Early small bowel obstruction: Clinical evidence of small bowel obstruction (abdominal pain, vomiting, and distension) with radiological evidence of a dilated small bowel

-Pseudomembranous Colitis (PMC): Clinical evidence of colitis (abdominal pain and diarrhea) with *Clostridium difficile* toxin or Polymerase Chain Reaction (PCR) positivity

-Leakage: Clinical or radiological evidence of leakage with fluid collection

-Voiding difficulty: Difficulty voiding that requires Foley catheter insertion

Results

Between January 2008 and December 2017, 354 patients underwent loop ileostomy closure in our center. The median age was 63 years (range, 20 to 89 years), with 244 men (68.9%). The primary diagnoses were rectal cancer (234, 66.1%), left colon cancer (60, 16.9%), ovarian cancer (14, 4.0%), familial adenomatous polyposis (5, 1.4%), diverticular disease (3, 0.8%), Crohn's disease (2, 0.6%), and other conditions (35, 9.9%). The previous types of surgeries were low anterior resection (221, 62.4%), ultra-low anterior resection or coloanal anastomosis (52, 14.7%), left hemicolectomy or anterior resection (29, 8.2%), total or subtotal colectomy (13, 3.7%), Hartmann's repair (12, 3.4%), and miscellaneous (27, 7.6%). ASA score 2 was most common, with 268 patients (75.7%). Fifty-eight patients had Diabetes Mellitus (DM) (16.4%), 37 patients were current smokers at the time of operation (10.5%), and 181 patients had comorbidities of any sort (51.1%). Ninety-nine patients (28.0%) received preoperative concurrent chemoradiotherapy. Before ileostomy closure, 221 (62.4%) underwent adjuvant chemotherapy.

Two hundred forty-six (69.5%) patients underwent a handsewn anastomosis with stoma resection; 56, a handsewn anastomosis without stoma resection; and 52, a stapled anastomosis. The mean interval from ileostomy creation to closure was 130 days (range, 30 to 1,089). The mean operation time was 86.2 min (range, 35 min to 230 min). The mean length of hospital stay after ileostomy closure was 10 days (range, 4 to 44). The patient's demographics are summarized in Table 1.

There were 84 patients with postoperative complications

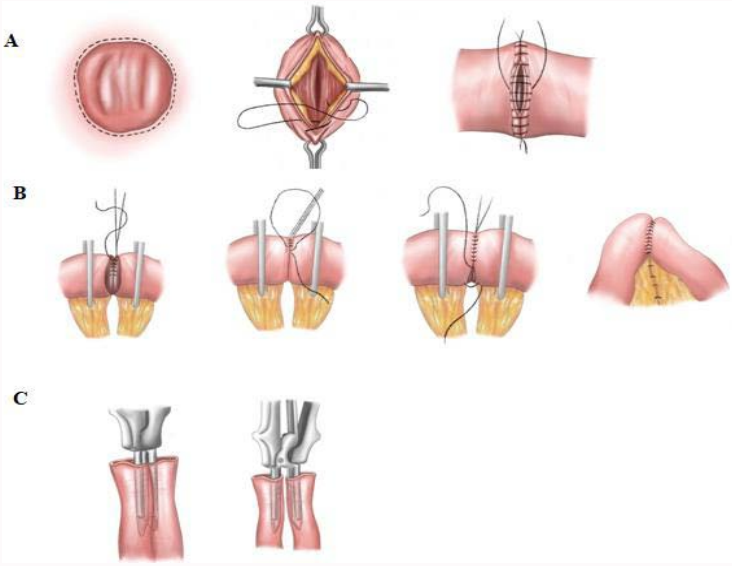

Figure 1: Stoma closure techniques. (A) Handsewn end-to-end anastomosis without resection. (B) Handsewn end-to-end anastomosis with resection. (C) Stapled closure with linear stapler, a functional end-to-end anastomosis.

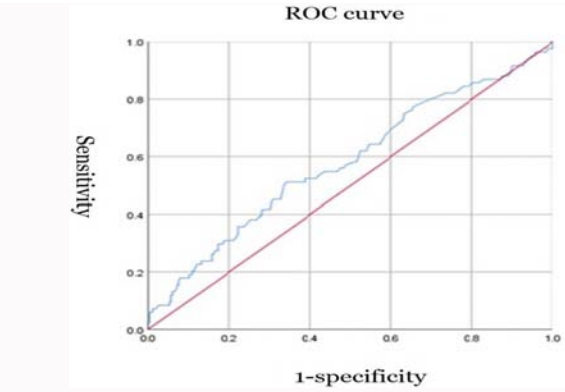

Figure 2: ROC curve for validation of cutoff for time to ileostomy closure.

(23.7%), with Clavien-Dindo classification 1 being the most common (56 patients, 15.8%). Eight patients (9.5%) had a Clavien-Dindo classification of ≥ 3 (Table 2). The two most common complications were wound infection (41, 11.6%) and small bowel obstruction (17, 4.8%); 3 patients required reoperation. *Clostridium difficile* infection was found in 6 patients (1.7%), of whom 3 (0.8%) had anastomotic leakage that required reoperation. Three patients died (0.8%), of whom two died of small bowel obstruction and consequent surgeries and complications, and one died from postoperative pneumonia. Morbidities and mortalities of IC are summarized in Table 3.

Using the ROC curve, the cutoff for time to IC was evaluated as 116 days (Figure 2). In the univariable analysis, DM, underlying pulmonary disease, the patients with low preoperative serum albumin level (<3.5 g/dL), and longer interval from initial surgery to ileostomy closure showed the p-value <0.1 associated with complications (Table 4).

In the multivariable analysis, low preoperative serum albumin level (<3.5 g/dL; Odds Ratio [OR], 7.248; 95% Confidence Interval [CI], 2.416 to 22.838, p=0.0005) and longer interval from initial surgery to ileostomy closure (OR, 1.977; 95% CI, 1.167 to 3.350, p=0.0113) were independent contributing factors associated with IC complications (Table 5).

Discussion and Conclusion

In the era of increasing number of anal sphincter saving surgery in minimally invasive techniques, ileostomy creation and IC has become a crucial part of the surgery in order to mitigate the effects of anastomotic leakage and protect low anastomosis [14-16]. Hence, researches analyzing complications of IC and possible risk factors are needed for better outcomes of surgical managements [9,17-20].

In a nationwide retrospective study that used data from the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) with 5,401 patients who underwent IC, the complication and mortality rates were 17.7% and 0.6% respectively, with the most common complication being wound infection (6.7%) [17]. In our 354 patients, the morbidity rate was 23.7% and mortality rate was 0.8%, which is comparable with those reported in other studies with morbidity ranging from as low as 5% to as high as 40% and mortality ranging from 0 % to 4% [3,5,6,21]. The most common complication in our study was wound infection (11.6%), followed by intestinal obstruction (4.8%), the incidence being similar with those in other studies with wound infection ranging from 3.8% to 12.9% and intestinal obstruction ranging from 3.8% to 12% [5,6,18,22]. Other complications such as pseudomembranous colitis, voiding difficulty, anastomotic leakage and pneumonia were reported in our study with rates comparable to other studies. The incidence of serious complications, such as anastomotic leakage was only 0.8%, which was a little lower rate than the reported incidence rate of small bowel anastomosis leakage, which is 2% to 4% [23].

Many attempts have been made to identify the possible risk factors of postoperative complications after IC. However, there is no definite attributable factor to the complications. In this study, we found that the hypoalbuminemia was the strongest independent risk factor of IC complications (preoperative serum albumin <3.5 g/dL; p=0.0005; OR, 7.248; 95% CI, 2.416 to 22.838). Serum albumin is the single powerful nutritional marker in surgical patient and hypoalbuminemia is well known representative risk factor for wound healing failure. Saha et al. reported that preoperative hypoalbuminemia was significantly associated with postoperative

Table 1: Patient demographics.

Clinical characteristics	Total number of patients n=354 (%)
Age (years, median (range))	63 (20-89)
Sex	
Male	244 (68.9)
Female	110 (31.1)
Types of disease	
Rectal cancer	234 (66.1)
Left colon cancer	60 (16.9)
Ovarian cancer	14 (4.0)
Familial adenomatous polyposis	5 (1.4)
Diverticular disease	3 (0.8)
Crohn's disease	2 (0.6)
Others	35 (9.9)
Previous types of surgery	
Low anterior resection	221 (62.4)
Ultra-low anterior resection/coloanal anastomosis	52 (14.7)
Left hemicolectomy/anterior resection	29 (8.2)
Total/ subtotal colectomy	13 (3.7)
Hartmann's repair	12 (3.4)
Miscellaneous	27 (7.6)
BMI (Asian guideline) (kg/m^2)	
Underweight (<18.5)	37 (10.5)
Normal weight (18.5–23)	141 (39.8)
Overweight (23–25)	86 (24.3)
Obese (≥ 25)	90 (25.4)
ASA score	
1	48 (13.6)
2	268 (75.7)
3	38 (10.7)
Smoking history	
Yes	37 (10.5)
No	317 (89.5)
Comorbidities	
Yes	181 (51.1)
No	173 (48.9)
Diabetes mellitus	
Yes	58 (16.4)
No	296 (83.6)
Preoperative concurrent chemoradiotherapy	
Yes	99 (28.0)
No	255 (72.0)
Adjuvant chemotherapy	
Yes	221 (62.4)
No	133 (37.6)
Closure technique	
Handsewn with resection	246 (69.5)
Handsewn without resection	56 (15.8)
Stapled	52 (14.7)
Preoperative serum albumin level	
<3.5 g/dL	16 (4.5)
≥ 3.5 g/dL	338 (95.5)
Time to ileostomy repair (days, mean (range))	130.3 (30-1089)
Operative time (minutes, mean (range))	86.2 (35-230)
Hospital stay (days, mean (range))	10.7 (4-44)

Table 2: Clavien-Dindo classification of complications.

Clavien-Dindo classification	n	%
1	56	66.7
2	20	23.8
3	5	5.9
4	0	0
5	3	3.6

Table 3: Morbidities and mortalities.

Type of complication	n	%
Wound infection	41	11.6
Early small bowel obstruction	17	4.8
Pseudomembranous colitis	6	1.7
Voiding difficulty	5	1.4
Anastomotic leakage	3	0.8
Pneumonia	2	0.6
Miscellaneous	10	2.8
Total	84	23.7

Table 4: Univariable analysis of factors associated with complications.

Factors	P value
Age	0.451
Male sex	0.57
BMI	0.1082
ASA	0.2708
Smoking	0.7503
Comorbidities	0.2077
Diabetes mellitus	0.0795
Underlying pulmonary disease	0.0787
Preoperative chemoradiotherapy	0.2129
Postoperative adjuvant chemotherapy	0.2319
Ileostomy closure technique	0.6655
Serum albumin level <3.5 g/dL	0.0002
Time to ileostomy closure (cutoff: 116.5 days), days	0.0052
Operative time	0.3621

BMI: Body Mass Index; ASA: American Society of Anesthesiologist

mortality, occurring in 2.5% of all mortality cases [24]. The authors suggested that this is likely to be the effect of chronic sepsis, which may result in reduced healing capacity. Several studies have also suggested that preoperative hypoalbuminemia is a potent risk factor of postoperative complications in colorectal surgery [25-28].

The second strong risk factor of IC complication in this study was longer interval from initial surgery to IC surgery (p=0.0113

Table 5: Multivariable analysis of factors associated with complications.

Factors	Odds ratio (95% CI)	P value
Serum albumin level <3.5 g/dL	7.248 (2.416–22.838)	0.0005
Time to ileostomy closure (cutoff: 116.5 days), days	1.977 (1.167–3.350)	0.0113

(OR, 1.977; 95% CI, 1.167 to 3.350). We found that the 116th day after initial surgery was the cutoff time as a critical point to increase complication rate after IC through the ROC curve analysis.

Rubio-Perez's findings showed that delay in IC (>6 months) is a risk factor of increased complications [29]. Figueiredo et al. [30] have also reported in their study with 259 patients that the later the closure, the greater the complications, and thus early closure is recommended even if the patient is undergoing adjuvant chemotherapy. On the other hand, Perez et al. suggested that the optimal closure time was >8.5 weeks, and shorter intervals could result in an increased risk of postoperative complications (sensitivity, 88%; specificity, 44%) [5]. Menahem et al. [31] have reported in their meta-analysis that early closure, defined as ≤ 14 days from the index operation in which the ileostomy was performed, showed no significant difference in overall morbidity rate as compared with late closure in carefully selected patients. Recent interest regarding early closure reflects patients' poor QoL and stoma-related complications. The authors would like to suggest that considering this study's results and patients' QoL, it seems reasonable to consider early IC.

Effects of chemotherapy on surgical complications remain controversial. It is generally believed that chemotherapy may interrupt the healing process, which makes surgeons delay IC if patient undergoes adjuvant chemotherapy [32,33]. However, recent findings suggest that this may not always be the case; there is no definite proof that chemotherapy impairs healing [30,34]. In our study, since most patients received 5-fluorouracil based chemotherapy, adjuvant chemotherapy was not a significant risk factor. Nevertheless, chemotherapy such as doxorubicine is a well-known factor inhibiting wound healing. Thus, depending on the types of chemotherapy used in patients, there may be an increase in complication rates, but further studies are needed to validate this.

Surgical technique is nonetheless a key risk factor of surgical complications in many studies. In our study, 246 patients underwent stoma closure using handsewn end-to-end anastomosis with resection; 56, with handsewn end-to-end anastomosis without resection; and 52, with staples. The anastomosis technique was not a risk factor of morbidity in our study. However, all 17 patients who had early small bowel obstruction underwent stoma closure with a handsewn maneuver. Statistical significance was not achieved because of the small sample size, but our result is compatible with those of previous studies, indicating a more common small bowel obstruction with handsewn repair in meta-analysis [35], therefore favoring stapled closure over handsewn closure [18,36-38].

The limitations of this study include its retrospective nature and small sample size. The timing and method of closure may be reflections of the surgeon's preference, which creates selection bias. However, this study has its value in confirming hypoalbuminemia and late closure as potential strong risk factors of morbidity in ileostomy closure. Therefore, normalization of preoperative hypoalbuminemia reflecting patient's nutritional status and performing early closure no later than 4 months if possible may necessary to further reduce morbidity rates of IC. Large prospective randomized multicenter studies are needed to validate these findings.

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References

1. Alberts JC, Parvaiz A, Moran BJ. Predicting risk and diminishing the consequences of anastomotic dehiscence following rectal resection. Colorectal Dis. 2003;5(5):478-82.
2. D'Haeninck A, Wolthuis AM, Penninckx F, D'Hondt M, D'Hoore A. Morbidity after closure of a defunctioning loop ileostomy. Acta Chir Belg. 2011;111(3):136-41.
3. Mansfield SD, Jensen C, Phair AS, Kelly OT, Kelly SB. Complications of loop ileostomy closure: A retrospective cohort analysis of 123 patients. World J Surg. 2008;32(9):2101-6.
4. Garcia-Botello SA, Garcia-Armengol J, Garcia-Granero E, Espí A, Juan C, López-Mozos F. A prospective audit of the complications of loop ileostomy construction and takedown. Dig Surg. 2004;21(5-6):440-6.
5. Perez RO, Habr-Gama A, Seid VE, Proscurshim I, Sousa AH, Kiss DR, et al. Loop ileostomy morbidity: Timing of closure matters. Dis Colon Rectum. 2006;49(10):1539-45.
6. Williams LA, Sagar PM, Finan PJ, Burke D. The outcome of loop ileostomy closure: A prospective study. Colorectal Dis. 2008;10(5):460-4.
7. Tulchinsky H, Shacham-Shmueli E, Klausner JM, Inbar M, Geva R. Should a loop ileostomy closure in rectal cancer patients be done during or after adjuvant chemotherapy? J Surg Oncol. 2014;109(3):266-9.
8. Harries RL, Ansell J, Codd RJ, Williams GL. A systematic review of Clostridium difficile infection following reversal of ileostomy. Colorectal Dis. 2017;19(10):881-7.
9. Thalheimer A, Bueter M, Kortuem M, Thiede A, Meyer D. Morbidity of temporary loop ileostomy in patients with colorectal cancer. Dis Colon Rectum. 2006;49(7):1011-7.
10. Giannakopoulos GF, Veenhof AA, van der Peet DL, Sietses C, Meijerink WJHJ, Cuesta MA. Morbidity and complications of protective loop ileostomy. Colorectal Dis. 2009;11(6):609-12.
11. Lasithiotakis K, Aghahoseini A, Alexander D. Is early reversal of defunctioning ileostomy a shorter, easier and less expensive operation? World J Surg. 2016;40(7):1737-40.
12. Danielsen AK, Park J, Jansen JE, David Bock, Skullman S, Wedin A, et al. Early closure of a temporary ileostomy in patients with rectal cancer a multicenter randomized controlled trial. Ann Surg. 2017;265(2):284-90.
13. Bakx R, Busch OR, van Geldere D, Willem Bemelman A, Frederik Slors JM, Jan van Lanschot JB. Feasibility of early closure of loop ileostomies: A pilot study. Dis Colon Rectum. 2003;46(12):1680-4.
14. Boyce SA, Harris C, Stevenson A, Lumley J, Clark D. Management of low colorectal anastomotic leakage in the laparoscopic Era: More than a decade of experience. Dis Colon Rectum. 2017;60(8):807-14.
15. Matthiessen P, Hallbook O, Rutegard J, Simert G, Sjödahl R. Defunctioning stoma reduces symptomatic anastomotic leakage after low anterior resection of the rectum for cancer: A randomized multicenter trial. Ann Surg. 2007;246(2):207-14.
16. Gastinger I, Marusch F, Steinert R, Wolff S, Koeckerling F, Lippert H, et al. Protective defunctioning stoma in low anterior resection for rectal carcinoma. Br J Surg. 2005;92(2):1137-42.

17. Sharma A, Deeb AP, Rickles AS, Iannuzzi JC, Monson JRT, Fleming FJ. Closure of defunctioning loop ileostomy is associated with considerable morbidity. Colorectal Dis. 2013;15(4):458-62.

18. Man VC, Choi HK, Law WL, Foo DC. Morbidities after closure of ileostomy: Analysis of risk factors. Int J Colorectal Dis. 2016;31(1):51-7.

19. Bakx R, Busch OR, Bemelman WA, Veldink GJ, Slors JFM, van Lanschot JJB. Morbidity of temporary loop ileostomies. Dig Surg. 2004;21(4):277-81.

20. Shellito PC. Complications of abdominal stoma surgery. Dis Colon Rectum. 1998;41(12):1562-72.

21. Bhama AR, Batool F, Collins SD, Ferraro J, Cleary RK. Risk factors for postoperative complications following diverting loop ileostomy takedown. J Gastrointest Surg. 2017;21(12):2048-55.

22. Chow A, Tilney HS, Paraskeva P, Jeyarajah S, Zacharakis E, Purkayastha S. The morbidity surrounding reversal of defunctioning ileostomies: A systematic review of 48 studies including 6,107 cases. Int J Colorectal Dis. 2009;24(6):711-23.

23. Hesp WL, Lubbers EJ, de Boer HH, Hendriks T. Anastomotic insufficiency in small bowel surgery-incidence and treatment. Langenbecks Arch Chir. 1986;368(2):105-11.

24. Saha AK, Tapping CR, Foley GT, Baker RP, Sagar PM, Burke DA, et al. Morbidity and mortality after closure of loop ileostomy. Colorectal Dis. 2009;11(8):866-71.

25. Hu WH, Chen HH, Lee KC, Liu L, Eisenstein S, Parry L, et al. Assessment of the addition of hypoalbuminemia to ACS-NSQIP surgical risk calculator in colorectal cancer. Medicine (Baltimore). 2016;95(10):e2999.

26. Lohsiriwat V, Lohsiriwat D, Boonnuch W, Chinswangwatanakul V, Akaraviputh T, Lert-akayamanee N. Pre-operative hypoalbuminemia is a major risk factor for postoperative complications following rectal cancer surgery. World J Gastroenterol. 2008;14(8):1248-51.

27. Hennessey DB, Burke JP, Ni-Dhonochu T, Shields C, Winter DC, Mealy K. Preoperative hypoalbuminemia is an independent risk factor for the development of surgical site infection following gastrointestinal surgery: a multi-institutional study. Ann Surg. 2010;252:325-9.

28. Hardt J, Pilz L, Magdeburg J, Kienle P, Post S, Magdeburg R. Preoperative hypoalbuminemia is an independent risk factor for increased high-grade morbidity after elective rectal cancer resection. Int J Colorectal Dis. 2017;32(10):1439-46.

29. Rubio-Perez I, Leon M, Pastor D, Dominguez JD, Cantero R. Increased postoperative complications after protective ileostomy closure delay: An institutional study. World J Gastrointest Surg. 2014;6(9):169-74.

30. Figueiredo MN, Mege D, Maggiori L, Ferron M, Panis Y. When is the best time for temporary stoma closure in laparoscopic sphincter-saving surgery for rectal cancer? A study of 259 consecutive patients. Tech Coloproctol. 2015;19(8):469-74.

31. Menahem B, Lubrano J, Vallois A, Alves A. Early closure of defunctioning loop ileostomy: Is it beneficial for the patient? A Meta-analysis. World J Surg. 2018;42(10):3171-8.

32. Robertson I, Leung E, Hughes D, Spiers M, Donnelly L, Mackenzie I, et al. Prospective analysis of stoma-related complications. Colorectal Dis. 2005;7(3):279-85.

33. Biagi JJ, Raphael MJ, Mackillop WJ, Kong W, King WD, Christopher Booth M. Association between time to initiation of adjuvant chemotherapy and survival in colorectal cancer: A systematic review and meta-analysis. JAMA. 2011;305(22):2335-42.

34. Choi YJ, Kwak JM, Ha N, Lee TH, Baek SJ, Kim J, et al. Clinical outcomes of ileostomy closure according to timing during adjuvant chemotherapy after rectal cancer surgery. Ann Coloproctol. 2019;35(4):187-93.

35. Leung TT, MacLean AR, Buie WD, Dixon E. Comparison of stapled versus handsewn loop ileostomy closure: a meta-analysis. J Gastrointest Surg. 2008;12(5):939-44.

36. Phang PT, Hain JM, Perez-Ramirez JJ, Madoff RD, Gemlo BT. Techniques and complications of ileostomy takedown. Am J Surg. 1999;177(6):463-6.

37. Shelygin YA, Chernyshov SV, Rybakov EG. Stapled ileostomy closure results in reduction of postoperative morbidity. Tech Coloproctol. 2010;14(1):19-23.

38. Loffler T, Rossion I, Goossen K, Saure D, Weitz J, Ulrich A, et al. Hand suture versus stapler for closure of loop ileostomy-a systematic review and meta-analysis of randomized controlled trials. Langenbecks Arch Surg. 2015;400(2):193-205.