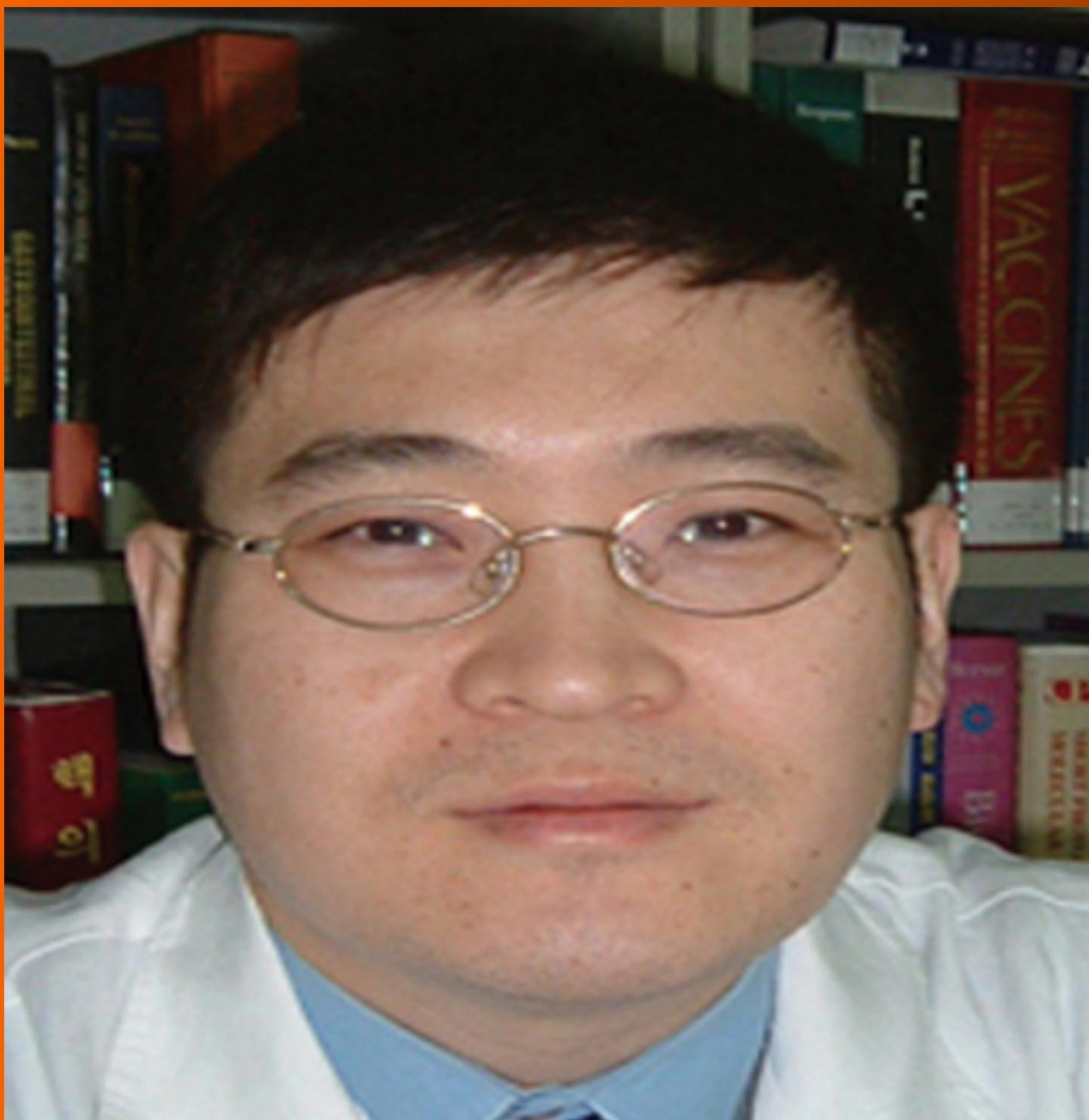


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Retrospective Study

Predictors of dehydration and acute renal failure in patients with diverting loop ileostomy creation after colorectal surgery

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Author contributions: Omar Vergara-Fernández, and Mario Trejo-Avila designed this work, collected and interpreted the data, and drafted the manuscript. Mario Trejo-Avila performed statistical analyses. Oscar Santes, Danilo Solórzano-Vicuña, Noel Salgado-Nesme contributed to study concept, critically revised the manuscript, and performed overall supervision. All authors contributed to the final approval of the manuscript.

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Abstract**BACKGROUND**

Despite the potential benefits of fecal diversion after low pelvic anastomosis in colorectal surgery, diverting loop ileostomy construction is related to significant rates of complications.

AIM

To determine potential predictors of high output related complications in patients with diverting loop ileostomy creation after colorectal surgery.

METHODS

Patients who underwent open and laparoscopic colorectal surgery requiring a diverting loop ileostomy from January 2010 to March 2018 were retrospectively analyzed. We included patients older than 18 years, who underwent colorectal surgery with primary low pelvic anastomosis, and with the creation of a diverting loop ileostomy, at elective or emergency settings for the treatment of benign or malignant conditions. Univariate and multivariate logistic regression analysis was used to determine the effect of the potential predictors on the rate of high output related complications. The high output related complications were dehydration and acute renal failure that required visits to the emergency department and hospitalizations.

RESULTS

Of the 102 patients included in the study, 23.5% ($n = 24$) suffered high output related complications. In this group of patients at least one visit to the emergency department (mean 1.6), and at least one readmission to the hospital was needed. The factors associated with high-output ileostomy, in the univariate analysis, were: urgent surgical intervention (OR = 2.6; $P = 0.047$), the development of postoperative complications (OR = 3; $P = 0.024$), have ulcerative colitis (OR = 4.8; $P = 0.017$), use of steroids (OR = 4.3; $P = 0.010$), mean output at discharge greater than 1000 mL/24 h (OR = 3.2; $P = 0.016$), and use of loperamide at discharge (OR

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= 2.8; $P = 0.032$). Multivariate logistic regression analysis identified two independent risk factors for high output related complications: ulcerative colitis [OR = 7.6 (95%CI: 1.81-31.95); $P = 0.006$], and ileostomy output at discharge ≥ 1000 mL/24 h [OR = 3.3 (1.18-9.37); $P = 0.023$].

CONCLUSION

In our study, patients with ulcerative colitis and those with an ileostomy output above 1000 mL/24 h at discharge, were at increased risk of high output related complications.

Key words: Loop ileostomy; High-output ileostomy; Loop ileostomy complications; Dehydration; Colorectal surgery

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Core tip: In this retrospective study involving 102 patients who underwent colorectal surgery resections with primary low pelvic anastomosis and with the creation of a diverting loop ileostomy for the treatment of benign and malignant conditions, we evaluated the risk factors for high output related complications. The high output related complications were dehydration and acute renal failure that required visits to the emergency department and hospitalizations. We found that patients with ulcerative colitis and those with an ileostomy output above 1000 mL/24 h at the moment of discharge, were at increased risk of high output related complications.

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INTRODUCTION

Diverting loop ileostomy is commonly performed to protect a distal anastomosis when there is a high risk of anastomotic leakage^[1,2]. Although fecal diversion does not prevent an anastomotic leak, it decreases the mortality and morbidity associated with this condition^[3].

Despite the potential benefits of fecal diversion, loop ileostomy construction is related to significant complications, with an incidence rate of 20% to 60%^[4]. Patients with a diverting loop ileostomy will require an additional operation to take down the ostomy and may develop small bowel obstructions, parastomal hernia, stoma stenosis, stoma retraction or prolapse, skin problems, dehydration, electrolyte abnormalities, and acute kidney injury due to a high-output stoma^[5-5]. Patients with ileostomies represent the group with the highest readmission rates after a colorectal procedure^[6]. Hospital readmissions and visits to the emergency department put patients at risk for morbidity (*e.g.*, nosocomial infections) and raise health care costs associated with these procedures^[7]. In patients with a small bowel stoma, dehydration and related complications are the most frequent cause of hospital readmissions in the first 3 wk following surgery, reported in up to 40% of cases, at least a third of which require long-term treatment^[6-10].

The majority of studies reporting high-output complications include in the analysis terminal ileostomies and diverting loop ileostomies^[6-11]. Due to the increased use of protective or diverting loop ileostomies in open and laparoscopic colorectal surgery and because there is a lack of articles analyzing the risk of readmission focusing only on this population, we decided to analyze this group of patients. The aim of the study was to determine the potential clinical predictors of high output-related complications (dehydration and acute renal failure) in patients with diverting loop ileostomy creation after open and laparoscopic colorectal surgery.

MATERIALS AND METHODS

From January 2010 to March 2018, all patients who underwent colorectal surgery requiring a diverting loop ileostomy at Instituto Nacional de Ciencias Médicas y Nutrición “Salvador Zubirán” in Mexico City, Mexico, were included. Data for these patients were retrospectively retrieved and analyzed. This study was conducted in accordance with local audit and governance protocols.

We included patients older than 18 years who underwent benign or malignant colorectal surgery with a primary low pelvic anastomosis, with the creation of a diverting loop ileostomy in elective or emergency settings. An index surgery was defined as the operation in which a colon or rectal resection, primary anastomosis, and diverting loop ileostomy were performed. In all patients, the diverting loop ileostomies were performed at a distance of 15 to 30 cm from the ileocecal valve. Patients who had diverting loop ileostomy not related to colorectal diseases and those with incomplete data were excluded.

Demographic information was categorized as follows: sex (female and male), age (< 59 or ≥ 60 years), and body mass index (BMI < 29.9 or ≥ 30 kg/m²). Comorbidity was assessed using the Charlson Comorbidity Index (CCI)^[12]. Other variables examined were tobacco use, previous treatments (systemic steroids, immunomodulators, TNF inhibitor drugs, radiotherapy, or chemotherapy), and history of previous abdominal surgeries. The drugs classified as immunomodulators were azathioprine, methotrexate, and mycophenolate mofetil. Variables regarding index surgery were the type of operation (elective or urgent; laparoscopic or open), complications unrelated to the ileostomy, and reintervention. The mean ostomy output at the moment of discharge was analyzed as less than 1000 mL/24 h, and equal to or greater than 1000 mL/24 h. Information on the use of loperamide at discharge was collected. All patients underwent loop ileostomy closure, which was cataloged for statistical purposes in less or more than 3 mo.

Two groups of patients were formed: Those who did not have high-output-related complications after discharge (N-HORC: Non-high-output-related complications group) and those who did have high-output-related complications (HORC: High-output-related complications group). The high-output-related complications included in the study were dehydration with electrolyte disturbances and acute renal failure. Ileostomy high-output was defined as more than 1500 mL in 24 h, at the moment of emergency department visit or readmission in the HORC group^[6]. Patients in the N-HORC had an output of less than 1500 mL in 24 h during their follow-up and did not require emergency department visit nor readmissions. We employed an operational definition of dehydration proposed by Fish *et al.*^[9], where clinical criteria or objective signs could support the diagnosis at the time of readmission. Electrolyte imbalances included hypo- or hyponatremia, hypo- or hyperkalemia, hypo- or hypermagnesemia, and hypo- or hyperchloremia. Acute renal failure was diagnosed following the Acute Kidney Injury Network consensus definitions^[11].

In the HORC group, the time from the index surgery to the first visit to the emergency department or readmission, as well as the number of visits to the emergency department or readmissions, were registered. Patients who visited the emergency department (due to a high-output loop ileostomy) and received intravenous hydration but were subsequently discharged not requiring admission to the hospital were also included in this group (HORC). Data regarding high-output-related complications were retrieved and registered from discharge until the elective loop ileostomy closure was performed.

Statistical analysis

All the data were collected retrospectively in a digital database. Categorical data were presented as totals (*n*) and proportions as percentages (%). Categorical data were compared using the 2 test or Fisher’s exact test (analyzing patients in two groups: HORC *vs* N-HORC groups). All the tests were two-sided and used an alpha of 0.05.

Univariate binomial logistic regression analysis was performed. All the variables with a *P*-value less than 0.05 in the univariate analysis were considered potential risk factors (predictors of high-output-related complications) and were entered manually into the multivariate backward logistic regression analysis. The variables representing the lowest risk for each complication were considered to be the reference group (OR = 1.0). Odds ratios and 95% confidence intervals (95%CI) were calculated. All the *P*-values were 2-tailed, and a *P*-value < 0.05 was considered statistically significant. All the data were analyzed using SPSS statistic Version 22.0 (IBM Corporation, Armonk, New York, NY).

RESULTS

Our selection criteria yielded 102 cases of patients with a diverting loop ileostomy after open and laparoscopic colorectal surgery. We found 78 (76.5%) patients without high-output-related complications (N-HORC) and 24 (23.5%) patients with high-output-related complications (HORC). The patient characteristics are described in [Table 1](#). No differences were found regarding sex, age, BMI, or comorbidities. The frequency of a preoperative colorectal diagnosis was similar in both groups, except for ulcerative colitis, which was more frequent in the HORC group (6.4% *vs* 25%, $P = 0.010$). Regarding previous medical treatments, the use of steroids (10.3% *vs* 33.3%, $P = 0.007$) and immunomodulators (2.6% *vs* 12.5%, $P = 0.049$) was significantly more frequent in the HORC group.

Index colorectal surgery was performed more frequently in the elective setting in both groups, with no difference in the type of operation (open or laparoscopic) or in the rate of reintervention. The rate of postoperative morbidity related to the index colorectal surgery was higher in the HORC group (21.8% *vs* 45.8%, $P = 0.021$).

At discharge an ileostomy output greater than 1000 mL was associated with the development of an output > 1500 mL/24 with concurrent acute renal failure or electrolyte imbalance during follow-up in 54.2% of patients in the HORC group. In the N-HORC, 26.9% of patients were discharged with an output greater than 1000 mL, but patients in this group tended to normalize output and did not develop high output nor complications during follow-up.

The use of loperamide was more frequent in the HORC than in the N-HORC (62.5% *vs* 37.2%, $P = 0.029$). Patients with high-output-related complications had a mean of 1.6 visits to the emergency department and at least one readmission to the hospital (see [Table 2](#)). The rates of acute renal failure and dehydration with electrolyte imbalances were 75% and 79.2%, respectively.

The univariate and multivariate results are summarized in [Table 3](#). Index colorectal surgery performed as an emergency, the presence of complications following the index surgery, diagnosis of ulcerative colitis, previous treatment with immunomodulators and steroids, daily in-hospital ileostomy output of more than 1000 mL/24 h, and discharge with loperamide were considered potential risk factors for the occurrence of high-output related complications. Multivariate logistic regression analysis identified two independent risk factors for high-output-related complications: the preoperative diagnosis of ulcerative colitis [OR = 7.6 (95%CI: 1.81-31.95); $P = 0.006$], and daily in-hospital ileostomy output ≥ 1000 mL/24 h [OR = 3.3 (1.18-9.37); $P = 0.023$].

DISCUSSION

In this retrospective study, we found that 23.5% of patients with diverting loop ileostomy creation after open or laparoscopic colorectal surgery suffered from high-output-related complications, namely dehydration with electrolyte imbalances and acute renal failure. In this group of patients, at least one visit to the emergency department for evaluation and at least one readmission to the hospital was needed. Despite the potential advantages of a diverting loop ileostomy, surgeons should take into account the high rate of morbidity associated with this procedure.

There is a trend toward sphincter-sparing procedures with the use of very low pelvic anastomoses in colorectal surgery^[13]. The most dreaded complication of a low pelvic anastomosis is an anastomotic leak. Anastomotic leakage could result in generalized peritonitis, pelvic abscess, prolonged length of hospital stay, decreased quality of life, cancer recurrence and higher mortality^[1,14,15]. Fecal diversion is aimed at minimizing these complications^[1,14]. The absence of a diverting stoma in low anterior resection is associated with a higher rate of anastomotic leakage^[16]. For ultra-low resections with subsequent coloanal anastomosis, a diverting ostomy is almost always constructed^[3]. The incidence of anastomotic leakage after colorectal surgery ranges from 1% to 25%^[13,17], and mortality ranges from 6% to 22%^[18].

The benefits of a diverting loop ileostomy should be contrasted with the potential of complications. We found in our study that 23.5% of the patients who underwent a diverting loop ileostomy after an open or laparoscopic colorectal procedure presented at least one visit to the emergency department and at least one readmission to the hospital due to high-output-related complications. Similar rates of readmission have been previously published^[4,6,9,19]. The all-cause readmission rate of patients with ileostomy (including both terminal and loop ileostomies) is 28% to 35%, with dehydration being the most common reason for readmission^[4,6,9,19]. Dehydration in patients with ileostomies is associated with longer, later, and multiple readmissions as well as additional morbidity^[9]. It is essential to consider the fact that readmission rates are a measure of surgical quality^[20].

Table 1 Characteristics of patients with diverting loop ileostomy after colorectal surgery

	N-HORC (n = 78)	HORC (n = 24)	P < 0.05
Sex			0.913
Female	40 (51.3)	12 (50)	
Male	38 (48.7)	12 (50)	
Age, n (%)			0.475
< 59 yr	39 (50)	14 (58.3)	
≥ 60 yr	39 (50)	10 (41.7)	
BMI, n (%)			0.919
< 29.9	72 (92.3)	22 (91.7)	
≥ 30	6 (7.7)	2 (8.3)	
Smoking, n (%)			0.779
Yes	30 (38.5)	10 (41.7)	
Diabetes mellitus, n (%)			0.459
Yes	11 (14.1)	2 (8.3)	
Hypertension, n (%)			0.829
Yes	21 (26.9)	7 (29.2)	
Charlson morbidity index			0.985
0-1	29 (37.2)	9 (37.5)	
2-3	25 (32.1)	7 (29.2)	
4-5	19 (24.4)	6 (25)	
≥ 6	5 (6.4)	2 (8.3)	
Colorectal diagnosis, n (%)			
Rectal cancer	33 (42.3)	6 (25)	0.127
Colon cancer	7 (9)	3 (12.5)	0.611
Ulcerative colitis	5 (6.4)	6 (25)	0.010
Diverticular disease	24 (30.7)	9 (37.5)	0.537
FAP	9 (11.6)	0	0.111
Previous abdominal surgery, n (%)	14 (17.9)	2 (8.3)	0.257
Yes			
Previous Treatments, n (%)			
Steroids	8 (10.3)	8 (33.3)	0.007
Immunomodulator	2 (2.6)	3 (12.5)	0.049
Biologics (anti-TNF)	1 (1.3)	2 (8.3)	0.074
Radiotherapy	28 (35.9)	6 (25)	0.322
Chemotherapy	33 (42.3)	7 (29.2)	0.249
Index surgery, n (%)			0.078
Elective	59 (75.6)	13 (54.2)	
Urgent	19 (24.4)	11 (45.8)	
Modality of index surgery, n (%)			0.244
Open	52 (66.7)	19 (79.2)	
Laparoscopic	26 (33.3)	5 (20.8)	
Complications after index surgery, n (%)	17 (21.8)	11 (45.8)	0.021
Yes			
Re-intervention after index surgery, n (%)	13 (16.7)	7 (29.2)	0.177
Yes			
Ileostomy output at discharge, n (%)	21 (26.9)	13 (54.2)	0.013
≥ 1000 mL			
Discharge with loperamide, n (%)	29 (37.2)	15 (62.5)	0.029
Yes			
Time until ileostomy closure, n (%)			0.038
< 3 mo	9 (11.5)	7 (29.2)	
> 3 mo	69 (88.5)	17 (70.8)	

N-HORC: Non-high output related complications group; HORC: High output related complications group;

BMI: Body mass index; ASA: American Society of Anesthesiologists; IQR: Interquartile range.

In a recent study, the presence of ileostomy high-output at any time during the index admission was associated with a 3-fold increased risk of readmission for dehydration^[6]. We found a similar 3.3-fold increased risk of presenting a high-output-related complication (either dehydration or acute renal failure) in patients with more than 1000 mL/24 h the day of discharge. Loperamide reduces the daily output and decreases the losses of sodium and potassium in patients with an ileostomy^[21]. The use of loperamide was associated with a greater incidence of complications and hospital readmissions (OR = 2.8, 95%CI: 1.09-7.24). This may reflect the difficulties in controlling the output in this group of patients shortly after surgery.

A high-output stoma is characterized by an increased loss of water and sodium, which may produce dehydration, hyponatremia, hypomagnesemia, and hyperaldosteronism^[4]. In patients with normal preoperative glomerular filtration rates, approximately 20% show significant reductions in glomerular filtration rates after ileostomy creation, and some patients require hospitalization for IV fluid hydration^[7,10]. Impairment of renal function was evident in 75% of our patients who presented with high-output-related complications, all of whom required admission to the hospital for IV fluid hydration.

The identification of patients at risk of developing high ileostomy output and its related complications is of paramount importance to implement interventions to decrease readmissions^[6]. In our institution, diverting loop ileostomies are performed at a distance of 30-15 cm from the ileocecal valve. Some recognized causes of high output are proximal stomas, intraabdominal sepsis, enteritis, intermittent bowel obstruction, less than 200 cm of small bowel length, recurrent disease in the remaining bowel (*e.g.*, inflammatory bowel disease or radiation enteritis), bacterial overgrowth, and medications^[4,10]. In our study, patients with ulcerative colitis had a 7.6-fold increased risk of presenting with high-output complications.

In a recent study, Chen *et al*^[21], developed the so-called "Dehydration Readmission After Ileostomy Prediction Scoring System". They found seven predictors, based on the American College of Surgeons National Surgical Quality Improvement Program database, and they assigned different points for each predictor: ASA class III (4 points), female sex (5 points), IPAA (4 points), age \geq 65 years (5 points), shortened length of stay (5 points), ASA class I to II with IBD (7 points), and hypertension (9 points). Patients with $>$ 15 points are at increased risk for readmission for dehydration. In our study, we found a high prevalence of the previously mentioned predictors in the patients who were readmitted: 33.3% were ASA class III, 50% were females, 25% required an IPAA, 41.7% were $>$ 65 years, 25% had ulcerative colitis, and 29.2% of patients had hypertension.

Patients with an ileostomy warrant special attention, and preventing dehydration represents an opportunity to improve outcomes^[9]. After the creation of a diverting loop ileostomy, the aim is to close it within 8-12 wk^[22-24]. Although the objective is to close all diverting loop ileostomies, the reversal percentage ranges from 75% to 86%^[22-27]. Chun *et al*^[26], reported that in 23.6% of patients, the ileostomy was not closed, with obesity (OR = 4.61, 95%CI: 1.14-18.54) and smoking (OR = 4.47, 95%CI: 1.43-13.98) being risk factors for non-closure. Therefore, there should be a focus on the prevention of high output (and subsequently the readmission rates) until the loop ileostomy can be closed. We found in our study that the mean time from discharge after index surgery to the first visit to the emergency department was 78.3 d. This time-lapse is essential because the majority of our patients (overall 84.3%) had to wait more than three months to have their ileostomy closed.

Several ileostomy care pathways have been implemented and reported with the purpose of reducing readmissions due to dehydration^[19]. For example, Nagle *et al*^[19], reported decreased hospital readmissions (the readmission rate for dehydration dropped from 15.5% to 0%) with the "ileostomy pathway" that included a set of patient education tools throughout the perioperative process with post-discharge tracking of intake and output.

Although many studies have identified predictors of morbidity and readmission, many risk factors are non-modifiable, such as age, sex and comorbidities^[6-9]. Aside from the protocols that we can implement to reduce readmissions, we should possibly focus on the selection of patients who would benefit the most with the construction of a diverting loop ileostomy and define the minimal time in which the patients could have their ostomies closed to reduce the time-at-risk for developing complications^[28]. More studies are needed to answer these questions.

The limitations of our study are largely attributable to the sample size and retrospective design. The single institutional nature of our investigation is prone to

Table 2 Characteristics of patients with high output related complications (high-output-related complications group)

	HORC group (n = 24)
Number of visits to the ED, mean (range)	1.6 (1-4)
Time from index surgery to first visit to the ED (d), mean (range)	78.3 (3-360)
Number of readmissions to the hospital, mean (range)	1 (1-2)
Presentation with acute renal failure, n (%)	
Yes	18 (75)
No	6 (25)
Presentation with dehydration or electrolyte imbalances, n (%)	
Yes	19 (79.2)
No	5 (20.8)

HORC: High-output-related complications; ER: Emergency department.

selection bias. The sample size could represent a risk of bias for a multivariate analysis, which could lead to underestimation of the independent variables. However, we consider that this study provides evidence of different risk factors associated with high-output-related complications that should be weighed at the time of diverting loop ileostomy construction. These data can be used by colorectal and general surgeons for surgical decision-making and counseling patients on the pros and cons of diverting loop ileostomy after open and laparoscopic colorectal surgery.

In our study, 23.5% of patients who required diverting loop ileostomy creation after open or laparoscopic colorectal surgery suffered from high-output-related complications, namely dehydration with electrolyte imbalances and acute renal failure. In this group of patients, at least one visit to the emergency department for evaluation and at least one readmission to the hospital was needed. Patients with ulcerative colitis and those who were discharged after index surgery with a daily in-hospital ileostomy output of more than 1000 mL were at increased risk for high-output related complications.

Despite the potential benefits of fecal diversion after low pelvic anastomosis in colorectal surgery, diverting loop ileostomy construction is related to significant rates of complications.

Table 3 Univariate and multivariate analysis of clinical factors associated with high-output related complications (dehydration and acute renal failure)

Factors	Univariate analysis		Multivariate analysis	
	OR (95%CI)	P value	OR (95%CI)	P value
Index surgery	1.0			
Elective				
Urgent	2.6 (1.01-8.82)	0.047		
Complications after index surgery	3 (1.15-7.97)	0.024		
Yes				
Ulcerative Colitis	4.8 (1.33-17.75)	0.017	7.6 (1.81-31.95)	0.006
Immunomodulators	5.4 (0.85-34.63)	0.074		
Steroids	4.3 (1.42-13.41)	0.010		
Biologics (anti-TNF)	7 (0.60-80.85)	0.119		
Ileostomy output at discharge \geq 1000 mL/24 h	3.2 (1.24-8.26)	0.016	3.3 (1.18-9.37)	0.023
Discharge with loperamide	2.8 (1.09-7.24)	0.032		
Yes				

The reference category has an odds ratio of 1.0. For multivariable backward logistic regression analysis, odds ratio (OR) and 95% confidence interval (CI) are presented, and only significant results are shown.

ARTICLE HIGHLIGHTS

Research background

Despite the potential benefits of fecal diversion after low pelvic anastomosis in colorectal surgery, diverting loop ileostomy construction is related to significant rates of complications.

Research motivation

There is a lack of articles analyzing the risk of complications related to high output complications focusing only in this population (patients with diverting loop ileostomies).

Research objectives

Our main purpose was to determine potential predictors of high output related complications in patients with diverting loop ileostomy creation after colorectal surgery.

Research methods

Patients who underwent open and laparoscopic colorectal surgery requiring a diverting loop ileostomy from January 2010 to March 2018 were retrospectively analyzed. Univariate and multivariate logistic regression analysis was used to determine the effect of the potential predictors on the rate of high output related complications.

Research results

Of the 102 patients included in the study, 23.5% ($n = 24$) suffered high output related complications. In this group of patients at least one visit to the emergency department (mean 1.6), and at least one readmission to the hospital was needed. The factors associated with high-output ileostomy, in the univariate analysis, were: urgent surgical intervention ($P = 0.047$), the development of postoperative complications ($P = 0.024$), ulcerative colitis ($P = 0.017$), use of steroids ($P = 0.010$), mean output at discharge greater than 1000 mL/24 h ($P = 0.016$), and use of loperamide ($P = 0.032$). Multivariate logistic regression analysis identified two independent risk factors for high output related complications: ulcerative colitis [OR = 7.6 (95%CI: 1.81-31.95); $P = 0.006$], and ileostomy output at discharge \geq 1000 mL/24 h [OR = 3.3 (1.18-9.37); $P = 0.023$].

Research conclusions

Patients with ulcerative colitis and those with an ileostomy output above 1000 mL/24 h at discharge, were at increased risk of high output complications.

Research perspectives

This article reflects that diverting loop ileostomy has become a surgical technique commonly employed after open and laparoscopic colorectal resections with low pelvic anastomosis. Despite the frequency of the employment of this technique, there is a lack of articles analyzing the risk of readmission focusing only in this population. Our results support that not only patients with terminal ileostomies, but also patients with diverting loop ileostomy represent a high risk group for presenting to the emergency department with dehydration and acute renal failure.

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