



REVIEW ARTICLE

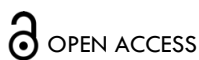
Stomas in Cytoreductive Surgery and Hyperthermic Intraoperative Peritoneal Chemotherapy for Colorectal and Appendiceal tumors: risk factors and outcomes

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ABSTRACT

Background: Cytoreductive surgery/hyperthermic intraperitoneal chemotherapy have evolved as promising treatments for peritoneal carcinomatosis of colorectal and appendiceal origin but are associated with high morbidity and mortality. For concomitant resections, stoma may mitigate against anastomotic leak or its adverse sequelae.

Objective Evaluate factors regarding decision-making and outcomes of stoma during cryoreductive/hyperthermic intraperitoneal chemotherapy.

Design: Retrospective review

Patients: All patients with appendiceal and colorectal neoplasms with peritoneal carcinomatosis who underwent cytoreductive surgery/hyperthermic intraperitoneal chemotherapy between 2009-2018. Patients were divided into those with and without a stoma.

Main outcomes: Surgical outcomes.

Results: 110 consecutive patients were identified. 78 (70.9%) did and 32 (29.1%) did not have a stoma: 46.9% loop ileostomies, 34.4% end ileostomies, 18.7% colostomies. 16.4% had diverting ileostomy. Preoperative factors associated with stoma formation included rectal tumor ($p=0.031$), body mass index <30 ($p=0.023$), hypoalbuminemia ($p=0.036$), and neoadjuvant chemotherapy ($p=0.043$). Peritoneal cancer index ≥ 10 ($p=0.002$), greater cytoreduction surgery ($p<0.001$), residual disease ($p=0.002$), more blood loss ($p < 0.001$), more blood transfusions ($p<0.001$), multiple small bowel resections ($p<0.001$), and multivisceral resections ($p<0.001$) also led to more stoma formation. Incidence of complications was 56.2% in patients with and 52.6% without a stoma ($p=0.7$). Patients with stomas had significantly more surgical site infections ($p=0.006$), severity of morbidity (Clavien-Dindo class 3/4; $p =0.017$), longer hospitalization ($p=0.028$), higher reoperation rate ($p=0.010$) and higher mortality ($p<0.002$). 8/32 (25%) patients underwent stoma reversal, one via laparotomy. Mean time to stoma closure was 5.3 ± 2.8 months with a 4.5% morbidity rate.

Limitations: Retrospective nature, heterogeneity of pathology/location, high-volume center with quaternary ancillary services leading to better resolution of complications but less generalizable results.

Conclusions: Patient with appendiceal or colorectal neoplasms with higher carcinomatosis burden requiring extensive cytoreductive surgery and blood transfusion are more likely to have a stoma. Only 25% undergo stoma reversal, highlighting the importance of preoperative counselling.

Keywords Stomas · Peritoneal carcinomatosis · Cytoreductive surgery · HIPEC · Intraperitoneal chemotherapy

Background

Since the 1980s, studies on cytoreductive surgery (CRS) followed by hyperthermic intraperitoneal chemotherapy (HIPEC) have prompted a new treatment option for peritoneal carcinomatosis of several malignancies, including colorectal, appendiceal, ovarian, among others.¹⁻⁷ Today, this multimodal approach is able to achieve long-term survival in select patients and has acceptable morbidity and mortality^{4,5,8}.

Nonetheless, CRS with HIPEC is still considered a complex and high-risk procedure⁹. This extensive surgery often requires multiple bowel resections and anastomoses in order to achieve complete cytoreduction (CC-0, CC-1), resulting in high complication rates¹⁰. When a concomitant resection is performed, a stoma might be employed in an attempt to mitigate against anastomotic leakage or at least its major adverse sequelae, and a diverting loop ileostomy has been recommended in this setting¹⁰⁻¹². In one series, loop ileostomies were almost always reversed, whereas non-loop ileostomies were almost always permanent¹³. Additionally, stoma reversal adds the additional morbidity associated with a future operation¹².

Predicting factors for stoma formation has been assessed by comparing patients who underwent stoma formation to those who did not¹⁰. Creation of a stoma during CRS/HIPEC has been correlated with a higher peritoneal carcinomatosis index (PCI) score, larger number of organs resected, greater number of anastomoses, prolonged operative time (OT), and longer hospital stay (LOS)¹⁰. In fact, in procedures requiring ≥ 2 anastomoses, formation of a stoma reduced the anastomotic leak (AL) rate, morbidity, and reoperation rate, therefore, a protective diverting loop ileostomy has been previously recommended for extensive CRS/HIPEC procedures¹⁰. Analyzing the various factors leading to stoma formation in this setting and the short-term outcome of this group of patients may improve both preoperative assessment and intraoperative decisions.

The primary aim of this study was to evaluate factors regarding the decision-making process and outcomes of performing a stoma during CRS and HIPEC for colorectal and appendiceal tumors and to examine whether fecal diversion reduces postoperative morbidity.

Materials and Methods

STUDY POPULATION

A retrospective analysis of an IRB-approved prospective registry was performed. All patients >18 years of age who underwent CRS and HIPEC for appendiceal and CRC between November 2009 and February 2018 at our institution were included. Patients were divided into two groups: those with and those without a stoma. A protective stoma was defined as any stoma with at least one distal anastomosis. The two groups were compared for demographics, preoperative baseline characteristics, operative details, and postoperative outcomes. This retrospective study was approved by the Institutional Review Board.

DATA COLLECTION

Patient demographics including age, gender, body mass index (BMI), albumin level, preoperative carcinoembryonic antigen (CEA), tumor location, and neoadjuvant chemotherapy were retrieved from the patient's medical record. Peritoneal cancer index (PCI), intraoperative complications, estimated blood loss (EBL), major cytoreductive surgery, small bowel resection, multivisceral resection, type of anastomosis, and type of stoma creation were obtained from the operative report. Outcome measures including length of hospital stay (LOS), overall and specific complications, reoperation, pathology, residual disease, and mortality were obtained from the patient's medical record. Complications included ileus, small bowel obstruction (SBO), abscess, surgical site infection (SSI), anastomotic leak, enterocutaneous fistula, perforation, pulmonary edema, and blood transfusion. Ileus was defined as a failure to pass gas or stool or the inability to tolerate a diet at postoperative day four or later. SBO was defined as any of the above-described symptoms with radiologic confirmation of mechanical obstruction. Abscess was confirmed by radiologic imaging and anastomotic leak was defined as any disruption of the anastomosis proven by radiology at reoperation. Morbidity was graded according to the Clavien–Dindo (CD) classification¹⁴: Grades I–II were considered minor and grades III–V were considered major.

SURGICAL TECHNIQUE

The abdominal cavity was evaluated as to establish the extent of the peritoneal spread using the PCI score, as described by Sugarbaker¹⁵. Lesions were resected by sharp dissection or ablation using a variety of thermal methods (cautery, bipolar, or argon beam). The abdominal cavity was carefully inspected for peritoneal carcinomatosis in all quadrants, diaphragm, on the surface of the small bowel, lesions on the serosal surface of the small bowel mesentery, and in the pelvis, after which surgery was initiated. Complete omentectomy was performed, as was additional organ resection when indicated. Following irrigation, the HIPEC cannulas were placed, after which the skin was closed with a watertight seal. After filling the abdomen with 3 L of sterile lactated Ringer's, HIPEC was undertaken with 40 mg/m² of mitomycin C (MMC) circulated at 42–43 degrees Celsius for 60–110 minutes with a perfusion flow rate of 1000 mL/min. At the completion of HIPEC, irrigation of the abdominal cavity, removal of the inflow and outflow cannulas, reintroduction of trocars, and further suction of fluid was undertaken after which the anastomoses and/or stoma formation were performed. Assessment of the CC score was performed according to the residual tumor size¹⁶.

STATISTICAL ANALYSIS

Statistical analyses were performed using SPSS 24.0 software. Simple descriptive analyses were performed including mean and standard deviation (SD) for normally distributed factors. Univariate analysis comparing patients with stoma and without stoma were undertaken using the cross-table Pearson χ^2 test or Fisher exact test, when appropriate, was used for categorical factors, while the Student's t-test was applied for continuous factors. In order to assess the impact of stoma creation at

the HIPEC surgery setting among other perioperative factors, we performed a multivariate regression analysis to the preoperative and intraoperative factors statistically significant after univariate analysis. Stoma reversal analysis was calculated using the Fischer's exact test. Survival probabilities were calculated using the Kaplan–Meier method. p value < 0.05 was considered statistically significant.

Results

PATIENTS

A total of 110 patients underwent CRS/HIPEC for colorectal and appendiceal neoplasms; 32 (29.1%) with stoma and 78 (70.9%) without stoma (**Figure 1**). Mean

age for patients with stoma was 53.3 ± 13.3 ; 16.4% were female versus 12.7% males ($p = 0.114$). Three types of stomas were performed: 15 (46.9%) loop ileostomies, 11 (34.4%) end ileostomies, and 6 (18.7%) end colostomies. In 18/110 (16.4%) patients, the ileostomy was diverting a colorectal or small bowel anastomosis. Preoperative factors associated with stoma creation are shown in **Table 1** and included rectal tumor (21.9% vs. 7.7%, $p = 0.031$), body mass index (BMI) < 30 (81.3% vs. 58.4%, $p = 0.023$), hypoalbuminemia (12.5% vs. 2.6%, $p = 0.036$), carcinoembryonic antigen (CEA) (67.8 ± 241.2 vs. 17.6 ± 49.1 , $p = 0.021$), and neoadjuvant chemotherapy (78.1% vs. 57.7%, $p = 0.043$).

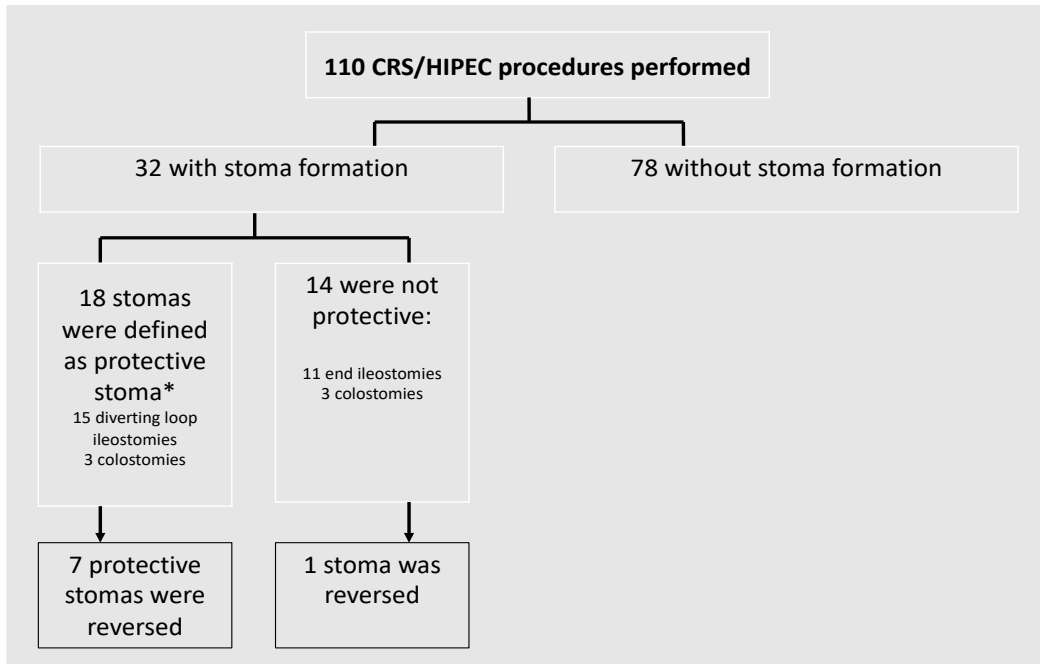


Figure 1. Flowchart of patient allocation. *Protective stoma: either loop ileostomy (n = 15) or double barrel colostomy (n = 3)

PCI, peritoneal cancer index, HIPEC, hyperthermic intraperitoneal chemotherapy

Table 1. Univariate analysis of perioperative factors associated with stoma creation at cytoreductive surgery and hyperthermic intraperitoneal chemotherapy procedure

Variable	Stoma N = 32	No stoma N = 78	P value
Age (years), mean \pm SD	53.3 \pm 13.3	55.8 \pm 11.3	0.315
Male, n (%)	14 (12.7)	47 (42.7)	0.114
BMI ≥ 30 (kg/m ²), n (%)	6 (18.7)	32 (41.0)	0.023
Albumin < 3.5 gr/dL, n (%)	4 (12.5)	2 (2.6)	0.036
Preoperative CEA, mean \pm SD	67.8 \pm 241.2	17.6 \pm 49.1	0.021
Preoperative chemotherapy, n (%)	25 (78.1)	45 (57.7)	0.043
Colorectal location, n (%)			0.031
- Right colon	6 (18.7)	25 (32.0)	
- Left colon	0 (0)	1 (1.3)	
- Sigmoid colon	8 (25.0)	6 (7.7)	
- Rectum	7 (21.9)	6 (7.7)	
PCI ≥ 10 , n (%)	19 (59.4)	23 (29.5)	0.002
EBL (cc), mean \pm SD	662.5 \pm 687.4	250.0 \pm 305.6	0.000
Major CRS, n (%)	28 (87.5)	25 (32.0)	0.000
Multivisceral resection, n (%)	19 (59.4)	20 (25.6)	0.000
Small bowel resection, n (%)	23 (71.9)	27 (34.6)	0.000
Resection with hypaque, n (%)	27 (84.4)	30 (38.5)	0.000
Anastomosis type, n (%)			0.000

Variable	Stoma N = 32	No stoma N = 78	P value
- Ileocolic	7 (21.9)	26 (33.3)	
- Ileorectal	3 (9.4)	2 (2.6)	
- Colocolic	1 (3.1)	0 (0)	
- Colorectal	9 (28.1)	0 (0)	
- Coloanal	3 (9.4)	0 (0)	
Intraoperative complication (re-do anastomosis), n (%)	3 (9.4)	1 (1.3)	0.039
Transfusion, n (%)	14 (43.7)	9 (11.5)	0.000
LOS, mean ± SD	10.5 ± 4.6	7.1 ± 3.7	0.028
ICU length of stay, mean ± SD	2.8 ± 2.6	1.6 ± 2.3	0.036
Pathology report, n (%)			0.000
- *Positive malignancy	32 (100)	56 (71.8)	
- *Negative malignancy	0 (0)	15 (19.2)	
- Focal atypical cell/mucin deposits	0 (0)	7 (9.0)	
Abscess, n (%)	0 (0)	5 (6.4)	0.000
Surgical site infection, n (%)	8 (25)	5 (6.4)	0.006
Clavien-Dindo class, n (%)			0.017
- 1	3 (9.4)	17 (21.8)	
- 2	7 (21.9)	20 (25.6)	
- 3	7 (21.9)	3 (3.8)	
- 4	1 (3.1)	1 (1.3)	
Reoperation, n (%)	4 (12.5)	1 (1.3)	0.010
**Overall mortality, n (%)	16 (50.0)	16 (20.5)	0.002
Residual disease, n (%)	16 (50.0)	4 (5.1)	0.024

SD standard derivation, BMI body mass index, EBL estimated blood loss, CEA carcinoembryonic antigen, PCI, peritoneal cancer index, CRS, cytoreductive surgery, LOS length of hospital stay, ICU intensive care unit, SSI surgical site infection

*positive malignancy = malignancy of deposits or tumor found

*negative malignancy = pathological study negative for malignancy

**Over an 80-month follow up period

SURGICAL PARAMETERS

The intraoperative factors that significantly led to more stoma formation were peritoneal cancer index (PCI) ≥ 10 (59.4% vs. 29.5%, p = 0.002), a more extensive cytoreductive surgery (CRS) (87.5% vs. 32%, p < 0.001), residual disease (50% vs. 20.5%, p = 0.002), a higher estimated blood loss (EBL) (662.5 ± 687.4 vs. 250.0 ± 305.6, p < 0.001), more red blood cells (RBC) transfusions (43.7% vs. 11.5%, p < 0.001), multiple small bowel resections (71.9% vs. 34.6%, p < 0.001), and multivisceral resections (59.4% vs. 25.6%, p < 0.001).

POSTOPERATIVE OUTCOMES

The incidence of complications was 56.2% in patients with stoma versus 52.6% in those without stoma (p = 0.7). Patients with stomas had significantly more surgical site infections (25% vs. 6.4%, p = 0.006), severity of morbidity (Clavien-Dindo class 3 and 4: 25% vs. 7.7%, 21.9% vs. 7.7%, respectively, p = 0.017), longer hospitalization (10.5 ± 4.6 vs. 7.1 ± 3.7, p = 0.028),

higher reoperation rate (12.5% vs. 1.3%, p = 0.010) and mortality (50% vs. 20.5%, p < 0.002). Among diverted patients, 7 had dehydration, 3 had small bowel obstruction, one intraabdominal abscess, and one pulmonary complication. All patients with anastomotic leak (AL) were non-stoma patients. Eight of 32 patients (25%) underwent stoma reversal, one by laparotomy. The mean time to stoma closure was 5.3 ± 2.8 months with a morbidity rate of 4.5%. As noted in **Table 2**, multivariate analysis among perioperative factors, multiple small bowel resections and multivisceral resections were significantly associated with stoma creation. **Figure 2** demonstrates Kaplan-Meier curves of overall survival (OS) after CRS/HIPEC for appendiceal and colorectal cancer based on stoma and no stoma patients. Stoma patients had more mortality at 12 months (40% vs. 20%, p < 0.001). OS after CRS/HIPEC based on end ileostomy, loop ileostomy, and colostomy creation was 38%, 75%, and 80%, respectively (p < 0.029) as noted in **Figure 3**.

Table 2. Multivariate analysis of perioperative factors associated with stoma formation at cytoreductive surgery and hyperthermic intraperitoneal chemotherapy

Prognostic factor	OR	Lower 95%CI	Upper 95%CI	P value
BMI ≥ 30 kg/m²	1.136	0.089	1.153	0.082
Albumin <3.5 gr/dL	1.471	0.459	41.322	0.200
Preoperative chemotherapy	0.358	0.360	5.682	0.611
PCI ≥10	0.696	0.617	6.526	0.247
EBL	0.001	0.999	1.002	0.239

Multivisceral resection	1.522	1.343	15.627	0.015
Small bowel resection	1.674	1.472	19.316	0.011

OR, odds ratio; CI, confidence interval; BMI, body mass index; PCI, peritoneal cancer index; EBL, estimated blood loss

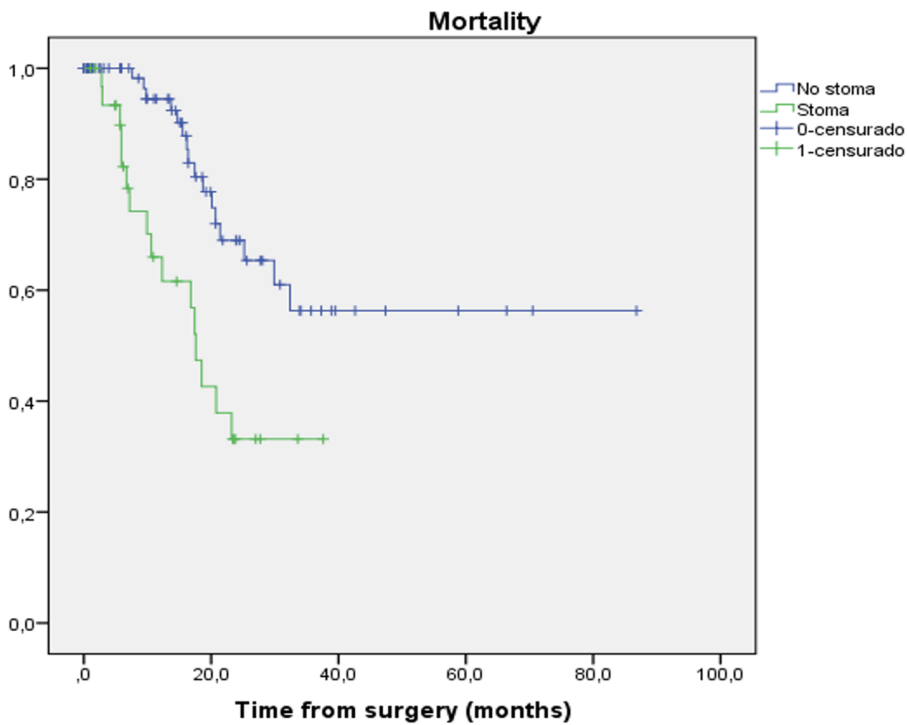


Figure 2. Kaplan-Meier curves of overall survival after at cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for appendiceal and colorectal neoplasms based on stoma and no stoma patients

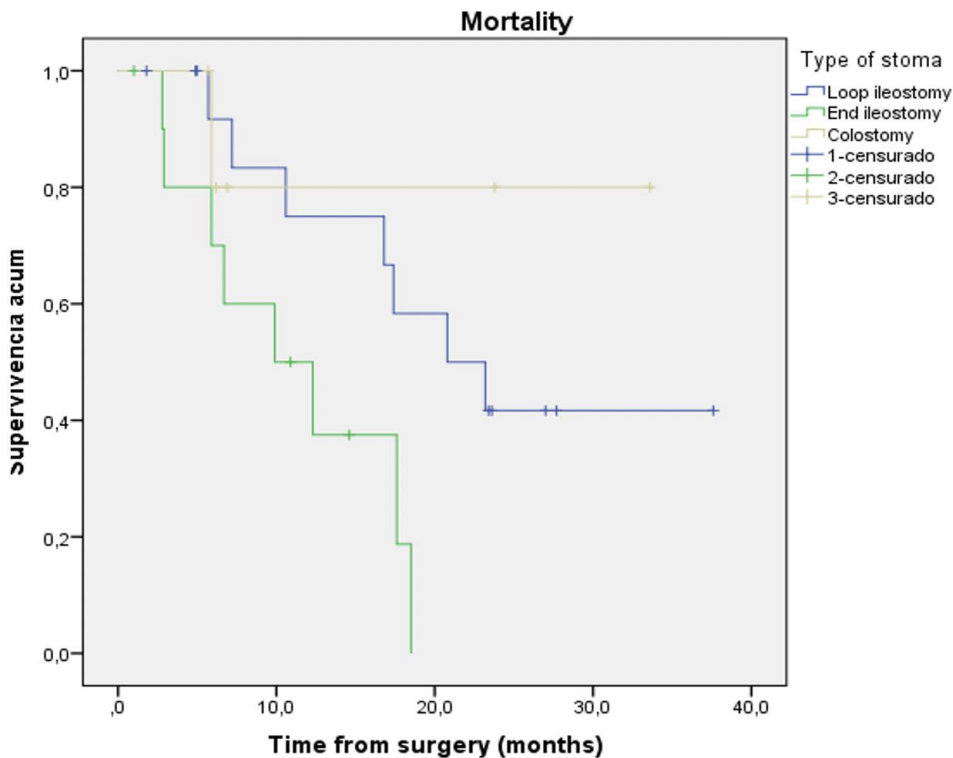


Figure 3. Kaplan-Meier curves of overall survival after at cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for appendiceal and colorectal neoplasms based on loop ileostomy, end ileostomy, or colostomy creation

Discussion

Peritoneal carcinomatosis of gastrointestinal primary origin has been considered a fatal clinical entity to be treated palliatively in the past 40 years¹. Currently, the development of surgical techniques such as CRS/HIPEC have provided new hope for a potential increase in overall survival in select patients¹⁻⁷. Although CRS/HIPEC is still considered a complex and high-risk procedure, it is associated with an acceptable morbidity and mortality^{4,5,8,9}. Achieving complete cytoreduction (CC-0, CC-1) is crucial as it has been shown to correlate with prognosis^{10,16}.

Formation of stoma via diverting loop ileostomy or colostomy as part of CRS/HIPEC is a technique frequently used to protect a high-risk anastomosis and may be an effective tool in reducing leaks, thus decreasing the postoperative morbidity¹⁰⁻¹². In the past, colorectal anastomoses required a diverting ileostomy in 50% of these patients, and its incidence was reduced to 7%¹⁷. In our series, we identified 29.1% of patients with stoma formation, higher than some studies in the literature at 17%¹⁰, and 4.8%¹⁸, but in keeping with what other authors have described¹⁹. The majority of stoma patients in our study had rectosigmoid colon resection (46.9%) with ileorectal, colorectal or coloanal anastomoses^{11,12}. The majority of our patients with right colon or appendiceal neoplasms underwent CRS/HIPEC with ileocolic anastomosis and no diversion, similar to what other studies have described¹².

In pelvic cytoreduction with rectal resection, the resection margin usually is just below the peritoneal surface; therefore, rectal resections in CRS/HIPEC are more likely high anterior resection than low anterior resections. With this in mind, a colostomy may not be necessary in all cases²⁰. In our study, we identified 18.7% of colostomies, lower than previously published (21%)¹⁰. Loop ileostomy was 46.9%, also lower than other studies (67%)¹⁰, and end ileostomy 34.4%, higher than other studies (12%)¹⁰. Verwaal et al. performed a protective colostomy in 42% of their patients, but complications occurred in almost 18% of them despite the stoma^{20,21}. Furthermore, Sugarbaker suggested that preservation of a 10–15 cm length of rectum allows a two-layered anastomosis which may reduce the need for diverting ileostomy in patients who undergo CRS and HIPEC¹¹.

In the current series, preoperative factors significantly associated with stoma formation included rectal tumor (21.9%), non-obese patients (BMI <30), malnutrition defined as hypoalbuminemia (albumin <3.5 gr/dL), higher CEA, and neoadjuvant chemotherapy. Even though a defunctioning stoma is feasible in most cases, it may be difficult in edematous small bowel after a prolonged procedure such as CRS/HIPEC or in obese patients¹⁹. Although patients with stoma were slightly younger than patients without stoma¹², and they are more likely to be female, it was not statistically significant as other authors have reported¹⁰.

On univariate analysis we found that operations with stoma formation were more extensive. In fact, procedures requiring two or more number of anastomoses, formation

of stoma reduced the anastomotic leak (AL) rate, the morbidity, and reoperation rate, therefore, protective diverting loop ileostomy should be considered in extensive CRS/HIPEC procedures^{8,10}. In our study, patients with PCI ≥ 10 , greater cytoreduction, residual disease (CC-2, CC-3), a higher estimated blood loss (EBL), more red blood cells (RBC) transfusions, multiple small bowel resections, multivisceral resections, and re-do anastomosis were intraoperative factors that significantly led to more stoma formation. This finding is in keeping with other reports¹⁰; however, prolonged operative time (OT) was not correlated and it is similar for both groups as seen in another report¹². On multivariate logistic regression analysis among perioperative factors, multiple small bowel resections and multivisceral resections are significant factors predicting stoma formation. Our findings also raise the question of the exact impact of organs resection on patient outcome¹⁰. Otherwise, a study regarding this issue showed that PCI was the single most dominant factor for stoma formation²².

Intuitively, patients with higher PCI undergo more extensive surgery (more bowel and solid organ resections) in order to render the patient CC-0 status, and thus these patients are at higher risk of complications^{4,23,24}. In the present study, the incidence of complications was slightly higher among patients who required stoma, although it was not statistically significant¹⁰. Overall, AL occurred in 3 cases (2.7%) which is lower than other reported series (7.5%-12.3)^{8,10,12,18}. CRS with HIPEC can take up to 12 hours and frequently requires large-volume resuscitation during and after the operation. After CRS and HIPEC, patients often have significant fluid shifts, development of pleural effusions, and requirement of peritoneal drains¹². Nonetheless, within the body of CRS and HIPEC literature, the anastomotic leak rate is reported to be as high as 10%²⁵, but most of the studies included all intestinal anastomoses and did not focus on high-risk pelvic anastomoses¹².

Our patients with stomas had significantly more intra-abdominal abscess and surgical site infections, as well as higher severity of morbidity (Clavien-Dindo class 3 and 4) and reoperation rate. Surprisingly, postoperative ileus was not significantly lower for stoma patients. Patients in the present series received a mitomycin C-based regimen for HIPEC, and the literature contains evidence that intraperitoneal administration of this drug may reduce postoperative adhesion formation²⁶. Conversely, a 1996 study by Jacquet and Sugarbaker²⁷ showed increased intraabdominal adhesions after intraperitoneal chemotherapy with mitomycin C. Consequently, we assume that the difference in stoma-related morbidity rate is attributable to higher volume of disease in the stoma group that required multiple organs resections and GI anastomoses, and not to the creation of the stoma itself. Previous studies on extreme CRS/HIPEC (defined as either resection of ≥ 5 organs or ≥ 3 bowel anastomoses) showed that extensive CRS/HIPEC procedures are associated with higher major morbidity, including greater rate of intra-abdominal abscess/leak, and inferior oncological outcomes²⁴, whereas other studies have shown lower rate of severe morbidity (41 vs. 6%) and

lower reoperation rate (28 vs. 0%) for patients who underwent stoma creation¹⁰. Unlike our study, other reports established that loop ileostomy may be omitted for patients with low risk for AL after colorectal resection in experienced centers with adequate postoperative care, possibilities for postoperative assessment and radiological intervention to avoid stoma-related complications and increase the quality of life of patients with peritoneal metastases¹⁷.

Overall, 8 of our patients (25%) underwent stoma reversal²², which is not on par with previous studies reporting stoma closure rates of approximately 70% for colorectal cancer^{12,28}. However, other studies of CRS and HIPEC patients have reported lower rates of stoma reversal although still higher than ours (44%)¹⁰. They grouped both loop and end stomas (colostomy and ileostomy) together, which likely explains the low reported closure rates^{22,29}. Only one bowel continuity restored required a laparotomy for reversal due to dense adhesions, much lower than 18% of previous publications¹². Among patients with stoma reversal, only one was non-loop ileostomy and 5 of whom had complications treated non-operatively; four patients had postoperative ileus, one patient fistula, and anastomotic leak rate of 0% after ileostomy closure, lower than other publications²², reporting a morbidity rate for stoma reversal up to 50% which is similar to other publications¹². Overall morbidity rate of stoma reversal was 4.5%, more than 1.6% reported by other authors¹⁰. No patients died due to stoma reversal, whereas other authors reported a 30-day mortality rate of 4.7%¹². Avoiding excess of intestinal discontinuity, mean time to stoma closure in our series was 23 weeks, which is similar to what other authors have reported¹². As expected, factors to avoid stoma reversal were formation of non-loop ileostomy and evidence of disease progression¹⁰. Non-reversal of loop ileostomy was considered very poor survival¹³.

This study has some limitation including its retrospective nature and the heterogeneity of the pathology/location. In addition, these patients were treated at a high-volume

center with quaternary ancillary services, which leads to better resolution of complications and makes the results less generalizable with other lower volume centers.

Conclusions

Patients with appendiceal or colorectal neoplasms with higher carcinomatosis burden requiring major cytoreductive surgery and RBC transfusion are more likely to have stoma constructed in CRS/HIPEC procedure. Only one quarter of the patients with a diverting ileostomy in this study had bowel continuity restored within 6 months after their index operation highlighting the importance of preoperative counselling. Diverting ileostomy reversal required a laparotomy in one case due to dense adhesions and had an associated overall morbidity rate of 4.5%. The use of protective stoma should be considered in extensive CRS/HIPEC procedures requiring multiple bowel resections although additional studies are needed to evaluate risk factors for anastomotic leak.

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