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Perioperative Management of Patients Undergoing CRS and HIPEC

Akhil Chawla[1], Cheng-Cheng Zhu[2], Grant Backer[3], Julia O'Gara[3], Zhi ven Fong[3], Hao M Deng[2], Xiaodong Bao[2], James C Cusack[3]*

[1]Department of Surgery, Division of Surgical Oncology, Northwestern University Feinberg School of Medicine, USA

[2]Department of Anesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital, USA

[3]Department of Surgery, Division of Surgical Oncology, Massachusetts General Hospital, USA

Abstract

Background and Objectives: We conducted a retrospective review to assess the outcomes of our initial five-year experience of Cytoreductive Surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) at the Massachusetts General Hospital.

Methods: A prospective database was maintained to understand the effect of our multidisciplinary approach using a dedicated perioperative anesthesia and nursing team and goal-directed fluid-restrictive resuscitation for CRS and HIPEC performed with 40 mg of mitomycin C at 42°C for 90 min. ERAS protocol included strict fluid-replacement guidelines, early ambulation, and early resumption of enteral intake.

Results: We performed 97 cases from 2011-2016. The median PCI was 14.5. Completeness of Cytoreduction score was 0 or 1 in 88.5%. Patients had a median estimated blood loss of 300 mL with a transfusion requirement in 14.4% of patients. 88.7% of patients were extubated immediately postoperatively. The intraoperative complication rate was 4.1%. The median ICU and hospital stays were 2 and 8 days, respectively. The 30-day readmission rate was 16.5%. The 90-day mortality rate was 0%.

Conclusion: The outcomes from our initial experience using a multidisciplinary approach in patients undergoing CRS and HIPEC demonstrate short postoperative ICU and hospital stays, acceptable postoperative morbidity and readmission rates, and low perioperative mortality.

Keywords: Cytoreductive surgery; Hyperthermic intraperitoneal chemotherapy; Pseudomyxoma peritonei; Enhanced recovery after surgery

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Correspondence:

James C. Cusack., Jr., M.D., Department of Surgery, Massachusetts General Hospital, Yawkey Building 7th Floor, 55 Fruit Street, Boston, MA 02214, USA, Tel: (617) 724-4093; E-mail: jcusack@mgh.harvard.edu

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Introduction

The treatment of peritoneal surface malignancies has evolved significantly over the past three decades. Prior to the use of Cytoreductive Surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC), the discovery of peritoneal metastases was broadly regarded as a lethal condition. In the current era, national guidelines offer CRS and HIPEC as an option for patients with isolated peritoneal disease, specifically for metastatic colorectal cancer and appendiceal mucinous neoplasms [1,2]. Furthermore, for the first time, recently reported randomized phase III prospective data have supported the use of HIPEC plus CRS in metastatic ovarian cancer patients, demonstrating its superiority in terms of recurrence-free survival and overall survival over CRS alone [3].

With the increasing use of CRS and HIPEC, there has been a surge in the establishment of centers specializing in this multidimensional treatment modality. This concentration of care at dedicated peritoneal surface malignancy centers has allowed for better surgical outcomes, which are well-known to be driven by the association of case volume in a field burdened by nontrivial morbidity and mortality [4]. The optimal number of patients required to achieve volumes which predict favorable oncologic and operative outcomes range in the literature between 73 to 180 [4-6]. Much like other complex disease entities, the evolution of the treatment of peritoneal disease by CRS and HIPEC has also seen a change in morbidity and mortality rates over time. With the early reports of HIPEC citing mortality rates as high as 9% [7], Sugarbaker et al. were one of the first to establish the procedure as one with an acceptable toxicity profile with the reporting of their

prospective experience, citing morbidity and mortality rates of 27% and 2.7%, respectively [8].

The Massachusetts General Hospital began its experience in CRS and HIPEC in 2011. We began our effort with the establishment of a multidisciplinary team involving members crucial to the success of the program, which included Surgical Oncology, Anesthesia and Critical Care, as well as the perioperative nursing staff. The protocolization of an anesthesia-driven stringent fluid-restrictive method of resuscitation, a dedicated nursing team assigned to all HIPEC cases, experienced pump technicians, as well as the addition of an Enhanced Recovery After Surgery (ERAS) pathway in 2013, have all together contributed to the success of the program. Importantly, since its inception, we have prospectively tracked our anesthesia and surgical outcomes for quality control. Here, we report our initial five-year experience with CRS and HIPEC along with our perioperative outcomes utilizing our multidisciplinary approach.

Methods

We reviewed our prospectively maintained anesthesia and surgery outcomes database from 2011-2016. This was our initial 5-year experience with CRS and HIPEC at Massachusetts General Hospital. Clinical and pathologic data as well as postoperative outcomes were prospectively entered into an anesthesia and surgical database. Experimental protocols were approved by the Massachusetts General Hospital institutional review committee.

Preoperative management

All patients received mechanical bowel prep prior to surgery. In 2013, an ERAS protocol was introduced to guide pre- and perioperative fluid management. All patients received DVT prophylaxis including compression boots and subcutaneous heparin administration.

Anesthesia

We assembled a dedicated anesthesia and perioperative nursing team specific for CRS and HIPEC cases. With regards to protocol, a central venous catheter for central venous pressure monitoring and an arterial line placed were by anesthesia preoperatively. A strict fluid-restrictive method of perioperative resuscitation was employed. This included intraoperative infusion of Plasma-Lyte, and postoperative infusion of Lactated Ringers' solution at 1 mL per kg per hour, as well as colloid in the form of 250 mL 5% albumin boluses as needed to maintain a urine output nearing 0.5 mL per kg per hour. Postoperatively, patients would be planned for extubation if appropriate. Given the large fluid shifts associated with HIPEC and prolonged operative time needed for the operation [9], patients would require admission to the Surgical Intensive Care Unit (SICU) for a mandatory one-night stay or longer if deemed necessary, the dedicated anesthesia/critical care team would continue to follow the patient closely while in the SICU to ensure appropriate fluid-restrictive resuscitation.

Cytoreductive surgery

CRS included a full evaluation of the burden of metastatic disease upon exploration, with the goal of removing all visible disease, and, if not previously performed, resection of the primary tumor. Laparoscopic exploration was performed sparingly to evaluate the extent of carcinomatosis prior to CRS and HIPEC. Patients deemed suitable for CRS were those in which removal of all macroscopic disease was deemed possible using a combination of resection, stripping, and ablation. Patients that were deemed unsuitable were generally those who progressed on systemic chemotherapy, had poor functional status, had unresectable disease burden due to location of metastases within liver, small bowel mesentery, and/or serosal surface of the small bowel.

A large midline laparotomy incision was performed in most cases for CRS. To objectively document the burden of disease, the Peritoneal Cancer Index (PCI) was documented upon exploration. CRS was performed to achieve the lowest possible remaining tumor burden assessed by a post-CRS PCI assessment as well as the Completeness of Cytoreduction (CC) score. Sites of disease were systematically addressed, resecting disease in a counter-clockwise fashion beginning in the left upper quadrant of the abdomen. All areas of disease on the parietal and visceral peritoneal as well as visceral resections were performed as necessary. If bowel resection was performed, the remaining bowel was left in discontinuity until after HIPEC was completed. Anastomoses were performed in standard hand-sewn or stapled fashion followed by confirmation of hemostasis and closure of the abdomen.

Hyperthermic intraperitoneal chemotherapy

After CRS, the abdomen was temporarily closed. Infusion catheters for inflow and outflow were inserted. Flow rates were maintained by a roller pump and managed by an experienced pump technician. HIPEC was performed using 40 mg of mitomycin C with an average inflow temperature of 42°C for 90 min using a closed technique. Temperature was monitored with temperature probes placed into the inflow and outflow segments of the circuit, and core temperature was monitored by an esophageal temperature probe placed by the anesthesia team. The abdomen was gently massaged throughout the 90-min HIPEC period. After completion of HIPEC, the abdomen was reopened to complete any anastomoses and confirm hemostasis.

Pathology

An experienced gastrointestinal pathology team was involved in reviewing CRS cases. The primary cancer type, nodal status, grade and differentiation, as well as mucinous or signet-ring cell features were assessed during review.

Postoperative course

An Enhanced Recovery after Surgery (ERAS) protocol was implemented to streamline care of patients treated with CRS and HIPEC. After at least a one-night stay in the SICU, patients were transferred to the regular nursing floor when appropriate. Patients were aggressively encouraged to participate in early ambulation which was generally started on postoperative day 0 or 1, depending on extubation. The nasogastric tube was removed routinely on postoperative day 3 or 4, depending on the extent of the resection or at the earliest sign of bowel function, generally indicated by flatus. The following day, a clear liquid diet was initiated. Patients would be discharged home on a full liquid diet for 1 week, after which a soft solid diet was introduced, followed by out-patient follow up with the surgeon at three weeks. A nurse practitioner would be assigned to contact the patient within the first five days of discharge to ensure the patient was progressing appropriately.

Outcomes

Peri-operative outcomes including length of stay, perioperative complications, readmission and mortality were documented in the prospectively maintained database.

Table 1: Patient characteristics.

Patient Characteristics	Median/total (Interquartile Range/ Percentage)
Age (years)	55 (43.5-63.5)
Sex, male	45 (46.4%)
ASA	
1	2 (2.1%)
2	43 (45.3%)
3	46 (48.4%)
4	4 (4.2%)
Clinical History	
History of ascites	14 (14.4%)
Ischemic heart disease	2 (2.1%)
Diabetes mellitus	4 (4.1%)
Previous Abd. Surgery	90 (92.8%)
Previous systemic chemotherapy	52 (54.6%)
Previous radiotherapy	2 (2.1%)
Postoperative Cr	0.88 (0.72-1.1)
Postoperative Hb	8.40 (7.5-10.6)
Postoperative INR	1.2 (1.1-1.3)

Statistical analysis

Descriptive statistical analyses were performed on all predefined outcomes. Continuous variables were summarized and reported using median and Interquartile Range (IQR). Categorical variables were reported using frequencies and relative percentages.

Results

Patient characteristics

In total, 97 patients underwent both CRS and HIPEC at Massachusetts General Hospital within the first five years of our experience. Patient characteristics are shown in Table 1. The median age of was 55 years with 46.4% of patients being male. Most patients had an American Society of Anesthesia (ASA) score of 2 or 3 (93.7%). Of the 97 patients that underwent CRS and HIPEC, 90 had undergone a previous abdominal surgery in the past. These operations included those in which the diagnosis of peritoneal metastases was made, the primary tumor was resected, diagnostic laparoscopy was performed to assess the burden of disease, or in which a laparotomy or laparoscopy was performed for an unrelated reason. Out of all patients, 54.6% had undergone previous systemic chemotherapy. Only 2 of 97 patients underwent prior radiotherapy. Postoperative laboratory values are shown in Table 1 as an indication of postoperative organ function.

Anesthesia outcomes

Using a fluid-restrictive method of resuscitation, the median amount of fluid infused intraoperatively was 5000 mL, of which a median of 4500 mL was Plasma-lyte infusion, and a median of 500 mL was colloid infusion. The median urine output for all patients during the case was 750 mL. The median case length from the time of patient entrance into the operating suite to the time of extubation was 517 min or 8.6 h.

The estimated blood loss was 300 mL and ranged from "minimal" which was counted as 0 mL to 3000 mL in one case. As such, given the low amount of blood loss in combination with fluid-restrictive resuscitation, only 14 of 97 (14.4%) patients needed any blood

Table 2: Anesthesia characteristics.

Anesthesia Characteristics	Median/total (Interquartile Range/ Percentage)
Infusion	
Crystalloid (mL) Colloid (mL)	4500 (3000-5500) 500 (0-1000)
Urine output (mL)	750 (545-1155)
Estimate blood loss (mL)	300 (200-700)
Any transfusion needed	14 (14.4%)
PRBC transfusion needed	11 (11.3%)
Units PRBC transfused	0 (0-0)
Length of case, in-room to extubation (minutes)	517 (401-616)
Immediate extubation postoperatively	86 (88.7%)

Table 3: Intraoperative characteristics.

Intraoperative Characteristics	Median/total (Interquartile Range/ Percentage)
Peritoneal Cancer Index	14.5 (7-323)
Completeness of Cytoreduction Score	
0	43 (44.3%)
1	39 (40.2%)
2	7 (7.2%)
3	3 (3.1%)
Resections performed	
Small bowel (SB)	31 (32.0%)
Colon	45 (46.4%)
Rectum	25 (25.8%)
Spleen	18 (18.6%)
Pancreas	1 (1.0%)
Gallbladder	9 (9.3%)
Bladder	1 (1.0%)
Greater omentum	72 (74.2%)
Lesser omentum	19 (19.6%)
Liver metastasectomy	10 (10.3%)
Partial gastrectomy	4 (4.1%)
Uterus	14 (14.4%)
Ovary (or ovaries)	12 (12.3%)
Parietal peritoneum	47 (48.5%)
Pelvic peritoneum	51 (52.6%)
Omental bursa	36 (37.1%)
Other	15 (15.5%)
Anastomoses performed	
SB-SB	5 (5.2%)
Gastro-SB	1 (1.0%)
SB-Colon	45 (46.4%)
Colocolonic	4 (4.1%)
Colorectal	19 (19.6%)
Intraoperative complications	4 (4.1%)
Need for ostomy	
Temporary colostomy	1 (1.0%)
Permanent colostomy	0 (0%)
Temporary ileostomy	23 (23.7%)
Permanent ileostomy	1 (1.0%)

product transfusion, of which 11 (11.3%) were transfused Packed Red Blood Cells (PRBC). The median number of units of PRBC given for all patients was 0. The vast majority of patients, 88.7%, were extubated immediately after completion of the operation (Table 2).

Intraoperative outcomes

The median PCI upon exploration was 14.5. Out of all patients, CC was 0 in 44.3%, 1 in 40.2%, and either 2 or 3 in 10.3%.

Multi-organ resection was not uncommon during CRS in order to address all disease burden (Table 3). In terms of bowel resections, colon resection was performed in 46.4%, proctectomy in 25.8% and small bowel resection in 32%. The most commonly performed anastomosis was small bowel to colon, which was performed in 45 of the 97 patients. A colorectal anastomosis was performed in 19 patients of the 97 patients. 25 patients required an enterostomy and 23 patients required temporary diverting ileostomies. These ileostomies were primarily for the purposes of protecting low rectal anastomoses after low anterior resection.

Omentectomy was always performed when tumor was present (74.2%), as this was critical to reducing disease burden in patients with peritoneal metastases. All parietal and visceral peritoneum with macroscopic disease was stripped and removed, which often included Glisson's capsule. However, in 10 patients, liver parenchymal resection was performed in order to ensure margin-negative resection. The spleen was the most often resected solid organ and was resected in 18.6% of patients. Hysterectomy was performed in 14 and oophorectomy was performed in 12 of the 52 females in the study.

The overall rate of intraoperative complications was 4.1%. The four complications which occurred intraoperatively were the following: One patient had a brief period of hypoxia in which a postoperative transthoracic echocardiogram demonstrated right heart strain. Another patient developed temporary ventricular fibrillation during fascial closure which subsequently stabilized. One patient developed a rash which was noticed at the completion of surgery. The source of this rash was not identified. Finally, one patient developed gastrointestinal bleeding secondary to a staple line bleed which was discovered after 60 min of HIPEC. This was quickly addressed, and the total intended 90-min period of HIPEC for this patient was not completed. The remainder of the 93 patients in this study did not have an intraoperative complication.

Pathology

The pathologic characteristics of the cohort are summarized in Table 4. The primary site of malignancy of the 97 patients was appendiceal in origin in 55 patients (56.7%). Out of these, 22 were appendiceal mucinous neoplasms and 33 were appendiceal adenocarcinomas. Colorectal adenocarcinomas accounted for the next most common type of primary pathology, totaling 26 patients (26.8%), of which 24 were colon and 2 were rectal in origin.

There was a broad range of nodal disease information available. Nodes were most often harvested with the intent of reducing disease burden when the primary tumor was being resected along with CRS. However, when enterectomy was being performed for disease burden on the serosa or mesentery, it was done by including the associated nodal basin by high ligation. In addition, nodal tissue was harvested at other common locations when indicated including the hepatoduodenal ligament, retroperitoneum, gastroepiploic arcade, and pelvis. The median number of nodes examined by pathology was 16.5. The median number of nodes in which malignancy was identified was 0.5.

Table 4: Pathology.

Pathology	Median/total (Interquartile Range/ Percentage)
Primary Cancer	
Appendiceal mucinous neoplasm	22 (22.7%)
Appendiceal adenocarcinoma	33 (34.0 %)
Colon	24 (24.7%)
Rectal	2 (2.1%)
Mesothelioma	8 (8.3%)
Small bowel	1 (1.0%)
Other	6 (6.2%)
Unknown	1 (1.0%)
Lymph node status	
Total positive nodes	0.5 (0-4)
Total nodes examined	16.5 (9-26)
Cytoreduction	
Mucinous features	47 (48.5%)
Signet cell features	8 (8.2%)
Well differentiated adeno.	23 (23.7%)
Mod. differentiated adeno.	10 (10.3%)
Poorly differentiated adeno.	16 (6.2%)

In terms of pathology of the peritoneal metastases, mucinous features were identified in 48.5% of patients. Signet ring cell features were identified in 8.2% of patients. Peritoneal metastasis were graded according to the highest grade identified within the specimen and was found to be well-differentiated in 23.7%, moderately differentiated in 10.3%, and poorly differentiated in 6.2% of patients.

Postoperative outcomes

Using the ERAS-protocol, post-operative outcomes were acceptable and are displayed in Table 5. As patients were required to have at least a one-night stay in the SICU, the median ICU Length of Stay (LOS) was 2 days, and the median total hospital LOS was 8 days. The total hospital LOS was most commonly dependent on the time to resumption of oral intake.

The median time to nasogastric tube removal was 3 days with resumption of oral intake by clear liquid diet occurring at a median of 4 days. In a minority of patients (17.5%), enteral nutritional intake was not adequate at postoperative day 7 and thus required total parenteral nutrition *via* a peripherally inserted central catheter with which the patient was discharged. In only one patient, enteral supplementation in the form of tube feeds was used. Only one patient in our cohort was discharged to a skilled nursing facility, and not home.

The most common complication which occurred within thirty days of CRS and HIPEC was a pleural effusion. This occurred in 41.7% of all patients. However, the extent to which this was clinically significant and needed drainage was only present in 6.2%. The other common complication which occurred within thirty days was hematologic in origin and reflected a commonly seen side effect of HIPEC [10]. These hematologic toxicities included low cell counts of white blood cells, platelets, or neutrophils. Out of 97 patients, venous thromboembolism was seen in 4 patients, of whom 3 had Pulmonary

Table 5: Postoperative characteristics.

Postoperative Characteristics	Median/total (Interquartile Range/ Percentage)
Length of Stay (LOS)	
ICU LOS (days)	2 (1-3)
Total hospital LOS (days)	8 (7-11)
NGT removal (postoperative day)	3 (2-5)
Resumption of PO intake (postoperative day)	4 (3-6)
Need for tube feeds	1 (1.0%)
Need for parenteral nutrition	17 (17.5%)
30-day reoperation	
Overall rate	6 (6.2%)
30-day postoperative complications	
Hematologic	21 (21.9%)
Bleeding	5 (5.2%)
Wound infection	5 (5.2%)
Wound dehiscence	3 (2.7%)
Pneumonia	3 (3.1%)
Pleural effusion	40 (41.7%)
Drained pleural effusion	6 (6.2%)
Myocardial infarction	2 (1.8%)
Respiratory failure requiring intubation	1 (1.0%)
Deep space infection	3 (3.2%)
Pancreatitis	1 (1.0%)
Fistula	2 (2.1%)
Anastomotic leak	6 (6.2%)
PE	3 (3.2%)
DVT	1 (1.0%)
Clavian Dindo Classification	
Grade I	71 (73.2%)
Grade II	16 (16.5%)
Grade IIIa	4 (4.1%)
Grade IIIb	5 (5.2%)
Grade IV	1 (1.0%)
Discharge disposition	
Home	94 (99.0%)
Facility	1 (1.0%)
30-day readmission	16 (16.5%)
30-day mortality	0 (0%)
90-day mortality	0 (0%)

Embolism (PE) and 1 had Deep Vein Thrombosis (DVT). However, it is not known in these cases if venous thromboembolism was present prior to CRS and HIPEC. In terms of Clavian-Dindo grading of complications, there were 71 grade I, 16 grade II, 4 grade IIIa, 5 grade IIIb, and 1 grade 4 complication. Over 90% of patients were able to graduate from close surgical oncology follow-up and return to their medical oncologist for their intended systemic treatment at a median of 90 days.

The thirty-day readmission rate was 16.5%. The thirty and ninety-day mortality rate was 0%. Median follow-up from date of surgery was 35.1 months. Median overall survival was 44.6 months for the entire cohort of patients.

Discussion

We report the initial five-year experience in CRS and HIPEC for peritoneal surface malignancies at the Massachusetts General Hospital. We organized a multidisciplinary team to establish perioperative protocols to guide the care of our clinicians. Using fluid-restrictive resuscitation, a dedicated anesthesia and perioperative nursing team, and establishing protocols to guide postoperative management of patients undergoing CRS and HIPEC led to short postoperative ICU and hospital stays, acceptable postoperative morbidity and readmission rates, and low perioperative mortality. These tools may be implemented by institutions which are developing a program in peritoneal surface malignancies and to enhance outcomes for patients with CRS and HIPEC.

The utilization of a fluid restrictive method of resuscitation during abdominal surgery has been shown to increase tissue perfusion, improve pulmonary function, and decrease postoperative complications [11-14]. From the onset of our experience in CRS and HIPEC, this critical component was a hallmark of our perioperative management and was guided by the anesthesia department. A specified team of anesthesiologists was assigned to all CRS and HIPEC cases and followed these patients into their postoperative course ensuring standardized management in the SICU. Given that CRS requires meticulous technique and thorough exploration to achieve an R0 resection; these cases are often burdened with long anesthesia times in addition to the time needed for HIPEC. In our cohort, the median time of CRS and HIPEC was 500 min, including time for induction, line placement, cystoscopy and ureteral stent placement in many cases and extubation postoperatively. HIPEC is known to cause significant fluid changes throughout infusion and can pose challenges in the form of major hemodynamic shifts, lactic acidosis, fluid balance, and thermal variations [15-17]. Traditional resuscitative methods call for a maintenance of urine output of at least 100 mL every 15 min sustained by colloid and crystalloid infusion of up to 1800 mL per hour [17]. Given our experience in fluid restrictive resuscitation in other disease sites, we hypothesized that restricting fluid may specifically benefit patients with CRS and HIPEC who are particularly susceptible to perioperative morbidity. Given this premise, we maintained end-organ perfusion intraoperatively using Plasma-lyte, which has isotonic properties and a "balanced" profile in terms of its relationship with blood plasma, and furthermore avoids supraphysiologic blood levels of chloride which can lead to kidney injury [18,19]. This is particularly meaningful for preventing or reducing lactic acidosis which develops as a side effect of HIPEC, thus avoiding large fluid boluses for correction. Additionally, postoperatively, we utilized low-volume colloid boluses in the form of 250 mL of 5% albumin as needed, in order to resuscitate patients based on low urine output as a marker of end-organ perfusion, allowing for quicker volume expansion in the intravascular space [20]. In addition to meticulous technique during CRS, our low EBL may also partly be attributed to by the use of low-volume resuscitation, which limits hemodilution and hypothermia which has been shown to compromise coagulation and worsen blood loss [21,22]. Almerey et al. [23] have demonstrated that the use of fluid restriction during HIPEC contributes to low volumes of PRBC transfusion and low Clavian-Dindo grade III-IV events, similar to what we have demonstrated.

Our postoperative outcomes, while certainly are contributed

to by a combination of anesthesia, surgical and ICU management, are also benefited by the introduction of our ERAS protocol. Our management protocol defines a limited stay in the SICU, early patient mobilization due partly due to timely discontinuation of the Foley catheter and monitoring devices, as well as better availability of mobility assistance by nursing staff and physical therapy. While the use of HIPEC is associated with high rates of post-operative ileus which oftentimes leads to readmission [24], our median time to NGT removal and resumption of oral intake were 3 and 4 days, respectively. A minority of patients required a need for parenteral nutrition which was used as a bridge to enteral nutrition when needed and could be easily administered at home. We educated patients with a nutritionist during the hospital stay and instructed all patients to remain on a full liquid diet for one week after discharge before progressing to a soft solid diet. This diet was reassessed during the postoperative visit with the surgeon and advanced or kept the same depending on recovery of bowel function and symptomology. An additional tool which we implemented was the use of a nurse practitioner to call our patients after discharge during the first week, to not only ensure adequate recovery from surgery, but to also address any issues or questions regarding diet and fluid intake that could be managed at home, avoiding a visit to the emergency room, or even a potential readmission. We believe this had a significant effect on reducing our 30-day readmission rate of 16.5%.

Our most common complications included pleural effusion and hematologic pathology. These have been well described complications after HIPEC [25-27]. In terms of Clavian-Dindo classification of complications, out of 97 patients, we had 4 grade IIIa, 5 grade IIIb, and 1 grade 4 complication which is in line with other reports [23,28]. Our rate of reoperation was 6.2%.

The uniformity of treatment of all patients by a single surgeon at one institution using a protocol based approach, as well as one type of intraperitoneal chemotherapy agent for all cases should be underscored as a strength of this report, as it controls for many of the variables which would make such results uninterpretable. However, our study has certain limitations. First, this retrospective study defines a period of time during which our volume in terms of CRS and HIPEC increased as a referral center. Thus, our perioperative outcomes reflect both the earlier as well as the latter portion of the experience, during which we had gained valuable insight in caring for such patients. Secondly, based on our data, we were not able to define specific numerical limits to infusion volume in terms of the resuscitation that are ideal. Rather, this report is purposed to highlight the important themes that we implemented, including fluid restriction, dedicated anesthesia and nursing care teams, and post-operative treatment protocols, which when delivered as a package, allowed for desirable outcomes in an initial experience with a morbid procedure.

Take home points for developing a new peritoneal surface malignancy program from this single-institution initial experience include the following: Firstly, for those charged with developing the program should visit and subsequently be proctored by others who have similarly established a program. There should be a standardized communication scheme with anesthesia providers that begins the day before surgery in order to establish goals for the case. In terms of technical caveats, it is important for less experienced surgeons to liberally use the services of their colleagues from other specialties. As an example, challenging hysterectomies were originally performed with help from our gynecology colleagues, and we have now migrated away from that practice and generally perform these ourselves. Ureteral stents should be used liberally as well particularly when involvement is suspected on the basis of CT imaging. Urology should perform procedures such as ureteral and bladder dome reconstructions, unless there is experience in these procedures by the primary surgeon. In terms of minimizing blood loss, temperature management is key. Aggressively warming the patients with the help of forced air warming blankets until the start of HIPEC should be a goal in order to keep patients normothermic.

Conclusion

Taken together, our data highlight the value of fluid-restrictive resuscitation, the assignment of a dedicated CRS/HIPEC perioperative team, and a perioperative ERAS protocol in delivering care with acceptable perioperative morbidity and mortality to patients with peritoneal disease. This report may be used as a guide to enhance quality and perioperative outcomes for HIPEC programs under development or in their infancy. Future work to further enhance perioperative outcomes in such patients should include multi-institutional collaboration.

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