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Outcomes of complex abdominal wall reconstruction at the time of CRS and HIPEC

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ABSTRACT

Introduction: Cytoreduction Surgery with Hyperthermic Intraperitoneal Chemotherapy (CRS/HIPEC) is a treatment option for patients with peritoneal metastatic cancer. This procedure has been shown to improve survival, however, patients are often left with abdominal wall and soft tissue defects requiring further surgical correction. We aim to assess the safety and clinical outcomes of abdominal reconstruction performed concurrent with CRS/HIPEC.

Methods: We conducted a retrospective chart review on patients with peritoneal metastases who received CRS/HIPEC therapy and abdominal wall reconstruction at tertiary center from 2012 to 2018. Records were evaluated for the patient characteristics, oncologic history, operative details, and postoperative course. Complications were graded with the Clavien-Dindo classification.

Results: Five patients aged 29–54 years old met the inclusion criteria. The most common type of cancer within this cohort was colorectal cancer. To close the abdomen, four patients underwent component release, biologic mesh placement, and primary fascial closure. The last patient was closed with adjacent tissue transfer. Two patients experienced Grade I complications: deep vein thrombosis and leukocytosis (both self-resolved). Three patients experienced Grade II complications: atrial fibrillation, anemia, and a wound infection which required readmission. No patients experienced grades III, IV or V complications. The follow up period was a median of 5.3 months [r: 2.6–21.9 months].

Conclusion: The patients benefitted therapeutically from combined abdominal reconstruction and CRS/HIPEC with minimal complications and good long-term survival. We advocate for the coupling of these procedures as the benefits outweigh the risks, and allows wound closure at the time of surgery.

1. Introduction

Cytoreduction with Hyperthermic Intraperitoneal Chemotherapy (CRS/HIPEC) presents a promising treatment option for patients with advanced abdominal cancer and peritoneal metastases. It may improve the poor survival outlook of this population [1]. Aggressive cytoreduction is first done to surgically excise visible tumors and cancer cells. Chemotherapy is administered directly to the peritoneal surface immediately following the surgery to eradicate microscopic disease and decrease the chances for cancer cell regrowth. Following this procedure, patients are often left with muscle, fascial and soft tissue defects that require abdominal wall reconstruction and complex closure. Correction of these defects may minimize wound infections and improve patient survival.

Successful reconstruction relies on the assessment of any muscle loss and soft tissue deficit. Abdominal wall reconstruction has progressed since the component separation technique was first described by Ramirez et al. [2]. The technique of component separation has been adapted to include the use of adjunct modalities, such as acellular dermal matrix (mesh) or negative therapy pressure, when necessary to repair a wide array of abdominal wall defects [3]. The main goals of a successful reconstruction include restoration of abdominal wall integrity including muscle and soft tissues, and prevention of hernia formation and evisceration in order to prevent recurrent hernia and infection. A prior study investigated the management of complex abdominal wall defects found the hernia recurrence rate was lower in

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Table 1
Patient characteristics.

Case	Age/ years	Gender	BMI	Diagnosis	PCI	Previous chemotherapy	Previous radiation	Previous tumor resection	Hernia present	Hernia type
1	29	F	24	Colorectal	< 5	Y	Y	Y	N	–
2	35	F	46	Colorectal	10	Y	N	Y	Y	Incisional
3	49	F	30	Mucinous appendiceal neoplasm with pseudomyxoma peritonei	32	Y	N	Y	Y	Multiple incisional
4	54	F	28	Mesothelioma	10	Y	N	Y	N	–
5	52	M	28	Colorectal	20–25	Y	N	Y	N	–

F – female, *M* – male, *Y* – yes, *N* - no.

patients who underwent component separation with mesh reinforcement compared to those without component separation or mesh reinforcement. Furthermore, a lower rate of infection after component separation compared to primary closure was found [3].

Use of component separation technique and biologic mesh for abdominal wall reconstruction has proven to be successful for preventing ventral hernias in otherwise healthy patients [4], its success as a technique for tissue that has previously been subject to irradiation, chemotherapy, and immunosuppression is still unknown. In this study, we report our experience in performing combined CRS/HIPEC and abdominal wall reconstruction. Additionally, we aim to determine the safety and clinical outcomes of this unique population.

2. Methods

Our Institution Review Board approved the conduction of a retrospective chart review of all patients who had undergone abdominal reconstruction at time of CRS/HIPEC in 2012–2018 at a single center, tertiary university hospital. Patients were identified through a search in the UMMS database and subsequent chart review was performed on the identified patients. Prior to their operations, the patients attempted previous management of their respective cancers. All had at least one cycle of chemotherapy and most of the patients had received previous tumor resection. Lack of success of chemotherapy or tumor reoccurrence prompted these patients to be considered for a combined HIPEC/CRS and abdominoplasty treatment.

Data were collected on patient characteristics, preoperative cancer grading, length of hospital stay, post-operative complications, and 90-day readmission rate. Complications were classified by the Clavien-Dindo system [5]. All patients included in the study were evaluated by the Peritoneal Cancer Index (PCI), a cancer grading system which preoperatively grades 13 abdominal regions based on the largest tumor size in that region [6,7]. The PCI evaluates the extent of cancer metastases throughout the peritoneal cavity. The Cytoreduction Score (CCR) represents the success of treatment to decrease the tumor.

2.1. Operative technique

A multidisciplinary team approach was used for all surgeries with the inclusion of both surgical oncology and plastic surgery teams. The patients were taken to the operation room and cytoreduction was accomplished first, wherein the abdomen was explored, and all possible tumor burden was resected. The completeness of cytoreduction is assessed by a CCR Score where CCR grades 0–1 represent complete cytoreduction and CCR grades 2–3 represent incomplete cytoreduction. CCR0 indicates that no macroscopic residual disease remains, and CCR1 indicates that residual tumors less than 2.5 mm remain [6]. Following cytoreduction, HIPEC was performed.

Finally, the abdominal wall was reconstructed by components separation. All abdominal wall reconstructions were performed by a plastic surgeon. To perform abdominal wall reconstruction to address the muscle layer an assessment was made on fascial and muscle deficit, in addition to the need for soft tissue reconstruction. Bilaterally, the skin and subcutaneous planes were elevated from the underlying musculature and a plane between the internal and external obliques was created to allow muscle advancement to the midline. If Strattice biologic mesh was used to reinforce the repair, it was inset with anchoring sutures to offset the tension on the incision line. Local tissue transfer was performed to address any soft tissue defect. The incisions were closed with interrupted figure-of-eight sutures allowing soft tissue to be reapproximated. An incisional wound vacuum-assisted device was then applied. Progressive tension sutures were placed along the lateral abdominal wall to secure the skin flap in place.

2.2. HIPEC regimen

Inflow and outflow catheters were placed and connected to a perfusion circuit, the abdomen and skin were temporarily closed, and the peritoneal cavity was perfused with warm saline until the temperature reached 42° Celsius. Thirty milligrams of mitomycin C was added to the closed perfusion circuit for 60 min and another 10 mg was added for additional 30 min for a total dose of 40 mg of mitomycin C and a total perfusion time of 90 min. Abdominal wall reconstruction followed completion of HIPEC.

3. Results

Five patients were identified for inclusion in the study. The majority of whom were female (80%) and ages ranged from 29 to 54 years old with a mean body mass index of 30 kg/m^2 [range: 24–46]. All patients presented with peritoneal metastases. Colorectal cancer ($n = 3$) was the most common underlying malignancy followed by mucinous appendiceal neoplasm with pseudomyxoma peritonei ($n = 1$), and mesothelioma ($n = 1$). Further patient details are provided in Table 1.

Mean operative time was 584 min [range: 249–694 min]. Time for CRS/HIPEC represented 68% (399 min) of total mean operative time with abdominal reconstruction contributing only 185 min, on average, to the combined procedure (Table 2).

Mean length of hospital stay was 8 days [range: 6–13]. The post-operative course for patients is detailed in Table 3. There was 1 readmission for 1 patient within 90 days. Illustrative cases are described below. Three Grade II complications occurred in three patients, and two Grade I complications occurred in two patients. Complications were classified according to the Clavien-Dindo classification [5] and listed in Table 4.

3.1. Case 1

A 29 year old female with metastatic colon cancer underwent exploratory laparotomy, full-thickness right abdominal wall resection, omentectomy, excision of a mesenteric nodule, and HIPEC. Component release, placement of biologic mesh, and tissue transfer were performed concomitantly. To reconstruct the abdomen, components release was performed and Strattice mesh underlay was used to reinforce the right abdominal wall defect measuring approximately 10 cm × 8 cm, and the fascia was approximated in the midline over the mesh. One week

Table 2
Operative details.

Case	Total surgical time (mins)	Length of CRS/HIPEC (mins)	Length of PRS (mins)	Tissue removed	Component release	Biologic mesh	Location of mesh	iVAC present
1	249	180	69	Abdominal wall (skin, fascia, rectus) with tumor, mesenteric nodule, omentum	Y	Y Strattice	Underlay	Y
2	618	413	205	Rectum, omentum containing two masses, small bowel mesenteric nodules, pelvic mass with distal ureter, pelvic mass with adjacent peritoneum, two liver biopsies	Y	Y Strattice	Underlay	Y
3	694	562	132	Terminal ileum and cecum, sigmoid colon, abdominal wall tumor nodules, intra-abdominal tumor nodules with adjacent omentum, two distal stomach/proximal duodenum serosal nodules, tumor with ligamentum teres and adjacent peritoneum, tumor with falciform ligament and adjacent peritoneum, gallbladder with porta hepatis nodules, pelvic mass with adjacent peritoneum, small bowel mesenteric nodules	Y	Y Strattice	Underlay	Y
4	459	297	162	Small bowel, sigmoid colon, three pericolonic tumors	Y	N	None	Y
5	899	542	357	Right colon, three small bowel segments, gallbladder, left kidney, rectum and anus (abdominoperineal resection), peritoneal implants, abdominal wall tumor	Y	Y Strattice	Overlay	Y

Mins – minutes, *CRS/HIPEC* – cytoreduction surgery with hyperthermic intraperitoneal chemotherapy, *PRS* – plastic reconstructive surgery, *RUQ* – right upper quadrant, *N/A* – not available, *iVAC* – incisional vacuum-assisted device.

postoperatively, the patient presented to the emergency room (ER) with dehydration and malaise, but no acute abnormality was found. She was given 2L of intravenous fluids and discharged. One week later, she was admitted to the hospital for a *Pseudomonas* wound infection and treated with a course of oral antibiotics. Despite wound infection and repeat presentations to the ER, the patient achieved a satisfactory aesthetic result (Fig. 1) and has no recurrence of her metastases at 4 months of follow-up.

3.2. Case 2

A 35 year old female with metastatic colorectal cancer underwent combined CRS/HIPEC/abdominal wall reconstruction with panniculectomy. She had a history of previous DVT and multiple abdominal surgeries including left colectomy and ventral hernia repair. To reconstruct the abdominal wall, components release was performed and muscle flaps were advanced to the midline. The ventral hernia measuring approximately 20 cm × 12 cm was repaired primarily, using Strattice underlay placed in the retromuscular space to reduce tension on the hernia, and an incisional wound vacuum-assisted device was used. On POD 2, she was noted to have a left lower extremity DVT which was not managed with anticoagulation due to high bleeding risk. Repeat duplex four days later did not show thrombus propagation. She was transfused 1 unit of blood on POD 3 for a hemoglobin of 7. She was found to have a UTI on POD 7 and was treated with ciprofloxacin. On POD 20 she went to the ER with upper abdominal pain and vomiting and was found to have leukocytosis. No evidence of infection was found.

3.3. Case 3

A 49 year old female with a history of CRS/HIPEC therapy nine years earlier underwent CRS/HIPEC with abdominal wall reconstruction for mucinous appendiceal neoplasm with pseudomyxoma peritonei. Components separation was performed and Strattice underlay was secured around the border of the ventral abdominal wall hernia defect measuring approximately 15 cm × 8 cm. The fascia was reapproximated in the midline over the mesh, and an incisional wound vacuum-assisted device was applied. Five days post-operatively, the patient experienced atrial fibrillation with rapid ventricular response. She was treated with metoprolol, Cardizem, and magnesium then maintenance Diltiazem. Two weeks postoperatively, the patient developed a right lower extremity DVT and was treated with Xarelto.

3.4. Case 4

A 54 year old female initially presented for peritoneal mesothelioma with a PCI of 20. She received an initial CRS/HIPEC achieving CCR0 cytoreduction at that time. Two years later she was found to have a recurrence of malignant disease. At that time, the patient also presented with banding of her laparotomy scar, distortion of the umbilicus and tethering of the scar to the midline. Following large debulking of her peritoneal lesions, her abdominal reconstruction at time of CRS/HIPEC involved primary closure of fascia, removal of chronically thickened and fibrotic tissue, amputation of the umbilicus and soft tissue reconstruction. Stable soft tissue coverage was achieved with local soft tissue flap advancement (Fig. 2). Her postoperative course was without complication.

3.5. Case 5

A 52-year-old male had a complicated history with colorectal cancer with a total of six abdominal surgeries for removal of tumor implants, an appendectomy, and incisional hernia repair before electing to proceed with CRS/HIPEC/abdominal wall reconstruction and bilateral gracilis muscle flap reconstruction of a large perineal defect.

Table 3
Postoperative course.

Case	LOS/days	Post-operative chemotherapy	Post-operative radiotherapy	Wound complication	Reoperations within 90 days	Readmission within 90 days	Post-operative cytoreduction	Follow up time/months
1	6	Y	N	Y	N	Y	CCR0	3.8
2	10	N	Y	N	N	N	CCR0	14.0
3	6	N	N	N	N	N	CCR1	2.6
4	7	N	N	N	N	N	CCR0	20.3
5	13	Y	N	N	N	N	CCR1	22.0

LOS – length of hospital stay, *Y* – yes, *N* - no.

Table 4
Complications.

Clavien-Dindo classification	Number of patients
Grade I	2
Grade II	3
Grade III	0
Grade IV/V	0

Grade I consisted of a lower extremity DVT and leukocytosis, both self-resolved.
Grade II consisted of atrial fibrillation treated with diltiazem, anemia treated with a single blood transfusion, and a surgical site infection treated with oral antibiotics.

Cytoreduction left the rectus abdominis muscles approximately 2 cm short of closure at the midline, so components separation was performed to achieve additional tissue excursion. The muscle flaps were reapproximated in the midline and Strattice mesh was overlaid to provide additional support to the abdominal wall, and an incisional wound vacuum-assisted device was applied. Postoperatively, the patient demonstrated good wound healing without complication or readmission and a good cosmesis was achieved (Fig. 3). At the last follow up appointment to date, he remained disease free.

4. Discussion

The patients included in this case series were offered CRS/HIPEC with abdominal wall reconstruction as a treatment option for diffuse peritoneal metastases in the setting of colorectal cancer, gastric cancer, and mesothelioma. Peritoneal metastases portend an extremely poor prognosis. However, more recent therapies such as CRS and HIPEC, have demonstrated improved survival time when compared with systemic chemotherapy alone [1] but frequently leave the abdominal wall considerably weakened [8] Several large studies have found re-operation rates ranging from 8 to 17.5% and a surgical site infection rate of 11.4% [9] following CRS/HIPEC. Although abdominal reconstruction is typically performed separated in time from CRS/HIPEC, it may be combined within the same surgery [10]. There is no standard technique for reconstruction in this unique patient subset. We have described different approaches to this operative task with successful outcomes of fewer complications, shorter hospital stays and fewer re-operations than that described in the literature. We believe this case series demonstrates the significance of concurrent soft tissue and abdominal wall reconstruction in the prevention of sequential abdominal wall weakness.

Soft tissue reconstruction was completed to provide stable soft tissue cover using local flap advancement. The local tissue rearrangement technique allows closure of the defect without excessive tension at the closure site that may result in ischemia [11]. This is of particular benefit in patients who have had a previous resection of the abdominal wall or other abdominal operations and, thus, accrued abdominal scar tissue and are at increased risk for further abdominal wall, weakness,

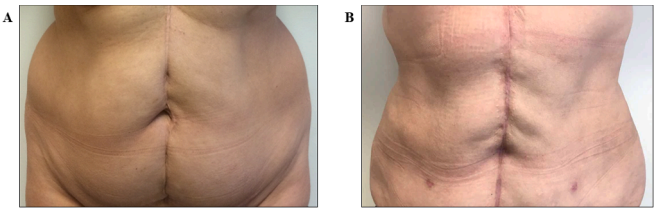

Fig. 2. (A) Preoperative photograph of a 54-year-old female with recurrent peritoneal mesothelioma. **(B)** Two year postoperative photograph of the same patient following primary closure of fascia and skin.

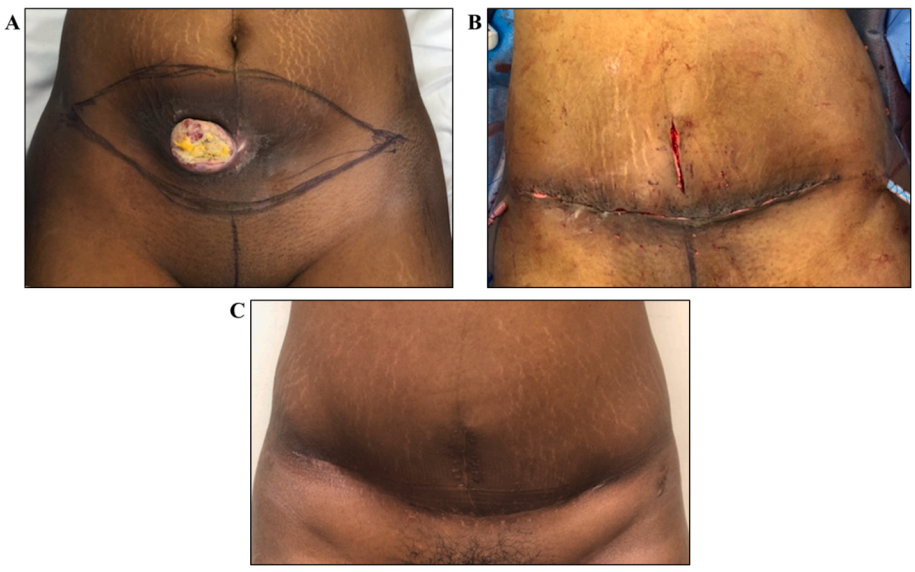

Fig. 1. (A) Preoperative photographs of a 29-year-old female with colorectal cancer that has eroded through her abdominal wall; **(B)** Immediate post-operative photograph of the same patient showing abdominal closure following component release, biologic mesh, and adjacent tissue transfer; **(C)** Four-month postoperative photograph of the same patient demonstrating fully healed incision.

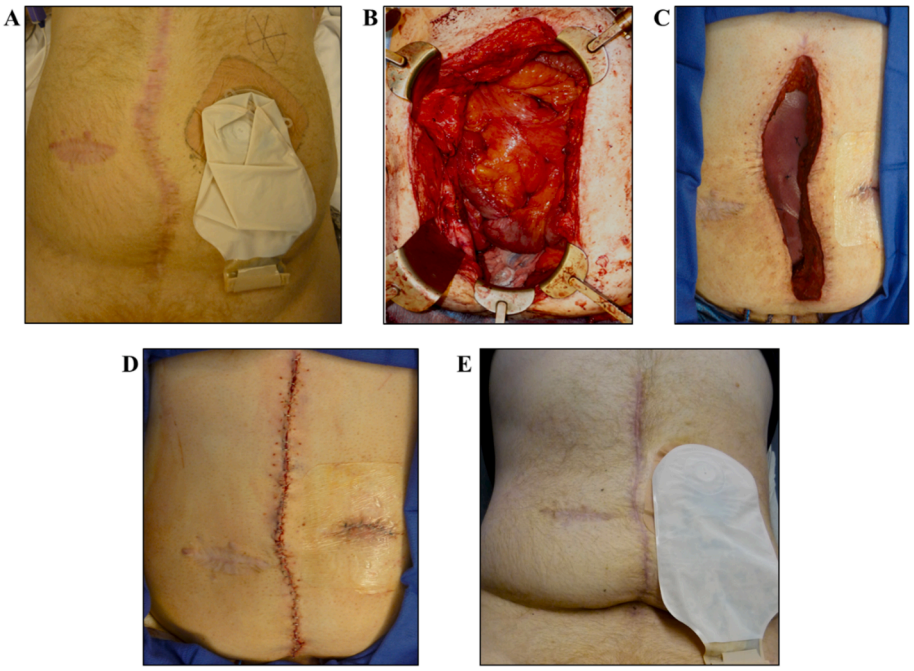

Fig. 3. Photographs of operative course of a 52-year-old male with colorectal cancer with a history of six previous abdominal surgeries for tumor resection and an incisional hernia repair. **(A)** Preoperative abdomen with colostomy situated in left hemiabdomen; **(B)** Intraoperative view following completion of oncologic resection; **(C)** Component release with Strattice mesh overlay; **(D)** Immediate postoperative photograph of abdominal closure; **(E)** Postoperative view three months after surgery demonstrating good wound healing.

herniation or additional procedures [10].

Abdominal wall reconstruction was accomplished by similar techniques through this study. Components separation was performed in all cases, whereby a plane was created between the internal and external oblique muscles, allowing additional excursion of the muscle flaps for primary closure. This was necessary in these cases to overcome sizable abdominal wall defects. The ultimate goal of components separation is minimization of tension at the incision and risk of hernia recurrence. The strength and stability of the abdominal wall closure prove exceptionally important in this patient cohort, who have often undergone multiple major abdominal surgeries, with personal histories of abdominal hernias.

Biologic mesh and closed incision negative pressure wound therapy, or iVACs, are additional tools to improve the strength of reconstruction and expedite the healing process; both of which were utilized in the cases described. Prosthetic mesh reinforcement can be used to achieve a tension-free repair, restore abdominal domain and reduce the incidence of hernia recurrence [12]. Cases 1, 2, and 3 employed a Strattice mesh underlay to offset tension at the incision and minimize the risk of hernia. Case 5 used Strattice mesh as an overlay as the rectus abdominis muscles were reapproximated at the midline in a tension-free manner. We have found in this series, that reinforcement of reapproximated muscle flaps with Strattice mesh produced long term abdominal wall strength without hernia recurrence. While these patients may remain at increased risk for further abdominal wall defects, we believe this tension-free abdominal wall reinforcement, at both the muscular and soft tissue levels, replenishes a portion of the tissue integrity inevitably lost by CRS and HIPEC. Additionally, all the patients in our series received negative pressure wound therapy. This is indicated for patients with incisions with a higher risk of surgical site complications, especially in the case of tissue deficit, where the use of sutures and staples elevates the stress placed on the tissue and can cause increased tissue injury, ischemia, or fibrosis [13][. Negative pressure wound therapy has been shown to decrease the incidence of dehiscence and infections by decreasing lateral stress at the skin level [13]. Use of these dual systems (biologic mesh and closed incision negative pressure wound therapy) may explain the excellent outcomes observed in our study.

Although HIPEC and abdominal wall reconstruction are both major surgeries with considerable individual risks, our case series indicates that performing a combined operation of abdominal wall reconstruction at the time of CRS/HIPEC is feasible with comparable risks and increased benefits. The literature suggests high rates of complications contributing to morbidity and mortality of CRS/HIPEC [9]. In this case series to this date, there were no incidences of grade III-IV morbidity, mortalities, or reoperations. One of the major contributing factors associated with post-operative complication of CRS/HIPEC procedures is due to the negative chemotherapeutic effect on wound healing. The benefit of abdominal wall reconstruction at the time of CRS/HIPEC is in part due to the improvement in the strength of wound closure, which decreases immediate complications of infection and wound breakdown; an effect that may be amplified by the use of biologic mesh and closed incision negative pressure wound therapy. We hypothesize that the subsequent abdominal wall reconstruction allows surgeons to be more daring in the extent of their resection and choice of patients. This is supported by the literature which showed that patients with HIPEC/CRS/abdominal wall reconstruction had a much higher rate of extensive abdominal wall resections at the time of surgery and were more likely to have a history of prior resection and prior concurrent ventral hernia compared to HIPEC/CRS alone[10]. Furthermore, our cohort had a length of stay that was on average 7 days shorter than that of an exclusively CRS/HIPEC cohort described in the literature [14]. This may indicate that the combined surgeries result in less morbidity in the immediate postoperative period than no abdominal wall reconstruction following CRS/HIPEC. Future studies may compare the outcomes of HIPEC/CRS/abdominal wall reconstruction versus HIPEC/CRS alone.

Finally, the abdominal wall reconstructions performed on all the patients in this series were equally successful despite the heterogeneity in the study subjects, such as previous surgical history, type of cancer, extent of cancer and extent of cytoreduction. Grading systems such as the PCI and CCR Score have been used to quantify some of these variables to serve as prognostic indicators for the ultimate success of cancer eradication. The extent of the combined surgical procedure depended greatly on the quantity of tissue that necessitated removal by cytoreduction. These five patients encompassed a wide range of PCI scores from < 5 to 32 and were able to attain comparable results following cytoreduction. Furthermore, abdominal wall reconstruction by component release, biologic mesh, and adjacent tissue transfer was utilized in all five of these patients. The quantity of tissue removed was vastly variable among patients due to the wide range in PCI, indicating

the reconstructive technique provides versatility with the ability to be applied to a wide range of abdominal defects. Furthermore, given the additional operating time needed for this multidisciplinary approach, prudence must be exercised when selecting surgical candidates and comprehensive disclosure of potential benefits and risk must be included in the consent process. However, we believe that the benefit of the reduced morbidity and index hospital admission stay outweigh the potential risks of prolonged anesthesia.

5. Conclusion

The results of this case series demonstrate that CRS/HIPEC in combination with abdominal wall reconstruction is a promising treatment option for patients with peritoneal metastases. The combined surgery yields comparable complication rates to CRS/HIPEC alone, but with the added benefit of the increased strength of closure and decreased reoperation rate. We achieved successful outcomes through stabilization and reinforcement of the complete abdominal wall via adjacent tissue transfer and component separation. Future studies will need larger sample sizes and stratification to determine what patient characteristics may suggest an increased risk for postoperative complication.

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