# Perianesthesia Measurement During Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy Procedure: A Case Report and Review of the Literature

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**Purpose:** *This purpose of this case study and review was to understand perianesthesia care of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy surgery (CRS+HIPEC).*
**Design:** *Case study.*
**Methods:** *The perianesthesiaa medical record of a patient under CRS+HIPEC was analyzed to study the characteristics of perianestheia care for CRS+HIPEC. The literature of perianestheisa care for CRS+HIPEC was reviewed.*
**Findings:** *The challenges that perianesthesia care for CRS+HIPEC include—but are not limited to—electrolyte abnormalities, hemodynamic instabilities, and temperature fluctuation. Optimal perianesthesia management of a patient treated with CRS+HIPEC requires control of a complex interplay of physiologic mechanisms.*
**Conclusions:** *Besides maintenance of clinical and laboratory parameters, and recognition and treatment of any changes, evidenced-based guidelines are needed, not only for the optimal perianesthesia management of these patients, but also to avoid potential life threatening intraoperative and postoperative complications. The standardization of perianesthesia management for CRS+HIPEC is a necessary step in meeting these goals.*

**Keywords:** *cytoreductive surgery, hyperthermic intraperitoneal chemotherapy, blood pressure, perianesthesia measurement.*


**PERITONEAL CARCINOMATOSIS,** regardless of primary tumor type, has been a lethal disease, not only is complete surgical removal impossible, but also systemic chemotherapy is powerless. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS + HIPEC) is a promising technique for peritoneal carcinomatosis by surgical oncologists, and it results in a significant increase in the survival rate for peritoneal carcinomatosis.[1] The surgical procedure of CRS + HIPEC involves multiple visceral organ resections and peritonectomies to achieve a maximal cytoreduction. A heated chemotherapy is administered intraoperatively into the abdomen to cover all raw peritoneal surfaces. CRS + HIPEC has been used with increasing frequency worldwide as the safety, morbidity rate, and therapeutic considerations with respect to CRS + HIPEC have become better understood and recognized.[2] Nevertheless, HIPEC presents

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several challenges for health care providers: (1) perioperative hemodynamic instability, (2) changes in the cardiovascular status because of increased intra-abdominal pressure by the closed abdomen technique, (3) increased oxygen consumption because of the increased body temperature, (4) impairment of coagulation because of the large volume shift and protein loss with high fluid turnover, and (5) hypothermia during the cytoreductive phase and during the HIPEC procedure.[3-7] These challenges render perianesthetic management more complicated than during general abdominal surgeries. The optimal perianesthetic management of a patient treated with CRS + HIPEC requires control of a complex interplay of physiological mechanisms. Moreover, the population typically receiving CRS + HIPEC is at a substantially increased risk of morbidity, mortality, and extended intensive care unit (ICU) stay because of complexities of surgery and perianesthetic management.

## Case Summary

A 50-year-old male was admitted to a hospital for CRS + HIPEC for treatment of pseudomyxoma peritonei of appendiceal origin. A diagnostic laparoscopy was performed 30 days before the current surgery. During the previous surgery, 5 L of mucinous ascites were drained from the patient's abdomen, and a catheter was placed to manage the ascites. After review of the anatomic specimen, pseudomyxoma peritonei was diagnosed. Vital signs were as follows: heart rate = 91 beats/min; blood pressure = 110/74 mm Hg; respiratory rate = 21 breaths/min; $SaO_2$ = 98% while breathing room air; and Mallampati degree = 2. After the preoperative evaluation, bilateral paravertebral nerve block catheters were placed in the preoperation holding area. Anesthesia was induced intravenously with the following medications: 150 mcg fentanyl, 50 mg lidocaine, and 140 mg propofol. After positive pressure ventilation, 50 mg of rocuronium was administered. After loss of train-of-four twitches, a 7.5-mm cuffed endotracheal tube was inserted. Anesthesia was maintained by sevoflurane, with an exhaled fraction of 1% to 1.5% and boluses of rocuronium at 10 to 20 mg, according to neuromuscular monitoring (train of four). After surgical preparation of the patient, a midline incision was made from the xiphoid to the pubic symphysis and carried down through midline fascia. After incision, an estimated 3 L of ascites was drained from the patient's abdomen. During the cytoreduction phase, surgeons performed an exploratory laparotomy with radical abdominal tumor debulking, which comprised multiple peritonectomies, the mobilization of hepatic and splenic flexures, and a complete omentectomy, cholecystectomy, distal gastrectomy, ileocolectomy with appendectomy, and a left hemicolectomy with low anterior resection and a bilateral ureterolysis. The peritoneal cancer index score for this patient was 33 (eg, ranges from 0 [absence of disease] to 39 [highest possible score]), and his completeness of cytoreduction score was 0 (eg, ranges from 0 [no residual tumor] to 3 [residual nodules greater than 25 mm]). The cytoreduction phase lasted 10 hours. The patient experienced a 400 mL blood loss and a 720 mL urine loss. During this cytoreduction phase of the surgery, 9,000 mL of crystalloids and 750 mL of 5% albumin were administered. Twenty-five minutes after beginning the HIPEC procedure, a scheduled cuffed blood pressure check of the patient reported a pressure of 129/58 mm Hg, with arterial blood pressure at 84/58 mm Hg. Noticing the discrepancy between the two blood pressures, all the connections for the arterial lines were checked and flushed. The patient's arterial blood pressure remained the trend of dropping. However, the cuffed blood pressure continued to climb. As a result, two more noninvasive blood pressure cuffs were placed: one on the left lower leg and one on the right arm. The original blood pressure cuff remained on the left arm. The three blood pressure cuffs all indicated hypertension. A second arterial line was placed on the left radial artery. The arterial blood pressures from left and right radial arterial lines showed the similar hypotension. The anesthesia monitor module (GE Solar 8000m) and all the cables were changed. Nevertheless, the huge discrepancy in blood pressure measurement persisted. The recorded blood pressures during the HIPEC phase are shown in Figure 1. During this time, the pulse oximeter's plethysmograph waveform was normal, $SpO_2$ was 100%, and $ETCO_2$ was 32 to 33 mm Hg. The patient's left carotid and radial pulse could be felt. A transesophageal echo (TEE) ultrasound was done by anesthesiologist. The TEE indicated that the patient's cardiac function was normal yet hypovolemic. Through

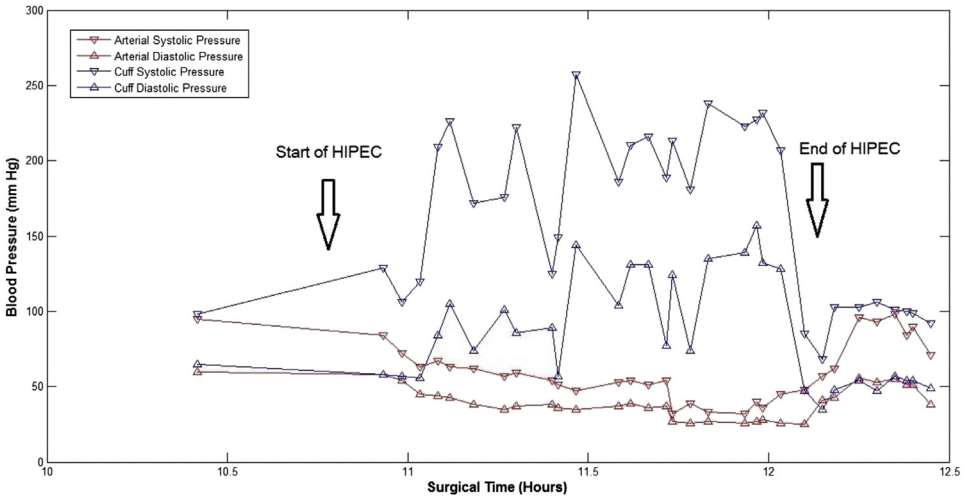


Figure 1. The cuff and arterial blood pressure discrepancy during the HIPEC phase. HIPEC, hyperthermic intraperitoneal chemotherapy. This figure is available in color online at www.jopan.org.

the entire HIPEC phase, 2,500 mL crystalloid and 500 mL 5% albumin were infused into the patient. Two units of packed red blood cells were transfused to the patient when arterial blood gas showed hemoglobin had dropped from 11.1 to 8.3 g/dL. The discrepancy between the cuffed and arterial blood pressures was not resolved. The highest recorded cuffed blood pressure was 257/144 mm Hg, with the arterial blood pressure 47/35 mm Hg at the same time. Soon after the HIPEC phase concluded, the cuff and arterial blood pressures correlated again and were similar to pre-HIPEC blood pressure. After 100 minutes of heated therapy, the patient's abdomen was flushed with large amounts of normal saline and drained. The abdomen was reopened for coloproctostomy, ileocolostomy, billroth II gastrojejunostomy, and diverting loop ileostomy. Then, the surgeons closed the patient's abdomen and concluded the 14-hour surgery. Throughout the entire procedure, the patient received 14 L of IV crystalloid, 1,250 mL 5% albumin, and two units of packed red blood cells. Blood loss was 750 mL, and urine output was 1,100 mL. At the end of the surgery, the patient was transferred intubated to the ICU, where he remained for 6 days. In 24 hours, the patient was extubated. The patient was asymptomatic and in good nutritional status when he was discharged from the hospital on the 11th postoperative day. Three months after the surgery, the patient underwent stoma closure and reconstruction of the intestinal tract.

## Discussion

### *Peritoneal Carcinomatosis*

Peritoneal surface oncology is a rapidly evolving subspecialty of oncology that manages peritoneal surface malignancies, which are categorized into (1) peritoneal carcinomatosis, secondary to abdominal, pelvic, or extra-abdominal malignancies, (2) pseudomyxoma peritonei, and (3) primary peritoneal tumors.[13] Peritoneal carcinomatosis is the leading cause of death for patients resected with intra-abdominal carcinomas.[14] The patients with untreated peritoneal carcinomatosis have median survival in less than 7 months for nongynecologic tumors and less than 15 months for gynecologic tumors.[15] Traditional cancer treatments, such as surgical resection, radiation therapy, and systemic chemotherapy, have not demonstrated efficacy in improving long-term survival.[16] Systemic chemotherapy and symptom-directed surgery may have a median survival ranging from 5.2 to 7 months under fluorouracil-only treatment.[17-20] In 2008, a multi-institutional study revealed that (1) the median survival was 19 months and (2) 3-year survival was 39% after CRS + HIPEC for 501 patients with colorectal peritoneal carcinomatosis.[21] From a retrospective analysis of contemporary data (2003 to 2011), 5-year survival after CRS + HIPEC varied by site of tumor origin and histology (eg, disseminated peritoneal adenomucinosis [91.3%], mesothelioma [80.8%],

appendiceal adenocarcinoma [38.7%], and colorectal adenocarcinoma [38.2%]).[22]

### *Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy*

CRS is performed in series or during a single operation to excise intra-abdominal macroscopic tumors.[23] CRS consists of the removal of a tumor or tumors and any affected organs, peritoneum, or tissue that are deemed technically feasible and safe to remove for the patient.[19,23] The resection status of patients after CRS has been judged using the following classification: R0, which is the complete removal of the tumor or tumors (that are visible) and negative cytologic findings or microscopic margins. The ultimate surgical goal is to debulk most tumors until the nodules are 1 mm in size to make cytotoxic drugs penetrate the remaining tumor cells.[24]

After CRS, HIPEC is performed with a suprahepatic inflow cannula and a pelvic outflow cannula is connected through a recirculating perfusion circuit that is driven by a roller pump heat exchanger.[24] Constant temperature monitoring is performed with temperature probes. The chemotherapy is introduced into the perfusion circuit with a target outflow temperature at the pelvis of 40°C. Surgeon will rock the abdomen throughout HIPEC to improve drug distribution to all peritoneal surfaces.[24] The direct intra-abdominal infusion of chemotherapeutic drugs into malignant tissue maximizes exposure to high concentrations of chemotherapeutic drugs (20 to 1,000 times greater than plasma levels), whereas minimizing exposure of the normal tissue.[25,26] Meanwhile, intra-abdominal infusing chemotherapeutic drugs are high-molecular-weight hydrophilic drugs that are unable to cross the peritoneal fluid-plasma barrier and demonstrate slow peritoneal clearance.[27-30]

Today, CRS + HIPEC is considered to be the "gold-standard" treatment for pseudomyxoma peritonei and peritoneal mesothelioma, and the procedure is covered by major health insurance companies such as Blue Cross Blue Shield, Aetna, and UnitedHealthcare.[31-33] Nevertheless, even with the promising results from previous studies,[21,22] peritoneal carcinomatosis from colorectal cancer, gastric cancer, ovarian cancer, or endometrial cancer is still in an experimental stage—data from randomized controlled trials are lacking to support the benefits of CRS + HIPEC. One major issue that has surfaced in previous studies is that the patients selected for CRS + HIPEC are in better health than patients in the larger population, so the improved 3- or 5-year survival may not reflect the benefit of CRS + HIPEC. In 2014, an estimated 1,900 CRS + HIPEC procedures were performed in the United States.[34]

### *Perianesthesia Management*

CRS + HIPEC represents a substantial operative undertaking for perianesthesia care. Average operative times are approximately 10 hours, with long ICU and hospital stays that consume substantial resources.[3-6] CRS + HIPEC features no general guidelines for perianesthetic management. Many heath care providers manage CRS + HIPEC patients in a way that is similar to the way they manage patients who undergo other types of major abdominal surgery. Nonetheless, the complexities of CRS + HIPEC make perianesthetic management much more challenging in the following ways.

**FLUID MANAGEMENT.** The large incision combined with surgery duration of up to 10 hours can cause large evaporative losses. For example, Arakelian et al[8] reported mean blood loss of 2,384 mL, with a range of 500 to 14,000 mL, during 76 CRS + HIPEC procedures. Schmidt et al[3] reported median blood loss of 600 mL, with a range of 200 to 9,000 mL, during CRS + HIPEC. It is a well-accepted established doctrine that 6 to 8 mL/kg/h fluid turnover rate for major abdominal surgery is too low for CRS + HIPEC. Rotruck et al[9] suggest that total fluid infusion should be 10 to 20 L according to their institute protocol. Schmidt et al[4] and Raspe et al[10] assert that up to 12 mL/kg/h should be administered during CRS + HIPEC, depending on the degree of debulking. Owusu-Agyemang et al[5] reported the combined average rate of crystalloid and colloid administration during CRS + HIPEC to be 9 mL/kg/h, with a range of 6 to 15 mL/kg/h for pediatric patients.

The choice of crystalloid or colloid infusions for intraoperative fluid management in abdominal

surgery is the subject of a heated debate within the perianesthesia community, and a definitive resolution to this controversy is still remote.[35-37] Considering that drainage of ascites and extensive debulking are associated with an enormous perioperative protein loss up to 700 g/d,[38] Schmidt et al[4] suggested a restrictive regime and the substitution of albumin only in the case of a profound decrease in albumin plasma levels (eg, less than 15 mg/dL). However, all these previous studies do not provide any evidence to support their fluid management strategy. Moreover, no study, thus far, has been conducted concerning the optimal replacement of fluids during CRS + HIPEC. For the CRS + HIPEC case study described previously, we maintained an average crystalloid infusion of 12 mL/kg/h, supplemented with 1,250 mL 5% albumin and two units of packed red blood cells. Considering that the patient experienced only 750 mL of blood loss, and his urine output was 1 mL/kg/h, we were satisfied with the fluid management for this case. However, the patient was still hypovolemic on the first postoperative day and needed extra crystalloid and colloid infusion.

**HEMODYNAMIC STABILITY.** Because CRS + HIPEC is a lengthy and invasive procedure, the patients are carefully selected by surgical and perianesthesia management teams to decrease perioperative morbidity and mortality. Patients with compromised cardiac or pulmonary function rarely undergo this procedure. Hemodynamic stability during this procedure is mainly decided by volume and temperature status[8,9] or primary disease (eg, mesothelioma vs peritoneal carcinomatosis).[11] During the CRS phase of our case study, the patient experienced significant decreases in the mean arterial pressure and increases in the heart rate. Hemodynamic change during this phase is similar to major abdominal surgery. During the HIPEC phase, the heated chemoperfusion triggers the body's responses to heat stress. The peripheral vasculature dilatation increases heat loss from the core to the environment. The heart rate increases to maintain vascular output in the face of decreasing peripheral vascular resistance.[3,4,39] Without proper fluid resuscitation, blood pressure decreases with decreasing peripheral vascular resistance. During CRS + HIPEC, all anesthetics are conducted using standard (eg, electrocardiography, noninvasive blood pressure, pulse oximetry, and capnography) and continuous central venous and invasive arterial pressure monitoring.[4] The routine use of extended invasive hemodynamic monitoring such as pulmonary artery catheters and transesophageal echocardiography occurs in some institutes, but this monitoring is not recommended.[4] In our case, the patient presented with mild hypotension, but this was easily controlled to a mean arterial pressure of over 65 mm Hg (and 20% within normal range) by aggressive fluid management and vasoactive medications. However, the situation that occurred during the HIPEC phase not only was quite challenging, but also has never been reported before. In most cases, cuffed blood pressure shows severe and consistent hypertension; simultaneously, arterial blood pressure shows severe and consistent hypotension. The huge discrepancy makes intraoperative anesthesia management very difficult. During the case described previously, we lacked the third method for monitoring blood pressure, so we did not have direct evidence to determine which blood pressure reading was the correct one. Hypovolemia from TEE can indicate that hypotension from arterial blood pressure is close to its actual amount, and this is consistent with previous studies. However, the normal pulse oximeter's plethysmograph waveform, 100% $SpO_2$, the steady 32 to 33 mm Hg $ETCO_2$, palpable left carotid and radial pulses, and consistent urine output all indicate that the actual blood pressure is not as low as the indicated arterial blood pressure. After consulting the certified registered nurse anesthetists and anesthesiologists in the same facility, it is learned that the blood pressure discrepancy is common during HIPEC phase. We suspect that the surgeon rocking the patient during the HIPEC phase may have something to do with the blood pressure discrepancy. A retrospective study including anesthesia records for CRS + HIPEC for last 5 years has been initiated to research the cause of blood pressure measurement discrepancy during CRS + HIPEC.

**TEMPERATURE MANAGEMENT.** During CRS, the intra-abdominal space will be exposed and the intra-abdominal organs will be carefully debulked by surgeons for several hours. Body heat may be lost to vaporization. In addition, the intra-

abdominal space may be irrigated by cold, normal saline solution. As a result, the patient faces the risk of hypothermia. Moreover, during HIPEC, the carrier solution is heated to 40°C to 43°C, which will put the patient at significant risk for hyperthermia. Either hyperthermia or hypothermia may cause consumptive coagulopathies, arrhythmias, liver or renal injury, peripheral neuropathies, and seizures.[40-43] Even with multiple tools, such as the forced-air warmer, warm infusion, and the cooling pad, maintaining normothermia for patients during the entire CRS + HIPEC procedure is still difficult. For our case, the temperature management during the CRS phase was successful. The patient's core temperature increased to 36.5°C before we turned off the forced-air warming blanket and fluid warmer. With the highest core temperature of 40.5°C, the forced-air warming blanket with ambient air was not enough to lower the patient's core temperature to the normal range. Therefore, extra actions are needed during this phase.

**COAGULATION MANAGEMENT.** CRS + HIPEC may impair the coagulation function, but the reasons for this are unknown.[4] Disturbance of coagulation may be caused by (1) the large volume shift, (2) protein loss with high fluid turnover, and (3) the hyperthermic chemotherapy. The effects of CRS and HIPEC on the coagulation system are insufficiently understood and should be a focus of further investigation. For this case, no coagulation test was done during surgery because of the patient's mild blood loss. In the ICU, the patient's international normalized ratio (INR) was 2.5, and it dropped to 1.8 after two units of fresh frozen plasma (FFP) were transfused. No other intervention for coagulation was undertaken. The patient's INR was 1.1 before being discharged, which was the same as the preoperative INR value. We assert that the intraoperative coagulation test is necessary, even for patients without massive blood loss.

**PAIN MANAGEMENT.** Thoracic epidural analgesia for pain management in patients undergoing CRS + HIPEC is recommended for most institutes if no contraindications exist.[12] Desgranges et al[44] pointed out that (1) the arterial and venous vasodilatation by blockade of the sympathetic nervous system from epidural infusion may show hemodynamic intolerance, and acute episodes of hypotension may be enhanced by systemic effects of HIPEC and (2) disturbances in coagulation during CRS + HIPEC are a risk factor of spinal hematoma after epidural analgesia.

Our institute uses a bilateral paravertebral block for perioperative management for CRS + HIPEC. Compared with thoracic epidural analgesia, the bilateral paravertebral block causes less hemodynamic instabilities.[45] The patient in this case described previously did benefit from the advantage of a bilateral paravertebral block. A bilateral paravertebral block also can help reduce narcotic usage and achieve satisfactory postoperative pain control.

In addition to these challenges concerning fluid management, hemodynamic stability, temperature management, coagulation management, and pain management, the anesthetic management of CRS + HIPEC is further complicated by the systemic absorption of peritoneal fluid, elevated abdominal pressures by intraperitoneal chemotherapy perfusion, acute kidney injury from nephrotoxic chemotherapeutic drugs, electrolyte abnormalities, and cardiac malfunction because of shifts in volume and changes in temperature. All these issues may affect perianesthesia care outcomes. Although (1) many studies have examined the surgical outcomes for CRS + HIPEC, and (2) oncology surgeons have never ceased in making an effort to standardize CRS + HIPEC, studies of the pathophysiological changes that accompany CRS + HIPEC are rare.

## Conclusion

CRS + HIPEC is a high-risk surgical procedure associated with major hemodynamic and metabolic changes throughout the perianesthetic phase. It requires coordinated and patient-centered perianesthetic management. Health care providers need evidence-based guidelines not only for the optimal perianesthetic management of these patients, but also to avoid potentially life threatening intraoperative complications. The standardization of perianesthetic management for CRS + HIPEC is a necessary step in meeting these goals.

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