

Combined Hyperthermic Intraperitoneal Chemotherapy and Hyperthermic Intrathoracic Chemotherapy in Stage IVA Ovarian Carcinoma: Single Institution Experience from North India

Abstract

Introduction: Treatment of Stage IVA ovarian carcinoma needs a combined multidisciplinary team approach. The peritoneal disease needs adequate local treatment with cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC). Hyperthermic intrathoracic chemotherapy (HITHOC) is a reasonable treatment option for ovarian carcinoma with malignant pleural effusion or pleural deposits. The CRS with HIPEC and HITHOC needs collaborative surgical and anesthetic skills and is a more technically demanding procedure. **Methods:** We are sharing the experience of three advanced cases diagnosed with Stage IVA ovarian carcinoma with subdiaphragmatic deposits along with malignant pleural effusion, which were treated with CRS with combined HIPEC and HITHOC. The feasibility of combined HIPEC and HITHOC along with surgical sequelae and follow-up treatment outcomes are individually summarized. **Results:** All patients underwent the proposed surgery without any significant intraoperative complications. The postoperative morbidity was acceptable with no recorded mortality. One patient developed recurrent pleural disease on follow-up. **Conclusions:** HIPEC/HITHOC is an effective and safe therapeutic option to prevent recurrence in Stage IVA ovarian carcinoma, which has previously a dismal prognosis. In addition, the patient's general condition improved symptomatically and the respiratory distress level significantly reduced after the curative-intent treatment.

Keywords: Cytoreduction surgery, hyperthermic intraperitoneal chemotherapy, hyperthermic intrathoracic chemotherapy, multidisciplinary approach, neoadjuvant chemotherapy

Introduction

Cytoreductive surgery (CRS) followed by hyperthermic intraperitoneal chemotherapy (HIPEC) is an evolving modality of treatment for peritoneal carcinomatosis including carcinoma ovary.^[1] The treatment of Stage IVA ovarian carcinoma needs combined multidisciplinary team approach of surgeon, onco-anesthesiologist, radiologist, pathologist, and medical oncologist. It has a poor prognosis with a median overall survival of 6–18 months.^[2] Systemic chemotherapy followed by interval CRS is the treatment of choice in the real world for a selected group of patients.^[3] This approach may reduce the risk of recurrence and result in increased disease-free survival. However, it alone may not offer the optimal treatment for International Federation of Gynecology and Obstetrics (FIGO)

Stage IVA (metastatic pleural effusion/pleural deposits). The important aims of surgery are staging of the disease and assessment of disease extent and removal of all visible disease (CRS) or as much as possible (debulking), but there is no standard treatment for patients with malignant pleural effusion/pleural deposits in such kind of aggressive cancer. However, recently hyperthermic intrathoracic chemotherapy (HITHOC) with CRS was used as a surgical armamentarium for tackling the pleural disease.^[4]

Hypothetically, HITHOC may offer an additional benefit in the form that the tumor cells are destroyed by direct exposure to cytotoxic with hyperthermia.

Literature suggests the survival benefit after optimal cytoreduction for intrathoracic metastasis of ovarian cancer.^[4] Complete/optimal CRS followed by HIPEC and HITHOC procedure is gradually becoming

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Ray MD, Raghuram K, Kumar N. Combined hyperthermic intraperitoneal chemotherapy and hyperthermic intrathoracic chemotherapy in stage IVA ovarian carcinoma: Single institution experience from North India. Clin Cancer Investig J 2021;10:84-90.

M. D. Ray,
K. Raghuram,
Navin Kumar¹

Department of Surgical
Oncology, All India Institute of
Medical Sciences, New Delhi,
¹Department of Surgical
Oncology, Mahavir Cancer
Sansthan, Patna, Bihar, India

Submitted: 25-Oct-2020
Revised: 23-Jan-2021
Accepted: 23-Jan-2021
Published: 23-Apr-2021

Address for correspondence:
Dr. Navin Kumar,
Department of Surgical
Oncology, Mahavir Cancer
Sansthan, Patna, Bihar, India.
E-mail: navin2k1@gmail.com

Access this article online

Website: www.cci-j-online.org

DOI: 10.4103/ccij.cci_j_154_20

Quick Response Code:



a well-validated treatment modality for peritoneal and pleural metastasis. As per the literature, microscopic as well as up to 2.5 mm tumor deposits are destroyed by the synergistic effects of hyperthermia (41°C–43°C) and chemotherapy.^[5] However, the procedures are not well standardized yet due to its technically demanding surgery with potential perioperative morbidity and mortality.^[6] A couple of case series with few case reports and review articles were reported in the literature.^[7-9] This research aims to share our experience of CRS with HIPEC and HITHOC in three patients with technical specifications and survival outcomes.

Case Reports

Case report I

A 55-year-old, homemaker, uniparous presented with complaints of dry cough, shortness of breathing, right chest pain, and dysphagia for 1 month. On examination, her Eastern Cooperative Oncology Group Performance Status (ECOG PS) was 3. Routine hematological workup was normal. The chest X-ray was suggestive of the right pleural effusion. Contrast-enhanced computed tomography (CECT) chest revealed massive right pleural effusion with the mild enhancement of pleura, complete right lung atelectasis, subcentimetric mediastinal lymphadenopathy and subtle left lung ground-glass opacity suggestive of pleural metastasis. CECT abdomen revealed peritoneal thickening, soft-tissue thickening in the mesentery, left subphrenic space and perihepatic space, subcentimetric mesenteric, left paraaortic, aortocaval and bilateral inguinal nodes. Pleural fluid adenosine deaminase, glucose and protein values were within the normal range. Ziehl–Neelsen staining of pleural fluid was negative for acid-fast bacilli. Furthermore, the culture sensitivity of pleural fluid test was sterile. Pleural fluid cytology was positive for adenocarcinoma.

Pleural nodule biopsy was suggestive of adenocarcinoma. In immunohistochemistry (IHC), CK7, WT-1, and P53 were positive; however CK20, TTF-1, calretinin, and P40 were negative. CA125 was 312 ng/ml (Normal: 0-35 ng/ml). She was diagnosed as carcinoma ovary with right pleural effusion (FIGO stage – IVA). Serum CEA and CA 19-9 were within the normal range.

The bilateral mammogram was normal. Upper gastrointestinal endoscopy and colonoscopy were normal. Pulmonary function test was suggestive of restrictive pattern with forced expiratory volume (FEV1), forced vital capacity (FVC), and FEV1/FVC were 55.2%, 60.76%, and 95.77%, respectively. Room air oxygen saturation of the patient was 96%–98%. In prehabilitation, incentive spirometry, steam inhalation, high protein high-calorie diet, hematinic, and chest physiotherapy were started. She was planned for neoadjuvant chemotherapy (NACT) followed by interval cytoreduction surgery with HIPEC and

HITHOC. The patient received 3 cycles NACT (paclitaxel and carboplatin). Given the partial response to NACT, she was planned for definitive surgery.

Intraoperatively, there were moderate ascites. Multiple tumor deposits were present over the liver, segment 5 and segment 2 with dense adhesions to the diaphragm. Hemorrhagic pleural effusion was present. Tiny military deposits were present on the right parietal pleura, along with collapsed right lower lobe lung. Bilateral tubal-ovarian masses (right side – 5 cm × 3 cm and left side 4 cm × 3 cm) were present. Small multiple deposits were present in the pouch of Douglas. There were small deposits over the upper rectum and rectosigmoid junction. Cervix was bulky; however, the uterus appeared to be normal. Both parietal and pelvic peritoneum was normal. Multiple omental deposits were present, the largest 5 cm × 5 cm. Multiple bilateral pelvic, aortocaval, and paraaortic nodes were present. There were multiple diaphragmatic deposits. The peritoneal carcinomatosis index (PCI) was 15 out of 39.

During surgery, there was approximately 1.5 L blood loss, which was replaced with 2 units of packed red blood cells and crystalloids fluid. The cytoreduction surgery completed in approximately 6 h, which consisted of total abdominal hysterectomy with bilateral salpingo-oophorectomy, bilateral pelvic node dissection, paraaortic node dissection, and total omentectomy. Diaphragmatic stripping was done after the right lobe liver mobilization to excise the diaphragmatic nodule [Figure 1a]. Hemorrhagic pleural fluid drained. Right side diaphragm was opened from the abdomen to excise pleural-based nodules [Figure 1b]. Hence, CRS with combined HIPEC and HITHOC was performed. No separate thoracotomy incision was made for HITHOC, as there was no gross pleural disease left after cytoreduction surgery (CC = 0). HIPEC was performed by a semi-open technique (modified Coliseum), using Cisplatin 100 mg (70 mg/m²) in 2.5 L normal saline perfusate at 41°C–43°C for 60 min at the rate of 1200 ml/min using roller pump. Pleurectomy was not performed only chemotherapy fluid was allowed to flow freely intrathoracically through the diaphragmatic space.

Intraoperatively vitals, urine output and temperature were monitored by the anesthesia team. Urine output was maintained at 0.5–1.0 ml/kg/h during cytoreduction and 2–3 ml/kg/h in HIPEC and HITHOC phase. During CRS, transient hypotension developed which was managed with vasopressor and fluid challenge. During the HIPEC/HITHOC procedure, the temperature of the patient was increased from 35.4°C to 38.2°C. The cold intravenous fluid was administered. In addition, forced air warmer was stopped. Urine output, temperature, hemodynamics, arterial blood gas analysis, and other vital parameters monitored regularly during the procedure. After the completion of the procedure, the perfusate was sucked out. Hemostasis was ensured. Diaphragmatic defect was closed with

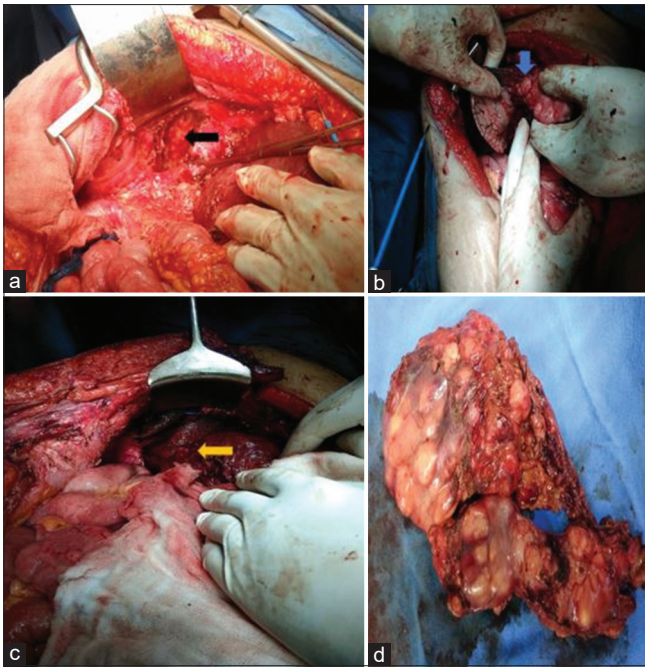


Figure 1: (a) Post sub-diaphragmatic deposit excision along with liver mobilization and diaphragmatic rent creation (black arrow). (b) Depicting excision of the pleural based nodule (solid blue arrow), adherent to the right lower lobe lung parenchyma. (c) Postcombined hyperthermic intraperitoneal chemotherapy and hyperthermic intrathoracic chemotherapy diaphragmatic rent closed with polypropylene mesh. (d) Specimen of the excised sub-diaphragmatic nodule with part of the diaphragm

the polypropylene 1–0 suture [Figure 1c]. Intercostal drainage (ICD) tube was placed in the right fifth intercostal space in the “safety triangle.” The abdomen was closed in layers over 2 drains (one in subhepatic space and other in the pelvis). The total duration of the procedure was 8 h 30 min. Total fluids administered were 5000 ml of balanced salt solution and 2 units of packed red cells. The patient shifted to the intensive care unit (ICU) in the intubated state for mechanical ventilation and vitals monitoring. The patient was weaned off from the ventilator on postoperative day 2. Vasopressor support was gradually tapered and stopped on postoperated day 3. In the postoperative period, renal functions and coagulation profiles were deranged which were conservatively managed. Abdominal drains were removed on the 5th and 7th postoperative days consequently. ICD tube was removed on the 6th postoperative day. The urinary catheter was removed on the 4th postoperative day and the patient was discharged in a healthy state on the 8th day following surgery. Follow-up period was uneventful and sutures removed on day 21.

Final histopathology report rendered the diagnosis of FIGO IVA serous ovarian carcinoma, because of similar metastatic tumor in excised pleural-based deposits [Figure 1d]. The patient was advised for further systemic chemotherapy and periodic follow-up. Till the date of 7 months of treatment-free interval, the patient was having overall good performance status with no radiological and biochemical evidence of malignancy.

Case report II

A 49-year-old female with known medical comorbidity of hypothyroidism was a known case of ovarian carcinoma. She was diagnosed and treated outside in 2015. Staging laparotomy was done and intraoperatively, there was a large left solid-cystic lesion size 15 × 12 × 10 cm with papillary projection on the capsular surface. The right ovary and uterus were normal. Outside histopathology revealed papillary adenocarcinoma, FIGO stage IB. After a treatment-free interval of 9 months, the patient presented with bloating and abdominal distension to our tertiary cancer care center in August 2016. CA 125 was 1900 ng/ml (normal: 0–35 ng/ml). CECT chest and whole abdomen revealed gross pleural effusion (right>left), mild ascites and peritoneal deposits. Pathological block/slide review conferred the diagnosis of high-grade serous adenocarcinoma. The final diagnosis assigned was recurrent ovarian carcinoma, FIGO Stage IVA. Six cycles of taxanes and platinum-based chemotherapy were administered. After treatment-free interval of 11 months, the patient received 6 cycles of gemcitabine and carboplatin-based chemotherapy until April 2018. She was referred for surgical treatment after a multidisciplinary tumor board discussion. Prehabilitation and pre-anesthesia check-up were done as per institution protocol. Preoperative CECT chest, abdomen and pelvis suggested gross ascites, omental cake/deposits, perihepatic peritoneal deposits with no pelvic or retroperitoneal lymphadenopathy. Secondary cytoreduction surgery with HIPEC and HITHOc was done. Intraoperatively, there were moderate ascites, diffuse pelvic peritoneal and bilateral subdiaphragmatic deposits. The root of mesentery was studded with nodular peritoneal deposits. Disease-specific peritonectomy, total omentectomy, right hemicolectomy with ileotransverse anastomosis with mesenteric and diaphragmatic stripping were done. HIPEC was performed by semi-open technique (modified Coliseum), using chemotherapy drug “Mitomycin” 30 mg in 2.5 L normal saline perfusate at 41°C–43°C for 60 min at the rate of 1200 ml/min using roller pump. PCI was 23 out of 39. CC-score was 1. Final histopathology showed the features of high-grade serous carcinoma mesenteric, omental and peritoneal deposits, FIGO IIIC2. Three cycles of taxane-based adjuvant chemotherapy were administered to the patient. Five months’ postsurgery, the patient is under follow-up with no evidence of local or systemic disease recurrence.

Case report III

A 46-year female with known medical comorbidity of abdominal Koch’s, presented with right-sided chest pain for one month. She was evaluated and diagnosed as right side malignant pleural effusion. The right pleural biopsy was suggested for poorly differentiated carcinoma. IHC of specimen was positive for CK7, ER, and CA125. The rest of IHC markers such as calretinin, CK20, TTF-1,

synaptophysin, and mammaglobin were negative. PET CT was done. There were hypermetabolic right pleural nodular lesions involving costal, mediastinal, and diaphragmatic pleura along with right pleural effusion. Hypermetabolic bilateral solid cystic adnexal lesions with nodular deposits in recto-uterine space and perihepatic space were present. The bilateral mammogram was normal. On examination, ECOG performance status was 2. Vitals were normal. No lymphadenopathy was noticed. On per abdomen examination, there was no lump palpable, no organomegaly or ascites. Per vaginal and per rectal examination were normal.

Hence, the patient was diagnosed as carcinoma ovary with right side malignant pleural effusion (FIGO Stage IVA). She was planned for neoadjuvant chemotherapy (NACT) followed by surgery in the multidisciplinary team. A total of nine cycles of taxane- and platinum-based chemotherapy was administered. Post-NACT, computed tomography (CT) scan revealed good partial response, because of the decrease in size of the lesion. After NACT, she underwent interval CRS with combined HIPEC and HITHOC. Intraoperatively, there were multiple deposits in the “pouch of Douglas” and perihepatic space. Multiple small right pleural deposits, pelvic, and retroperitoneal nodes were present. Complete cytoreduction surgery with cc score ‘0’ was achieved. Peritoneal carcinoma index was seven out of 39. For HIPEC and HITHOC, 100 mg Cisplatin chemotherapy drug was used in 2 L normal saline perfusate at -41°C – 43°C , over 45 min in a similar fashion as that of the previous patient. Intraoperative fluid management, temperature, and vitals monitoring were performed by the expert anesthesiologist. The patient was shifted to ICU for postoperative monitoring. She was extubated on the 2nd day of surgery. The inotropes support was tapered down gradually and stopped on the 3rd day of surgery. The patient was shifted out from ICU on the 3rd postoperative day to the surgical ward. The urinary catheter was taken out on the 4th day of surgery. Drains were removed on the 5th and 7th days of surgery. She was discharged from hospital on the 9th postoperative day. The postoperative period was uneventful and sutures were removed on postoperative day 21. The patient was advised for further systemic chemotherapy and periodic follow-up with routine clinical examination and CA 125.

Discussions

After a thorough review of published literature so far on combined CRS with HIPEC and HITHOC in carcinoma ovary, we found a couple of literature studies addressing the same.^[8,9] One retrospective study was done earlier by Paul H Sugarbaker *et al.* regarding combined HIPEC and HITHOC.^[10] It was described as hyperthermic intraoperative thoracoabdominal chemotherapy (HITAC), which was advocated for gastrointestinal cancers (appendix, colon, mesothelioma, and gastric cancers) but not used for ovarian

carcinoma. In that study, HITAC was compared with HIPEC and HITHOC separately. They observed a significant ipsilateral thoracic recurrence (6 out of 8 operated cases of pseudomyxoma peritonei), which occurred intrathoracically in cases of CRS and HIPEC alone (without HITAC). Diaphragmatic resections were performed for HITAC. Among HITAC cases, only one patient developed ipsilateral thoracic recurrence out of 16 in the appendiceal malignancy subgroup. They strongly suggested that HITAC was an essential part of the treatment for peritoneal metastases if diaphragm resection required for complete cytoreduction.^[10]

This is applicable in the case of carcinoma ovary also. Hence, it can be postulated that by doing combined HIPEC and HITHOC (by diaphragmatic resections) in cases of carcinoma ovary with pleural dissemination, ipsilateral thoracic recurrences can be reduced. This could be observed with the presence or absence of microscopic intrathoracic disease. In addition, in cases of diaphragmatic resection when there is no tumor in the pleural surface, tumor permeation may occur directly because of the resection of the anatomical barrier. It caused the pavement for the tumor to cross the diaphragm. Apart from HIPEC, doing prophylactic HITHOC in these cases will help in reducing intrathoracic recurrences. There is no need for any added extra procedure rather than allowing the chemotherapy containing fluid to flow freely in the pleural space through the diaphragmatic rent and closing the defect primarily with delayed absorbing suture, later the combined procedure of HIPEC and HITHOC.

Sugarbaker *et al.* reported grade 3 or 4 toxicity of 43% for this combined procedure.^[10] However, in the present three cases, apart from mild derangement of RFT and coagulation profile (grade 1 toxicity) with no major toxicity was observed. Even though, there is the large increase in total diffusion surface when the pleural space is added to the abdominal space for Chemotherapy, the authors found the absorption of chemotherapy from the pleural space through the parietal and visceral pleura was considerably less efficient than from the abdominal and pelvic cavity.^[11] We also did not modify the dosage of chemotherapy drugs for combined HIPEC and HITHOC and no adjustments were made to standard HIPEC protocol.

Perioperative management of Stage IVA ovarian cancer is a nightmare for onco-anesthesiologist, especially doing CRS with HIPEC and HITHOC in the same setting. It is not only a long duration surgical procedure with hyperthermic chemotherapy, but also includes major blood loss, fluid shifts, nephrotoxicity, exposure to hypothermia during HIPEC and HITHOC, electrolytes imbalance, acid-base disturbances, and deranged coagulation profile.^[12] Cardiovascular/Respiratory pathophysiological changes exacerbated with HIPEC + HITHOC.

The drugs commonly used as Cisplatin and Mitomycin at 41°C – 43°C . Cisplatin is well known for nephrotoxicity.^[13]

Intraoperatively and postoperatively, these patients can have reduced cardiopulmonary reserve, which with super-added respiratory tract infection may lead to pneumonia, even acute respiratory distress syndrome. Apart from these, pneumothorax and pleural inflammations are also common sequelae.

Paralytic ileus, surgical site infections, anastomotic leak, abdominal abscess, enterocutaneous fistula, and venous thromboembolism are the common complications of this kind of surgery. The common complications of HIPEC and HITHOC are enlisted in Table 1. HITHOC has a few additional risks along with CRS.^[13-15] Pathophysiological changes in HIPEC and HITHOC are summarized in Table 2.

CRS is itself a challenging surgery but it gets more challenging when HIPEC and HITHOC added with it. It takes a long time, may need multiorgan resection with multiple anastomoses along with significant blood loss. Hyperthermic exposure to pleural and peritoneal cavities may lead to significant pathophysiologic changes such as increased basal metabolic rate, oxygen demand with tachycardia.

Surgeon fatigue is an unspoken truth in hampering surgical quality. This combined treatment strategy has been considered to show acceptable morbidity and mortality for the treatment in primary thoracic disease.^[16]

Lim *et al.* reported the feasibility and acceptable morbidity of HIPEC after CRS in ovarian cancer.^[17] Apart from the usual complications of opening the thoracic cavity along

with one-lung ventilation, exposure to heated chemo thereby may lead to arrhythmia and may cause mediastinal shift leading to decrease venous return, cardiac output, and direct cardiac compression.^[18] Impairment of tissue oxygenation and in airway pressure can occur both during HIPEC and HITHOC. After CRS, HIPEC, and HITHOC, it is an anesthetist challenge to maintain optimum volume, adequate tissue perfusion intraoperatively. Postoperative comprehensive care starting from fluid and electrolyte balance, maintenance of albumin and hemoglobin levels to renal function monitoring and respiratory care. Goal-directed fluid therapy has shown better outcomes.^[19] The measurement of urine output is a reliable way to monitor renal function. Urine output 0.5–1 ml/kg/h during CRS 2–3 ml/kg/h during HIPEC and 1–2 ml/kg/h during HITHOC are essential.^[20]

These patients require mechanical ventilation, correction of chemotherapy-induced coagulopathy, replacement of protein loss in continuous ascites and glycemic control. Thromboprophylaxis with mechanical maneuvers and pharmacological agents should be started as soon as feasible.

Three doses of aprepitant (substance P/neurokinin 1 receptor antagonist) should be administered to prevent post-HIPEC/HITHOC nausea and vomiting in the following schedule.

1. 120 mg tablet 1 day before surgery
2. 80 mg tablet 2 h before surgery
3. 80 mg on 1st postoperative day through the nasogastric tube.

Postoperative wound care, infection control, intake output monitoring, prophylactic antibiotics, nutrition, monitoring of kidney and liver function with electrolytes imbalance management, chest physiotherapy and incentive spirometry are important aspects to improve the expected perioperative outcome.

We need to add surgical issues in the discussion. How much the surgery difficult! – The long exhaustive procedure, two cavities; thorax and abdomen, chemotherapy toxicities, health personnel chemotherapy drug exposure, blood loss, more respiratory compromise, increase abdominal pressure, and lung collapse with atelectasis.

Conclusions

CRS with HIPEC and HITHOC is a complex and challenging procedure but it is the viable treatment option in cases of carcinoma ovary in the presence of malignant pleural effusion/pleural deposits, where diaphragmatic resection is performed. It can lead to reducing the ipsilateral thoracic recurrences. However, further research with multicentric, well-powered randomized controlled trials with adequate sample size is warranted for the validation of the therapeutic advantages of HIPEC and HITHOC together for abdominal disease as well as the

Table 1: Complications of hyperthermic intraperitoneal chemotherapy and HITHOC

HIPEC morbidities*	HITHOC morbidities
DVT - 8%	Pulmonary edema
Paralytic ileus/SAIO - 6%	Cardiomyopathy
Burst abdomen/SSI - 4%	Cardiotoxicity (doxorubicin induced)
Lymphocele - 4%	Interstitial pneumonitis
Ureteric injury - 4%	Cytotoxic agent-induced pleural inflammation
Deranged RFT - 4%	Atrial fibrillation
Enterocutaneous fistula - 4%	Pneumothorax
Pulmonary complications - 2%	Pulmonary embolism
ARDS - 1%	Air leaks
Myelosuppression - 1%	Empyema
GTCS + cardiomyopathy - 1%	Bronchopleur
Bile leak - 1%	Fistula

*The major morbidity data from our tertiary cancer care center, overall 35% in 123 patients. DVT: Deep vein thrombosis, SAIO: Subacute intestinal obstruction, SSI: Surgical site infection, ARDS: Acute respiratory distress syndrome, GTCS: Generalized tonic-clonic seizure, HIPEC: Hyperthermic intraperitoneal chemotherapy, HITHOC: Hyperthermic intrathoracic chemotherapy, RFT: Renal function test

Table 2: Pathophysiological changes in hyperthermic intraperitoneal chemotherapy and hyperthermic intrathoracic chemotherapy

Organ/systems	HIPEC	HITHOC
Cardio-vascular system	Increase in HR, BP, CVP, CI (hyperdynamic circulation) Decrease in SVR and MAP Increase in intra-abdominal pressure	Decrease in venous return and cardiac output (direct cardiac compression and IVC/SVC obstruction) Increase in myocardial wall tension and oxygen demand Decrease in coronary perfusion pressure
Respiratory system	Increase in intrathoracic and airways pressure Decrease in FRC	Increase in intrathoracic pressure Mediastinal shift with increase in airway pressure and decrease in FRC
Hematological system	Decrease in platelet count Prolonged PT/INR	Decrease in platelet count Prolonged PT/INR
Metabolism and pathophysiology	Metabolic acidosis (increased lactate level) Increase in ETCO2 Increase in oxygen extraction and consumption Hypomagnesemia (cisplatin induced) Hyperglycemia, lactic acidosis, hyponatremia (5% dextrose used as carrier with oxaliplatin)	Metabolic acidosis (increased lactate level) Increase in ETCO2 Increase in oxygen extraction and consumption Hypomagnesemia (cisplatin induced) Hyperglycemia, lactic acidosis, hyponatremia (5% dextrose used as carrier with oxaliplatin)
Systemic	Neurotoxicity, nephrotoxicity (cisplatin induced)	Pulmonary edema, nephrotoxicity (cisplatin induced), cardiotoxicity (doxorubicin induced)

HR: Heart rate, BP: Blood pressure, CVP: Central venous paper, CI: Cardiac index, SVR: Systemic vascular resistance, MAP: Mean arterial pressure, FRC: Forced respiratory capacity, PT/INR: Prothrombin time/international normalized ratio, ETCO2: End-tidal CO2, SVC: Superior vena cava, IVC: Inferior vena cava, HIPEC: Hyperthermic intraperitoneal chemotherapy, HITHOC: Hyperthermic intrathoracic chemotherapy

disease with diaphragmatic involvement with or without malignant pleural effusion. The perioperative management of this procedure requires good communication between the surgeon and anesthesiologist and intensivist. As per the current study of limited experience, it is an effective and safe therapeutic procedure for improving the patient's longevity of life and controlling disease progress in a selected group of patients. Thereby, it improves the quality of life of the patient along with the assumption to improve disease-free and overall survival.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Acknowledgment

We would like to acknowledge our Head of Department Professor (Dr.) S V S Deo, Dr BRA IRCH, AIIMS, New Delhi for constant support and inspiration. The acknowledgment extends to all faculty and senior residents of the Department of Surgical Oncology and Department of Onco-anesthesia and Palliative Care for intraoperative and postoperative patient care.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

- Mulier S, Claes JP, Dierieck V, Amiel JO, Pahaut JP, Marcelis L, et al. Survival benefit of adding hyperthermic IntraPERitoneal chemotherapy (HIPEC) at the different time-points of treatment of ovarian cancer: Review of evidence. *Curr Pharm Des* 2012;18:3793-803.
- Bristow RE, Tomacruz RS, Armstrong DK, Trimble EL, Montz FJ. Survival effect of maximal cytoreductive surgery for advanced ovarian carcinoma during the platinum era: A meta-analysis. *J Clin Oncol* 2002;20:1248-59.
- Raspe C, Piso P, Wiesenack C, Bucher M. Anesthetic management in patients undergoing hyperthermic chemotherapy. *Curr Opin Anaesthesiol* 2012;25:348-55.
- Zhou H, Wu W, Tang X, Zhou J, Shen Y. Effect of hyperthermic intrathoracic chemotherapy (HITHOC) on the malignant pleural effusion: A systematic review and meta-analysis. *Medicine (Baltimore)* 2017;96:e5532.
- Akahira JI, Yoshikawa H, Shimizu Y, Tsunematsu R, Hirakawa T, Kuramoto H, et al. Prognostic factors of stage IV epithelial ovarian cancer: A multicenter retrospective study. *Gynecol Oncol* 2001;81:398-403.
- Erasmus JJ, Goodman PC, Patz EF Jr. Management of malignant pleural effusions and pneumothorax. *Radiol Clin North Am* 2000;38:375-83.
- Stojiljkovic D, Nikolic S, Cvetkovic A, Jokic V, Spurnic I, Jokic S, et al. Hyperthermic intrathoracic chemotherapy (HITHOC) in ovarian carcinoma a propos of a case. *J BUON* 2018;23:153-5.
- Hua Z, Wu W, Tang X, Zhou J, Shen Y. Effect of hyperthermic intrathoracic chemotherapy (HITHOC) on the malignant pleural effusion: A systematic review and meta-analysis. *Medicine* 2017;96:e5532.
- Stojiljkovic D, Nikolic S, Cvetkovic A, Jokic V, Kocic M,

- Filipovic J. Hyperthermic intrathoracic chemotherapy (hithoc) in ovarian carcinoma review of literature and a case report. *Eur J Surg Oncol* 2019;45:e64.
10. Sugarbaker PH, Chang D, Stuart OA. Hyperthermic intraoperative thoracoabdominal chemotherapy. *Gastroenterol Res Pract* 2012;2012:623417.
 11. Sugarbaker PH, Stuart OA, Eger C. Pharmacokinetics of hyperthermic intrathoracic chemotherapy following pleurectomy and decortication. *Gastroenterol Res Pract* 2012;2012:471205.
 12. Ramegowda JK, Salam MA, Nayak V, Zaveri S. Anaesthetic management of extra-pleural pneumonectomy and hyperthermic intrathoracic chemotherapy procedure. *Indian J Anaesth* 2015;59:807-10.
 13. Zhao ZY, Zhao SS, RenM, Liu ZL, Li Z, Yang L. Effect of hyperthermic intrathoracic chemotherapy on the malignant pleural mesothelioma: A systematic review and metaanalysis. *Oncotarget* 2017;8:100640-47.
 14. Sheshadri DB, Chakravarthy MR. Anaesthetic Considerations in the perioperative management of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. *Indian J Surg Oncol* 2016;7:236-43.
 15. Chua TC, Yan TD, Saxena A, Morris DL. Should the treatment of peritoneal carcinomatosis by cytoreductive surgery and hyperthermic intraperitoneal chemotherapy still be regarded as a highly morbid procedure? A systematic review of morbidity and mortality. *Ann Surg* 2009;249:900-7.
 16. Ried M, Potzger T, Braune N, Neu R, Zausig Y, Schalke B, *et al.* CRS and HITHOC perfusion for malignant pleural tumours: Perioperative management and clinical experience. *Eur J Cardiothoracic Surg* 2013;43:801-7.
 17. Lim MC, Kang S, Choi J, Song YJ, Park S, Seo SS, *et al.* Hyperthermic intraperitoneal chemotherapy after extensive cytoreductive surgery in patients with primary advanced epithelial ovarian cancer: Interim analysis of a phase II study. *Ann Surg Oncol* 2009;16:993-1000.
 18. Kanakoudis F, Petrou A, Michaloudis D, Chortaria G, Konstantinidou A. Anaesthesia for intraperitoneal perfusion of hyperthermic chemotherapy. Haemodynamic changes, oxygen consumption and delivery. *Anaesthesia* 1996;51:1033-6.
 19. Schumann R, Wilson G, Hariskov S, Buck D, Goodman M, Balonov K, *et al.* Impact of Intraoperative anaesthetic and fluid management on 30 day postoperative outcomes in a newly established surgical peritoneal surface malignancy program. *J Anesth Clin Res* 2012;3:1-4.
 20. Cooksley TJ, Haji-Michael P. Postoperative critical care management of patients undergoing cytoreductive surgery and heated intraperitoneal chemotherapy (HIPEC). *World J SurgOncol* 2011;9:169.