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Original Research

Incidence of Post-operative Pulmonary Complications Following Cytoreductive Surgeries and HIPEC: A Retrospective Analytic Study

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Background and objective: Cytoreductive surgery (CRS) is performed to treat macroscopic disease, while Hyperthermic intraperitoneal chemotherapy (HIPEC) is used to address microscopic residual disease. Abdominal surgeries may be associated with pulmonary complications and prolonged hospital stays. This retrospective study aimed to determine the incidence of post-operative pulmonary complications occurring within 30 days following CRS and HIPEC, as well as identify the responsible risk factors.

Materials and methods: The retrospective study included patients who underwent CRS and HIPEC. Patient data was retrieved from May 31, 2018, to June 30, 2022. Data was obtained from patient records and registers kept in the medical records library. Post-operative pulmonary complications were noted, and risk factors were identified.

Results: A total of 27 CRS with HIPEC surgeries were performed during the study period. The procedures were conducted on patients with primary tumors of the ovary, colon, appendix, Ewing's sarcoma pelvis, and peritoneum. Six patients developed post-operative pulmonary complications, including pleural effusion in four patients and acute respiratory distress syndrome (ARDS) in two patients.

Conclusion: The incidence of post-operative pulmonary complications in our study following CRS and HIPEC was 22%. Pleural effusion was the most common complication observed, followed by ARDS. Intrinsic disease in association with hypoalbuminemia (< 2 gm/dl) was identified as an important factor contributing to pleural effusion.

Introduction

Peritoneal carcinomatosis (PC) is usually associated with a poor prognosis. The combination of cytoreductive surgery (CRS) and Hyperthermic intraperitoneal chemotherapy (HIPEC) has shown to be an effective therapeutic option for certain selected patients with primary and secondary

peritoneal carcinomatosis (PC). Cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) has been nicknamed the ‘mother of all surgeries’ due to the magnitude of resection and peri-operative haemodynamic alterations [1].

Cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) is a major undertaking with profound peri-operative metabolic and haemodynamic alterations. It requires standardised protocols for immediate postoperative intensive care management to improve patient-related outcomes.

CRS is theoretically performed to treat the macroscopic disease and HIPEC is used to treat any microscopic residual disease with the intention of treating the PC by a single procedure. Such patients are routinely admitted to the ICU postoperatively. Abdominal surgeries are sometimes associated with pulmonary complications and also prolonged hospital stays [2]. Historically the morbidity and mortality rates documented in the literature for CRS and HIPEC ranged from 40 to 60% and 10 to 20%, respectively [3].

The aim of this study was to determine the incidence of post-operative pulmonary complications occuring within 30 days following cytoreductive surgeries and HIPEC.

Materials and Methods

This was a retrospective analytic study. The study was initiated after approval by the Institutional review board. The study was done in patients who underwent CRS and HIPEC in Malabar Cancer Centre. Patient’s data was retrieved from 31st May 2018 to 30th June 2022. The data was obtained from the patient records and registers kept in the medical records library.

The primary objective was to determine the incidence of post-operative pulmonary complications within 30 days following cytoreductive surgeries and HIPEC. The secondary objective was to identify the risk factors associated with the pulmonary complications.

Inclusion criteria

• All those patients who underwent CRS and HIPEC surgeries during the mentioned period.

Exclusion criteria

• Immediate mortality (within 2 hours of surgery)

The variables recorded were

Gender, age, comorbidities, body, primary cancer location,peritonectomy procedures, visceral resections and anastomoses done, time in the operating room in intraoperative events, blood products given,post operative pulmonary complications, duration of mechanical ventilation, Glisson’s capsulectomy and chest drainage tube insertion. Anaesthesia-All patients had received epidural and general anesthesia.Central venous and arterial line catheterisation was also performed in these patients. The HIPEC protocol at our centre is cisplatin for ovarian/gastric and other rare tumours, and mitomycin was used for pseudomyxoma peritonei and colorectal malignancies. The method used is closed technique, hyperthermic perfusion at 41 to 42 °C maintained for 60-90 minutes. All patients after CRS and HIPEC were transferred to our intensive care unit for postoperative management. We opted for overnight elective mechanical ventilation (MV) postprocedure if the following factors were present: massive resection due to higher PCI (PCI ≥ 8), diaphragmatic resection or subdiaphragmatic peritoneal stripping performed, duration of surgery≥6 h, intraoperative haemodynamic instability/ cardiac arrhythmias, abnormalities in the

arterial blood gas analysis (ABG), DIC and patient-related risk factors for postoperative pulmonary complications such as obesity, smoking history and chronic obstructive airway disease (COAD).

Statistical analysis

The data was entered using Microsoft Excel 2021 and the data was analysed using SPSS version 23.

Results

In this study there were 27 surgeries of CRS with HIPEC. 21 patients were females (77.77%). The characteristics of the patients have been given in Table 1and 2.

Mean Age (years)	46.59
BMI (kg/m²)	24.24
Comorbidities	
Diabetes mellitus	6
Hypertension	2
Hypothyroidism	2
Gender	
Male	6
Female	21
Primary tumour	
Ovary	16
Appendix	4
Colon	4
Peritoneal carcinomatosis	2
Ewings sarcoma pelvis	1
Average operative time (hours)	7.36 ± 1.5
Average blood loss (ml)	1081.48 ± 859.69
Average packed RBC transfused	2.41± 1.67
Inotropic support	9 patients
Glisson’s capsulectomy	6 patients
Chemotherapy drug used	
Mitomycin	9
Cisplatin	18
Duration of mechanical ventilation	38 ± 8
Pulmonary complications	
Pleural effusion	4
ARDS	2

Table 1. Characteristics of the Patients in this Study.

	Number	Intervention done
Pleural effusion	4	Chest drainage/ reintubation
Respiratory distress	2	NIV/Reintubation/ Tracheostomy

Table 2. Pulmonary Complication.

The duration of HIPEC done (dwell time) was 60 minutes in 26 patients 1 patient had a dwell time of 90 minutes All the patients had undergone total peritonectomy. Four patients had undergone bowel resection and anastomoses. Inotropic support was started in 9 patients, majority of which was stopped by the post operative day 1. Glissons capsulectomy was done in 6 patients.The

complications included pleural effusion and ARDS. The details of the complications have been given in Table 1. Chest drainage tubes were inserted ,anticipating pleural effusion in 9 patients after diaphragmatic peritonectomy.

There was no statistical difference between the patients with pulmonary complications from those without pulmonary complications (p=0.09).

Discussion

The incidence of grade ¾ pulmonary complications was in the range of 10–16 % in several studies [4-7]. Table 3 shows the pulmonary adverse events scored from grade I through grade IV.

Adverse event	Grade I	Grade II	Grade III	Grade IV
Respiratory distress	Mild symptoms	Oxygen therapy or medications required	Endotracheal intubation	Tracheostomy required
Pleural effusion	Asymptomatic	Diuretics required	Thoracocentesis required	Compromised, chest tube insertion
Pneumonia	Minimal symptoms	Antibiotics and respiratory therapy	Bronchoscopy	Intubation required

Table 3. Grades of Pulmonary Adverse Events.

Pleural effusion was found to be a relatively common event which is described in many reports and it could be due to several factors. The diaphragmatic peritoneal stripping leads to a mechanical and thermal injury of the muscle. This injury leads to fluid access to the thorax from the abdomen of the chemotherapy solution used during HIPEC.

In the absence of systematic thoracic drainage, stripping of the diaphragmatic peritoneum leads to significant increase in post-operative pleural effusions, [8,9]. This strategy can decrease but not abolish the intrinsic risk of pleural effusion [3].

There is a significant risk of post-operative infectious complications and pneumonia , approximately reported in 3.2–10% of patients who have undergone peritonectomy procedures [4,7-13].

The incidence of postoperative pulmonary complications was 22 % following CRS and HIPEC in our study. The most common complication was pleural effusion followed by ARDS.

In our study 4 patients developed pleural effusion. Of these 4 patients, 3 patients with carcinoma ovary had full thickness diaphragmatic rents which was repaired and chest drainage tubes were inserted prophylactically. In the 4^{th} patient, a case of carcinoma appendix,chest drainage tubes were inserted after detecting pleural effusion in the post operative period. All the 4 patients had hypoalbuminemia, (<2.0gm/dl) post operatively. The intrinsic disease in association with hypoalbuminemia was found to be an important factor for causing pleural effusion.

The two patients who had ARDS post operatively had features of sepsis. Both patients had features suggestive of pneumonia in the chest X-ray.

Diaphragmatic peritonectomy per se was found not to be solely associated with pleural effusion.

Sand et al in a study done in 417 patients found that (17%) of patients developed severe postoperative pulmonary complications. A full thickness diaphragmatic injury or diaphragmatic resection were the risk factors noted [14].

Preti et al conducted a study in 147 patients.Pulmonary adverse events were noted in 10% of their patients who underwent CRS and HIPEC. They concluded that subphrenic peritonectomy was not a

specific risk factor for developing these pulmonary adverse events [5].

Arakelian et al conducted a study in 76 patients and found that, 6 patients required thoracocentesis and the another 6 needed chest tube insertion. There was no statistically significant difference in post-operative recovery between the non-intervention and intervention groups [15].

In our study although chest drainage tubes were inserted prophylactically in 9 patients anticipating pleural effusion, 5 patients did not have any features of pleural effusion.

Several factors have to be considered while performing CRS and HIPEC. It should be done in a multidisciplinary setting with due consideration of the risks and benefits. The timing in relation to systemic chemotherapy, patient factors and operative factors are some factors to be considered.Patient factors such as age, nutrition status and performance status; and operative factors such as peritoneal cancer index (PCI), the organs affected by disease, tumor histology, and surgeon experience are some factors affecting morbidity and mortality. A good understanding of the patient and operative factors associated with morbidity and mortality allows for more better patient selection and decision making.

CRS and HIPEC performed for disseminated intra-abdominal malignancies is a complex procedure with a high risk for morbidity and mortality.When CRS and HIPEC is performed at high volume centers and experienced hands, it can be associated with prolonged survival with acceptable morbidity and mortality rates.

The limited existing data suggests that the contribution of the intraperitoneal chemotherapy to overall morbidity is small, and that the majority of morbidity is because of the abdominal surgery. Therefore larger studies which evaluate the individual contribution of intraperitoneal chemotherapy to CRS and HIPEC morbidity and mortality and to long-term outcomes are required.

Several predictive factors responsible for moderate to severe morbidity following CRS and HIPEC have been analysed. Several studies have shown a direct relationship between the extent of disease and grade 3/4 morbidity and mortality. Extended peritoneal carcinomatosis definitely requires more extensive surgery, longer operating time, greater blood loss and is therefore consequently associated with higher complication rates.

There are a few limitations of this study. a) This is a retrospective study, b) The sample size used is small. Therefore there is a need for a prospective study in a larger population to find out the associated outcomes.

In conclusion, in our study the incidence of postoperative pulmonary complications was 22 % following CRS and HIPEC surgeries.The most common complication was pleural effusion followed by ARDS. The intrinsic disease in association with hypoalbuminemia (<2gm/dl) was found to be an important factor for causing pleural effusion.

References

References

1. 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 [Internet]. Database of Abstracts of Reviews of Efects (DARE): quality-assessed reviews [Internet]. Centre for Reviews and Dissemination (UK); 2009 [cited 2023 Feb 24]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK76965/. 2009.
2. Lawrence VA, Hilsenbeck SG, Mulrow CD, Dhanda R, Sapp J, Page CP. Incidence and

hospital stay for cardiac and pulmonary complications after abdominal surgery. *Journal of General Internal Medicine.* 1995; 10(12)DOI
3. Foster JM, Sleightholm R, Patel A, Shostrom V, Hall B, Neilsen B, Bartlett D, Smith L. Morbidity and Mortality Rates Following Cytoreductive Surgery Combined With Hyperthermic Intraperitoneal Chemotherapy Compared With Other High-Risk Surgical Oncology Procedures. *JAMA network open.* 2019; 2(1)DOI
4. Kusamura S, Younan R, Baratti D, Costanzo P, Favaro M, Gavazzi C, Deraco M. Cytoreductive surgery followed by intraperitoneal hyperthermic perfusion: analysis of morbidity and mortality in 209 peritoneal surface malignancies treated with closed abdomen technique. *Cancer.* 2006; 106(5)DOI
5. Preti V, Chang D, Sugarbaker PH. Pulmonary Complications following Cytoreductive Surgery and Perioperative Chemotherapy in 147 Consecutive Patients. *Gastroenterology Research and Practice.* 2012; 2012DOI
6. Sugarbaker P, Van der Speeten K, Stuart O, Chang D, Mahteme H. Patient-and treatment-related variables, adverse events and their statistical relationship for treatment of peritoneal metastases. In: Sugarbaker PH (ed) Cytoreductive surgery and perioperative chemotherapy for peritoneal surface malignancy: textbook and video atlas. Cine-Med, Connecticut. 2012.
7. Yan TD, Zappa L, Edwards G, Alderman R, Marquardt CE, Sugarbaker PH. Perioperative outcomes of cytoreductive surgery and perioperative intraperitoneal chemotherapy for non-appendiceal peritoneal carcinomatosis from a prospective database. *Journal of Surgical Oncology.* 2007; 96(2)DOI
8. Chéreau E, Ballester M, Selle F, Cortez A, Pomel C, Darai E, Rouzier R. Pulmonary morbidity of diaphragmatic surgery for stage III/IV ovarian cancer. *BJOG: an international journal of obstetrics and gynaecology.* 2009; 116(8)DOI
9. Dowdy SC, Loewen RT, Aletti G, Feitoza SS, Cliby W. Assessment of outcomes and morbidity following diaphragmatic peritonectomy for women with ovarian carcinoma. *Gynecologic Oncology.* 2008; 109(2)DOI
10. Glehen O, Osinsky D, Cotte E, Kwiatkowski F, Freyer G, Isaac S, Trillet-Lenoir V, et al. Intraperitoneal chemohyperthermia using a closed abdominal procedure and cytoreductive surgery for the treatment of peritoneal carcinomatosis: morbidity and mortality analysis of 216 consecutive procedures. *Annals of Surgical Oncology.* 2003; 10(8)DOI
11. Capone A, Valle M, Proietti F, Federici O, Garofalo A, Petrosillo N. Postoperative infections in cytoreductive surgery with hyperthermic intraperitoneal intraoperative chemotherapy for peritoneal carcinomatosis. *Journal of Surgical Oncology.* 2007; 96(6)DOI
12. Stephens AD, Alderman R, Chang D, Edwards GD, Esquivel J, Sebbag G, Steves MA, Sugarbaker PH. Morbidity and mortality analysis of 200 treatments with cytoreductive surgery and hyperthermic intraoperative intraperitoneal chemotherapy using the coliseum technique. *Annals of Surgical Oncology.* 1999; 6(8)DOI
13. Schmidt U, Dahlke MH, Klempnauer J, Schlitt HJ, Piso P. Perioperative morbidity and quality of life in long-term survivors following cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. *European Journal of Surgical Oncology: The Journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology.* 2005; 31(1)DOI
14. Sand O, Andersson M, Arakelian E, Cashin P, Semenas E, Graf W. Severe pulmonary complications after cytoreductive surgery and hyperthermic intraperitoneal chemotherapy are common and contribute to decreased overall survival. *PloS One.* 2021; 16(12)DOI
15. Arakelian E, Torkzad MR, Bergman A, Rubertsson S, Mahteme H. Pulmonary influences on early post-operative recovery in patients after cytoreductive surgery and hyperthermic intraperitoneal chemotherapy treatment: a retrospective study. *World Journal of Surgical Oncology.* 2012; 10DOI