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Updates on Peritoneal Surface Malignancy Cytoreductive Surgery and Hyperthermic Intraoperative Peritoneal Chemotherapy Morbidity and Mortality Outcomes from the Shiraz Surgical Oncology Group

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Abstract

Background: Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) are well-known in the treatment of different types of peritoneal carcinomatosis (PC). CRS and HIPEC are associated with several major comorbidity and can affect patients short-term and long-term outcomes. The present study aimed to evaluate the short term follow up, mortality and morbidity rate of CRS and HIPEC of recent period surgery compared with our previously reported study patients.

Method: Short-term follow-up data were collected and analyzed for 150 PC patients who underwent CRS-HIPEC between 2017 and 2021 compared with 43 patients from our retrospective cohort study. Data were analyzed using SPSS 23. The statistical significance was determined by a *P*-value < 0.05.

Results: Mortality at 60 days of the 2017-2021 group and the 2016 group was 1.33% (2/150) and 7 % (3/43), respectively. The 2017-2021 group showed less minor and major complications according to Clavien-Dindo classification. Overall, the mortality and morbidity rates were lower as compared with our previous reported study.

Conclusion: Our center has achieved an acceptable and progressive route through the use of CRS and HIPEC for PC, as demonstrated by our study.

Keywords: Peritoneal neoplasms, Cytoreductive surgery, Chemotherapy, Morbidity, Mortality

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Introduction

The standard treatment for certain peritoneal malignancies is cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC). Surgical

Table 1. Patient clinical characteristics, operative, morbidity and mortality and complication data in both 2016 and 2107-2021 groups

	2016 group (n=43, range, %)	2107-2021 group (n=150; range; %)	*P*-Value
Bleeding, mL	528.84 ± 564.64	415.15 ± 315.50	0.08
Duration of procedure (minutes)	368.79 ± 95.88	359.56 ± 78.55	0.51
PCI score	8.79 ± 5.83	10.3 ± 6.7	0.18
ICU Stay, median day (range)	2 (0-32)	2(0-34)	0.99
Hospital Stay, median day (range)	7 (2-48)	6(2-35)	0.49
Mortality at 60 days, No. (%)	3 (7)	2(1.3)	0.04
Overall survival, No. (%)	31 (72.1)	111(74)	0.80
Surgical morbidity, No. (%)			
No complication	35 (81.4)	125(83.3)	0.94
Wound infection	1 (2.3)	3(2)	0.99
Intra-abdominal abscess/collection	2 (4.7)	6(4)	0.99
Ileus or DGE >7 days (delayed gastric emptying)	4 (9.3)	11(7.33)	0.47
Leak/fistula	1 (2.3)	5 (3.3)	0.11
Minor and major complications, Clavien-Dindo classification, 60 days post-op			
Deviation from Normal post-operative course without the need for intervention (Grade 1)	10 (23.25)	35 (23.33)	0.99
Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions, antibiotics and total parenteral nutrition are also included (Grade 2)	10 (23.25)	12 (8)	
Requiring surgical or endoscopic or radiologic intervention (Grade 3)	5 (11.62)	13(8.66)	
Organ dysfunction (Grade4)	3 (6.97)	11(7.33)	
Patient demise (Grade 5)	3 (6.97)	2(1.33)	

PCI: Peritoneal carcinomatosis index; ICU: Intensive care unit; DGE: Delayed gastric empty

treatment focuses on eradicating all or almost all macroscopically visible tumors, while HIPEC concentrates on eradicating microscopic residual tumors.[1]

For 40 years, treating peritoneal malignancy with CRS in combination with HIPEC has been widely practiced improved survival[2] has been recorded, particularly in patients with colorectal cancer and peritoneal carcinomatosis,[3] pseudomyxoma peritonei (PMP),[4] peritoneal mesothelioma,[5] locally advanced ovarian cancer.[6]

The mortality rate ranges from 7.6 to 9% and the morbidity rate varies from 39 to 67.6% in older publications.[2, 7]

Sugarbaker's introduction of CRS and HIPEC in 1996 resulted in a mortality rate of 5% and a morbidity rate of 35%, but the rates were decreased to 1.5% and 27% after a few years.[2]

It seems that teams who use the method attain the global learning curve and reach a plateau. Not using the learning curve will lead to unacceptably high morbidity and mortality rates.[8,9]

This article is aimed at presenting a brief comparison that focuses on the efficacy and safety of CRS and HIPEC for patients with peritoneal malignancies in two periods of time in our center.

Materials and Methods

This retrospective study analyzed data from patients undergoing CRS/HIPEC for peritoneal tumors between 2017 and 2021. Clinical records and follow-up assessments were used to collect data on perioperative outcomes, complications, and short-term survival rates. The documentation included patient demographics, tumor characteristics, and treatment details.

Short-term follow-up data were collected and analyzed for 150 peritoneal carcinomatosis (PC) patients who underwent CRS-HIPEC between 2017 and 2021 compared with 43 patients from our retrospective cohort study. Written informed consent was obtained from all study participants.

The Ethics Committee of Shiraz University of Medical Sciences approved the study protocol. The Ethics Committee reference number was IR.SUMS.REC.1398.1061. The difference in morbidity and mortality rates during this period was compared using data from our previous study.[8]

The laparotomy was used for CRS and HIPEC procedures by making a long midline incision, exploring the abdominal cavity, and evaluating the resectablity of the lesions. To eliminate all visible tumor nodules, careful dissection was performed. Peritoneal carcinomatosis index (PCI) was used to evaluate the extent of PC. As previously mentioned, the completeness of CRS score (CSS) was used to evaluate the effectiveness of CRS. All gross tumors and involved tissues, including the peritoneum and supracolic omentum, were removed during CRS, as was the objective of the procedure. After completing CRS, an open abdomen was used to carry out all HIPEC procedures with a HIPEC device. Continuous monitoring was conducted by placing temperature probes on the inflow and outflow tubing. A perfusion circulation was recognized with about 3 L of Ringer's lactate. A HIPEC device was used to maintain flow rates of approximately 1.2 L/min. Following the initial chemotherapy dose, we planned a total perfusion time of 90-110 minutes, with outflow temperature of 42oC. In heated intraperitoneal chemotherapy through HIPEC device, Mitomycin C 30 mg and 10 mg, respectively at 0 and 45 minutes, were entered into the abdomen and circulated for 90 minutes for colorectal, appendiceal, and PMP. At 0 o'clock, CDDP Cisplatin 50 mg/m2 was put in the abdomen to treat primary peritoneal carcinomatosis for 90 minutes. During the 90-minute circulation for ovarian cancer PC, CDDP Cisplatin 75 mg/m^2 was inserted into the abdomen.

Statistical analysis

The statistical analyses were carried out through statistical package for the social sciences (version 23; IBM SPSS Inc. Chicago, IL, USA). All the data were collected retrospectively and descriptive statistics were generated for all measures, including means, median, ranges, and standard deviations for continuous measures and frequencies and proportions for categorical data. The statistical significance was determined by a *P*-value < 0.05.

Results

The retrospective cohort study compared outcomes between two periods: 2016 (n=43) and 2017-2021 (n=150). The mortality rate at 60 days decreased significantly from 7% (3/43) in 2016 to 1.33% (2/150) in 2017-2021 (P = 0.04). Major complications, as defined by Clavien-Dindo Grade III-V, were reduced, with fewer Grade V complications observed (6.97% in 2016 vs. 1.33% in 2017-2021). Hospital stay also showed improvement, with a median of 7 days in 2016 reduced to 6 days in 2017-2021.

There was no significant difference in terms of intraoperative bleeding, duration of procedure, PCI score, ICU stay, and overall Survival between two study groups.

Overall, these findings indicate a substantial improvement in patient outcomes and perioperative safety following CRS-HIPEC (Table 1).

Discussion

This retrospective cohort was initially analyzed and found to have lower morbidity and mortality compared with our previous reported study. Our patient cohort has shown a significant decrease in hospital stay, mortality at 60 days, post-operative complications morbidity, and Clavien-Dindo classification morbidity score, all of which demonstrate the safety of CRS/HIPEC in our center.

According to the international literature, experience leads to a reduction in the incidence of morbidity and mortality rates for CRS and HIPEC. According to experts, achieving the learning curve requires at least 1109 or 140 to 150 cytoreductions.[10, 11] Morbidity and mortality can be acceptable if the selection of candidates for CRS and HIPEC is limited to patients who can undergo complete or near-complete cytoreduction.[10-14]

Possible predictors of morbidity include the extent of peritoneal malignancy and the number of anastomosis. There is a low mortality rate. The

learning curve is confirmed to be safe for CRS and HIPEC, resulting in low and acceptable incidence of morbidity and mortality.

At present, the majority of Western guidelines advocate for the combination of cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) as the standard treatment for specific patients with colorectal peritoneal metastases (PM).[15-16] Asian oncological societies suggest that patients with minimal colorectal PM should consider CRS/HIPEC.[17] However, there is limited clinical evidence derived from Iranian patients.[8, 18, 19]

Asian-Pacific and Iranian centers have recently published retrospective cohort studies with limited median follow-up (16-37 months), with at-least 40% of procedures performed for appendiceal, colorectal, and ovarian PM.[8, 18-24]

Our findings were comparable, indicating a 5.3% complication rate for those who are in grade III or higher and a 60-day mortality rate of 1.3%. We believe that our morbidity and mortality rates are acceptable since CRS/HIPEC learning curve is short and only requires less than 200 cases to master.

In Asia, the survival rate for appendiceal PM patients after CRS/HIPEC was equivalent to that found in Western centers, but colorectal PM patients appeared to have a worse prognosis. Differences in patient selection and tumor biology, as well as experience in performing this complex procedure may be behind this. To determine the long-term oncological outcome of CRS/HIPEC in Asian patients, more studies, especially large prospective trials, are necessary. In order to maximize oncological benefit and minimize risks, it is crucial to select patients carefully.

The major morbidity and mortality rates in Asian-Pacific and Iranian centers 17.1-40.4% and 0-3.7%,[18-24] were comparable to those in the West, respectively.[8]

This work experienced numerous limitations, including a small population and being retrospective. Other confounding factors related to the different PC origins and the role of systemic therapy on the performance of isolated peritoneal disease.

Conclusion

Our findings were comparable, suggesting that there were fewer 60-day post-operative complications and mortality rates in the 2017-2021 group. The learning curve of CRS/HIPEC has reached an acceptable level in our center recently, which has resulted in an improvement in our morbidity and mortality rates.

Authors' Contribution

M.A: Study design, Hypothesis, surgical procedure, data gathering, drafting and reviewing the manuscript; MYK: Study design, data gathering and analysis and reviewing the manuscript; All authors have read and approved the final manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Conflict of Interest

None declared.

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