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The evaluation of morbidity in gastrointestinal tumor patients underwent cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (HIPEC)

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ABSTRACT

Objective: In this study, we aimed to determine the postoperative morbidity rate and identify demographic, clinical, and treatment-related variables that may be potential risk factors for morbidity in gastrointestinal tumor patients undergoing hyperthermic intraperitoneal chemotherapy (HIPEC) with or without cytoreductive surgery (CRS).

Material and Methods: In this retrospective study, 60 patients who had undergone HIPEC due to gastrointestinal tumor between October 2017 and December 2019 were included. Systemic toxicities were graded and evaluated according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 3.0 criteria.

Results: Mean age of the patients was 60.43 ± 12.83. Primary tumor localization was the stomach in 33 patients (55%), colon in 21 (35%), rectum in five (8.3%), and appendix in one patient (1.7%). PCI mean value was 9.51 ± 10.92. CC-0 was applied in 37 (61.7%) patients, CC-1 in 11 (18.3%), CC-2 in 6 (10%), and CC-3 in six patients (10%). Morbidity was observed in 50 (83.33%) of the 60 patients participating in the study according to NCI-CTCAE v3.0 classification. Mild morbidity rate was 46.6%, severe morbidity rate was 36.6%, and mortality rate was 11.66%. Enteric diversion application, length of stay in the ICU, and length of hospital stay were shown to have a statistically significant effect on the NCI-CTCAE morbidity score ($p= 0.046$, $p= 0.004$, $p< 0.001$).

Conclusion: With proven beneficial effects on survival in patients with locally advanced gastrointestinal tumors, CRC and HIPEC are acceptable in these patients despite their increased morbidity and mortality rate. With new studies on this subject, morbidity and mortality rates may be reduced.

Keywords: Gastrointestinal tumor, cytoreductive surgery, hyperthermic intraperitoneal chemotherapy, morbidity, HIPEC

INTRODUCTION

Peritoneal spread that occurs in primary gastrointestinal cancers (such as the stomach, colon, rectum and appendix) is a common cause of treatment failure (1). The effectiveness of chemotherapy and immunotherapy alone in the treatment of peritoneal carcinomatosis (PC) is limited. Therefore, effective treatments have been sought. Methods such as various combinations of systemic chemotherapy and hyperthermic intraperitoneal chemotherapy (HIPEC) with or without cytoreductive surgery (CRS) have been studied to improve survival and prevent complications. CRS/HIPEC has been used since the 1980s to treat peritoneal malignancy caused by colorectal adenocarcinoma, appendix mucinous carcinoma, and gynecological malignancies (2).

Combined CRS/HIPEC therapy performed in specialized centers has been shown to be an effective treatment option for selected patients with primary and secondary PC. In this dual combination, CRS is used to treat macroscopic disease and HIPEC is used to treat microscopic residual disease. This combination method has slowly become the accepted standard treatment for diseases such as pseudomyxoma peritonei and peritoneal mesothelioma (3-5). In addition, the best long-term results for PC from colorectal cancer have been reported with CRS/HIPEC (6,7). Although there has been quite a bit of research showing that CRS/HIPEC is beneficial, some oncologists remain uncertain of this therapeutic approach due to its high toxicity (8).

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For peritoneal metastases, the benefit of CRS-HIPEC is well defined, and the toxicities associated with treatment are well known. Major morbidity rates of 24-34% and mortality rates of 2-4% have been reported following CRS/HIPEC in large patient series (5,9-13). The most commonly used morbidity and mortality classification systems that assist surgeons in characterizing postoperative complications are Clavien, Feldman, Elias, Bozetti and the National Cancer Institute's (NCI) Common Terminology Criteria for Adverse Events (CTCAE) (14-22). In our study, we chose NCI-CTCAE version 3.0 to classify surgical morbidity, HIPEC toxicity, and mortality (14). The aim of our study was to determine the postoperative morbidity rate and identify demographic, clinical, and treatment-related variables that may be potential risk factors for morbidity in gastrointestinal tumor patients undergoing HIPEC with or without CRS.

MATERIAL and METHODS

This retrospective study was held in the General Surgery Clinic of Trakya University Faculty of Medicine Hospital, Türkiye between October 2017 and December 2019. Institutional human study review committees of Trakya University Faculty of Medicine (2019/397) approved the study which was conducted in accordance with the tenets of the Declaration of Helsinki, and written informed consent was obtained from all subjects. Data of 60 patients (41 males, 19 females) that had undergone HIPEC were evaluated. Patients under the age of eighteen, who were pregnant, who were unable to give their consent to the procedure, or whose data could not be accessed were excluded from the study.

Age, sex, comorbidities, primary tumor focus (cecum, ascending colon, hepatic corner, transverse colon, splenic corner, descending colon, sigmoid colon tumors in a single group; colon tumors), the operation performed, PCI and complete cytoreduction score (CC), whether they received neoadjuvant therapy or not, duration of hospital stay, intensive care unit (ICU) stay, operation time and data of side effects, morbidity and complications that occurred during the follow-up of the patients were collected after obtaining consent from the patients. The CC score was calculated over the residual tumor in the patient after cytoreduction was complete. In this study, scoring was assessed as CC-0, no residual disease; CC-1, minimal residual disease (0-2.5 mm residual); CC-2, residual disease between 2.5 mm and 2.5 cm; and CC-3, residual disease above 2.5 cm. PCI scores were further divided into three groups, No PC: PCI= 0; Mild PC: 0< PCI< 13; and Severe PC: PCI> 13. The number of patients was determined according to Bozzetti, Elias, Feldman and NCI-CTCAE v.3 scoring. NCI-CTCAE scores were also grouped into no morbidity: grade 0, mild morbidity: grade 1 and 2, and severe morbidity: grade 3, 4 and 5. NCI-CTCAE v.3 scores and groups formed according to these scores, age, sex, PCI score and the groups formed from this score, CC score, primary tumor focus, whether neoadjuvant was taken or not, splenectomy or enteric diversion performed during the surgery, hypertension, type II diabetes, coronary artery disease, previous cerebrovascular disease, surgery time, length of stay in the hospital and ICU were evaluated. Similarly, the duration of surgery, length of hospital stay, and length of stay in the ICU were compared with the CC score and PCI score and the groups formed from this score.

Statistical Analysis

Normal distribution was evaluated by Shapiro-Wilk test. For comparisons of more than two groups, one-way analysis of variance was used for normally distributed variables, and Kruskal-Wallis test was used for variables that were not normally distributed. The relations between qualitative variables were evaluated using Pearson Chi-square test, and the relations between quantitative variables were evaluated with Spearman correlation analysis. As descriptive statistics for quantitative variables, mean and standard deviation were used for normally distributed variables, and medians and quartiles were used for variables that were not normally distributed. Frequency and percentage were given for qualitative variables. The level of significance was set at 0.05 in all statistical analyses. All statistical analyses were performed using the TURCOSA (www.release.turcosa.com.tr) statistical package program.

RESULTS

Demographic characteristics of the patients included in the study are given in Table 1. Mean of the patients was 60.43 ± 12.83 (range, 23-83). Twenty-nine patients (48%) had hypertension, 13 (22%) type II diabetes mellitus, 10 (17%) coronary artery disease and two (3.3%) previous cerebrovascular disease as comorbidity. Thirty-three of the patients (55%) underwent operation for gastric tumor, 21 for colon originated tumor (35%), five for rectal tumor (8.3%) and one for appendix origin tumor (1.7%). Ten of the patients (16.6%) received neoadjuvant therapy. While 12 of the patients did not have PC, 30 patients had mild PC and 18 patients had severe PC. The PCI mean value was 9.51 ± 10.92. Complete cytoreductive surgery (CC-0) for 37 (61.7%) patients, CC-1 for 11 (18.3%), CC-2 for 6 (10%), and CC-3 cytoreductive surgery for 6 (10%) was applied. Median surgery time of the patients was 292.5 (range, 115-555) minutes, and median length of hospital stay was 14 (10-47) days. Splenectomy was performed in eight (13.34%) patients, and enteric diversion was performed in eight (13.34%) patients during surgery.

Morbidity classification of the patients according to Feldman, Bozzetti, Elias and NCI-CTCAE v3.0 is shown in Table 2. According to the new classification of NCI-CTCAE v3.0, 10 patients had no morbidity, 28 patients had mild morbidity, and 22 patients had severe morbidity. Morbidity was observed in 50 (83.33%) of the 60 patients participating in the study according to NCI-CTCAE v3.0 classification. Mild morbidity rate was 46.6%, severe morbidity rate was 36.6%, and mortality rate was 11.66%.

Table 1. Demographic characteristics and perioperative characteristics of the patients included in the study

Variables	n (%)
Age, (years) Mean ± SE (min-max)	60.43 ± 12.83 (23-83)
PCI, Mean ± SE (min-max)	9.51 ± 10.92 (0-39)
Surgery time (minutes) Median (min-max)	313.51 ± 86.55 (115-555)
Length of hospital stay (days) Median (min-max)	15.61 ± 6.89 (10-47)
Receiving neoadjuvant therapy	10 (16.7%)
Splenectomy	8 (13.34%)
Enteric diversion	8 (13.34%)
Length of ICU stay (days) Median (min-max)	2.05 (0-33)
Gender	
Female	19 (31.7%)
Male	41 (68.3%)
PC	
Mild PC (PCI score between 0 and 13)	42 (40%)
Severe PC (PCI score 13 and above)	18 (30%)
CC Scores	
CC-0	37 (61.7%)
CC-1	11 (18.3%)
CC-2	6 (10%)
CC-3	6 (10%)
Primary Tumor Origin	
Stomach	33 (55%)
Colon	21 (35%)
Rectum	5 (8.3%)
Appendix	1 (1.7%)
Comorbidities	
Hypertension	29 (48%)
Type II diabetes mellitus	13 (22%)
Coronary artery disease	10 (10%)
Cerebrovascular disease	2 (3.3%)

CC: Complete cytoreduction, ICU: Intensive care unit, PC: Peritoneal carcinomatosis PCI: Peritoneal carcinomatosis index.

Morbidities observed in patients are shown in Table 3. Ninety-six morbidities were observed in total. The most common morbidity was pneumonia. Of the seven patients who died, four died due to pneumonia, one due to sepsis following esophagojejunostomy leakage in the ICU, one patient due to hemotoxicity concurrent with nephrotoxicity, and one patient because of cerebrovascular disease. Following surgery, a total of three patients had leakage: one esophagojejunostomy anastomotic leak, one duodenal stump leak, and one ileotransverostomy leakage. Pancreatic-cutaneous fistula developed in one patient. It was observed that one patient developed acute myocardial infarction on the 27th day of hospitalization following surgery.

Predictive factors that may affect the NCI-CTCAE morbidity score are shown in Table 4. It was observed that age, sex, primary tumor origin, neoadjuvant therapy, having hypertension, having Type II Diabetes Mellitus, presence of coronary artery disease, had a cerebrovascular disease, having had splenectomy, surgery time, PCI scores, and CC scores did not affect the NCI-CTCAE morbidity score. It was observed that the application of enteric diversion, the length of stay in the ICU, and the length of hospital stay had a statistically significant effect on the NCI-CTCAE morbidity score ($p= 0.046$, $p= 0.004$, and $p< 0.001$, respectively).

The relation of PC distribution of the patients with other parameters is shown in Table 5. A statistically significant correlation was observed between the PCI scores and surgical time ($p= 0.017$, $p= 0.017$). There was a weak correlation between the PCI score and surgical time (correlation coefficient= 0.31). There was no significant relation between PCI scores and PC subgroups and in the length of ICU stay ($p = 0.484$) and length of hospital stay ($p= 0.383$).

The relation between CC scores and other parameters is shown in Table 6. It was observed that there was a statistically significant relation between CC scores and surgery time, and this relationship was due to the difference between CC-0 and CC-2 ($p= 0.004$). As the CC score increases, so does the average duration of surgery; but in CC-3, the average duration fell below CC-0. There was no statistically significant relationship between CC scores and length of stay in the ICU ($p= 0.735$) and length of hospital stay ($p= 0.270$).

Table 2. Number of patients according to Feldman, Bozzetti, Elias and NCI-CTCAE v.3 morbidity classification systems

	Feldman	Bozzetti	Elias	NCI-CTCAE v.3
Grade 0			10	10
Grade 1	13	10	4	7
Grade 2	32	35	31	21
Grade 3	8	8	2	7
Grade 4	7	7	6	8
Grade 5			7	7

Table 3. Morbidities and patient numbers according to the National Cancer Institute's (NCI) Common Terminology Criteria for Adverse Events (CTCAE) v.3

	Grade 1-2	Grade 3-4-5		Grade 1-2	Grade 3-4-5
Wound infection	5		Bradycardia	1	
Evisceration		2	Atrial fibrillation	1	
Fever	6		Supraventricular tachycardia	1	
Ileus	2		Myocardial infarction		1
Atelectasis	7		Hypertension		2
Pleural effusion	8	8	Cerebrovascular disease		1
Pneumonia	16	5	Encephalopathy	2	1
Urinary tract infection	3		Duodenal stump leak		1
Central catheter infection	1		Esophagojejunostomy leakage		1
Abdominal abscess	1	1	Pancreatic fistula	1	
Intraabdominal bleeding		2	Ileotransverostomy leakage		1
Diarrhea	1		Nephrotoxicity	1	7
Hematochezia		1	Hematotoxicity	3	2

DISCUSSION

In this study, we retrospectively examined morbidity after HIPEC with or without CRS and the factors that may affect morbidity. According to the NCI-CTCAE morbidity score, total morbidity rate was 83.33%, light morbidity rate was 46.6%, severe morbidity rate was 36.6%, and mortality rate was 11.66%. It was observed that the application of enteric diversion, length of stay in the ICU, and length of stay in the hospital had a statistically significant effect on the NCI-CTCAE morbidity score. In addition, it was determined that the operation time was significantly correlated with CC scores and PCI.

Previously, patients with peritoneal metastases were considered to have an incurable disease. With the addition of CRS/HIPEC to the treatment protocol, however, there has been increasing evidence that this treatment modality is effective in treating selected patients with peritoneal metastases from the appendix (7,23), colon and rectum (8,14,24), small intestine (25,26), ovarian (27) and peritoneum (mesothelioma) cancers (28). Still, the association of this procedure with significant morbidity makes patient selection more important than anything else.

Park et al. (24) have reported a mean operative time of 9.4 hours (range 3.4-19.6) and hospital stay of 20.2 days (8-70). In another study of 420 patients undergoing HIPEC/CRS, they have observed a mean operative time of 563 minutes and a hospital stay of 22 days (25). Polanco et al. (8) have reported that median operative time was 430 minutes and hospital stay was 15.86 days in their study with 370 patients. In our study, median operative time of the patients was 292.5 (range, 115-555) minutes and median hospitalization was 14 (10-47) days. These results are similar to the results of previous studies.

The rate of severe morbidity (class 3 and 4) calculated according to NCI-CTCAE scoring after CRS/HIPEC varies between 20.8% and 53.3% in various sources (26-28). Park et al. (24) have reported that 74.2% of the patients had postoperative complications in the short-term and 10.6% in the long-term. Hematological abnormalities [neutropenia (15.2%) and thrombocytopenia (6.1%)] have been reported as the most common complications of grade II in the same study (24). Baumgartner et al. (29) have reported that 148 (59.9%) of 247 patients experienced complications in the first 60 days after CRS/HIPEC. Among 20 patients (8.1%) with Grade 1 complications, the most common complication has been found as superficial wound infection in five patients and postoperative blood product transfusion in 87 patients (35.2%) with grade 2 complications (29 patients). They have observed grade 3-4 complications in 41 (16.6%) patients (29). In another study, it has been found that the overall complication rate was 42% and the incidence of severe complications (grade III +) in the entire study cohort of patients undergoing CRS/HIPEC was 24% (30). Several studies have established that the incidence of 3/4 grade pulmonary complications was 10-16% (3,25,31,32), hematological toxicity was 4-39%, renal failure was 2-4% (33,34), and venous thromboembolism was 4-4.4% (6,35). In our study, morbidity was observed in 50 (83.33%) of the 60 patients who participated in the study according to NCI-CTCAE v3.0 classification. Mild morbidity rate was 46.6%, severe morbidity rate was 36.6%, and mortality rate was 11.66%. A total of 96 morbidities were observed in 26 different ways. The most common morbidity was pneumonia. Chua et al. (36) have observed that morbidity rates in colorectal patients with CRS/HIPEC varied between 12% and 52%, and mortality rates varied between 0.9% and 5.8%. Fujimura et al. (37) have reported 50% morbidity and

Table 4. Analysis of potential risk factors for NCI-CTCAE scores. According to the NCI-CTCAE scoring grade 0; no morbidity, grade 1 and 2; mild morbidity, grade 3, 4 and 5; severe morbidity

Variables	No morbidity (grade 0) n= 10	Mild morbidity (grade 1-2) n= 28	Severe morbidity (grade 3-4-5) n= 22	p	Test statistic
Age, mean ± SE	64.4 ± 3.77	60.89 ± 2.02	58.04 ± 3.30	0.423	0.8731
Sex					
Male (n= 41)	6 (14.64%)	20 (48.78%)	15 (36.58%)	0.800	0.4451
Female (n= 19)	4 (21.06%)	8 (42.10%)	7 (36.84%)		
Primary tumor origin					
Stomach (n= 33)	7 (21.22%)	16 (48.48%)	10 (30.30%)		
Colon (n= 21)	2 (9.52%)	8 (38.10%)	11 (52.38%)	0.240	7.9691
Rectum (n= 5)	1 (20%)	4 (80%)	0		
Appendix (n= 1)	0	0	1 (100%)		
Neoadjuvant therapy					
No (n= 50)	7 (14%)	24 (48%)	19 (38%)	0.463	1.5397
Yes (n= 10)	3 (30%)	5 (50%)	2 (20%)		
Hypertension					
No (n= 31)	3 (9.68%)	16 (51.61%)	12 (38.71%)	0.318	2.2891
Yes (n= 29)	7 (24.15%)	12 (41.37%)	10 (34.48%)		
Type II diabetes mellitus					
No (n= 47)	7 (14.90%)	23 (48.93%)	17 (36.17%)	0.718	0.6632
Yes (n= 13)	3 (23.08%)	5 (38.46%)	5 (38.46%)		
Coronary artery disease					
No (n= 50)	8 (16%)	22 (44%)	20 (40%)	0.485	1.4462
Yes (n= 10)	2 (20%)	6 (60%)	2 (20%)		
Cerebrovascular disease					
No (n= 58)	10 (17.25%)	27 (46.55%)	21 (36.20%)	0.798	0.4501
Yes (n= 2)	0	1 (50%)	1 (50%)		
Splenectomy					
No (n= 52)	10 (19.23%)	25 (48.07%)	17 (32.70%)	0.184	3.3847
Yes (n= 8)	0	3 (37.5%)	5 (62.5%)		
Enteric diversion					
No (n= 52)	10 (19.23%)	26 (50%)	16 (30.77%)	0.046	6.1663
Yes (n= 8)	0	2 (25%)	6 (75%)		
CC scores					
CC-0 (n= 37)	7 (18.92%)	19 (51.35)	11 (29.73%)		
CC-1 (n= 11)	2 (18.18%)	5 (45.46%)	4 (36.36%)	0.675	4.0119
CC-2 (n= 6)	0	2 (33.33%)	4 (66.66%)		
CC-3 (n= 6)	1 (16.67%)	2 (33.33%)	3 (50%)		
PCI, median (min-max)	3.50 (0-39)	4.00 (0-32)	9.00 (0-39)	0.185	3.3724
PC					
Mild PC (n= 42)	7 (16.66%)	22 (52.38%)	13 (30.96%)	0.329	2.2263
Severe PC (n= 18)	3 (16.66%)	6 (33.34%)	9 (50%)		
Surgery time (minute) Median (min-max)	255 (225-375)	300 (210-555)	312 (115-495)	0.166	3.5976
Length of ICU stay (day) Median (min-max)	0 (0-3)	0 (0-3)	1.5 (0-33)	0.004	10.8360
Length of hospital stay (day), Median (min-max)	12 (10-14)	14 (10-17)	18.5 (10-47)	<0.001	17.4415

CC: Complete cytoreduction, ICU: Intensive care unit, PC: Peritoneal carcinomatosis PCI: Peritoneal carcinomatosis index.

Table 5. Analysis of potential risk factors for peritoneal carcinomatosis index (PCI) scores. PCI scores were divided into three groups, No PC: PCI= 0, Mild PC: 0< PCI< 13, Severe PC: PCI> 13

Variables	No PC (n= 12)	Mild PC (n= 30)	Severe PC (n= 18)	p	Test statistic
Length of ICU stay (day) Median (min-max)	0 (0-3)	0 (0-33)	0 (0-20)	0.484	1.4506
Surgery time (minute) Median (min-max)	270 (210-420)	270 (220-495)	375 (115-555)	**0.017**	**8.2079**
Length of hospital stay (day), median (min-max)	14 (10-18)	14 (10-47)	14 (10-33)	0.383	1.9185

Table 6. Analysis of potential risk factors for Complete cytoreduction (CC) scores. CC-0; no residual disease, CC-1; minimal residual disease (0-2.5 mm residual), CC-2; residual disease between 2.5 mm and 2.5 cm and CC-3; residual disease above 2.5 cm

Variables	CC-0 (n= 37)	CC-1 (n= 11)	CC-2 (n= 6)	CC-3 (n= 6)	p	Test statistic
Length of ICU stay (day) Median (min-max)	0 (0-33)	0 (0-20)	0 (0-6)	1 (0-8)	0.735	1.275
Surgery time (minute) Median (min-max)	270 (210-420)	335 (220-495)	382 (375-495)	255 (115-555)	**0.004**	**13.371**
Length of hospital stay (day), median (min-max)	14 (10-47)	14 (10-27)	13.5 (11-28)	17 (12-33)	0.270	3.925

33.3% reoperation rate in gastric cancer patients with CRS/HIPEC. It has been suggested that higher mortality observed with CRS and HIPEC for gastric cancer may be associated with gastrectomy (38). Our morbidity rates are similar to some studies (24,29), and higher than others (27,30). In our study, we think that 55% of the patients had gastric cancer, contributing to high mortality and morbidity. In addition, significant variations among the reported studies may be related to a variety of factors such as heterogeneity in data collection and reporting, differences in the rating and recording of major complications (such as Clavien scoring, NCI-CTCAE scoring and NSQIP definitions), institutional practices, experience of centers, and differences in patient populations or surgical techniques (8).

Many factors such as sex, age, number of visceral resections, number of peritonectomy procedures, disruption of umbilical fissure, primary colon anastomosis, number of anastomoses, incomplete cytoreduction, chemotherapeutic agent dose, and histopathological classification have been reported as predictive factors of morbidity following CRS/HIPEC (3,25,39-41). Simkens et al. (42) have identified patient's recent smoking history, surgical history, physical performance status, and the extent of cytoreduction as important prognostic factors for severe morbidity. In another study, only the CC score has been found to be a risk factor (29). Saxena et al. (43) have defined operative time greater than 10 hours and ASA greater than 3 as independent risk factors for complications of grade 3/4 in patients with pseudomyxoma peritonei. However, we did not observe most of these factors in our study. Furthermore, we observed that the application of enteric diversion, length of stay in the ICU, and length of stay in the hospital had statistically significant effects on the NCI-CTCAE morbidity score. However, based on this result, it would not be scientifically correct to say that the length of hospitalization and length of stay ICU directly increase morbidity. Patients with high morbidity scores will stay longer in the hospital to treat the associated morbidity as needed. The way to test this hypothesis is to prolong the non-indicative hospitalization periods of patients with lower morbidity scores and determine whether these patients will experience different or severe morbidities. However, this is not possible within the framework of general medical rules.

CONCLUSION

Studies have shown that there is a direct relationship between PCI and grade 3/4 morbidity and mortality. As a result of extending the PC, more extensive surgery, more blood loss, and consequently higher complication rates have been observed. High PCI (PCI> 17 for colorectal and PCI> 12 for stomach) in peritoneal metastases originating from stomach and colorectal has also been associated with poorer overall survival (44,45). In addition, it has been reported that both PCI and CC scores are prognostic factors affecting clinical and oncologic outcomes after HIPEC and CRS according to some study results (4,10,31). High CC-0 rates were observed in patients with low PCI, low CC-0 rates, and high CC-2 rates in patients with high PCI. These correlations suggest that incomplete resections and poor prognosis can be observed in cases of extensive peritoneal seeding (46). The necessity of obtaining complete cytoreduction has been emphasized in a number of publications in order to increase the chances of success of the treatment (47,48). It was

agreed that the PCI threshold value for CRS + HIPEC application in gastric cancer patients should be below 12 points (49). Coccolini et al. (47) have reconfirmed in their last meta-analysis that the PCI score threshold should be below 12 points. In our study, the mean value of PCI was 9.51 ± 10.92 and was below the reported value of 12. However, we did not observe any relationship between PCI rates and the NCI-CTCAE morbidity score in our study. Similarly, Verwaal et al. (50), using the same PCI scores as our study, have not found a relation between PCI scores and morbidity. Similar to PCI, CC scores did not affect the NCI-CTCAE morbidity score. There are studies (26,50) showing that CC scores affect the NCI-CTCAE morbidity score as well as those (25,28) showing that they do not. In our study, there was a statistically significant relation between CC scores and the duration of the surgery, which was due to the difference between CC-0 and CC-2. The mean surgery time increased as the CC score increased; but in CC-3, the mean time fell below CC-0. Therefore, it is thought that in patients with CC-3, the extent of peritoneal tumor spread, and possible resection is at a level that will increase the risk of perioperative mortality. Therefore, the operation time may be shortened because there is no resection attempt.

The limitations of the present study are the nuances of a single-center series and its evaluation of short-term results following HIPEC with or without CRS. However, this study is still valuable as we show the short-term clinical consequences of HIPEC with or without CRS used to treat peritoneal metastasis from gastrointestinal cancer.

In the literature, it has been shown that the addition of cytoreductive surgery combined with hyperthermic intraperitoneal chemotherapy to modern chemotherapy regimens significantly prolongs survival in patients with locally advanced cancer of the gastrointestinal tract. The morbidity rate of the current procedure is higher than conservative surgical techniques. However, this rate is expected considering the size of the surgery and the chemotherapeutic cytotoxic effect. Presenting different clinical experiences on this subject will be effective in determining the factors associated with unexpected events that may occur following operation and for reducing morbidity rates by better managing complications.

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ORİJİNAL ÇALIŞMA-ÖZET
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Hipertermik intraperitoneal kemoterapi (HIPEC) ile sitoredüktif cerrahi uygulanan gastrointestinal tümör hastalarında morbiditenin değerlendirilmesi

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ÖZET

Giriş ve Amaç: Çalışmada, sitoredüktif cerrahi (CRS) ile veya CRS olmaksızın hipertermik intraperitoneal kemoterapi (HIPEC) uygulanan gastrointestinal tümör hastalarında postoperatif morbidite oranını belirlemeyi ve morbidite için potansiyel risk faktörleri olabilecek demografik, klinik ve tedavi ile ilgili değişkenleri belirlemeyi amaçladık.

Gereç ve Yöntem: Çalışmaya Ekim 2017 ile Aralık 2019 tarihleri arasında gastrointestinal tümör nedeniyle opere edilen ve HIPEC uygulanan 60 hasta dahil edildi. Postoperatif morbiditeler retrospektif olarak, Ulusal Kanser Enstitüsü (NCI) Advers Olaylar için Ortak Terminoloji Kriterleri (CTCAE) sürüm 3.0 kriterlerine göre derecelendirildi ve değerlendirildi.

Bulgular: Hastaların yaş ortalaması 60,43 ± 12,83 idi. Primer tümör lokalizasyonu 33 hastada (%55) mide, 21'inde kolon (%35), beşinde rektum (%8,3) ve bir hastada apendiks (%1,7) idi. PCI ortalama değeri 9,51 ± 10,92 idi. 37 (%61,7) hastaya CC-0, 11'ine (%18,3) CC-1, 6'sına (%10) CC-2 ve altısına (%10) CC-3 uygulandı. NCI-CTCAE v3.0 sınıflamasına göre çalışmaya katılan 60 hastanın 50'sinde (%83,33) morbidite gözlendi. Hafif morbidite oranı %46,6, şiddetli morbidite oranı %36,6 ve mortalite oranı %11,66 idi. Enterik diversiyon uygulaması, yoğun bakımda kalış süresi ve hastanede kalış süresinin NCI-CTCAE morbidite skoru üzerinde istatistiksel olarak anlamlı bir etkisi olduğu gösterildi (p= 0,046, p= 0,004, p< 0,001).

Sonuç: Lokal-ileri gastrointestinal tümör hastalarında sağkalım üzerinde kanıtlanmış faydalı etkileri olan CRC ve HIPEC, artan morbidite ve mortalite oranlarına rağmen bu hastalar için kabul edilebilirdir. Bu konuda yapılacak yeni çalışmalarla morbidite ve mortalite oranları düşürülebilir.

Anahtar Kelimeler: Gastrointestinal tümör, sitoredüktif cerrahi, hipertermik intraperitoneal kemoterapi, morbidite, HIPEC

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