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Evaluation of Enhanced Recovery After Following a Surgical Protocol for Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy for Peritoneal Carcinomatosis

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ABSTRACT

Introduction: Cytoreductive surgery with or without hyperthermic intraperitoneal chemotherapy (CRS ± HIPEC) has positive effects on the survival of patients with peritoneal carcinomatosis (PC) due to intra-abdominal tumors. Currently, the available literature on the safety of the Enhanced Recovery After Surgery (ERAS) protocol for PC, which is associated with severe morbidity and mortality, is insufficient. **Aim:** This study aimed to present our results from treating patients using the ERAS protocol for PC that developed due to intra-abdominal tumors. **Material and Methods:** The data of 120 consecutive patients with PC due to different etiologies of abdominal origin and who underwent CRS ± HIPEC were analyzed. The patients were divided into two groups according to whether the ERAS protocol was applied. Information on demographics, length of hospital stay, cost, morbidity, and mortality was statistically compared between groups. **Results:** A total of 102 patients were included in the study. The first 40 patients did not undergo the ERAS protocol, whereas 62 patients did undergo the protocol. The mean length of hospital stay was 10 days in the non-ERAS group and 7 days in the ERAS group. The ERAS group was observed to have earlier mobilization, earlier gas and stool release, lower oral intake, and fewer respiratory problems than the non-ERAS group. **Conclusion:** CRS ± HIPEC has a positive effect on survival. The simultaneous application of the ERAS protocol with the aforementioned procedure has positive effects on intestinal motility and postoperative outcomes. In addition, this protocol may reduce costs by shortening the length of hospital stay.

Keywords: cytoreductive surgery, hyperthermic intraperitoneal chemotherapy, peritoneal carcinomatosis, ERAS.

1. INTRODUCTION

Enhanced Recovery after Surgery (ERAS) was introduced for clinical use by Wilmore and Kehlet in 1997; this approach was transformed into the ERAS working group in 2001 and was named the ERAS Society in 2010 (1-3). In 2012, the ERAS Society issued the first general surgical guidelines concerning colonic resections. These suggestions were followed by guidelines for rectal, gastric, liver, breast, and esophageal resections as well as pancreaticoduodenectomy (3-9). Advances in minimally invasive surgery and postoperative pain control have particularly allowed for effective applications of this protocol (10). In addition to minimally invasive surgery, another recent positive

development is the use of the hyperthermic intraperitoneal chemotherapy procedure together with cytoreductive surgery (CRS ± HIPEC), particularly for patients whose survival times are measured in months. Although this complex procedure has positive effects on survival, a complete patient preparation process needs to be conducted using a thorough multidisciplinary approach before performing the operation.

Complications are observed even in the resection of nonadvanced organ-limited cancers. Although these complications can be detected early using radiological methods and can be controlled by percutaneous procedures, their morbidity and mortality rates are as high as 52% and 6%,

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respectively (11). In terms of complications with CRS, concurrent excess organ resections, peritonectomy, and concurrent hepatobiliary interventions may be required. Each additional procedure may increase the incidence of complications in the patient. Another important issue in this regard is that possible complications may cause long-term hospitalizations and therefore increase the associated costs.

Over the last two decades, minimizing these potential complications through interventions has been a separate research topic at large research centers. In this regard, significant improvements have been made in reducing costs and adhering to a health care budget while providing benefits for both patient survival and quality of life. The most important development in this area is the ERAS protocol, which has been implemented in many surgical procedures. The promising results of the ERAS protocol have been presented in the literature (11, 12). The ERAS protocol has been applied for gastrointestinal and colorectal surgeries and has found widespread use in general surgical practices (12). CRS ± HIPEC is currently the gold standard for patients with pseudomyxoma peritonei, mesothelioma, and PC due to abdominal tumors (13). However, information is limited regarding the use of the ERAS protocol in patients with PC who undergo CRS ± HIPEC.

2. AIM

In this study, we aimed to evaluate the effectiveness of the ERAS protocol in patients who underwent CRS ± HIPEC.

3. MATERIAL AND METHODS

After obtaining approval from the ethics committee (approval number 144; date 28/11/2018), the data of 120 patients who underwent CRS ± HIPEC for PC at the General Surgery Clinic of the Health Sciences University, Ümraniye Training and Research Hospital, between May 2016 and January 2019 were prospectively collected and retrospectively analyzed. Eighteen patients with incomplete data regarding the ERAS protocol were excluded from the study. Therefore, a total of 102 patients were included in the study. The first 40 patients who did not undergo the ERAS protocol (non-ERAS group) and 62 patients who underwent the ERAS protocol (ERAS group) were included in the study. The patients in both groups who underwent CRS ± HIPEC were evaluated in terms of age, sex, primary disease, and the 12 parameters of the ERAS protocol during the preoperative, perioperative, and postoperative periods (Table 1).

Statistical analysis

Data obtained from the raw data were recorded in the IBM SPSS 22 software (IBM SPSS, Turkey), and the average, mode, median, and percentile distribution of the data were calculated and are presented in the tables in the results section. Based on the number of samples, the Shapiro–Wilk test was used to evaluate the distribution of the data. For normally distributed data, parametric tests were used, whereas in the absence of a normal distribution, nonparametric tests were used. The chi-square

test was used to compare nominal data, and p-values of <0.05 were considered statistically significant.

Preoperative evaluation period

In this period, patients who were examined in the outpatient clinic were informed about the surgery, complications that may be encountered, and details of the ERAS protocol. The patients were advised to abstain from alcohol consumption and smoking 4 weeks before the surgery. Patients who exhibited a weight loss of >10% in the preoperative period were provided ambulatory care in terms of nutritional support and care at their homes by nutrition experts. Nutritional status was assessed by the nutritional risk score (NRS, 2002). If the total NRS score was higher than 2, a nutrition plan was started (14). After the patients were admitted to the surgical unit, general information was provided by trained personnel. Triflow or balloon blowing exercises were performed along with gum chewing exercises. Thromboembolism prophylaxis was initiated in patients; moreover, the patients were instructed to wear pneumatic compression socks. No bowel cleaning was performed for any of the patients.

Perioperative period

Patients were provided pneumatic compression socks by operating room nurses who were experienced in the ERAS protocol. The operating room temperature was adjusted to 18°C–24°C with a relative humidity of approximately 30%–60%. A thoracic epidural catheter was opened by the anesthesia team in the operating room, the use of long-acting sedative drugs was avoided, and antibiotherapy was performed 30 min prior to the operation. The therapy was repeated every 4 h. Heating devices were used to maintain normothermia. During the operation, the volume of fluid loss, hourly urine output and blood pressure were monitored, and fluid resuscitation was performed. Routine fluid therapy was applied at 4 ml/kg/h according to the restrictive fluid management protocol. Blood samples were collected, and blood counts were measured every 3 h. Patients with hematocrit values less than 30% were given erythrocyte suspensions. Although the operation time, incision length, and period of drain usage were restricted and kept to minimum, in compliance with the ERAS protocol, these parameters were excluded in the present study due to their lack of practical application for CRS ± HIPEC.

Postoperative period

All patients were admitted to the intensive care unit after undergoing CRS ± HIPEC. After extubation, the nasogastric (NG) catheters were removed, and the patients were instructed to drink one cup of water. Postoperative pain management was provided by epidural anesthesia. For patients whose pain was inadequately managed despite the epidural analgesia, 100 mg tramadol and a nonsteroidal anti-inflammatory drug (NSAID) (ibuprofen 600 mg) were given as an additional dose on the first postoperative day. Additional drugs were given as a half dose on the 2nd day after surgery and stopped on the 3rd day. Antithrombotic therapy was performed at 10:00 pm on the day of surgery unless hemorrhagic drainage was noted from the drains. Treatment using pneumatic compression socks was continued. Triflow exercises and

tapotement were regularly performed. The patients were administered metoclopramide and were encouraged to chew gum. The Foley catheters were removed when the patients were taken to their rooms. All patients were encouraged to walk for a minimum of 2 h on the first day and 6 h on the second day postoperative. All patients wore abdominal corsets. The fluid treatment that was intraoperatively started at 4 ml/kg/h was continued during the early postoperative period. The patients were allowed to consume 40 ml/kg/h liquid food on the first day in the surgical unit. Liquid resuscitation was terminated for patients who were able to tolerate oral food intake, and liquid food was continued at a dosage of 80 ml/kg/h. The patients could begin to intake solid food after passing gas for the first time post operation, regardless of the presence of intestinal anastomosis. Patients with a stoma received training from stoma therapy nurses.

All patients were given a 24 h mobile phone number they could use to report any complaints after discharge. For the group of patients with a short hospital stay, primary education was provided to the patients and their relatives after discharge. In case of any complications, especially in the first 30 days after the operation, we ensured that a specialist examined the patient within 30 min of being admitted to the emergency ward without any interviews. Each patient was routinely followed up at the outpatient clinic 7, 15, and 30 days after the operation. Patients who did not attend their follow-up sessions were contacted via phone, and we ensured that all patients visited the hospital and were examined by a doctor.

4. RESULTS

Of the 120 patients, 18 patients who had incomplete data were excluded from the study; thus, 102 patients were included in the study. Among these 102 patients, the ERAS protocol was not applied to the first 40 patients, as the ERAS protocol was not available in our clinic. After deciding to use the ERAS protocol, an onsite training program was implemented, and 62 patients with PC were treated using the ERAS protocol. The mean age of the patients who did not undergo the ERAS protocol was 56 (31–70) years, including 23 (57.5%) females and 17 (42.5%) males. The mean age of the patients who did undergo the ERAS protocol was 57 (29–74) years, in-

Components of the ERAS protocol applied for CRS ± HIPEC		
Preoperative	Intraoperative	Postoperative
Preadmission education	Warming	Removed NG tube and drains
No bowel preparation	TEA	Early oral nutrition
Prophylaxis against VTE	Goal-directed liquid management	Early ambulation
Nutrition		Use of chewing gum
Physiotherapy		

Table 1. Components of the ERAS protocol applied for CRS ± HIPEC. Abbreviations: VTE: Venous thromboemboli, TEA: Thoracic epidural analgesia, NG: Nasogastric, CRS: Cytoreductive surgery, HIPEC: Hyperthermic intraperitoneal chemotherapy, ERAS: Enhanced Recovery After Surgery

Characteristics	ERAS group (n=62)	Non-ERAS group (n=40)	P-value
Age (years)	57 (29-74) (57.33±12.47)	56 (31-70) (56.12±12.17)	.056
Sex n,%			
Male	26 (41.9%)	17 (42.5%)	.06
Female	36 (58.1%)	23 (57.5%)	.05
BSA (du Bois)	130-206 (177.56±13.62)	132-202 (175.32±12.89)	.068
ASA n,%			
I	n=24 (38.7%)	n=19 (38%)	NA
II	n=13 (20.9%)	n=11 (22%)	
III	n=25 (40.3%)	n=20 (40%)	
NRS			
0	n=11 (17.7%)	n=8 (16%)	.04
1	n=30 (48.3%)	n=25 (50%)	.03
2	n=21 (33.8%)	n=17 (34%)	.02
Diagnosis n,%			
Colorectum	n=26 (41.9%)	n=20 (40%)	NA
Over	n=11 (17.7%)	n=8 (16%)	
Sarcomatosis	n=8 (12.9%)	n=6 (12%)	
Stomach	n=5 (8%)	n=5 (10%)	
Other	n=12 (19.3%)	n=11 (22%)	
PCI mean	12.84±6.26	12.44±6.14	.05
CC n,%			
0	n=50 (80.6%)	n=40 (80%)	NA
1	n=1 (16.1%)	n=8 (16%)	
2	n=2 (3.2%)	n=2 (4%)	
Ileostomy n,%	n=15 (24%)	n=14 (28%)	NA
Colostomy n,%	n=3 (4.8%)	n=3 (6%)	NA
Prior chemotherapy	n=40 (64.5%)	n=30 (75%)	NA
Prior surgery	n=50 (80.6%)	n=33 (82.5%)	NA
Comorbidities			
Diabetes mellitus	n=13 (20.9%)	n=11 (22%)	NA
Cardiovascular	n=25 (40.3%)	n=25 (50%)	
COLD	n=11 (17.7%)	n=8 (16%)	
Operation time (h, median)	4-13 (7.86±4.88)	3-14 (6.59±2.66)	NA
Mechanical ventilation dependence postoperative (h)	4	6	.04
Intraoperative fluid requirement (mean, min-max)	2100 (800-8500)	3500 (700-11.500)	.03
Crystalloid (ml)	320 (100-200)	761 (0-2500)	
Colloid (ml)			
Transfusion requirement (unit)			
Erythrocyte suspension	1.31 (0-10)	1.62 (1-12)	NA
Fresh frozen plasma	0.53 (0-1)	0.53 (0-1)	
Postoperative morbidity n,%			
Wound infection	5 (8%)	6 (15%)	.05
Hemorrhage	2 (3.2%)	2 (3%)	
Pneumonia	1 (1.6%)	2 (3%)	
Neutropenia	1 (1.6%)	2 (3%)	
Anastomotic Leak	0	2 (3%)	

Table 2. Demographic data. Abbreviations: ERAS: Enhanced Recovery After Surgery, BSA: Body surface area, ASA: American Society of Anesthesiologists, NRS: Nutritional risk index, PCI: Peritoneal carcinomatosis index, CC: Completeness of cytoreduction, COLD: Chronic obstructive lung disease, NA: Not available

cluding 36 (58.1%) females and 26 (41.9%) males. Of the patients who were treated using CRS ± HIPEC in the ERAS group, 26 (41.9%) had colorectal cancers, 11 (17.7%) had ovarian cancer, 8 (12.9%) had sarcomatosis, 5 (8%) had stomach cancers, and 12 (19.3%) had other (mesothelioma, breast, and pancreas) cancers. Of the patients who were treated using CRS ± HIPEC and in the non-ERAS group, 20 (40%) had colorectal cancers, 8 (16%) had ovarian cancers, 6 (12%) had sarcomatosis, 5 (10%) had stomach cancers, and 11 (22%) had mesothelioma, breast, and pancreatic cancers. The NRS was 0 in 11 (17.7%) patients in the ERAS group and in 8 (16%) patients in the non-ERAS group. The NRS score was 1 in 30 (48.3%) patients in the ERAS group and in 25 (50%) in the non-ERAS group. A total of 21 (33.8%) patients in the ERAS group and 17 (34%) patients in the non-ERAS group were found to have the worst possible nutritional status score, and this group received nutritional support in the preoperative period. The demographic data of the patients are shown in Table 2.

In the non-ERAS group, the mean length of stay in the intensive care unit was 2.3 days, and the mean length of stay in the hospital was 10 days. After extubation, the NG tubes were removed at an average of 2.5 days, and the Foley probes were removed at an average of 3.3 days. Gas and stool releases were noted at an average of 2.9 and 4.1 days, respectively, and the first oral food intake was initiated at an average of 3.1 days. No patients were mobilized on the first day. The transition to complete oral feeding was performed on the 6th day. The patients were discharged on the 10th day. In the ERAS group, the mean length of stay in the intensive care unit was 1.1 days, and the length of stay in the hospital was 7 days. The NG probes were removed on the same day as extubation, and the Foley probes were removed on the 1st day the patients were taken to the ward. Gas and stool releases were observed at an average of 1.8 and 3.1 days, respectively; after extubation, 200 ml oral fluid was started. The volume of fluid was increased to 500 ml on the 2nd day. The patients were mobilized for 2 h on the same day they were taken to the ward. The next day, the patients were mobilized for at least 6 h. The transition to complete oral feeding was performed on the 3rd day. The patients were discharged on the 7th day (Table 3). The ERAS group was observed to have earlier mobilization, earlier gas and stool release, earlier oral intake, and fewer respiratory problems than the non-ERAS group. The incidence score of grade 3/4 complications according to the Clavien-Dindo classification was 1.85 ± 0.88 in the ERAS group and 2.155 ± 1.02 in the non-ERAS group. Four patients (two from the ERAS and two from the non-ERAS groups) underwent reoperation due to anastomosis leakage. Mortality was observed in the following six patients: three patients in the ERAS (4.8%) and three patients in the non-ERAS groups (6%). The mortality rates were 4.8% and 6% in the ERAS and non-ERAS

Characteristics	ERAS group (n=62)	Non-ERAS group (n=40)	P-value
Number of additional doses of analgesics <i>n, %</i>	n: 5 (8%)	n=11 (22%)	.03
Time to liquid intake <i>d, median</i>	0.7 ± 0.4	3.1 ± 0.3	<.001
Time to solid intake <i>d, median</i>	3.1 ± 1.6	5.2 ± 1.3	<.001
Time to ambulation <i>n, %</i>			
POD 1 <i>n, %</i>	n=41 (66.1%)	n=15 (30%)	NA
POD 2 <i>n, %</i>	n=15 (24.2%)	n=25 (50%)	
POD >2 <i>n, %</i>	n=6 (9.6%)	n=10 (20%)	
Time to first flatus <i>d, median</i>	1.8 ± 0.6	2.9 ± 1.2	.01
Time to first stool <i>d, median</i>	3.1 ± 1.5	4.1 ± 1.4	.03
Removal of NG tube <i>d, median</i>	0.5 ± 0.4	2.5 ± 0.6	.01
Removal of catheter <i>d, median</i>	0.9 ± 0.8	3.3 ± 1.3	.01
ICU stay <i>d, median</i>	1.1 ± 0.8	2.34 ± 3.15	.02
Hospital stay <i>d, median</i>	7 ± 1.1	10 ± 4.5	.04
Health care costs \$, <i>median</i>	2100	3300	.03
Clavien-Dindo complication score (n)			
minor=CD 1-2	8	10	.05
major=CD >3	1	4	
Mortality <i>n, %</i>	n=3 (4.8%)	n=3 (6%)	.06

Table 3. Characteristics of gastrointestinal function, length of stay in the intensive care unit, morbidity and mortality. Abbreviations: ICU: Intensive care unit, ERAS: Enhanced Recovery After Surgery, POD: Postoperative day, NG: Nasogastric, d: Day, CD: Clavien-Dindo, NA: Not available groups, respectively. However, no statistically significant differences were noted (Table 3).

5. DISCUSSION

According to the World Health Organization data, the mortality rate associated with cancer ranks second highest after that associated with circulatory system diseases (15). Despite significant advances in treatment strategies, there has been little deviation in this ranking in the past 20 years. Of these developments, the introduction of cancer screening programs into clinical practice has helped enable early diagnosis of the disease; however, there have not been major changes in the incidence of abdominal tumors that cause PC, which worldwide, is associated with a survival of a few months. This problem has led researchers to concentrate on identifying and developing new treatment strategies. From this point of view, tomotherapy, which evaluates patients using a multidisciplinary application, has resulted in positive survival results by allowing for the application of radiotherapy to inaccessible cancerous regions, the use of next-generation chemotherapeutics and rational drugs in medical oncology, and the simultaneous use of CRS ± HIPEC (11-13). In addition, the use of pressurized intraperitoneal aerosol chemotherapy, which has been adopted for neoadjuvant and palliative treatment in the past 5 years in cases where CRS cannot be administered to PC, has provided hope for patients with advanced-stage cancers (16). In fact, during the 11th International Workshop on Peritoneal Surface Malignancy Meeting of the Peritoneal Surface Oncology Group International held in 2018, a paper presented by Cecil et al (17).from Bas-

ingstoke demonstrated small bowel transplantation after aggressive small bowel resections in patients with pseudomyxoma peritonei. All of these applications ultimately aimed to reveal key points for increasing the quality of life within the current survival duration and to increase overall survival and disease-free survival for patients with cancer. Moreover, many common complications related to existing malignancies have been described as well as types of surgical treatment that can be used with these malignancies. From the surgeons' point of view, the majority of these complications can be prevented by measures taken by the patient during the preoperative and postoperative periods. Although these measures initially seemed to be temporary and individualized actions rather than standard protocols, over the past 20 years, the ERAS protocol has become an accepted practice in the surgical treatment of many diseases, especially those related to the gastrointestinal system (GIS). A multi-centered study based in the Netherlands compared centers that used the ERAS protocol with those that did not use the ERAS protocol. The results showed that physicians involved with GIS surgeries reported high efficacy with the ERAS protocol, and the centers that did not use the protocol were recommended to start using the procedures (18). Although the literature has demonstrated that this protocol has important benefits for patients and has positive effects on factors that affect cost (such as hospitalization costs), data on the use of CRS ± HIPEC to treat PC are very limited, as demonstrated by our searches of PubMed and Google Scholar. In the present study, the mean length of hospital stay was significantly shorter for patients treated using this protocol than for patients treated without the protocol; these results are consistent with those reported by Teixeira et al. (19), Piskarska et al. (20) and Bennedson et al. (21) in their studies comparing patients who were and were not treated using this protocol.

An essential component of most ERAS pathways is multimodal pain management. Poorly controlled postoperative pain may result in adverse events that could prolong the patient's hospital stay, delay recovery, and affect the patient's experience with the health care system. Unlike traditional perioperative care, ERAS pathways typically use a standardized multimodal analgesic regimen with nonopioid agents or techniques to minimize the use of perioperative opioids and to decrease the incidence of opioid-related adverse effects (e.g., nausea, vomiting, sedation, ileus, pruritus, and respiratory depression) with the goal of improving and expediting patient recovery after surgery. In our practice, the ERAS protocol involves epidural analgesia, rather than opioids, since this method has been shown to have significant benefits, provide superior postoperative analgesia, decrease perioperative pulmonary-cardiac morbidity, and facilitate the early return of gastrointestinal tract function. In addition to epidural analgesia, tramadol and NSAIDs were given to patients when needed. Apart from analgesic therapy, fluid resuscitation was also performed. In previous ERAS studies, the appropriate dosage for fluid resuscitation was 3-6 ml/kg/h. In our protocol, we performed fluid

resuscitation with a dosage of 4 ml/kg/h in accordance with the literature. A review of the data on excess perioperative fluid administration suggests that overhydration may have deleterious effects on cardiac and pulmonary function, as well as on the recovery of gastrointestinal motility, tissue oxygenation, wound healing and coagulation (22, 23). Several studies suggest that avoiding fluid overload and providing only the amount of intravenous fluid necessary to maintain fluid balance, which is often guided by body weight, may significantly reduce postoperative complications and shorten the length of hospital stay (24, 25). In addition, some preliminary studies have shown that intraoperative fluid administration guided by transesophageal Doppler monitoring, called "goal-directed fluid therapy," resulted in better ejection fraction, better oxygenation, and fewer postoperative complications than traditional fluid administration techniques (26, 27).

In addition to benefiting patient health, this protocol offers another important advantage over other treatments in the health sector to facilitate the treatment and recovery process of patients. One inevitable factor associated with this protocol is the cost associated with treatment and hospitalization services. Currently, one of the top priorities of the global health sector is to reduce health care costs. An important factor for reducing costs is shortening the length of hospital stay because the average daily hospital-bed fee in the US is approximately \$1700, and this fee increases to \$5200 in intensive care units (28). Fees in health centers in European countries are also similar to the aforementioned fees. In Turkey, the daily bed-service fee in private institutions is approximately \$300, while this service fee is slightly less in level-three health facilities within the scope of general health insurance. The most important benefit of the ERAS protocol is a reduction in the costs associated with the length of hospital stay and in the psychosocial impact of long hospital stays.

In our case series, the shortened length of stay in centers that fully implemented the ERAS protocol was reflected in the costs, and a statistically significant difference was noted between patients who were and were not treated using the ERAS protocol in the initial stage of their treatment. In this study, the costs related to health care services decreased, and patients who were discharged early from the hospital experienced positive changes in their life quality indexes (18, 28).

Recently, it has become a routine practice to adequately inform patients about even the simplest applications of surgical procedures. Another important aspect of preoperative information programs is providing early information regarding problems, such as pain and complications, that patients may encounter; such programs make the application of the ERAS protocol more effective (29,30). In our own practice, after multidisciplinary teams evaluated the patients, the surgical oncologists provided the patients with all the relevant information regarding their current situation, disease, disease stage, interventions, and treatment strategies that can be applied. Although there are no qualitative or quantitative data indicating

its effectiveness, the information-providing stage is believed to facilitate patient-physician communication and to ease the internal struggle of the patients to adapt to their diseases. After observing the benefits at this stage, we believe that including a clinical psychologist on the ERAS team at this information-providing stage is beneficial; we have been preparing to implement this change.

One of the most important applications of the ERAS protocol, other than in current surgical interventions, is to prevent the deterioration of gastric motility due to mechanical or functional factors (30, 31). In general, malnutrition is a common condition in patients who require CRS. In the present study, we provided patients with general information and analyzed the nutritional index of the patients using the NRS 2002; then, we provided nutritional support by consulting nutritional experts on our team and evaluating the nutritional condition of the patients using objective findings and biochemical markers. We ensured maximum oral intake of high-calorie and high-protein foods during this process. The NRS was calculated on a weekly basis through an active screening method for all patients, and the operations were planned after the NRS was reduced to being <1 (31). Furthermore, in the present protocol, the period of oral intake was extended to the last stage of the preoperative period for all patients, and the patients were encouraged to start oral intake as early as possible after being weaned from the ventilator and admitted to the intensive care unit.

In contrast to colorectal cancers that have a genetic etiology, other malignancies that cause PC are observed at old ages (32). Comorbid diseases (diabetes, hypertension, coronary artery diseases, and chronic obstructive pulmonary diseases) are also more common in at old age. Such comorbidities may introduce additional risks to the surgical intervention. Although the ERAS protocol seems to shorten the time between admission and discharge, controlling comorbidities is becoming an important issue because of risk factors such as old age. In this regard, Luther et al. (33) reported a significant difference in the length of hospital stay between patients with diabetes and those without diabetes, even when the ERAS protocol was used. In our routine practice, patients who follow the routine ERAS protocol are instructed to perform breathing exercises under the supervision of a respiratory physiotherapist. Subsequently, the patients are given preoperative training to ensure that they adapt to the pre- and postoperative Triflow breathing device. We believe that these exercises may prevent postoperative respiratory complications. In our study, when the two groups were evaluated in this respect, we found that the incidence of pulmonary complications was significantly lower in the ERAS group than in the non-ERAS group. Additionally, patients who undergo CRS routinely have their blood glucose levels monitored, particularly those who require pancreatic interventions; the administration of short-acting insulin can prevent high glucose levels. These treatments also prevent wound infections that may develop as surgical site infections; the reported incidence of these infections in our study was different from that reported in other published studies; the inci-

dence of infection was also significantly lower in patients treated with the ERAS protocol than in those treated without the protocol, which we believe was a result of the measures taken.

Intestinal clearance was once specified as a procedure that should be strictly performed before operations, particularly before colorectal surgeries; however, in the last 10 years, this procedure has been recommended only for interventions involving rectal tumors, even though the utility of intestinal clearance for rectal interventions is currently being questioned. Although the protective effect of intestinal clearance on wound infection has been identified, the adverse effects on gastrointestinal flora and motility have become more prominent, and this practice is now being avoided (34, 35). In fact, to ensure that the patient experiences minimal surgical stress, the ERAS protocol recommends initiating oral intake in the early postoperative period and continuing oral intake until the last stage. In our case series, nutritional measures and intestinal cleansing were both performed, and no intolerance to oral intake was observed in the patients treated using the ERAS protocol. Another issue in this process is the practice of chewing gum, which has been recently prioritized in the literature. Atkinson et al. (35) reported that chewing gum did not affect the return of bowel function or length of hospital stay after colorectal resection. In our own practice, although there was no quantitative parameter to evaluate this practice and despite the findings of Atkinson et al. (35) we believe that chewing gum has positive effects on early motility based on the feedback we received from our patients.

6. CONCLUSION

In summary, we applied 12 out of a total of 24 ERAS parameters in our study, and the use of the ERAS protocol had a positive effect on morbidity and mortality by reducing the length of hospital stay for patients with PC caused by abdominal tumors who underwent CRS \pm HIPEC. Our results show that the ERAS protocol yields good results not only for elective general surgeries such as colorectal, gastric, and pancreatic surgeries but also for CRS \pm HIPEC, which uses a serious and aggressive multidisciplinary approach. We believe that these findings will contribute to the literature, and in light of these results, we believe that the use of the ERAS protocol for aggressive surgical procedures such as CRS \pm HIPEC results in early oral intake, early discharge, minimal complications, and considerably low hospital costs.

- **Declaration of patient consent:** The authors certify that they have obtained all appropriate patient consent forms.
- **Author's contribution:** O.D. gave substantial contribution to the conception or design of the work and in the acquisition, analysis and interpretation of data for the work. O.D. had role in drafting the work and revising it critically for important intellectual content. O.D. gave final approval of the version to be published and they 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.
- **Conflicts of interest:** There are no conflicts of interest.

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