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Enhanced recovery after surgery for gastric cancer with HIPEC: feasibility and outcomes in a complex setting

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ABSTRACT

Background: Enhanced Recovery After Surgery (ERAS) pathways improve outcomes following gastrectomy, but their applicability to procedures involving hyperthermic intraperitoneal chemotherapy (HIPEC) remains uncertain.

Methods: All patients undergoing total or subtotal gastrectomy for gastric cancer at our center between January 2017 and June 2024 were included. The institutional ERAS protocol, originally designed for standard gastrectomy, was prospectively applied to patients undergoing concomitant cisplatin-based HIPEC (CB-HIPEC). Twelve ERAS items were assessed, and adherence ≥70% was considered optimal. Clinical and perioperative outcomes were analyzed retrospectively.

Results: Among 670 patients, 44 underwent gastrectomy with CB-HIPEC and 626 underwent gastrectomy alone. HIPEC patients were younger (median age 55 vs. 68 years, $p < 0.001$) and had more advanced disease. Overall ERAS compliance ≥70% was achieved in 75% of the standard group but only 25% of the HIPEC group ($p < 0.001$). Major deviations involved delayed removal of the nasogastric tube (77% retained postoperatively vs. 18%, $p < 0.001$) and urinary catheter (98% vs. 28%, $p < 0.001$), as well as slower progression to oral intake (liquids by POD 1: 52% vs. 88%; soft diet by POD 3: 36% vs. 76%, $p < 0.001$). Despite reduced adherence, rates of active ambulation by POD 2 were comparable (82% vs. 88%). Overall complication rates were higher after CB-HIPEC (54.5% vs. 38%, $p = 0.039$), but CB-HIPEC itself was not an independent predictor of morbidity.

Conclusions: HIPEC substantially impairs ERAS adherence, mainly due to delayed gastrointestinal and urinary recovery, without directly increasing postoperative morbidity. Procedure-specific ERAS adaptations are warranted for gastrectomy with CB-HIPEC.

1. Introduction

Surgery for metastatic gastric cancer is becoming more common, particularly in cases with limited peritoneal involvement, where it is considered after intensive chemotherapy. This often involves combining radical surgery with cisplatin-based intraoperative hyperthermic intraperitoneal chemotherapy (CB-HIPEC). Despite technical advancements, gastric cancer surgery remains associated with high rates of morbidity and mortality [1]. Over the past decade, Enhanced Recovery After Surgery (ERAS) protocols for gastric cancer surgery have been increasingly developed, with most studies originating from Eastern countries [2], although positive outcomes have also been reported in Western centers [3]. Recently, ERAS protocols have been evaluated for peritoneal surgeries, both with and without HIPEC [4]. However, their application is challenging due to the heterogeneity of the surgeries, which include various types of tumors, the majority being gynecological cancers and pseudomyxoma. Consequently, ERAS Society's guidelines for peritoneal diseases largely rely on evidence extrapolated from other types of surgeries [5,6]. At our Center, an ERAS protocol for gastric cancer surgery has been fully implemented since January 2017, resulting in a significant reduction in postoperative length of hospital stay (LOS) and lower costs compared to the standard pathway [3]. In this study, we aimed to assess whether the ERAS protocol for gastric cancer can be effectively applied to patients undergoing gastrectomy with CB-HIPEC.

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2. Methods

We included all patients that underwent gastrectomy for cancer in our Center from January 2017, coinciding with the full adoption of the Enhanced Recovery After Surgery (ERAS) protocol for gastrectomy at our institution. Patient inclusion ended in June 2024, ensuring at least 90 days of postoperative follow-up. Throughout the study period, five experienced surgeons performed all operations, in accordance with the latest international guidelines for gastric cancer [7–9]. HIPEC treatment for gastric cancer with peritoneal involvement consisted of mitomycin C (16.5 mg/m^2) and cisplatin (125 mg/m^2), administered over 1 h at 41–43 °C in 4-5 L of saline solution using a closed technique. Our ERAS protocol, first implemented in January 2017 and described in our initial 2021 report, was originally designed for patients undergoing gastrectomy without additional procedures such as CB-HIPEC [3]. We selected the ≥70% threshold for ERAS adherence based on previous evidence from our earlier, which demonstrated that compliance of at least 70% with ERAS items was associated with improved patient recovery and reduced hospital costs, without increasing readmission rates or the need for post-discharge care [3]. Nevertheless, ERAS principles were also applied to the HIPEC group, with adherence to individual items left to the discretion of the operating surgeon, based on clinical judgment, experience, and the patient's condition. Since January 2019, patients undergoing CB-HIPEC have received an initial intravenous bolus of 9 mg/m^2 of sodium thiosulfate, administered concurrently with the start of cisplatin intraperitoneal perfusion for 20 min, followed by a second infusion of 12 g/m^2 over 6 h at the conclusion of the CB-HIPEC procedure [10–12]. We did not establish a specific protocol for gastrectomy combined with CB-HIPEC. Instead, data were prospectively collected to assess which components of the ERAS protocol could be applied as in standard gastrectomy and which required specific indications for CB-HIPEC. All data were collected prospectively and analyzed retrospectively.

2.1. Outcomes

The primary aim of this study was to evaluate the compliance with a standardized ERAS protocol for gastrectomy when CB-HIPEC was performed during the primary surgery (HIPEC group) and compare this result with the cohort of patients that underwent gastrectomy alone (standard group).

Secondary objectives were to assess the rate and types of complications associated with adding CB-HIPEC to gastrectomy and to determine whether complications were the main risk factor for ERAS deviation among the two groups. The primary outcome was compliance rate with ERAS items, analyzed both individually and overall. Secondary outcomes included 90-day postoperative morbidity and mortality rates, the length of hospital stay (LOS) and readmission rates. Based on previous publications, optimal compliance was defined as adherence to ≥70% of ERAS items [3]. Compliance with the ERAS protocol was assessed using 12 items, divided into six pre-intraoperative and six postoperative items. The pre-intraoperative items included carbohydrate loading, multimodal analgesia, goal-directed fluid therapy (GDT), avoidance of nasogastric tube (NGT) placement, immediate extubation, and transfer to the surgical ward. The postoperative items included removal of the urinary catheter by postoperative day (POD) 2, early resumption of a liquid and soft diet, targeted physiotherapy. The physiotherapy program was based on an early mobilization protocol starting on postoperative day 1 (mobilization and respiratory physiotherapy), assisted ambulation on POD2 and progressive increase in daily physical activity according to patient tolerance. At the beginning of our experience, drain placement was routinary for total gastrectomy and selectively placed for subtotal gastrectomy, with a drain removal within 4 POD if no complications occurred. During the study period, our center led the ADIGE trial [13], which investigated the role of prophylactic drain placement in gastrectomy. Patients were therefore randomized to either a Drain or No-Drain group. Since the trial required drains to remain in place for at least 4 POD, we defined success in this study as either no drain placement or removal within 4 POD. Morbidity was defined as any complication occurring within 90 days postoperatively according to the GASTRODATA definitions [1]. Complications were graded using the Clavien-Dindo (CD) classification [14] and categorized as mild (CD grades I-II) or severe (CD grades III-V). Other resections were defined as the removal of any organ in addition to the stomach. Cholecystectomy was not included in this definition, as evidence supports its potential benefit in selected patients undergoing gastrectomy [15], and it does not appear to increase the morbidity or mortality of the primary procedure [16]. Nutritional status was evaluated using the Nutritional Risk Index [17]. Polyuria was defined as a urine output exceeding 3 L per day, regardless of renal function.

2.2. Statistical analysis

Data are expressed as mean ± standard deviation (SD) and range for continuous variables, counts, and percentage for categorical variables. Group comparisons were performed using the Mann–Whitney *U* test for continuous variables and the chi-squared test or Fisher's exact test (when expected frequency were ≤5) for categorical variables. Logistic regression models were created to estimate the unadjusted and the adjusted odds ratio (OR; 95 % confidence interval [CI]) for the adherence of ERAS items (at least of 70% of the total items) and for the occurrence of one or more major complications (dependent variables) in relation to socio-demographic and clinical characteristics (independent variables). Independent variables were selected based on exploratory analysis and clinical relevance. All tests were statistically significant at $p < 0.05$. Statistical analysis was performed using STATA statistical software version 17 (StataCorp, College Station, TX, USA).

3. Results

3.1. Patients and treatment features

Between January 2017 ad June 2024, a total of 700 patients underwent total or subtotal gastrectomy for gastric adenocarcinoma at our institution. Of these, 30 patients were excluded due to palliative procedures such as palliative gastro-jejunal bypass, feeding jejunostomy, or explorative laparotomy and/or emergency surgeries, leaving 670 patients eligible for analysis. Among the included patients, 44 underwent concomitant CB-HIPEC while the remaining 626 patients underwent gastrectomy alone (standard group) (Table 1). Across the entire cohort, males were more prevalent (64%), however, an opposite trend was observed in the HIPEC group, with fewer males compared to standard group (45% vs. 65%, $p = 0.010$). Patients in the HIPEC group were significantly younger (median age 55 vs. 68 years, $p < 0.001$) and had a lower median BMI (25.7 vs. 22.7, $p < 0.001$). No significant differences were observed between the two groups in terms of nutritional status, as assessed by the NRI (98.6 vs. 99.2) and serum albumin levels (38.4 vs. 39.2 g/L). ASA I–II status was more frequent in the HIPEC group (82% vs. 61%), whereas cardiovascular (57% vs. 32%) and metabolic comorbidities (29.5% vs. 7%) were significantly more common in the standard group ($p = 0.001$ for both). Adenocarcinoma was the predominant histology (96%). Clinical stage IV disease more frequent in the HIPEC group (61% vs. 14%, $p < 0.001$). Metastatic spread was mainly lymph nodal in the standard group (40.5%) and peritoneal in the HIPEC group (96%). Preoperative chemotherapy was administered to 93% of HIPEC patients compared with 42.5% of the standard group ($p < 0.001$). All HIPEC cases were performed via open surgery whereas 84% of the standard group underwent an open approach. Total gastrectomy (86% vs. 60%, $p < 0.001$), multivisceral resections (89% vs. 36%, $p < 0.001$), and specifically intestinal resections (20% vs. 3%, $p < 0.001$) were more frequent in the HIPEC group. Median operative time was longer in the HIPEC (464 vs. 297 min) (Table 1).

Table 1
Comparison of the demographic and clinical characteristics of patients who underwent HIPEC and those who did not, within the context of ERAS program.

	Total sample	Standard Group	With HIPEC	Standard Group vs. With HIPEC P Value
Patients, no. (%)	670	626 (93.4)	44 (6.6)	-
Sex, no. (%)				
Male	426 (63.6)	406 (64.9)	20 (45.4)	**.010**[C]
Female	244 (36.4)	220 (35.1)	24 (54.6)	
Age, yr, median (IQR)	67 (18)	68 (17)	55 (13)	**<.001**[M]
Body-mass index at diagnosis (kg/m2), mean (SD)	25.5 (5.1)	25.7 (5.1)	22.7 (3.4)	**<.001**[M]
Albumin (gL), mean (SD)	38.4 (5.4)	38.4 (5.4)	39.2 (4.4)	.441[M]
NRI	98.6 (8.9)	98.6 (8.9)	99.2 (8.4)	.765[M]
History of smoking, yes, n (%)	302 (45.1)	288 (46.1)	14 (31.8)	.068[C]
History of alcohol, yes, n (%)	20 (2.9)	19 (3.1)	1 (2.3)	1000[F]
Preoperative comorbidities, no. (%)	445 (66.4)	425 (67.9)	20 (45.4)	**.002**[C]
Cardiovascular	372 (55.5)	358 (57.2)	14 (31.8)	**.001**[C]
Respiratory	85 (12.7)	79 (12.6)	6 (13.6)	.845[C]
Metabolic diseases	188 (28.1)	185 (29.5)	3 (6.8)	**.001**[C]
Kidney	45 (6.7)	45 (7.2)	0	.064[F]
Charlson Comorbidity Index, mean (SD)	2.8 (2.1)	2.9 (2.1)	1.5 (1.1)	**<.001**[M]
American Society of Anesthesiologists score no. (%)				
I-II	420 (62.7)	384 (61.3)	36 (81.8)	**.007**[C]
III-IV	250 (37.3)	242 (38.6)	8 (18.2)	**.007**[C]
Tumor histology, no. (%)				
Adenocarcinoma (1)	645 (96.3)	601 (96.1)	44 (100)	.399[F]
Others (2)	25 (3.7)	25 (4)	0	
cStage				
0	10 (1.5)	10 (1.6)	0	**<.001F**
I	109 (16.8)	109 (18.1)	0	
IIA	31 (4.8)	31 (5.1)	0	
IIB	75 (11.6)	73 (12.1)	2 (4.5)	
III	309 (47.7)	294 (48.7)	15 (34.1)	
IV	114 (17.6)	87 (14.4)	27 (61.4)	
cM site				
Peritoneal disease and/or positive cytology	40 (40.4)	16 (21.6)	24 (96)	**<.001**[F]
Liver	19 (19.2)	19 (25.7)	0	
Ln	30 (30.3)	30 (40.5)	0	
Multiple sites[@]	10 (10.1)	9 (12.2)	1 (4)	
Tumor location, no. (%)				
Cardia (SII-SIII)	172 (25.7)	167 (26.7)	5 (11.4)	**<.001**[F]
Proximal	222 (33.1)	197 (31.5)	25 (56.8)	
Distal	250 (37.3)	241 (38.5)	9 (20.4)	
Linitis	14 (2.1)	9 (1.4)	5 (11.4)	
Gastric stump	12 (1.8)	12 (1.9)	0	
Preoperative chemotherapy, no. (%)	307 (45.8)	266 (42.5)	41 (93.2)	**<.001**[C]
Surgery, no. (%)				
STG	257 (38.4)	251 (40.1)	6 (13.6)	**<.001**[F]
TG	413 (61.6)	375 (59.9)	38 (86.4)	
Other resections, no. (%)	266 (39.7)	227 (36.3)	39 (88.6)	**<.001**[C]
Other resections: intestinal resections, no. (%)	28 (4.2)	19 (3)	9 (20.4)	**<.001**[F]
Mini-invasive surgery, no. (%)	101 (15.1)	101 (16.1)	0	**.004**[C]
Surgery duration min, mean SD	307.7 (89.3)	296.7 (79.6)	463.4 (73.3)	**<.001**[M]
Infusion SO ml, mean SD	2794.9 (1043.9)	2703.7 (924.2)	4249.5 (1632.5)	**<.001**[M]
Fluid Infusion mlproKgh ≤8, no. (%)	347 (53.9)	326 (53.8)	21 (55.3)	.869[C]
Fluid Infusion mlproKgh, mean SD	8.1 (2.9)	8.1 (2.9)	8.5 (3.8)	.747[M]
pSTAGE				
0	27 (4.2)	25 (4.1)	2 (4.5)	**<.001**[F]
I	126 (19.4)	124 (20.5)	2 (4.5)	
IIA	55 (8.5)	54 (8.9)	1 (2.3)	
IIB	92 (14.2)	88 (14.6)	4 (9.1)	
III	236 (36.4)	225 (37.2)	11 (25)	
IV	112 (17.3)	88 (15.6)	24 (54.6)	
pM site				
Peritoneal disease and/or positive cytology	47 (55.9)	26 (43.3)	21 (87.5)	**.002**[F]
Liver	11 (13.1)	11 (18.3)	0	
Ln	13 (15.5)	12 (20)	1 (4.2)	
Multiple sites[@]	13 (15.5)	11 (18.3)	2 (8.3)	
Discharge median (IQR)	7 (3)	7 (3)	9 (4.5)	**<.001**[M]
Anastomotic fistula, yes, no. (%)	7 (1.1)	7 (1.1)	0	1.000[F]
Clavien Dindo				
2	4 (57.1)	4 (57.1)	-	
3	2 (28.6)	2 (28.6)	-	
4	1 (14.3)	1 (14.3)	-	
Lung, yes, n (%)	68 (10.1)	60 (9.6)	8 (18.2)	.074[F]
Clavien Dindo				
0	6 (8.8)	6 (10)	0	-
1	16 (23.5)	16 (26.7)	0	
2	34 (50)	28 (46.6)	6 (75)	
3	2 (2.9)	2 (3.3)	0	
4	7 (10.3)	5 (8.3)	2 (25)	
5	2 (2.9)	2 (3.3)	0	
6	1 (1.5)	1 (1.7)	0	
Polyuria, n (%)				
No	644 (96.1)	626 (100)	18 (40.9)	**<.001**[F]
Yes	23 (3.4)	0	23 (52.3)	
Acute renal insufficiency	3 (0.4)	0	3 (6.8)	
Hospital readmission, yes, n (%)	60 (8.9)	58 (9.3)	2 (4.5)	.415[F]
90-day mortality, mean (SD)	13 (1.9)	13 (2.1)	0	1.000[F]

Abbreviations: HIPEC, hyperthermic intraperitoneal chemotherapy; SD, standard deviation; BMI, Body Mass Index; ERAS, Enhanced Recovery After Surgery program; Ln, Liph node; [@], two or more of the previous sites; SGT, Subtotal Gastrectomy; TG, Total Gastrectomy; Other resections includes removal of any organ in addition to the stomach except for cholecystectomy; [C], Chi-square test; [F], Fisher's exact test; [M], Mann–Whitney *U* Test; in bold: statistically significant values with $p < 0.05$.

Missing values: n = 1 BMI diagnosis; n = 11 Albumin (gL); n = 11 NRI; cStage n = 22; Surgery duration n = 1; Infusion SO ml n = 30; Fluid Infusion mlproKgh ≥8 n = 27; pSTAGE n = 22; Discharge n = 4.

3.2. ERAS items adherence

Preoperative protocol adherence was comparable between the two groups, with 87% receiving carbohydrate loading and 93% receiving exclusive antibiotic prophylaxis. Extubation at the end of surgery was achieved in 91% of HIPEC patients compared to 98% in the standard group, reflecting in a higher proportion of HIPEC patients requiring at least one night in the intensive care unit (20.5% vs. 8%, $p = 0.012$) (Fig. 1, Supplementary Table 1).

No difference in GDT application was evidenced between the two groups (p = 0.869). A NGT was maintained postoperatively in the majority of HIPEC patients (77%), whereas only 18% of patients in the standard group had an NGT in place after surgery ($p < 0.001$). Abdominal drain was removed within POD 4 in 79.5% of standard group patients compared with only 36% of HIPEC patients (p < 0.001). HIPEC patients showed a higher rate of failure in several postoperative recovery items. Only 52% resumed oral intake with liquids by POD 1 and 36% tolerated soft food by POD 3, compared to 88% and 76%, respectively, in the standard group ($p < 0.001$ for both). Passive physiotherapy on POD 1 was achieved in 66% of HIPEC patients versus 90% in the standard group ($p < 0.001$). By contrast, no significant difference was observed in the active ambulation by POD 2 (82% vs. 88%, $p = 0.213$). The urinary catheter was retained for more than two days in 98% of HIPEC patients, whereas in the standard group it was removed within the ERAS timeframe in 72% of cases. Overall compliance with the ERAS protocol exceeded the 70% threshold in 75% of patients in the standard group, compared to only 25% in the HIPEC group (p < 0.001) (Fig. 1, Supplementary Table 1). Multivariable analysis identified CB-HIPEC as an independent predictor of lower ERAS compliance. Other negative predictors included a low NRI, pathological T4 stage, ASA score III–IV, and the need for multiorgan resection (Table 2).

Table 2
Clinical, demographic variables associated with ERAS Adherence (70%) in patients with gastric cancer underwent HIPEC intervention.

Independent Variable	Unadjusted			Adjusted		
	OR	95% CI	P Value	OR	95% CI	P Value
Hipec, yes vs no	0.10	0.05-0.22	**<.001**	0.08	0.03-0.19	**<.001**
Age	0.98	0.96-0.99	**.008**	0.99	0.97-1.01	0.528
Sex male vs female	1.08	0.76-1.53	0.660	1.24	0.80-1.92	0.330
BMI	1.01	0.98-1.05	0.317	1.00	0.96-1.04	0.866
NRI	1.06	1.04-1.08	**<.001**	1.06	1.03-1.08	**<.001**
Preoperative chemotherapy, yes vs no	1.06	0.75-1.49	0.711	1.45	0.93-2.26	0.098
Pstage, IV vs 0-III	0.36	0.23-0.54	**<.001**	0.52	0.31-0.88	**.016**
ASA, 12 vs 34	2.84	2.01-4.03	**<.001**	2.75	1.77-4.26	**<.001**
Other resections, yes vs. no	0.44	0.31-0.63	**<.001**	0.57	0.37-0.87	**.010**
Surgery, TG vs STG	0.93	0.66-1.32	**.709**	0.95	0.61-1.46	0.824

Abbreviations: BMI, Body Mass Index; NRI, Nutritional Risk Index; ASA, American Society of Anesthesiologists score; TG, Total Gastrectomy; SGT, Subtotal Gastrectomy; Significant associations at P < 0.05; Bold indicates significant values. OR, odds ratio; CI, confidence interval; in bold: statistically significant values.

3.3. Complications and mortality

The overall complication rate was 40%, with a significantly higher proportion of patients in the HIPEC group experiencing at least one complication compared to the standard group (54.5% vs. 38.2%, $p = 0.039$) (Table 3). Medical complications were more frequent in the HIPEC group, particularly pleural effusion requiring drainage (14% vs. 3%, $p = 0.005$) and acute renal insufficiency (7% vs. 0.3%, $p = 0.002$). Similarly, surgical complications were more common, including postoperative bleeding (29.5% vs. 13.5%, $p = 0.004$) and bowel obstruction (14% vs. 4.5%, $p = 0.019$). The severity of complications, classified according to the Clavien-Dindo system, was predominantly grade II and IIIa, with a comparable distribution between the two groups. The overall mortality rate was 2%, observed exclusively in 13 patients from the Standard group. Multivariable analysis of factors associated with postoperative complications showed that CB-HIPEC was not an independent predictor (p = 0.377) (Table 3). Independent risk factors for postoperative complications included increasing age, low NRI, pathological stage IV, ASA score III–IV, total gastrectomy, and other major resections (Table 4).

3.4. Length of hospital stay

Discharge by POD 6 was achieved in 48% of patients in the standard

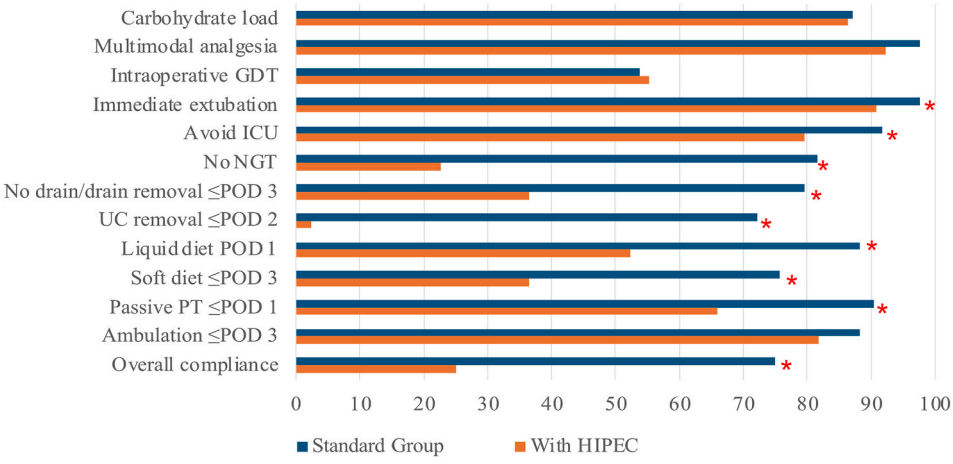


Fig. 1. Comparison of adherence to ERAS items between patients who underwent HIPEC versus those in the standard group. The red asterisk indicates a statistical significant difference between the two groups. **Abbreviation**: POD, postoperative days; GDT, goal-directed fluid therapy; ICU, intensive care unit; No NGT, nasogastric tube removal; UC, urinary catheter; PT, physiotherapy. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Table 3
Comparison of the intraoperative, postoperative general and surgical complications of patients who underwent HIPEC versus those who did not, within the context of ERAS program.

	Total sample (n = 670)	Standard Group (n = 626)	With HIPEC (n = 44)	Standard Group vs. With HIPEC P Value
Complications, n (%)	267 (39.8)	243 (38.2)	24 (54.5)	**.039**[C]
Intraoperative				
Unintended intraoperative damage to major vessels and/or organs requiring reconstruction or resection	-	-	-	-
Intraoperative bleeding requiring urgent treatment	102 (15.2)	98 (15.6)	4 (9.1)	.241[C]
Unexpected medical conditions interrupting or changing the planned procedure	-	-	-	-
Postoperative general complications				
Stroke causing patient's permanent deficit	-	-	-	-
Need for CPR	3 (0.4)	3 (0.5)	0	1.000[F]
Myocardial infarction with patient's transfer to CCU/ICU/other critical care facility	-	-	-	-
Cardiac dysrhythmia requiring invasive treatment	-	-	-	-
Acute myocardial failure with acute pulmonary edema or drop in EF > 50%	-	-	-	-
Pulmonary embolism with symptoms confirmed by urgent CT scan	1 (0.1)	1 (0.2)	0	1.000[F]
Need for prolonged intubation (>24 h after the surgical procedure)	2 (0.3)	2 (0.3)	0	1.000[F]
Respiratory failure requiring reintubation	8 (1.2)	6 (0.9)	2 (4.5)	.092[F]
Need for tracheostomy	-	-	-	-
Pleural effusion requiring drainage	26 (3.8)	20 (3.2)	6 (13.6)	**.005**[F]
Pneumothorax requiring treatment	3 (0.4)	3 (0.5)	0	1.000[F]
Acute liver dysfunction (the Child-Pugh score >8 for longer than 48 h)	1 (0.1)	1 (0.1)	0	1.000[F]
Acute renal insufficiency (postoperative creatinine twice its preoperative value)/ renal failure requiring CVVH or dialysis	5 (0.7)	2 (0.3)	3 (6.8)	**.002**[F]
Infections (gastrointestinal, respiratory, urinary, or other) with both symptoms and germ isolation	82 (12.2)	77 (12.3)	5 (11.4)	.855[C]
Postoperative surgical complications				
Postoperative bleeding requiring both urgent transfusions and invasive treatment	98 (14.6)	85 (13.5)	13 (29.5)	**.004**[C]
Postoperative bowel obstruction (clinical/ radiological signs of obstruction, inability to enteral feed, longer need for NG suction)	34 (5.1)	28 (4.5)	6 (13.6)	**.019**[F]
Postoperative bowel perforation or necrosis requiring surgical treatment (or cause of death)	3 (0.4)	3 (0.4)	0	1.000[F]
Duodenal leak (irrespective of presentation, method of identification, clinical consequences, and treatment)	7 (1.1)	7 (1.1)	0	1.000[F]
Anastomotic leak (irrespective of presentation, method of identification, clinical consequences, and treatment)	7 (1.1)	7 (1.1)	0	1.000[F]
Postoperative pancreatic fistula	9 (1.3)	9(1.3)	0	1.000[F]
Postoperative pancreatitis diagnosed both clinically and radiologically	5 (0.7)	5 (0.8)	0	1.000[F]
Other postoperative abnormal fluid from drainage and/or abdominal collections without gastrointestinal leak(s) preventing drainage removal or requiring treatment	20 (3)	16 (2.6)	4 (9.1)	**.036**[F]
Delayed gastric emptying (by 10th postoperative day) requiring treatment or delaying discharge	4 (0.6)	3 (0.5)	1 (2.3)	.238[F]
Other major complications requiring re-intervention or other invasive procedures	3 (0.4)	3 (0.4)	0	1.000[F]

Abbreviations: HIPEC, hyperthermic intraperitoneal chemotherapy; [C], Chi-square test; [F], Fisher's exact test; in bold: statistically significant values with $p < 0.05$.

group, compared with only 1 patient (2%) in the HIPEC group (Supplementary Table 1). Median length of hospital stay was 2 days longer in HIPEC group (9 vs 7 days, $p < 0.001$) (Table 1).

4. Discussion

This study represents the largest single-center experience directly comparing ERAS implementation in gastrectomy with and without CB-HIPEC. It delineates the influence of peritoneal disease and CB-HIPEC on ERAS adherence and postoperative outcomes. As expected, patients undergoing CB-HIPEC were highly selected and had a more advanced disease. Although complication rates were higher in this cohort, CB-HIPEC was not independently associated with increased morbidity; instead, age, low NRI, stage IV disease, ASA III–IV status, total gastrectomy, and extended resections were significant predictors. CB-

Table 4
Clinical, demographic variables associated with perioperative complications in patients with gastric cancer underwent HIPEC intervention.

Independent Variable	Unadjusted			Adjusted		
	OR	95% CI	P Value	OR	95% CI	P Value
Hipec, yes vs no	1.89	1.02-3.49	**.042**	1.37	0.67-2.80	0.382
Age	1.02	1.01-1.04	**<.001**	1.02	1.00-1.03	**.019**
Sex male vs female	1.28	0.92-1.77	0.130	0.76	0.52-1.11	0.158
BMI	0.98	0.95-1.01	0.262	0.97	0.94-1.01	0.218
NRI	0.94	0.93-0.96	**<.001**	0.96	0.94-0.98	**<.001**
Preoperative chemotherapy, yes vs no	1.04	0.76-1.42	0.793	0.98	0.66-1.43	0.918
Pstage, IV vs 0-III	2.92	1.92-4.44	**<.001**	2.36	1.46-3.84	**<.001**
ASA, 12 vs 34	0.40	0.29-0.55	**<.001**	0.46	0.31-0.68	**<.001**
Other resections, yes vs. no	1.96	1.43-2.69	**<.001**	1.78	1.22-2.59	**.002**
Surgery, TG vs STG	1.50	1.09-2.08	**.013**	1.59	1.08-2.35	**.017**

Abbreviations: BMI, Body Mass Index; NRI, Nutritional Risk Index; ASA, American Society of Anesthesiologists score; TG, Total Gastrectomy; STG, Subtotal Gastrectomy; Significant associations at $P < 0.05$; Bold indicates significant values. OR, odds ratio; CI, confidence interval; in bold: statistically significant values.

HIPEC substantially impaired ERAS compliance, mainly due to delayed removal of nasogastric tubes and urinary catheters, and was independently associated with ERAS failure in multivariable analysis. As shown by the preoperative characteristics, the HIPEC group consisted of a highly selected subset of patients with more advanced tumor stages, nearly all of whom required preoperative chemotherapy. However, these patients were also younger and had significantly fewer comorbidities, potentially providing a greater capacity for postoperative recovery. Interestingly, 39% of HIPEC patients were initially staged as non-metastatic prior to surgery but were upstaged intraoperatively due to positive cytology. This highlights the need for more accurate preoperative staging when selecting patients for resective treatment. Unfortunately, complete data on preoperative laparoscopic staging were not available, preventive definitive conclusions based on our current dataset. The laparoscopy was not systematically performed in all patients and, as a consequence, a proportion of patients were upstaged intra-operatively. This may have led to more extensive cytoreductive procedures, multiple organ resections, and the addition of HIPEC. Nevertheless, this did not affect the applicability of the ERAS protocol, which was implemented uniformly in all patients regardless of the intraoperative disease burden. ERAS adherence was significantly lower in the HIPEC group, supporting the hypothesis that these patients are perceived as requiring more intensive monitoring and a slower ERAS pathway. Compared with 75% of patients in standard group, only 25% of HIPEC patients achieved the 70% threshold for optimal ERAS compliance, primarily due to delayed removal of urinary catheter and drains, and slower resume of oral intake. The reduced adherence to standard ERAS items observed in HIPEC patients likely reflects the limited applicability of current ERAS recommendations in this complex setting rather than shortcomings in protocol compliance, highlighting the need for the development of dedicated ERAS pathways tailored specifically to HIPEC procedures. Interestingly, multivariable analysis showed that CB-HIPEC was independently associated with lower ERAS compliance but not with postoperative complications. Although HIPEC patients experienced higher postoperative complication rates, the multivariable analysis suggest that this morbidity was driven by the greater frequency of multiorgan resection and more advanced tumors, rather than CB-HIPEC itself. Based on our findings, postoperative complications and delayed recovery in HIPEC group appear to be driven not by the CB-HIPEC procedure itself, but by the greater surgical complexity. Higher rates of total gastrectomy and multiorgan resections are associated with increased morbidity, which in turn reduces adherence to ERAS protocols. These results are consistent with a recent meta-analysis on ERAS in patients undergoing cytoreductive surgery with or without CB-HIPEC, which reported that challenges in implementing certain postoperative measures were largely related to multiple bowel resections and the occurrence of polyuria [18]. Looking at postoperative complications, patients in the HIPEC group had a higher risk of postoperative bowel obstruction and renal insufficiency, which justifies a more conservative approach to NGT avoidance and early catheter removal. In our cohort, prolonged nasogastric tube retention and delayed urinary catheter removal were among the main contributors to reduced ERAS adherence. These deviations were largely driven by clinical considerations specific to cytoreductive surgery with CB-HIPEC, including extensive multivisceral resections and the increased risk of postoperative ileus necessitating prolonged nasogastric decompression. In addition, strict urine output monitoring was required to detect and prevent chemotherapy-related renal impairment and to manage the high incidence of postoperative polyuria, thereby justifying delayed urinary catheter removal. Moreover, a longer operative time and greater surgical invasiveness resulted in a higher proportion of patients requiring one night in ICU, potentially delaying postoperative ERAS items. This suggest that ERAS protocols should be adapted according to the invasiveness of surgery rather than CB-HIPEC itself, except for nephrotoxicity and its consequences, that are directly related with CB-HIPEC procedure. Focusing specifically on nephrotoxicity and its impact on the postoperative course, we observed that although GDT was implemented in fewer than 70% of cases in both groups, intraoperative fluid administration was comparable, averaging approximately 8 ml/kg/h across the entire cohort. This approach resulted in postoperative polyuria in 52% of patients in the HIPEC group, with an observed incidence of acute renal insufficiency of 6.8%. Acute renal failure rates after CB-HIPEC have historically reached 40% [19], with severe chronic renal failure up to 8.5% [20,21]. By contrast, Laplace et al. reported no cases of acute renal insufficiency following the introduction of sodium thiosulfate, consistent with our findings and supporting its role as an effective renal-protective strategy [11,12]. Based on the findings of the present study, routine sodium thiosulfate nephroprotection was introduced in our institution in January 2019, and its subsequent implementation was associated with a marked reduction in postoperative renal insufficiency. In the HIPEC group, adherence to the ERAS protocol regarding urinary catheter removal by POD 2 was seldom achieved, particularly in patients who developed postoperative polyuria. The median removal time was POD 6, which diverges not only from our study protocol but also from recent literature advocating for removal as early as POD 3 following CB-HIPEC [22]. Interestingly, this delay, did not hinder early ambulation with more than 80% of patients in both group reaching an active ambulation by POD 2. Compared with the existing literature on ERAS in the HIPEC setting, our study offers a large and homogeneous cohort of patients undergoing surgery for gastric cancer, with or without peritoneal involvement. By focusing exclusively on this patient population, it overcomes the limitations of previous studies that included heterogeneous tumor types and surgical procedures, thereby offering a clearer assessment of the true impact of HIPEC on surgical outcomes. The main limitations of the present study are its retrospective design and its single-center nature.

5. Conclusions

The addition of CB-HIPEC to gastrectomy for gastric cancer does not intrinsically increase postoperative morbidity; rather, the higher morbidity rates are mainly associated with multiorgan resections and

total gastrectomy. However, CB-HIPEC significantly reduces ERAS compliance, highlighting the need to design tailored perioperative pathways for these patients, particularly regarding the management of nasogastric tubes and urinary catheters. Further investigations across different clinical settings are warranted to validate these findings and to establish dedicated ERAS protocols supported by high-level quality of evidence.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The Ethical Committee for Clinical Trial of our Institute has approved the data collection with the following code: 2175CESC. Informed consent was obtained from all individual participants included in the study. This article does not contain any studies with animal subjects performed by any of the authors.

Author contributions

Conceptualization: FC, CG, JW, FM.
Methodology: FC, CG, FM, MB, EM, SC, JW.
Formal analysis and investigation: CG, SC, JW.
Writing - original draft preparation: FC, CG, JW.
Writing - review and editing: All authors.
All authors have made a significant contribution to this manuscript, have seen and approved the final version.

Data availability statement

The authors confirm that the data supporting the findings of this study are available within the article.

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Declarations of competing interest

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Appendix A. Supplementary data

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References

[1] Baiocchi GL, Giacopuzzi S, Reim D, Piessen G, Costa PMD, Reynolds JV, et al. Incidence and grading of complications after gastrectomy for cancer using the GASTRODATA registry: a European retrospective observational study. Ann Surg 2020;272(5):807–13.
[2] Wee IJY, Syn NL, Shabbir A, Kim G, So JBY. Enhanced recovery versus conventional care in gastric cancer surgery: a meta-analysis of randomized and non-randomized controlled trials. Gastric Cancer 2019;22(3):423–34.
[3] Weindelmayer J, Mengardo V, Gasparini A, Sacco M, Torroni L, Carlini M, et al. Enhanced recovery after surgery can improve patient outcomes and reduce hospital cost of gastrectomy for cancer in the west: a propensity-score-based analysis. Ann Surg Oncol 2021;28(12):7087–94.
[4] Dhiman A, Fenton E, Whitridge J, Belanski J, Petersen W, Macaraeg S, et al. Guide to enhanced recovery for cancer patients undergoing surgery: ERAS for patients undergoing cytoreductive surgery with or without HIPEC. Ann Surg Oncol 2021;28(12):6955–64.
[5] Hübner M, Kusamura S, Villeneuve L, Al-Niaimi A, Alyami M, Balonov K, et al. Guidelines for perioperative care in cytoreductive surgery (CRS) with or without hyperthermic IntraPEritoneal chemotherapy (HIPEC): enhanced recovery after surgery (ERAS®) society recommendations - Part I: preoperative and intraoperative management. Eur J Surg Oncol 2020;46(12):2292–310.
[6] Hübner M, Kusamura S, Villeneuve L, Al-Niaimi A, Alyami M, Balonov K, et al. Guidelines for perioperative care in cytoreductive surgery (CRS) with or without hyperthermic IntraPEritoneal chemotherapy (HIPEC): enhanced recovery after surgery (ERAS®) society recommendations - Part II: postoperative management and special considerations. Eur J Surg Oncol 2020;46(12):2311–23.
[7] Japanese gastric cancer treatment guidelines 2018. Gastric cancer. fifth ed., vol. 24; 2021. p. 1–21. 1.
[8] Smyth EC, Verheij M, Allum W, Cunningham D, Cervantes A, Arnold D. Gastric cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 2016;27(suppl 5):v38–49.
[9] De Manzoni G, Marrelli D, Baiocchi GL, Morgagni P, Saragoni L, Degiuli M, et al. The Italian Research Group for Gastric Cancer (GIRCG) guidelines for gastric cancer staging and treatment: 2015. Gastric Cancer 2017;20(1):20–30.
[10] van Driel WJ, Koole SN, Sikorska K, Schagen van Leeuwen JH, Schreuder HWR, Hermans RHM, et al. Hyperthermic intraperitoneal chemotherapy in ovarian cancer. N Engl J Med 2018;378(3):230–40.
[11] Laplace N, Kepenekian V, Friggeri A, Vassal O, Ranchon F, Rioufol C, et al. Sodium thiosulfate protects from renal impairement following hyperthermic intraperitoneal chemotherapy (HIPEC) with Cisplatin. Int J Hyperthermia 2020;37(1):897–902.
[12] Kurreck A, Gronau F, Alberto Vilchez ME, Abels W, Enghard P, Brandl A, et al. Sodium thiosulfate reduces Acute kidney injury in patients undergoing cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy with cisplatin: a single-center observational Study. Ann Surg Oncol 2022;29(1):152–62.
[13] Weindelmayer J, Mengardo V, Ascari F, Baiocchi GL, Casadei R, De Palma GD, et al. Prophylactic drain placement and postoperative invasive procedures after gastrectomy: the abdominal drain after gastrectomy (ADIGE) randomized clinical trial. JAMA Surg 2025;160(2):135–43.
[14] Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240(2):205–13.
[15] Miftode SV, Troja A, El-Sourani N, Raab HR, Antolovic D. Simultaneous cholecystectomy during gastric and oesophageal resection: a retrospective analysis and critical review of literature. Int J Surg 2014;12(12):1357–9.
[16] Bernini M, Bencini L, Sacchetti R, Marchet A, Cristadoro L, Pacelli F, et al. The Cholegas Study: safety of prophylactic cholecystectomy during gastrectomy for cancer: preliminary results of a multicentric randomized clinical trial. Gastric Cancer 2013;16(3):370–6.
[17] Buzby GP, Williford WO, Peterson OL, Crosby LO, Page CP, Reinhardt GF, et al. A randomized clinical trial of total parenteral nutrition in malnourished surgical patients: the rationale and impact of previous clinical trials and pilot study on protocol design. Am J Clin Nutr 1988;47(2 Suppl):357–65.
[18] Robella M, Tonello M, Berchialla P, Sciannameo V, Ilari Civit AM, Sommariva A, et al. Enhanced Recovery after Surgery (ERAS) Program for patients with peritoneal surface malignancies undergoing cytoreductive surgery with or without HIPEC: a systematic review and a meta-analysis. Cancers (Basel) 2023;15(3).
[19] Hakeam HA, Breakiet M, Azzam A, Nadeem A, Amin T. The incidence of cisplatin nephrotoxicity post hyperthermic intraperitoneal chemotherapy (HIPEC) and cytoreductive surgery. Ren Fail 2014;36(10):1486–91.
[20] Naffouje SA, Tulla KA, Chorley R, Armstrong N, Salti GI. Acute kidney injury increases the rate of major morbidities in cytoreductive surgery and HIPEC. Ann Med Surg 2018;35:163–8.
[21] Sin EI, Chia CS, Tan GHC, Soo KC, Teo MC. Acute kidney injury in ovarian cancer patients undergoing cytoreductive surgery and hyperthermic intra-peritoneal chemotherapy. Int J Hyperthermia 2017;33(6):690–5.
[22] Kefleyesus A, Bakrin N, Kepenekian V, Gerbaud-Coulas C, Li A, Vassal O, et al. Enhanced recovery for cytoreductive surgery and hyperthermic intraperitoneal Chemotherapy: an international survey to assess acceptance and feasibility. Eur J Surg Oncol 2025;51(9):110150.