

The effect of ERAS management in gastric cancer: assessment from the IMIGASTRIC study

Francesco Giovanardi^{1,2*}, Francesco Falbo³, Chiara Celano¹, Michele Casella¹, Marco Palisi¹

¹Department of General and Oncological Surgery, Azienda Ospedaliera Ordine Mauriziano “Umberto I”, Turin, Italy.

²Department of General Surgery and Organ Transplantation “Paride Stefanini”, Sapienza University of Rome, Rome, Italy.

³Department of Surgical Sciences, Sapienza University of Rome, Rome, Italy.

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*Correspondence to

Dr. Francesco Giovanardi
Department of General Surgery
and Organ Transplantation “Paride Stefanini”,
Sapienza University of Rome.
Viale del Policlinico, 155
00161, Rome, Italy.
giovanardi89@gmail.com
Telephone: +393202137231

ABSTRACT

Background:

Establish protocols to enhance the surgical management (ERAS) can improve outcomes, shortening hospital stay and save resources.

Several studies have carried out for colorectal surgery, while a lack of evidence for gastrectomy remains.

This study aims to evaluate the impact of ERAS strategies in a large series of patients underwent gastric cancer surgery.

Methods:

This is a propensity score-matched case-control study, comparing an ERAS group with a control group. Data were recorded through a tailored and protected web-based system. Primary outcomes: hospital stay, complications rate. Among the secondary outcomes, there are: POD of mobilization, POD of starting liquid diet and soft solid diet.

Results:

Patients in the ERAS and control groups were 1:1 matched by the closest propensity score on the logit scale and with a Caliber = 0.2. The successful matching resulted in a total sample of 440 patients.

The two groups showed no differences in all baseline patients characteristics, type of surgery (P=0.31) and stage of the disease (P=0.61).

A benefit in favor of the ERAS management was found in the length of hospital stay (P=0.0004) and complications rate (P=0.001).

Conclusion:

An ERAS program can safely be established in referral centers for gastric cancer, enabling to significantly improve the main clinical outcomes.

Key Words:

ERAS; Enhanced Recovery After Surgery; gastric cancer; gastric surgery; gastrectomy.

Background

Gastric cancer is the second leading cause of cancer death in the world and surgery plays the most important role in the treatment of this disease.

However, surgery for gastric cancer remains a high-risk procedure with clinically significant postoperative stress, complications, and significant sequelae.

Significant advances in the management of surgical patients have been in last decades for gastric cancer.

This has led to the concept of enhanced recovery after surgery (ERAS) with the objective of reducing the length of hospital stay accelerating postoperative recovery and reducing surgical stress.

The ERAS protocols have many items, including the pre-operative patient education, preoperative carbohydrate loading, early mobilization and feeding starting from the first postoperative days.

Most of studies on this field were published for colorectal surgery, while only few authors described ERAS protocols in gastric cancer surgery.

In the present study, we have evaluated the effects on postoperative functional recovery outcomes after gastrectomy in patients undergoing an ERAS program in comparison with a conventional surgical management.

Methods

Type of Study

This is a multi-institutional propensity score-matched case-control study, comparing patients undergoing a perioperative management based on the ERAS society principles (Table 1) and control patients undergoing conventional surgical management.

Data were collected in the context of the IMIGASTRIC study and after sharing a specific study protocol.[1]

The study was registered at clinical trials.gov with a registration number of NCT02325453.

Perioperative

- Education on the ERAS protocol administered;
- No routine use of mechanical bowel preparation;
- Allow oral meal intake until 6 hours before surgery;
- No routine use of nasogastric tube or abdominal drainage
- Maintain normal body temperature during surgery
- Antibiotic prophylaxis before skin incision without a postoperative prolonged use

Postoperative

- Avoid over-hydration and restricted fluid administration (20ml/kg/d) until full resumption of oral intake;
- Encourage early active ambulation from POD 1 (more than 2h/day);
- Remove urinary catheter as early as POD 1;
- Start early oral intake from POD 2;
- Evaluate patient recovery with discharge criteria to determine the discharge plan.

Table 1: ERAS management.

Time Period and Sites

Data entered into the IMIGASTRIC registry regarding procedures performed until data extraction (November 2019) were analyzed. All involved centers are referral institutions with a well-established gastric cancer program. All diagnostic and surgical interventions at these centers were done according to international guidelines and information stored in institutional prospective data collection systems.

Inclusion criteria

- Histologically proven gastric cancer
- Preoperative staging work-up performed by upper endoscopy and/or endoscopic ultrasound, and CT scan and in accordance to international guidelines
- Early Gastric Cancer[2, 3]
- Advanced Gastric Cancer[2, 3]
- Patients treated with curative intent in accordance to international guidelines[4, 5]

Exclusion criteria

- Distant metastases: peritoneal carcinomatosis, liver metastases, distant lymph node metastases, Krukenberg tumors, involvement of other organs
- Patients with high operative risk as defined by the American Society of Anesthesiologists (ASA) score > 4
- History of previous abdominal surgery for gastric cancer
- Synchronous malignancy in other organs
- Palliative surgery

Data Collection and Reported Outcomes

This study reported descriptive findings and outcomes among the two groups. Basic patient characteristics, tumor findings, and surgical procedure details were reported. The outcomes section offers a comparison regarding operative results, postoperative recovery, and complications.

Source of Data Analyzed

Data gathered were obtained from existing records, diagnostic tests, and surgical intervention descriptions. Data were collected and recorded by all institutions through a specific online shared protected system (<https://imigastric.logix-software.it/>).

The present study was reported in accordance with the STROBE guidelines and statement[6].

Propensity Score Matching

Propensity score matching analysis was carried out using SPSS software version 23 and R software version 3.1, through the Custom Dialog "PS Matching". Each patient's propensity score was calculated by a multivariable logistic regression model using the covariates of institution, age, sex, comorbidities, body mass index (BMI), surgical approach (open, laparoscopic, robotic) type of gastrectomy, stage of disease. Patients in the ERAS and Control group were 1:1 matched by the closest propensity score on the logit scale and with a Caliper = 0.2

Statistics

IBM SPSS Statistics V.23 was used to carry out the statistical analysis. An intention to treat analysis was performed.

The dichotomous variables were expressed as numbers and percentages, while continuous variables as mean and SD, or median and IQR (minimum and maximum values). Continuous variables were compared using independent T test.

Pearson's χ^2 test or Fisher's exact test, as appropriate, was used for analysis of categorical data. A P value of

<0.05 was considered statistically significant.

Results

At the time of this analysis, 1445 patients entered in the IMIGASTRIC registry had information on the ERAS management.

The matching analysis resulted in a total sample of 440 patients, 220 from the ERAS group and 220 from the Control group. The successful matching permitted to obtain a homogeneous distribution of all patient's characteristics (Table 2).

Table 3 shows no significant differences between groups in surgical approach (P=0.14), type of gastrectomy (P=0.31), stage of the disease (P=0.61).

A significantly shorter hospital stay (P=0.0004; Figure 1) was found in the ERAS group versus the Control group (Table 4).

The most relevant benefit was shown in the resumption of a liquid (P=0.01; Figure 2) and a soft solid diet (P=0.007; Figure 3).

No significant differences in patient mobilization (P=0.56) and first flatus (P=0.07) were found.

The ERAS group showed some advantages in the intravenous analgesic use (P<0.0001; Figure 4) than the control group, but no differences were found in the length of antibiotic use (P=0.31).

In this study the adoption of an ERAS protocol resulted in a significant reduction in post-operative complications (P=0.001) than the Control group.

Outcome	ERAS	Control	p value
Intraoperative complications no. (%)	8 (3.6)	10 (4.5)	0.81
Intraoperative death no. (%)	0 (0)	0 (0)	1
Hospital stay (days) mean±SD	10.35±4.76	13.77±13.61	<0.001
Mobilization (days) mean±SD	2.37±1.91	2.65±6.92	0.56
Liquid diet (days) mean±SD	3.89±2.7	4.76±4.41	0.01
Solid diet (days) mean±SD	6.79±4.91	9.05±10.87	0.007
Peristalsis (days) mean±SD	2.55±1	2.59±1.13	0.67
First flatus (days) mean±SD	3.31±1.18	3.54±1.52	0.07
Antibiotic use (days) mean±SD	4.75±3.86	5.24±5.83	0.31
Analgesic use (days) mean±SD	2.82±1.35	4.34±2.76	<0.001
Complications no. (%)	18 (8.2)	43 (19.5)	0.001
Complications after discharge no. (%)	11 (5)	10 (4.5)	0.5

Table 4: perioperative outcomes.

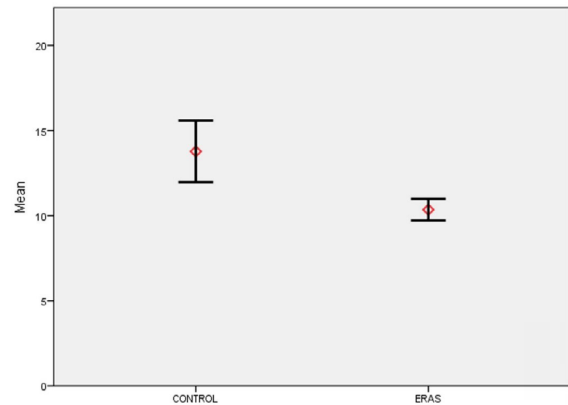


Figure 1: mean difference between groups in the length of hospital stay.

Variable	ERAS	Control	P value
Total no.	220	220	
Age mean±SD	67.14±13.03	67.18±12.62	0.97
BMI mean±SD	24.00±4.18	24.14±3.04	0.69
Sex no. (%)			0.77
M	132(60)	128(58.2)	
F	88(40)	92(41.8)	
ASA no. (%)			0.93
I	50 (22.7)	51 (23.2)	
II	109 (49.5)	114 (51.8)	
III	61 (27.8)	55(25)	
Comorbidities no. (%)	145 (65.9)	147 (66.8)	0.46

Table 2: Basic patients' characteristics.

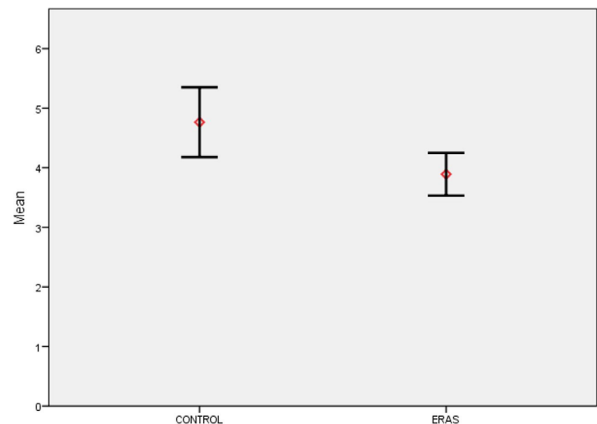


Figure 2: mean difference between groups in starting a liquid intake.

Variable	ERAS	Control	p value
Type of gastrectomy No. (%)			0.31
Distal	134 (60.9)	140 (63.6)	
Total	86 (39.1)	80 (36.4)	
Surgical approach No. (%)			0.14
Open	75 (34.1)	87 (39.5)	
MIS	145 (65.9)	133 (60.5)	
Tumor stage No. (%)			0.61
0	9 (4.1)	9 (4.1)	
IA	39 (17.7)	36 (16.4)	
IB	18 (8.2)	17 (7.7)	
IIA	29 (13.2)	32 (14.5)	
IIB	27 (12.3)	24 (10.9)	
IIIA	25 (11.4)	36 (16.4)	
IIIB	32 (14.5)	38 (17.3)	
IIIC	41 (18.6)	28 (12.7)	

Table 3: Surgical and pathological characteristics.

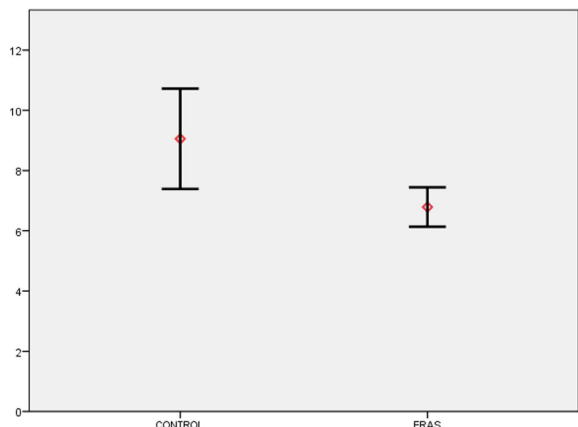


Figure 3: mean difference between groups in starting a soft solid diet.

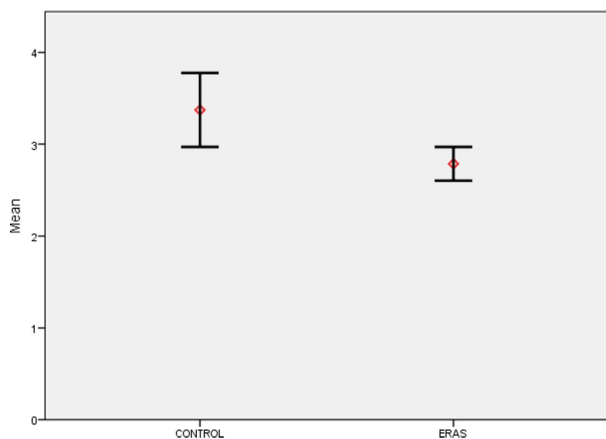


Figure 4: mean difference between groups in the length of intravenous analgesic use.

Discussion

The present study evaluated the role of the ERAS program in the management of gastric cancer patients using a propensity score case matched analysis to perform a comparison with a conventional care treatment.

A significant decrease in the length of hospital stay and in-hospital postoperative complications were the most relevant findings.

Important items in the ERAS protocol are early mobilization and feeding[7], which is especially facilitated by the absence of the NG tube and drainage, as well as an early removal of the urinary catheter. Smart[8] showed that failure of early patient mobilization is associated with prolonged hospital stay.

Yamada[9] in his study showed that the recovery of bowel function was significantly earlier in the ERAS group than in the conventional group.

In addition, Wang[10] reported that the first day of flatulence after gastric surgery was a mean of one day earlier in patients who received fast-track surgery compared to those who received conventional care.

Some factors such as prolonged fasting and placement of the nasogastric tube appear to cause nausea and contribute to a delay of intestinal recovery[11].

In our study, there was not a significant difference regarding the first flatus. However, we believe that this outcome is subject to a high risk of bias. Instead, variables regarding the oral recovery of food intake can be considered more reliable.

We found a significant advantage in favor of the ERAS group in all steps of food intake, from starting a liquid diet (3.89 ± 2.7 vs 4.76 ± 4.41 ; $P < 0.01$) to the resumption of a solid diet (6.79 ± 4.91 vs 9.05 ± 10.87 ; $P = 0.007$).

The ERAS protocols require the patient be not subjected to long periods of fasting.

Early postoperative nutrition reduces postoperative catabolism, accelerates the return of bowel function, and decreases the risk of complications. This was especially studied in colorectal surgery[12, 13].

Moreover, Lewis et al.[14] confirmed in their meta-analysis that keeping patients in a fasting state is not beneficial.

Several studies have shown that early oral feeding is feasible and brings benefits in gastric surgery[10, 15];

however, this point remains controversial.

Even if an early postoperative oral feeding has been shown to speed up the recovery after various types of surgery, this approach after gastrectomy has always been seen with suspicion because of some concerns, not actually well demonstrated in the literature, that early food intake may cause anastomotic leakage or intestinal obstruction.

In recent years, several studies have confirmed that early oral food intake after gastric surgery is safe and might be associated with enhanced recovery and shorter hospital stay[9, 16].

Particularly, a randomized controlled study has reported data on the safety of early oral feeding starting in the second postoperative day (POD 2) after gastrectomy[17]. The Makuuchi[18] and Pedziwiatr[19] studies, comparing ERAS and conventional management after gastrectomy, have confirmed that oral feeding in POD 2 is safe and allows the reduction of post-operative administration of intravenous fluids and an early discharge[20].

Sugisawa[21] focused on the rate of anastomotic leakage and aspiration pneumonia to evaluate the real risks of early nutrition.

In his study, the incidence of anastomotic leakage was 0.8%, a figure he highlighted as not only lower than that of the subjects in his historical cohort (1.7%), but also a result not different or lower (0.8-1.9%) when compared to previous data in studies in which conventional perioperative care was reported. Therefore, the author concluded that early oral nutrition is not able to adversely affect the anastomotic site. The same results were obtained by Yamada[9, 22], showing a similar incidence in anastomotic leaks (1.1%).

In our study, the adoption of an ERAS program resulted in a significant reduction in hospital stay with a mean difference of 3.42 days compared to conventional management.

Similar results were obtained by Sugisawa[21] and Wang[10].

In our study, a significant reduction in patients with postoperative complications (8.2% versus 19.5%; $P = 0.001$) was shown in the ERAS group. Moreover, no differences in readmissions for complications after discharge were shown ($P = 0.5$).

In conclusion, the adoption of a management based on the ERAS principles for gastric cancer can safely improve the patient's functional recovery, allowing an early discharge and a reduction of overall complications.

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Contributors

FG, FF, CC, MC, MP conceptualized and designed the study, acquired, and analyzed data, interpreted the study results, drafted the manuscript, and critically revised the final version of the manuscript.

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Competing interests

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

Availability of data and materials

Further information is available from the corresponding author on reasonable request.

Ethics approval

This study is conducted in compliance with ethical principles originating from the Helsinki Declaration, within the guidelines of Good Clinical Practice and relevant laws/regulations. Trial registration number: NCT02325453.

Provenance and peer review

Not commissioned; externally peer reviewed.

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