Effectiveness of Enhanced Recovery After Surgery (ERAS) in Gynecologic Oncology Surgery

Original Article

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ABSTRACT

Objective: The current study aimed to evaluate the effectiveness of implementation of enhanced recovery after surgery in patients with gynecologic cancer undergoing open surgery at our institute.

Methods: This was a randomized controlled trial done during the period of August 2022 to August 2023. The study included 100 participants with gynecologic cancer who were treated with open surgery at our institute. Patients were randomly assigned to conventional group (50 patients) who received the usual management, and the ERAS group (50 patients) who were managed by preoperative, intraoperative, and postoperative ERAS protocol. The outcome measures were length of hospital stay and perioperative complications.

Results: The mean time required for return of bowel function was significantly longer in group A (conventional) than in group B (ERAS) (30.72±7.72 hours versus 18.96±7.21 respectively; *P* value 0.001). The length of hospital stay was significantly longer in group A than group B (5.66±2.08 days versus 3.92±1.45 days respectively; *P* value 0.001). 17 cases (34%) of group A had postoperative nausea and vomiting (needing antiemetics) despite only 6 cases (12%) of group B (*P* value 0.01). Also 28 cases (56%) of group A had post operative moderate to severe pain despite only 14 cases (28%) of group B (*P* value 0.005). There was no significant difference in postoperative ileus, blood transfusion or readmission within 30 days between both groups.

Conclusions: We can conclude that implementation of ERAS protocol on patients with gynecologic cancers undergoing surgery had confirmed previous results of shorter length of hospital stay, early return of bowel function, less postoperative pain scores with no increase in perioperative complications. Implementation of ERAS guidelines should be encouraged in low resource countries.

Key Words: Enhanced recovery after surgery, gynecologic cancer, laparotomy, length of stay, postoperative pain.

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INTRODUCTION

Patients undergoing surgery are exposed to surgical stress, which is well known to induce a complex inflammatory response that is marked by production of a group of catabolic hormones and cytokines. These changes result in increased tissue demand and sometimes organ dysfunction[1].

Enhanced Recovery After Surgery (ERAS) is a global program aiming at improving the quality of surgery. This program is dependent on peri-operative recommendations which had been developed for different specialties of surgery[2,3].

Preoperative recommendations include several aspects, first is avoidance of mechanical bowel preparation. Second, incudes those concerned with duration of fasting before surgery, as the American Society of Anesthesiologists (ASA) Committee guidelines states that patients could be allowed to take solid meals until eight hours before elective surgical procedure, and clear fluids up to two hours[4].

It was found that the administration of fluids prior to the desired surgery may be associated with reduction in preoperative thirst, hunger, and anxiety[5]. Also, it was evidenced that prolonged dehydration before surgery may be associated with increased hazards of acute kidney injury (AKI) and even myocardial infarction[6].

Other preoperative recommendations by ERAS® Society included oral carbohydrate load two to three hours before surgery using isotonic complex carbohydrate solution. This practice was associated with reduction in insulin resistance (IR) and also more rapid normalization of associated metabolic abnormalities[7].

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The third preoperative recommendation includes medications that are allowed before surgery. Short acting oral anxiolytics could be used in selected cases with severe preoperative anxiety while long-acting sedating drugs should be used with caution within 12 hours from surgery for fear of delayed recovery[8]. Preoperative use of non-steroidal anti-inflammatory (NSIDs) drugs was associated with reduction in opioid requirements[9]. Also, the use of gabapentinoids prior to surgery may lead to reduction of postoperative pain, narcotic analgesic use, and nausea/vomiting with limitation of their use in elderly patients[10].

Intra-operative recommendations include proper use of antimicrobial prophylaxis, maintenance of normal body temperature, fluid management, and encouraging the use of regional anesthesia in selected cases[11]. High risk patients for venous thrombo-embolism (VTE) should have double prophylaxis through mechanical methods (compression) and pharmacologic methods (low molecular weight heparin) initiated preoperatively and may be extended in select cases[7].

Post-operative recommendations include early oral diet that could be initiated within 24 hours from surgery, minimizing use of intraperitoneal drains and nasogastric tubes, encourage early mobilization with use of multimodal opioid-sparing analgesia[12]. Early removal of bladder catheters within 24 hours after surgery (except in selected cases) is encouraged as it decreases risk of infection, urine retention, and supports early mobilization[13,14].

The implementation of these peri-operative practice recommendations was associated with faster recovery of the patient after surgery, better surgical outcome, and reduction in the overall costs of healthcare[15].

Despite these recommendations, a recent international survey on the implementation of ERAS protocol in open gynecologic oncology surgery revealed that only 37% of centers worldwide adhered to guidelines, with Africa being the lowest place (only 10%)[11]. From this point, our study aimed to evaluate effectiveness ERAS in patients with gynecologic cancers undergoing open surgery at our institute.

METHODS

This was a randomized controlled study carried out at the department of Obstetrics and Gynecology of Mansoura University Hospitals, Egypt during the period from August 2022 to August 2023. The study included 100 patients with gynecologic malignancies who underwent surgery for their primary cancer at our department. The study was approved by the Institutional review board (IRB MS.23.02.2296), Faculty of Medicine, Mansoura University.

Inclusion criteria:

All patients above the age of 20 years with gynecologic malignancies who underwent surgery in gynecologic oncology unit, Mansoura University Hospitals, Egypt.

Exclusion criteria:

- Advanced malignancy.
- Benign Lesions
- Surgery with resection anastomosis of the bowel
- Patients with organ failure
- Recurrent malignancy

Study methodology:

All patients were randomly divided into two groups:

- ERAS group: 50 Patients who will be treated with ERAS protocol.
- Conventional group: 50 Patients who will not be treated with ERAS protocol and will receive the traditional protocol.

Patients' demographic and clinical data were collected. After systematic examination, laboratory and radiologic evaluation were done. The procedure was explained to the patient, and written informed consent was obtained from all participants.

ERAS group patients were treated with Enhanced Recovery After Surgery Guidelines[12].

Preoperative Interventions:

- No prolonged fasting, fasting for fatty food 8 hours prior to surgery, and clear liquids 2 hours prior to the surgery.
- Carbohydrate loading to be completed 2 hours before procedure
- Avoid routine oral & mechanical bowel preparation
- Pre-operative hemoglobin stabilization and correction of anemia

Intra-operative ERAS protocol:

- Antibiotic prophylaxis first generation cephalosporins are the first line antimicrobials with anerobic coverage in cancer cases
- Skin Preparation: Patients wash themselves with chlorhexidine based antimicrobial soap before the surgery with pubic hair removal.

- Maintenance of normothermia: Maintaining the OR temperature (>72 F), forced air warming and intravenous fluids warming

- Avoidance of routine use of peritoneal, sub cutaneous and nasogastric tube after abdominal surgery.

- Maintenance of normoglycemia: blood glucose level should be maintained <200 mg/dl.

- Pain management: Decreasing the use of IV opioids, multimodal pain management using NSAIDs and acetaminophen and gabapentin with Regional anesthesia when possible

- Maintain euvolemia: Avoid very restrictive or liberal fluid regimens. Zero-sum fluid balance is obtained by minimizing crystalloid administration and increasing the use of colloids

- Prophylaxis of nausea and vomiting: Before surgery in high-risk patients' transdermal scopolamine 1.5mg patch, ondansetron 4mg IV during induction.

- Thromboprophylaxis: By compression stockings and the use of low molecular weight heparin in high-risk patients.

Postoperative Interventions:

- Early mobilization: include sitting in a chair not more than 8 hours after surgery, gradual walking two times per day and four times per day during postoperative days one and two respectively.

- Initiate regular diet within the first 24hours post operative starting with oral snips every 2 hours (after around 4 hours) then semisolid then solid with encourage of chewing gums.

- Multimodal pain management: minimizing use of opioids, and encourage use of acetaminophen, NSAIDs, and gabapentin.

- Early urinary catheter removal: on the same day with minimal invasive surgery and not more than 24 hours post operative with open surgery unless contraindicated.

- Maintain normal blood glucose levels

- Fluid optimization: to maintain euvolemia

- Nausea and vomiting prophylaxis: Ondansetron 4 mg oral every 6 hours

- Venous thrombosis prophylaxis by using low molecular weight heparin that is started on first post operative day and may be extended according to patient risk and surgery on cancer.

Conventional group patients will follow the current surgery guidelines of Mansoura University hospital:

Preoperative preparation:

- Food fasting for 12 hours before surgery and fluid fasting for 8 hours.

- Bowel preparation with Disflatyl (2 tablets) 4 times every 2 hours and rectal enema twice.

Intra operative:

- Normal operation room and fluids temperature.

- Antibiotic prophylaxis with 2 gm ceftriaxone.

- Routine Drains are allowed.

Postoperative intervention:

- Fluids 500mls normal saline/12hours, 500mls ringers solution/12hours.

- Analgesia ketolac amp (in 10cc saline) IV infusion/12hours,

- Antibiotics 1 gm ceftriaxone /12 hours after discharge from operation room.

- Foley catheter removal after 24 hours postoperative

- Delay starting oral intake for at least 24 hours

Outcome measures:

The primary outcomes were post-operative hospital length of stay (LOS), and perioperative complications including those occurring within 30 days after surgery.

Statistical analysis and data interpretation:

The collected data was coded, processed and analyzed utilizing a computer program (SPSS, version 26 (SPSS Inc., PASW statistics for windows version 26. Chicago: SPSS Inc.). Qualitative data were described using number and percent. Quantitative data were described using median inter quartile range for non-parametric data and mean, standard deviation for parametric data. in addition, the level of significance of the gotten results was judged *p* value at the (0.05) level or less (Figure 1).

RESULTS

Table (1) shows that, the mean age of group A (conventional group) was 60.18±10.17, and that of group B (ERAS group) was 55.74±13.17 with no significant difference, (*P* value 0.062). Mean BMI in group A 32.48±2.29 versus 33.16±1.89 in group B (*P* value 0.109). 26 cases (52%) of group A had hypertension, and 18 (36%) had diabetes which is the same in group B (48% and 36% respectively).

Table (2) shows no significant difference in intraoperative outcomes between both groups with mean operating time was 2.18±0.3 hours in group A versus 2.19±0.52 hours in group B (*P* value 0.907). 4 cases (8%) of each group had bladder injuries. 5 cases (10%) of group A had serosal bowel injury versus 4 cases (8%) of group B with no significant difference (*P* value 0.726).

Table (3) shows that the mean time required for return of bowel function was significantly longer in group A than in group B (30.72±7.72 hours versus 18.96±7.21 respectively; P value 0.001). The length of hospital stay was significantly longer in group A than group B (5.66±2.08 days versus 3.92±1.45 days respectively; P value 0.001). 17 cases (34%) of group A had postoperative nausea and vomiting (needing antiemetics) despite only 6 cases (12%) of group B (*P* value 0.01). Also 28 cases (56%) of group A had post operative moderate to severe pain despite only 14 cases (28%) of group B (*P* value 0.005). There was no significant difference in postoperative ileus nor blood transfusion between both groups.

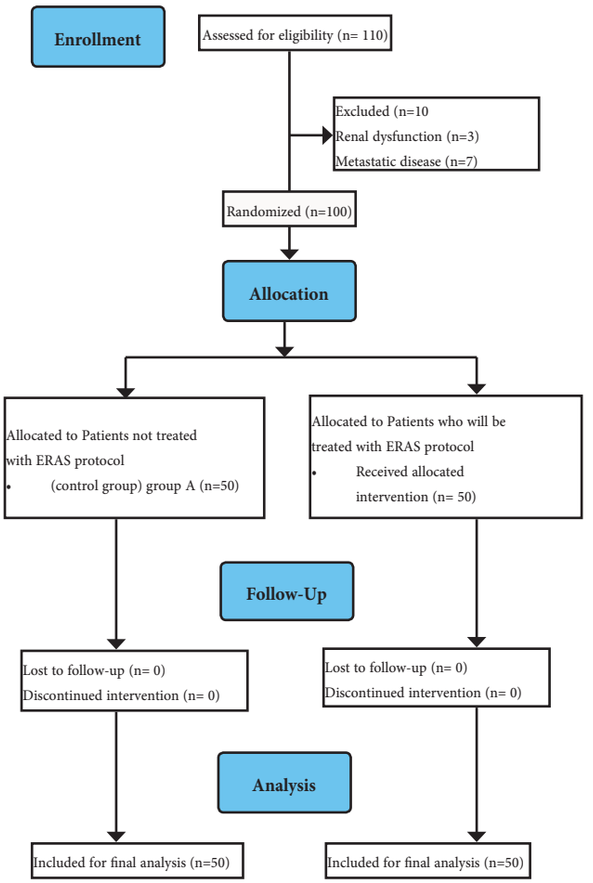

Fig. 1: Consort flow chart showing study design

Table 1: Demographic data and clinical characteristics of both groups:

	Group A (conventional) ***N*=50** **Mean±SD** **Median (min-max) *N* (%)**	**Group B (ERAS Group)** ***N*=50** **Mean±SD** **Median (min-max) *N* (%)**	***P* value**
Age (years)	60.18±10.17	55.74±13.17	0.062
Parity	4 (2-6)	3 (1-5)	0.001*
BMI (kg/m^2)	32.48±2.29	33.16±1.89	0.109
Hypertension	26 (52.0)	24 (48)	0.68
Diabetes	18 (36.0)	18 (36.0)	1.0
Other diseases	4 (8.0)	4 (8.0)	1.0
Primary site of cancer Uterus Cervix ovary	 38 (76.0) 4 (8.0) 8 (16.0)	 27 (54) 8 (16) 15 (30)	0.070
Stage Early Advanced	 39 (78.0) 11 (22.0)	 33 (66.0) 17 (34.0)	0.181

Table 2: Intraoperative patient outcomes of both groups:

	Group A (conventional) ***N*=50** **Mean±SD** **Median (min-max) Frequency (%)**	**Group B (ERAS Group)** ***N*=50** **Mean±SD** **Median (min-max) Frequency (%)**	***P* value**
Operative time (hours)	2.18±0.3	2.19±0.52	0.907
Bladder injury	4 (8.0)	4 (8.0)	1.0
Serosal bowel injury	5 (10.0)	4(8.0)	0.726

Table 3: Postoperative patient outcomes of both groups:

	Group A (conventional) ***N*=50** **Mean±SD** **Median (min-max) Frequency (%)**	**Group B (ERAS Group)** ***N*=50** **Mean±SD** **Median (min-max) Frequency (%)**	***P* value**
Return of bowel function (hours)	30.72±7.72	18.96±7.21	0.001*
Length of hospital stay (days)	5.66±2.08	3.92±1.45	0.001*
Postoperative ileus	3 (6.0)	2 (4.0)	1.0
Postoperative nausea and vomiting (needing antiemetics)	17 (34.0)	6 (12.0)	0.01*
Postoperative moderate to severe pain score	28 (56.0)	14 (28.0)	0.005*
Postoperative blood transfusion	8 (16.0)	4 (8.0)	0.218
Readmission within 30 days after surgery (Wound infection)	3 (6)	3 (6)	1.000

DISCUSSION

The principal finding of our study is that implementation of ERAS protocol in patients with gynecologic cancers undergoing open surgery was associated with significant shortening of time required for return of bowel function after surgery, shortening of hospital stay, reduction of post operative nausea\vomiting, and less postoperative pain with improved overall patient satisfaction, when compared with patients managed using traditional protocol. Also, this ERAS protocol was not associated with detrimental effect on patient's outcome nor increase in perioperative complications.

Our results came in agreement with a study done by Joshi TV on a total of 724 patients divided into two groups, 364 in the ERAS group and 360 in the non- ERAS group. This study revealed shorter length of hospital stay and earlier return of bowel function in ERAS group and the difference was significant. Also, this study showed a reduction in the use of narcotics in the ERAS group. There was no significant difference in postoperative complications and readmission within 30 days between the two groups[1].

Another trial done on 93 women who underwent laparotomy for gynecologic cancers and randomly assigned into an ERAS group, 46 cases or control group that received traditional care, 47 cases. The ERAS group had shorter hospital stay by 20 hours (P= 0.02), faster gastrointestinal function recovery, and lower pain scores during postoperative period with less narcotic requirements[16].

A recent meta-analysis concerning patients with gynecologic cancers revealed that the adherence to ERAS protocol was associated with a 1.6-day decrease in length of hospital stay, 32% reduction in complications during postoperative period, 20% reduction in readmission, and a US$ 2129 average saving of cost. There was a wide variation in the overall quality of included studies with only 5 studies being randomized controlled trials[17].

There were 5 previous randomized controlled trials examining the ERAS protocol in gynecologic surgeries (18-22). In three trials, the diagnosis of cancer was mandatory for all participants while in the other two, a significant number of the patients had benign disorders. Also, the primary site of cancer and the procedure performed showed a wide variability with one study was concerned mainly with patients who had advanced ovarian cancer, for home cytoreductive surgery was performed[18-20]. Another study concentrated mainly on patients with cervical cancer who had laparoscopic radical hysterectomy[22].

Our study is a prospective one and the strength point is the randomized design and the inclusion of patients with only gynecologic cancers. Limitations of the study include relatively small number of cohorts, and that the degree of difficulty of surgery was not determined with the presence of different personnel performing surgery which may reflect personal and behavioral variations.

We can conclude that implementation of ERAS protocol on patients with gynecologic cancers undergoing open surgery had confirmed previous results of shorter hospital stay, early return of bowel function, less postoperative pain scores with no increase in postoperative complications. Implementation of ERAS guidelines should be encouraged in low resource countries.

ABBREVIATIONS

AKI: acute kidney injury, **ASA:** American Society of Anesthesiologists, **ERAS:** Enhanced recovery after surgery, **IR:** Insulin resistance, **NSIDs:** Non-steroidal anti-inflammatory, **VTE:** Venous thrombo-embolism.

CONFLICT OF INTERESTS

There are no conflicts of interest.

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