A Comparative Study of Enhanced Recovery after Surgery Versus Non-Enhanced Recovery after Surgery in Emergency Surgery for Duodenal Ulcer Perforation

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ABSTRACT

Background

Enhanced recovery after surgery is a multimodal strategy, used to attenuate the loss and improve the restoration of functional capacity after surgery. Now widely used in elective surgery, the implementation of all of its components is not feasible in emergency surgery. Therefore, its tailored protocol is likely to give better outcome.

Objective

To investigate the feasibility and effectiveness of enhanced recovery after surgery in emergency surgery for Duodenal Ulcer Perforation.

Method

Hospital based study conducted at Nepalgunj Medical College, Kohalpur from September 2018 to 2020. Hundred patients underwent emergency laparotomy with Classical Graham's Patch Repair. Fifty patients in the enhanced recovery after surgery group were managed as per the protocol and the rest were managed conventionally. Both the groups were compared in terms of length of hospital stay, functional recovery parameters and complications.

Result

There were 48 (96%) males and 2 (4%) females in enhanced recovery after surgery group and 45 (90%) males and 5 (10%) females in non-enhanced recovery after surgery group. The mean length of hospital stay in enhanced recovery after surgery group was 4.9 ± 0.76 days together with early functional recovery compared to 9.06 ± 2.44 days in non-enhanced recovery after surgery group ($p < 0.05$). Complications as per Clavien-Dindo grading were more in the non- enhanced recovery after surgery group ($p=0.03$).

Conclusion

Enhanced recovery after surgery is feasible and effective strategy resulting in early recovery, reduced hospital stay and complications in patients undergoing emergency surgery for duodenal ulcer perforation.

KEY WORDS

Duodenal ulcer, Enhanced recovery after surgery, Length of hospital stay

INTRODUCTION

Enhanced recovery after surgery (ERAS), is a multimodal and multidisciplinary approach to perioperative management with the aim of minimizing stress response to surgery leading to early recovery and reducing surgical complications.[1] First outlined in Denmark by Professor Dr. Henrik Kehlet in 1990s, for patients undergoing colorectal surgeries, it has been widely adopted for favorable surgical outcomes.[2]

The implementation of many ERAS perioperative components such as cessation of smoking and alcohol may not always be feasible in emergency setting and also the patients undergo more complex operations. As a result, they have longer hospitalization and higher rates of morbidity and mortality compared to elective settings. Thus, feasibility and effectiveness of ERAS program in emergency surgery had been questioned.[3]

The rate of peptic ulcer disease (PUD) has decreased due to effective medical therapy however the complication like perforation has increased. Perforation occurs in 2% to 10% patients with PUD. Perforated duodenal ulcer (DU) is associated with 6% to 30% mortality. Graham's Patch Repair is the preferred surgical treatment. The postoperative management is predominantly based on conventional practices rather than being evidence based. Thus, conventional surgical practices are now being re-examined in the light of new evidence based ERAS protocol.[4,5]

As there is paucity of studies depicting the role of ERAS in such patients, this study was conducted to compare ERAS versus Non-ERAS in DU perforation in terms of length of hospital stay (LHS), early functional recovery and complications.

METHODS

This was a hospital based prospective study conducted in Department of Surgery, Nepalgunj Medical College Teaching Hospital from September 2018 to September 2020. All patients with DU perforation found during emergency surgery for perforation peritonitis were noted. Among them, the patients who had presented within 48 hours of onset of signs and symptoms of DU perforation and who were hemodynamically stable at presentation or responded to resuscitation with intravenous fluids were included in the study. The patients with refractory shock, coagulopathy or taking anticoagulants, associated comorbidities like Coronary Artery Disease (CAD), Uncontrolled Diabetes Mellitus (DM), Chronic Liver Disease (CLD), patients with intraoperative findings with spontaneously sealed off perforation and those who did not give consent for the study were excluded.

Demographic data at the time of admission was taken. A detailed history was taken. Thorough clinical examination was performed. Following laboratory investigations were

Table 1. ERAS versus Non-ERAS care

Components	ERAS Group	Non-ERAS Group
Preoperative (Both groups had RT, Foley catheter, IV antibiotics, analgesics and Pantoprazole)	Non opioid analgesia (IV acetaminophen 1 gm TDS)	Opioid analgesia (Inj. Tramadol 50 mg IV TDS)
Intraoperative (Patients in both groups underwent open Graham's patch repair under general anesthesia with endotracheal intubation)	Opioids (except short acting fentanyl) and benzodiazepines were avoided	Standard anesthesia protocol
Postoperative		
Antibiotics (Both groups) IV ceftriaxone and metronidazole till third POD Anti H. Pylori regimen/ as per pus culture and sensitivity started from fourth POD		
Postoperative Analgesia	Inj Drotaverine 80 mg IV TDS (POD one to two) Inj. Aectaminophen 1 gm IV on demand oral Drotaverine (after POD three)	Inj. Tramadol 50mg IV BD and SOS (POD one to two) oral Tramadol (after POD three)
IV fluids	Crystalloids till second POD fluids reduced to half on third POD and stopped on fourth POD	Crystalloids till third POD then reduced to half after first appearance of bowel sound and stopped after tolerating unrestricted liquid diet
Other medications	IV Metoclopromide 10 mg till second POD then on demand IV Pantoprazole 40 mg till second POD then oral pantoprazole 40 mg BD as per Triple regimen	IV Metoclopromide 10 mg IV on demand IV Pantoprazole 40 mg till second POD then oral pantoprazole 40 mg BD as per Triple regimen
Removal of tubes and drains (RT reinserted if patients developed paralytic ileus)	Foley catheter, RT- first POD AD- as early as possible	Foley catheter- after patient was ambulant RT- after the first appearance of bowel sound AD- after drain output is <100ml/day
Ambulation	Started on first POD	Mobilized from first POD then ambulated from third POD
Oral Diet (Oral feeding stopped if patients developed paralytic ileus)	Start sips of clear liquid on first POD Liquid diet on second POD Soft diet on third POD and normal diet since fourth POD onwards	Sips of water only on first POD Liquid diet started after first appearance of bowel sounds Solid food starte after passage of stool

RT: Ryle's Tube; IV: Intravenous; POD: Postoperative day; AD: Abdominal Drain

obtained: Complete blood count, Renal function test, Random blood sugar, Chest x-ray erect (PA view), ECG, Cross matching. The patients were divided into ERAS and Non-ERAS Groups, each consisting of 50 patients, randomly during surgery by lottery method. Many preoperative components of ERAS could not be instituted in emergency surgery for DU perforation. However most of the intraoperative and postoperative components could be applied in the ERAS group. In both groups the perforation was repaired by Classical Graham's Patch Repair technique. A single Abdominal drain (AD) was kept in Morrison's pouch in all. In Non-ERAS group, patients were managed in conventional way (Table 1).

Parameters like LHS, functional recovery after surgery and complications were compared in two groups. Complications were classified according to Clavien-Dindo grading. Any deviation from the normal postoperative course without need of intervention beyond the administration of anti-emetics, antipyretics, analgesics, diuretics, electrolytes, psychical therapy and also the wound infections are included in grade I. Grade II includes complications requiring pharmacological treatment with other medicines beyond the ones used for complications of grade I like parenteral nutrition, blood transfusion. Grade III includes complications requiring surgical, endoscopic or radiological intervention. Life threatening organ dysfunction requiring admission to intensive care unit (ICU) is included in grade IV and grade V includes death of the patients.

Ethical clearance was taken from the institution research committee. Statistical analysis was done using IBM Statistical Package for Social Science (SPSS) version 25. Categorical data was compared by Chi-squared test. Independent t-test was used to compare means. A p-value of < 0.05 was considered as statistically significant.

RESULTS

Over a period of two years, 100 patients were studied. There were 48 (96%) males and two (4%) females in ERAS Group and 45 (90%) males and five (10%) females in Non-ERAS Group. The demographics and most of the preoperative clinico- biochemical parameters were comparable in both groups (Table 2).

The LHS in the ERAS group was 4.9 ± 0.76 days compared to 9.06 ± 2.44 days in the Non-ERAS group (p < 0.05). As per the ERAS protocol RT was removed on the first postoperative day (POD) in the ERAS group. Whereas in the Non-ERAS group RT was required for an average of 4.36 ± 1.7 days. In the ERAS group, only one patient required RT reinsertion, while in the Non-ERAS group, two patients required RT reinsertion, all due to paralytic ileus (p=0.182).

All patients in the ERAS group were allowed sips of clear liquid from the first POD. Patients in the Non ERAS group were started on oral diet after the return of bowel sounds on an average of 2.5 days (p=0.04). All patients except three who developed paralytic ileus tolerated diet well and were progressively switched to solid fluids in the subsequent days.

Table 2. Patient Characteristics

Variables	ERSAS Group	Non-ERAS Group	p value
Sex			
Male	48	45	
Female	02	05	
Male : Female	24 : 01	09 : 01	0.24
Mean Age (Years)	46.76	42.32	0.07
Time of Presentation (Days)	1.38	1.60	0.02
Clinico-Biochemical Parameters			
Mean Haemoglobin (gm%)	12.78	13.01	0.59
Mean Systolic BP (mm Hg)	116.78	111.41	0.32
Mean Serum Albumin (mg/dl)	2.94	2.92	0.77
Acute Kidney Injury	9	10	0.79

None of the patients in the ERAS group required readmission whereas eight patients in the Non-ERAS group were readmitted which was statistically significant (p < 0.05). Three of those patients presented with pain abdomen where ultrasonography revealed pelvic, right sub-phrenic purulent collection and interspersed intra-peritoneal serous collection and were subsequently managed with pigtail insertion in first two and expectant management in third patient. Three patients with wound dehiscence were readmitted for resuturing. Two patients, one patient with omentopexy leak required pig tail drainage and another with recurrent epigastric pain was managed conservatively without any surgical intervention (Table 3).

Table 3. Post - Operative Parameters

Variables	ERAS Group (Mean POD)	Non-ERAS Group (Mean POD)	p value
LHS	4.9	9.06	< 0.05
RT Removal	1	4.36	< 0.05
RT Re-insertion	1	2	0.182
Foley Removal	1	3.78	0.03
IVF Stoppage	3.66	4.98	0.04
Oral Diet	1	2.50	0.04
AD Removal	4.66	5.54	< 0.05
Readmission	0	8	< 0.05

LHS: Length of Hospital Stay; RT: Ryle's Tube; IVF: Intravenous Fluid; AD: Abdominal Drain

Majority of the patients in both the groups had Grade II complications (ERAS-30%, Non-ERAS-20%). All six patients with grade III complications required surgical (resuturing under general anesthesia) and radiological interventions (Pig tail Drainage) and were from Non-ERAS group. Amongst the nine patients with mortality six were from the Non-ERAS Group (Table 4).

Table 4. **Clavien-Dindo Grading**

Clavien – Dindo Grade	ERAS Group	Non-ERAS Group	p-value
Grade I	7	10	0.09
Grade II	10	15	0.04
Grade III	0	6	<<0.05
Grade IV	2	3	0.18
Grade V	3	6	0.03
Total	22	40	0.03

The overall complication rate was found to be higher in the Non ERAS group (80%) than in the ERAS group (44%) which was statistically significant (p=0.03).

Most common complication observed in our study was Surgical Site Infection but it was statistically insignificant. Superficial SSI was observed in six (12%) patients in the ERAS group compared to eight (16%) patients in the Non-ERAS group (fig. 1).

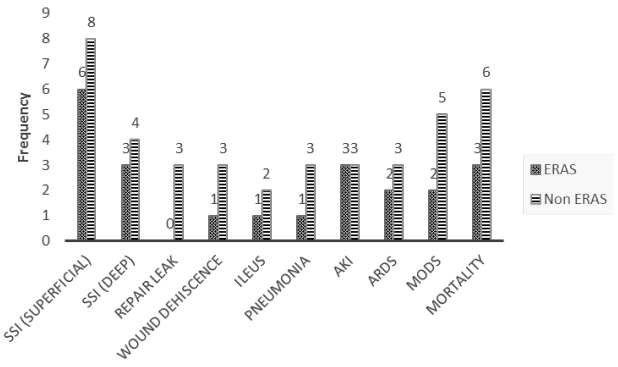

Figure 1. **Postoperative complications**

Fourteen patients required intensive care in their postoperative course. Among them 9 (18%) were in Non-ERAS group and 5 (10%) in ERAS. Three patients in ERAS group died, one due to ARDS and two due to MODS whereas six patients in Non-ERAS group died, one due to repair leak leading to sepsis, two due to ARDS and three due to MODS (fig. 1).

DISCUSSION

In an emergency setting, the limited literature is available demonstrating decreased LOH stay by utilization of ERAS protocols. Two studies on patients undergoing urgent colectomy showed reduction in LHS of 2-3 days.[3,8] In the present study, the hospital stay was reduced by 4.1 days in the ERAS group. This may be due to the application of more components of ERAS care in the intraoperative and postoperative period. Failure to implement the intraoperative components will lead to adverse postoperative outcomes even if the postoperative components are strictly followed.

Lohsiriwat et al. performed a survey on feasibility and beneficial effect of ERAS on emergency surgery comparing with those using traditional conventional care. Twenty five patients treated with ERAS protocol were compared with 40 patients with conventional postoperative care. They concluded that ERAS program in emergency surgery was associated with significantly shorter LOH stay and faster recovery of bowel function without increase in 30 day mortality and readmission.[3] In our study all 49 (98%) patients in ERAS tolerated oral diet right from the first POD day but average time to start orally in Non-ERAS was 2.5 days after the recovery of bowel function. Similarly there were early functional recovery parameters like ambulation, RT, urinary catheter and AD removal, and also none of the patients in the ERAS group required readmission whereas eight patients in the Non-ERAS group were readmitted.

In our study the mean postoperative hospital stay in the ERAS group was 4.9 ± 0.76 days compared to 9.06 ± 2.44 days in the Non-ERAS group ($p < 0.05$). The specific complications like SSI, pneumonia, AKI, wound dehiscence were similar in both groups however overall complications as per Clavien-Dindo grading and mortality were significantly lower in ERAS group. This is consistent with a study conducted by Gonenc et al. in 2018 where the length of hospital stay was significantly shorter (45%) in ERAS group but contrary to our study, there were no significant differences in the morbidity and mortality rates. They compared the outcomes in emergency laparoscopic surgery for DU perforation.[4]

Shida et al. divided 122 patients undergoing emergency abdominal surgery into ERAS group and traditional group.[6] They concluded that post-operative stay was 10 days in traditional group and seven days in ERAS group. More postoperative complication were seen in traditional group as compared to ERAS.[6] This is similar to our study where posts-operative stay was significantly shorter in ERAS group and variety of complications ranging superficial surgical site infection to death occurred in 40 (80%) in the Non-ERAS group and 22 (44%) patients in the ERAS group.

The evidence for removal of drains in emergency laparotomies is lacking where there is gross peritoneal contamination. In present study, all the patients in the ERAS group had the drains removed as early as possible, on an average of 4.66 POD. Likewise RT and urinary catheter were removed on first POD. Moreover, with tailored protocol, it was possible to attain shorter time to first flatus, first feeds and first walk, thus accelerate the recovery as in the previous reports. The overall postoperative complications were also significantly lower in ERAS group. One study had reported a reduction of 20% in the number of patients of emergency laparotomy requiring catheter beyond two days and also compared all emergency laparotomies in pre and post ERAS period revealing a significant reduction in the complications in the post-ERAS period thus stating that ERAS protocol is safe in emergency surgeries also.[7]

In the present study, oral diet was resumed at an average of one and 2.5 postoperative days, respectively, in ERAS

and Non-ERAS groups. Likewise, in one study oral diet was started on an average of 3.4 days in patients who had urgent colectomy managed with ERAS protocol.[8]

Moller et al. conducted a multicentric trial of perioperative protocols to reduce mortality in patients with DU perforation and concluded that the 30-day mortality rate in patients with DU perforation was reduced by more than one-third after the implementation of a multimodal and multidisciplinary perioperative care protocol, compared with conventional treatment.[9] Based on meta-analysis of three randomized controlled trials (RCTs), performed by Soreide et al. laparoscopic and open surgery for perforated peptic ulcers are equivalent and adherence to a perioperative protocol decreased mortality with a relative risk (RR) reduction of 0.63.[10] In our study, all six patients who required surgical (resuturing) and radiological interventions (Clavien Dindo Grade III) were from Non-ERAS group. Out of 14 patients who required ICU monitoring, nine were from Non-ERAS group and six had 30 day mortality, as compared to three (half of ERAS group) mortalities in ERAS group. This showed significant reduction in mortality ($p = 0.03$) in ERAS group.

Chndan et al. found that patients with DU perforation in ERAS group had a significantly early functional recovery for the time to first oral feeding and removal of drain (2.19 ± 0.39: $p < 0.001$), no readmission in ERAS group and also was a significant reduction in postoperative morbidity rate compared with standard care.[11] This is in consistent with our study where oral feeding was started, RT, urinary catheter was removed on first POD with only one patient requiring RT reinsertion and the overall complication rate was observed in 40 (80%) in Non-ERAS group compared to 22 (44%) in ERAS group ($p=0.03$).

We included only those patients who presented within 48 hours after the onset of symptoms. But the majority, with DU perforation comes much beyond 48 hours. So this conclusion cannot be applied to all patients with DU perforation.

CONCLUSION

ERAS protocol is an effective strategy that results in early recovery, reduced length of hospital stay, reduced morbidity and mortality in patients undergoing Graham's Patch Repair for duodenal ulcer perforation.

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