

Study of Enhanced Recovery after Surgery Protocol in Open Radical Cystectomy

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Abstract

Introduction: Bladder carcinoma is one of the most common carcinomas of urinary system. However, in India, it is the 17th leading cause of cancer and 19th leading cause of mortality. Surgical treatment i.e. Open radical cystectomy is the mainstay of treatment for invasive urothelial carcinoma. As the bladder cancer is associated with poor clinical outcome, there is clearly a need to improve the treatment outcome of patients with invasive bladder cancer. Enhanced recovery after surgery (ERAS) protocol is a multimodal- multidisciplinary approach which aims at improving the outcome of the patient's following surgery.

Method: Study design: Prospective comparative study population-Patients scheduled for open radical cystectomy at study area during the study period.

Inclusion criteria: All patients of Carcinoma Bladder undergoing open Radical cystectomy

Exclusion criteria: Patients not giving consent for the study. Detailed history regarding socio-demographic variables such as age, gender, residence, socioeconomic status and marital history was obtained and entered in questionnaire. All the patients were subjected to 2 groups using random number tables- Group A- ERAS, Group B- Control.

Result: Median (IQR) of first intake of clear fluids, ambulation, anal exhaust, and first defecation was significantly early in ERAS group as compared to control group. Vomiting was the most common complication in ERAS group (33.3%) followed by intestinal obstruction and pneumonia.

Conclusion: The protocol helps in avoiding mechanical stress and improving the postoperative recovery by promoting early mobilization after surgery, early return of bowel functions and reducing length of stay.

Keywords: ERAS- enhanced recovery after surgery, open radical cystectomy, urothelial carcinoma

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Introduction

Bladder carcinoma is one of the most common carcinoma of urinary system [1].

According to GLOBOCAN (2018), it is the seventh leading cause of carcinoma

worldwide [2]. However, in India, it is the 17th leading cause of cancer and 19th leading cause of mortality [3]. Transitional cell carcinoma, now replaced with the term urothelial carcinoma (UC) is the most common histological type of bladder carcinoma affecting approximately 90% of cases. The carcinoma is termed urothelial carcinoma when the neoplastic cells of urothelial origin invade basement membrane or lamina propria. According to World Health Organization, bladder cancer can be categorized into low grade (grade 1 and 2) or high grade (grade 3) carcinoma based upon differentiation [1].

Surgical treatment i.e. Open radical cystectomy (ORC) is the mainstay of treatment for invasive urothelial carcinoma. However, it is also recommended in management of high-risk cases of noninvasive urothelial cancers, in which BCG therapy fails [4]. The procedure involves the removal of urinary bladder along with associated organs such as prostate in males and uterus, part of vagina and ovaries in females [5]. The long term recurrence free survival rates following open radical cystectomy depend upon extent and stage of cancer. For cancers, confined to urinary bladder, the disease free survival rate has been reported to range between 75 to 85%, whereas it is 45 to 55% for extravesical disease and in presence of regional lymphnode metastasis, the disease free survival rate are reported between 25 and 35% [5-10]. Also, the requirement of urinary diversion, has been a challenging procedure even for experienced surgeon [11]. Radical cystectomy can also be performed laparoscopically, and has the potential advantage of maintaining oncological efficacy with improved morbidity and convalescence. However, the utility of laparoscopic radical cystectomy is yet not established [12].

As the bladder cancer is associated with poor clinical outcome, there is clearly a need to improve the treatment outcome of

patients with invasive bladder cancer. Certain principles such as preoperative mechanical bowel preparation, postoperative fasting until the first bowel movement have been previously used but are now outdated. These principles have been based upon the surgical dogma and their efficacy in terms of improving postoperative outcome is unproven [13]. ERAS protocol is a multimodal-multidisciplinary approach which aims at improving the outcome of the patients following surgery. This method was inspired by Dr. Henrik Kehlet. ERAS protocol stress at minimising the physiological stress caused by surgery and enhance recovery & outcome by modifying the endocrine and metabolic response to surgery rather than focusing solely on early discharge. These protocols also focus on avoiding prolonged fasting preoperatively, minimize systemic opioid use, avoid empirical IV fluids and promote early mobilization postoperatively [14].

Dr Henrik Kehlet implemented perioperative "fast track" program for colorectal surgery. The procedure was then transformed and adopted subsequently for other surgeries and has been associated with fast recovery, short duration of hospital stay, low hospital cost and lower rate of complications [15-17]. The procedure specific ERAS guidelines have been established for almost all the general surgeries by ERAS society, and the society is trying to standardize the protocol for urological surgeries especially radical cystectomy [18].

Though, adoption of ERAS protocol is associated with certain advantages following general surgeries in terms of patient's outcome, hospital stay and operative cost, its utility following radical cystectomy remains unknown, especially in Indian scenario. The present study was therefore conducted at a tertiary care centre to assess the utility of enhanced

postoperative recovery protocol after open radical cystectomy [19-24].

Aims and Objectives

To study enhanced post operative care after radical cystectomy

Materials and Methodology

The present prospective comparative study was conducted on patients scheduled for open radical cystectomy at Department of Surgery, Gandhi Medical College and associated Hamidia Hospital Bhopal during the study period of August 2019 to July 2021.

Inclusion Criteria: All patients posted for radical cystectomy

Exclusion Criteria: Patient not giving consent for the study

Methodology: After obtaining ethical clearance from ethical committee of Institute, all the patients fulfilling inclusion criteria who gave informed consent were enrolled. Detailed history regarding sociodemographic variables such as age, gender, residence, socioeconomic status and marital history was obtained and entered in questionnaire. All the patients were then subjected to detailed physical, general and local examination and findings were documented. Vitals such as Pulse, blood pressure, respiratory rate and temperature were recorded in questionnaire. Anthropometric variables such as height and weight were measured and BMI was calculated. Performance Status on ECOG (Eastern Cooperative Oncology Group) Scale was measured. All the patients were then subjected to detailed investigations.

Following surgery, cytological evaluation was also done in all the cases and findings were documented. All the patients were then subjected to 2 groups using random number tables.

- Group A- ERAS
- Group B- Control

In group A, ERAS protocol was followed with following key principles [4].

Statistical Analysis

Data was compiled using Ms Excel and analysed using IBM SPSS software version 20. Categorical data was expressed as frequency and proportion and since sample size was small, continuous variables were expressed as median and Inter quartile range. Chi square test was used to assess the difference in categorical variables between the groups whereas Mann Whitney U test was used to compare the median values between the groups. P value less than 0.05 was considered statistically significant.

Results

The present study entitled “Study Of Eras Protocol In Open Radical Cystectomy” was conducted on a total of 30 patients who were scheduled for open radical cystectomy. All the patients were randomly categorized into two groups

Group A- ERAS Group

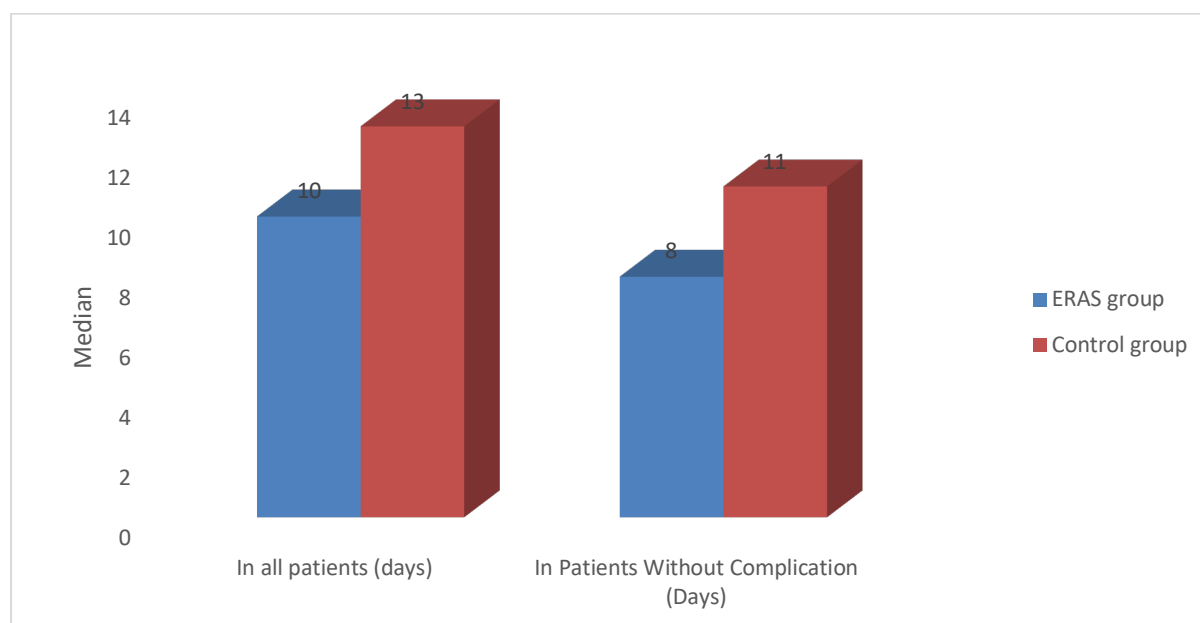
Group B- Control group

The findings of present study are tabulated as under

Table 1: Comparison of patients of two groups according to hospital events

Hospital events	ERAS group (n=15)		Control group (n=15)		P value
	Mean \pm SD	Median (IQR)	Mean \pm SD	Median (IQR)	
First Intake Of Clear Liquids (Hrs)	5.93 \pm 1.43	6 (4 - 7)	39.07 \pm 13.37	38(32 -48)	0.001
1st Ambulation (Hrs)	9.87 \pm 2.23	10 (8 - 12)	68.87 \pm 5.32	69(65 -73)	0.001
1st Anal Exhaust (Hrs)	20 \pm 4.24	20(17 -23)	47.47 \pm 12.74	48(34 -60)	0.001
1st Defecation 1(Hrs)	21.67 \pm 4.45	23(17 -25)	69.93 \pm 18.47	78(50 -84)	0.001
Drainage Tube Removal (Days)	5.07 \pm 1.58	5 (4 - 6)	6.2 \pm 2.27	6 (4 - 8)	0.17

In present study, median (IQR) of first intake of clear fluids, ambulation, anal exhaust, and first defecation was significantly early in ERAS group as compared to control group ($p < 0.05$). We observed no significant difference in median time for removal of drainage tube between the groups ($p > 0.05$).

**Figure 1: Comparison of length of stay of between the groups****Table 2: Comparison of two groups according to complications**

Complications	ERAS group (n=15)		Control group (n=15)		χ^2	P value
	N	%	N	%		
Vomiting	5	33.3	6	40	0.14	0.705
Urinary leakage	1	6.7	2	13.3	0.37	0.543
Intestinal obstruction	3	20	3	20	0	1
Pneumonia	3	20	3	20	0	1
UTI	2	13.3	3	20	0.24	0.624
DVT	0	0	1	6.7	1.03	0.309
Others	0	0	0	0	NA	NA

Vomiting was the most common complication in ERAS group (33.3%) followed by intestinal obstruction and pneumonia (20% each). UTI was seen in 13.3 % whereas urinary leakage was

observed in 1 patient (6.7%). None of the patient in ERAS group reported DVT. Overall, the complications were comparable between cases and controls ($p>0.05$).

Table 3: Comparison according to time of readmission

Readmission	ERAS group (n=15)		Control group (n=15)	
	N	%	N	%
None	12	80	7	46.7
30 days	2	13.3	6	40
90 days	1	6.7	2	13.3
χ^2	3.65			
P value	0.161			

Majority of the patient in ERAS group did not need readmission (80%) and among those who needed readmission, two were admitted in 30 days and one patient was admitted in 90 days. Though readmission rate was higher in control group as compared to ERAS group, we observed no significant difference in readmission rate between the groups ($p>0.05$).

Discussion

Bladder carcinoma is seventh most common carcinoma in World and 17th common cancer in India [2,3]. Though open radical cystectomy is the mainstay of treatment for invasive urothelial carcinoma, the outcome of patients remains poor and is suboptimal with higher risk of recurrence. Thus, it is important to identify the methods to improve the treatment outcome of patients with invasive bladder cancer. Various principles have been previously used for improving the outcome of patients with bladder cancer, these included preoperative mechanical bowel preparation and postoperative fasting until the first bowel movement [13].

ERAS protocols have been recommended following the radical cystectomy as a multidisciplinary approach which include the use of multimodal analgesia, epidural analgesia, limited fasting state, minimal use of systemic opioids, goal directed fluid therapy (GDFT) and early postoperative mobilization [25-27]. All the component of ERAS protocol helps in minimizing the physiological stress caused by surgery and ERAS protocol aims to modify the endocrine and metabolic response to surgery rather than focusing solely on early discharge [14].

We observed that implementing and following ERAS protocol is helpful in promoting early recovery with respect to first intake of clear fluids, ambulation, anal exhaust, and first defecation which was significantly earlier in ERAS group as compared to control group ($p<0.05$). However, median time for removal of drainage tube was comparable between the groups ($p>0.05$).

The findings of present study were concordant with the findings of Persson B *et al* (2015) in which mean time to first passage of stool was significantly shorter in ERAS group than the pre-ERAS group reflecting utility of ERAS protocol in improving bowel functions early [28,29]. Wei C *et al* (2018) also reported pelvic drainage tube removal, first ambulation, first water intake, first anal exhaust and first defecation to be significantly earlier in ERAS group as compared to non-ERAS group [30].

Earlier return of bowel activity was seen following ERAS protocol [23,24] and it could be attributed to use of chewing gum and magnesium tablets, which play an important role in reducing the bowel inflammation following surgery [28,29].

As ERAS protocol was significantly helpful in early return of bowel function, median length of hospital stay in patients with and without complication was significantly shorter in ERAS group (10 days and 8 days) as compared to control group (13 days and 11 day) ($p < 0.05$). Our study findings reported ERAS protocol implementation to promote early recovery of patients following surgery. Cerantola Y *et al* observed significantly shorter length of hospital stay in patients following surgery in ERAS group [28].

Two groups of patients in our study were compared with respect to complication rates. Radical cystectomy was associated with vomiting as the most common complication in majority of patients

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irrespective of group. Intestinal obstruction and pneumonia were observed in 20% cases in each group. We observed no significant difference in complications between the group ($p > 0.05$). Zhang D *et al* (2020) reported no significant differences in major complications between the groups supporting the findings of present study [31,32].

ERAS protocol group did not differ from conventional care group in readmission rate at 30 days and 90 days ($p > 0.05$).). Pramod SV *et al* (2020) noted no significant difference in readmission rate between the groups supporting our study findings [31].

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