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Enhanced recovery protocol versus standard protocol for patients undergoing radical cystectomy: results of a prospective randomized study

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Abstract

Background: To assess patients undergoing radical cystectomy using enhanced recovery protocol and standard protocol in terms of intraoperative and postoperative outcomes and complications.

Results: All operative and postoperative complications were recorded. In group B, time to normal bowel activity ranged from 1 to 4 days, and the mean was 1.8 days (± 1.02), while it ranged from 1 to 5 days, and the mean was 3.17 days (± 1.14) in group A which was statistically significant (p value < 0.001). The length of hospital stay in group B ranged from 6 to 50 days, the mean was 13.16 days (± 7.83), while it ranged from 8 to 35 days, and the mean was 14.71 days (± 5.78) in group A which was statistically significant (p value = 0.033). Postoperative mortality was similar in both groups.

Conclusion: In patients undergoing radical cystectomy, enhanced recovery protocol is considered as a safe procedure and not associated with any increase in intraoperative and postoperative complications compared to standard protocol. The length of hospital stay and time to return to full diet are reduced.

Keywords: Radical cystectomy, Complication, Enhanced protocol, Standard protocol, Bowel activity, Hospital stay

1 Background

In Egypt during the past 50 years, bladder cancer has been the most common cancer. Transitional cell carcinoma (TCC) replaced squamous cell carcinoma (SCC) as the more prevalent histopathological type with this declining rate suggesting possible changes in exposures related to bladder cancer induction, with reductions in schistosomal infection and increases in cigarette smoking and chemical exposures related to occupation [1]. The gold standard for treatment of muscle invasive bladder cancer (MIBC) is radical cystectomy (RC) with pelvic lymphadenectomy. Radical cystectomy is associated with greater morbidity and prolonged in-patient stay after surgery than other urological procedures despite improvements in surgical technique, anesthesia and perioperative care. Overall complication rates have been reported as high as 64% at 90 days, with an average in-patient stay of 17.4 days [2]. Since the early 1990s, enhanced recovery protocols have been used in various forms that improved perioperative outcomes of surgical patients [3].

Enhanced recovery after surgery (ERAS) protocols are multimodal perioperative care pathways designed to achieve early recovery after surgical procedures by maintaining preoperative organ function and reducing the profound stress response following surgery through preoperative counseling, optimization of nutrition, standardized analgesic and anesthetic regimens and early mobilization [4].

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Low level of evidence exists directly from RC studies where the majority of recommendations for RC ERAS protocols are based on extrapolation from colorectal surgery protocols [5].

2 Methods

This prospective randomized study was done between October 2014 and April 2016. We compared the outcome and complications of RC when using enhanced recovery protocol versus standard protocol in bowel preparation.

Informed consent was signed in each case after explaining the nature of the disease, the risks and potential benefits of the study and the procedure.

Seventy-five patients were included in this study who were candidates for RC. They were randomized in two groups (closed envelope): Group A (43 patients) where they followed the standard preoperative and postoperative protocol and Group B (32 patients) where they followed the enhanced recovery protocol. Patients were assessed by full history taking. Full examination includes general, abdominal, genitalia and digital rectal examinations. Routine laboratory investigations were done. Radiological investigations included chest X-ray, abdomino-pelvic ultrasound and computed tomography with intra-venous contrast while in patients with elevated creatinine, MRI abdomen and pelvis were done. In addition, all patients underwent urethrocystoscopy and biopsy. The preoperative evaluation was the stratified by age-adjusted Charlson's comorbidity index [6].

In group A, bowel preparation was started before surgery according to a standard 3-day bowel preparation regimen. On day 1, a low-residue diet, oral metronidazole 400 mg three times daily and oral neomycin 1 g three times daily were taken. On day 2, only clear fluids and oral antibiotics were taken with tap-water enema. On day 3, also clear fluids only and oral antibiotics were taken with rectal washouts until clear. Intravenous fluids were also administered to maintain hydration [7].

In group B, a day before radical cystectomy, the patients received a normal breakfast followed by unrestricted clear fluids and referred to stoma therapist to mark the site of the stoma.

The night before surgery, the region extending from the midchest to the midthigh was cleaned and prepared. Also, a prophylactic dose of enoxaparin sodium 40 IU subcutaneous was given and every 24 h thereafter until discharge.

All patients received general and epidural anesthesia with central venous line. A parenteral broad-spectrum antibiotic was given just before induction of anesthesia and continued postoperatively for 7 days. Intraoperative metronidazole was also given intravenously and continued 3 days after surgery. Compression stockings were used as prophylaxis for deep venous thrombosis.

A wide bore rectal tube (28 Fr) was placed after general anesthesia to avoid rectal injury during the operation. The patient was placed in the supine position with slight hyperextension of the table used to facilitate pelvic exposure and a Foley urethral catheter placed after draping. All male patients underwent a conventional RC, and anterior exenteration was done in female patients with standard lymphadenectomy. Two types of urinary diversions were planned, orthotopic urinary diversion and ileal conduit.

Wound closure was done by closure of the layers as 1 layer, in a simple running technique, using absorbable suture material (polyglactin) followed by closure of the subcutaneous layer and the skin. All postoperative events were graded according to an established five-grade modification of the original Clavien system [8].

Length of hospital stay (LOS) was recorded. Patients in group B started oral clear fluid from day 0, while in group A patients started oral fluid only after audible intestinal sounds or if they passed flatus, and they started to eat after tolerating clear fluids. Thus, patients in group B received free fluids as tolerated on day 1 with early mobilization. The epidural catheter was removed on day 2. Light diet as tolerated was introduced on day 3.

Data were coded and entered using the statistical package Statistical Package for the Social Sciences (SPSS) version 23. Data were summarized using mean, standard deviation, minimum and maximum in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data.

Correlations between quantitative variables were done using Spearman correlation coefficient. *P* values less than 0.05 were considered as statistically significant.

3 Results

The study group consisted of 64 males (85.3%) and 11 females (14.7%). The age of the patients ranged from 40 to 76 years with a mean of 58.49 years.

Comorbid conditions in patients are listed in Table 1.

The patients were sub-grouped according to Charlson's comorbidity index: eleven (14.7%) patients with 3 or less, 40 (53.3%) patients with 4–5 and 24 (32%) with more than 5 Charlson's index.

Three types of urinary reconstruction were performed in our study. Orthotopic neobladder was performed in 40 patients (53%), ileal conduit in 34 patients (45%) and rectal bladder with terminal colostomy in one patient (because sigmoid colon was injured during operation and we do colostomy and rectal bladder) (1.3%).

In our study, the length of hospital stay in Group A ranged from 8 to 35 days; the mean was 14.71 days

Table 1 Comorbid conditions

Comorbid condition	Number	Percent (%)
None	39	52
M.I.	1	1.3
C HF	1	1.3
PVD	1	1.3
COPD	8	10.7
Liver disease	4	5.3
Mild lung disease	20	26.7
DM	6	8.0
Hypertension	17	22.7
Cardiopulmonary	1	1.3
Renal impairment	8	10.7
≥ 2 Comorbid conditions	22	29.3

(±5.78). In Group B, it ranged from 6 to 50 days and the mean was 13.16 days (±7.83). This was a significant difference ($p=0.033$). Patients who underwent radical cystectomy (enhanced protocol) had a shorter hospital stay.

Forty-five patients (60%) had post-RC complications, and the remaining 30 patients (40%) had a smooth postoperative course. Table 2 shows different complications which occurred in both groups.

The differences between the two groups were not statistically significant as p value = 0.070. The complications were sub-grouped according to a five-grade modification of the original Clavien system as in Table 3.

The time to normal bowel activity in the enhanced protocol ranged from 1 to 4 days, the mean was 1.8 days (±1.02), while in the classic protocol it ranged from 1 to 5 days, and the mean was 3.17 days (±1.14) which was statistically significant ($p<0.001$).

4 Discussion

Successful application of an enhanced recovery protocol aims at improving postoperative recovery via early mobilization and quick return to oral diet which may lead to a shorter LOS. Mukhtar et al. [9] reported that mean time for return to normal bowel movement was significantly shorter for ERP group by 1.3 days (p value = 0.0005).

On the other hand, Arumainayagam et al. reported no significant difference between ERP and control groups in the time to bowel movement [4]. Also, Saar et al. [10] reported that the mean time to first bowel movement was 2.6 days in ERP group compared to 3.1 days in control group, although these differences were not statistically significant as p value = 0.3.

In comparison with our study, mean time for return to normal bowel movement was significantly shorter for ERP group by (p value < 0.001).

Saar et al. [10] found no significant difference between two groups in the LOS. In contrast to these results, the LOS was significantly shorter for ERP group in our study.

Saar et al. [10] reported no significant difference in total postoperative complications between ERP and control groups (p value = 0.60). Also, Mukhtar et al. [9] found no significant difference between ERP and control groups in postoperative complications which agreed with our study where there were no statistically significant values between both groups (p value = 0.070).

On the other hand, wound-related complications in the form of surgical site infection and tissue dehiscence occurred in 46.2% in both groups while it was in about 15% of patients in the series of Shabsigh et al. [11] and in 9% of the patients in Hautmann et al. [12]. These differences between our results and other studies may be contributed to advanced age of the patients and associated medical comorbidities.

Arumainayagam et al. [4] stated that there was no statistically significant difference ($p=0.934$) between both groups regarding genitourinary complications where urinary extravasation was the most common genitourinary complication which was in agreement with our series where also there was no statistically significant difference (p value = 0.727) between both groups.

Table 2 Complications occurred in both groups

	Method				*p* value
	Enhanced		Classic		
	Count	%	Count	%	
Postoperative complication	22	51.2	23	71.9	0.070
Urine leakage	7	17.1	4	14.3	0.727
Bowel leakage	3	7.3	0	0	0.266
Ileus	3	7.3	5	17.8	0.170
Thrombo-embolic	2	4.7	3	9.3	0.511
Wound infection	16	39	16	57.1	0.170

Table 3 Complications according to a five-grade modification of the original Clavien system

	Method				*p* value
	Enhanced		Classic		
	Count	%	Count	%	
Clavien grade					
1	8	36.4	9	39.1	0.539
2	5	22.7	7	30.4	0.539
3a	0	0	2	8.7	0.539
3b	3	13.6	1	4.3	0.539
5	6	27.3	4	17.4	0.539

Karl et al. [13] reported that 15% of patients in the ERP group had paralytic ileus, while in the classic protocol group 28% of patients had paralytic ileus. Analysis of comparison between the two groups showed no significant difference (p value = 0.93).

In our study, 7.3% of patients in the enhanced protocol group had paralytic ileus, while in the classic protocol group 17.8% of patients had Paralytic ileus, although these differences were not statistically significant (p value = 0.17).

5 Conclusion

In patients undergoing radical cystectomy, enhanced recovery protocol is considered as a safe procedure and not associated with any increase in intraoperative and postoperative complications compared to standard protocol. The length of hospital stay and time to return to full diet are reduced. With corroboration by further studies, we think that more urologic centers will shift to this form of patient care in the future.

Abbreviations

TCC: transitional cell carcinoma; SCC: squamous cell carcinoma; MIBC: muscle invasive bladder cancer; RC: radical cystectomy; ERAS: enhanced recovery after surgery; MRI: magnetic resonance imaging; LOS: length of hospital stay; SPSS: statistical package for the social sciences.

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Not applicable.

Authors' contributions

HI collected the patients' data, analyzed them and followed the patients postoperatively. SK drafted the article, revised it critically for important intellectual content, and wrote the paper with revision. AAA, AK, AS, MAH, AM, and IRS analyzed patient data and followed the patients postoperatively. HF, KM, and OAR gave idea and put study design. All authors have read and approved the final version of the manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This study was approved by the Research Ethics Committee of the Faculty of Medicine, Cairo University in Egypt. Ethics committee reference numbers is not available. All patients included in this study gave written informed consent to participate in this research.

Consent for publication

All patients included in this research gave written informed consent to publish the data contained within this study.

Competing interests

The authors declare that they have no competing interests.

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