

An adapted enhanced recovery protocol for adult augmentation cystoplasty in limited sources countries: A pilot clinical trial

Elham Jahantabi^{1,2} , Farzin Soleimanzadeh¹ , Hanieh Salehi-Pourmehr^{3,2} , Mahsa Zehi Saadat¹ , Maryam Nouri⁴ , Sakineh Hajebrahimi^{3,1} 

Cite this article as: Jahantabi E, Soleimanzadeh F, Salehi-Pourmehr H, Saadat MZ, Nouri M, Hajebrahimi S. An adapted enhanced recovery protocol for adult augmentation cystoplasty in limited sources countries: A pilot clinical trial. *Turk J Urol*. 2021; 47(6): 509-517

ABSTRACT

Objective: To investigate an adapted enhanced recovery after surgery (ERAS) protocol in adult augmentation cystoplasty (AC).

Material and methods: A total of 33 consecutive cases with a history of refractory idiopathic detrusor overactivity (IDO) or neurogenic bladder (NGB) with low capacity, poor compliance, high sustained detrusor pressure, and whose previous therapeutic methods had failed were enrolled. The adapted ERAS fasting 8 hours, high protein, low carbohydrate diet, antibiotics, did not use narcotics as much as possible during anesthesia, acetaminophen, early nasogastric tube removal, neostigmine injection postoperation, metoclopramide, early oral diet, and mobilization were applied, and morbidity and hospital stay duration were analyzed.

Results: Twenty-two patients had IDO, and the remained cases were NGB or had low bladder capacity or compliance. The mean age of patients in the IDO group was higher than in NGB cases ($P = .020$). Following the adapted ERAS protocol implementation, more than two-third of patients returned to a regular diet on the second day postoperation in both groups. The mean (SD) hospital stay duration was 7.7 (1.5) days. Postoperative fasting time was 8.8 ± 3.7 hours, and bowel function was returned 1 day postoperation in 82% of patients. Only 33.3% of adults need postprocedure acetaminophen for 2 days, and in 11 cases, it was prescribed for 1 day. All subjects except paraplegic patients had early mobilization 1 day postoperation.

Conclusion: Our findings revealed that adapted ERAS protocol could be safe and effective in adult AC. It accompanied by few complications, reduced intestinal motility problems, and a short length of hospital stay.

Keywords: Adapted; adults; augmentation cystoplasty; enhanced recovery protocol.

Introduction

Nowadays, with the implementation of enhanced recovery after surgery (ERAS) protocols, preserving the physiological homeostasis, and decreasing perioperative stress, the morbidity of postoperative and duration of urological cases hospital stay are reduced.¹ The goals of ERAS are to minimize pain and perioperative metabolic stress, fluid balance optimization, and convalescence times' decrement. Initially, it was assumed that applying ERAS might increase complication or readmission rates compared to traditional perioperative protocols; however, the implementation of ERAS

protocols in adult surgery demonstrated a significant reduction in hospital stay duration and lower postoperative complication rates without a concomitant increase in hospital re-admissions.² The revolution of ERAS in high-income countries led to the improvement of surgical and anesthesia complication rates and outcomes and saving dollars due to fewer complications and decreased length of hospital stay.³ However, not only ERAS is for high-income countries, but also a modified approach to ERAS may improve all types of surgery outcomes in low- and lower-middle-income countries.⁴ The ERAS society has established evidence-based enhanced recovery guidelines

¹Department of Urology, Tabriz University of Medical Sciences Faculty of Medicine, Tabriz, Iran

²Clinical Research Development Unit, Tabriz University of Medical Sciences, Imam Reza General Hospital, Tabriz, Iran

³Research Center for Evidence Based-Medicine, Iranian EBM Center: A Joanna Briggs Institute Center of Excellence, Tabriz University of Medical Sciences, Tabriz, Iran

⁴Student Research Committee, Tabriz University of Medical Sciences, Tabriz, Iran

Submitted:
02.04.2021

Accepted:
11.08.2021

Corresponding Author:
Sakineh Hajebrahimi
E-mail:
hajebrahimis@gmail.com

© Copyright 2021 by Turkish Association of Urology

Available online at
www.turkishjournalofurology.com

for adult colonic, pancreatic, rectal, and pelvic surgeries, and radical cystectomy patients.^{5,6} Based on our knowledge, ERAS protocol is performed in pediatric augmentation cystoplasty (AC), and in adults, this method is done only in radical cystectomy surgery.⁷ AC, which is used to serve urinary continence, prevent upper tract deterioration, and alleviate the symptoms of bladder dysfunction, remains an important approach in the cases with refractory overactive bladder (OAB), low compliance or capacity following neurogenic and non-neurogenic causes, or congenital urological anomalies, when the other treatment methods such as oral medications, intravesical botulinum toxin injection, and sacral neuromodulation have been failed.⁸⁻¹¹ This approach is associated with several complications. Some of them have early onsets like thromboembolism, wound and intra-abdominal infection, perforation, and mortality. Metabolic abnormalities, bacteriuria, urinary tract stones, incontinence, perforation, the need for intermittent self-catheterization, mucus production, growth retardation, vitamin deficiency, bone demineralization, and carcinoma may manifest late.¹²⁻¹⁴ In the current study, we aimed to investigate an adapted ERAS protocol in adult AC of consecutive cases referred to the tertiary teaching hospital between March 2016 and October 2020.

Material and Methods

Design and Ethic Statement

This study was a single-center case series report of an adapted ERAS protocol for adult patients undergoing reconstructive operations that included a bowel anastomosis. We introduced the outcomes of patients who underwent adapted ERAS protocol for AC. This study was approved by Tabriz University of Medical Sciences (IR.TBZMED.REC.1397.1052) and conducted in accordance with the ethical standards of the Declaration of Helsinki. All subjects provided a written informed consent before the procedure.

Main Points

- Nowadays, with the implementation of enhanced recovery after surgery (ERAS) protocols, the morbidity of postoperative and duration of urological cases hospital stay are reduced.
- ERAS is not only for high-income countries, and a modified approach to ERAS may improve all types of surgery outcomes in low- and lower-middle-income countries too.
- In the present study on 33 patients, adapted ERAS protocol was accompanied with few complications, low intestinal motility problems, and a short length of hospital stay.
- Adapted ERAS can be safe, practical, and effective in adult augmentation cystoplasty similar to pediatrics.

Study Population

A total of 33 consecutive cases with a history of refractory IDO or neurogenic bladder (NGB) were enrolled in this study. The patients were referred to the urology department of our teaching hospital between March 2016 and October 2020.

Eligibility criteria were as follows: low capacity; poor compliance; high sustained detrusor pressure according to the urodynamic results or imaging such as voiding cystourethrogram or refractory OAB cases whom the previous therapeutic methods such as conservative, pharmacotherapy, intradetrusor botulinum toxin-A injection, and sacral neuromodulation had failed to provide urinary storage; protect the upper urinary tract; preserve the renal function; provide continence and resistance to infection; and offer a convenient method for voluntary and complete emptying.

Preoperative Consideration

A comprehensive history and physical exam for all patients and laboratory tests, including complete blood count, electrolyte and creatinine, urinalysis, and urine culture, were performed. Patients underwent urodynamics, upper tract imaging, and colonoscopy if indicated.

Before ERAS protocol implementation, patients' counseling and education about the surgical procedure and the discharge criteria were the first steps. Since intermittent catheterization is a necessary adjunct postoperatively, the patients informed about its importance. The cases with cognitive disabilities or inadequate manual dexterity were not considered candidates for this approach.^{15,16}

Surgical Technique

To create a new reservoir with maximum surface area, different GI tract parts have been used for AC. Ileocystoplasty is the commonly reported technique, in which the patient gets supine or low lithotomy position. Then, standard midline laparotomy incision to access the intraperitoneal cavity is done. The native bladder is distended using a Foley catheter in the surgical field. By dissection, the loose tissue, and anterior and perivesical spaces are exposed, and the bladder is bivalved in the coronal or sagittal plane. To preserve the absorptive function of the terminal ileum, depending on the patient's age and the desired augmentation of bladder volume based on native bladder capacity, about 15 and 40 cm long (usually about 25 cm) of ileal segments are chosen just 15–20 cm away from the ileocecal valve.

Moreover, the adequate mesentery is required to reaching to the native bladder. Then, the mesentery is cleared from the intestine at either end, the bowel is divided at these ends, and

ileoileostomy is performed. The mesenteric window is closed for the prevention of hernia formation. After clearing, the dissected ileal segment is folded like U shape and anastomosed to itself, and thereafter anastomosed to the native bladder. This anastomosis is examined in order to ensure water tightness, and drains are inserted before closing the abdominal wall.¹⁵

ERAS Protocol

This is a multidisciplinary approach with an urologist's participation alongside the nutritionist, neurologist, anesthesiologist, preadmission nurses, recovery ward, and educator nurses.¹⁷

The principals of ERAS protocol include the following: (a) preoperative: preadmission counseling and education, medical optimization such as smoking cessation and weight loss or gain as required, control of comorbidities, fluid, and carbohydrate loading, no prolonged fasting, no/selective bowel preparation, avoidance of salt and water overload, antibiotic prophylaxis, thromboprophylaxis with low molecular weight heparin prior to surgery, compression stocking use, and extended prophylaxis postsurgery as indicated based on patient risk, thoracic epidural analgesia placement prior to surgery, single dose of antimicrobial prophylaxis 60 minutes prior to skin incision, and skin preparation with chlorhexidine-alcohol preparation; (b) intraoperative: short-acting anesthetic agents, midthoracic epidural anesthesia/analgesia, no drains, avoidance of salt and water overload, maintenance of normothermia (body warmer/warm intravenous fluids), and avoid the use of postoperative nasogastric intubation; and (c) postoperative: no nasogastric tubes (NGTs), prevention of nausea and vomiting, avoidance of salt and water overload, early removal of the catheter, early oral nutrition with clear liquid diet on the evening of surgery and regular diet on the day after surgery, nonopiod oral analgesia/Non-steroidal anti-inflammatory drugs (NSAIDs), early mobilization (out of bed day after surgery), discontinuation of maintenance intravenous fluids by postoperative day, and stimulation of gut motility.¹⁸⁻²³

Pharmaceutics such as metoclopramide, Alvimopan, and neostigmine is used to bowel function improvement in radical cystectomy. The peripherally acting μ -opioid antagonist alvimopan has been proven effective in published studies.²⁴ Neostigmine has a significant muscarinic effect on GI receptors, increasing the availability of acetylcholine and GI motility.

Adapted ERAS Protocol

Patients fasted only 8 hours, and a high protein, low carbohydrate diet was started 1 day before surgery. We administered antibiotics (the combination of cephalosporin, aminoglycoside, and metronidazole) just preprocedure and continued 1 day

postoperation. We did not use narcotics as much as possible during anesthesia, with continuous infusion of acetaminophen postoperation. Early NGT removal was the other part of this protocol. An urology resident injected neostigmine postoperation to ileus prevention with a dose of 0.5 mg/twice daily under cardiac monitoring and control of vital signs till the patient achieved a bowel movement. In addition, we injected 10 mg metoclopramide (Plasil, Lepetit) (i.v./three times a day) to prevent postoperative nausea and vomiting. Early oral diet and mobilization were also other parts of this protocol. The regular diet was started 1 day postoperation if the patients have bowel function (stool or repeated flatus). The duration of hospitalization in the new method was lower than the conventional technique, and the patients were discharged 7 days postoperation. Discharge criteria were adequately control of postoperative pain with oral analgesics, mobilization (out of bed \geq 6 hours daily), return of bowel function, and no complications in need of treatment in the hospital. All patients were revisited after discharge by an urologist and interviewed by a trained nurse to evaluate any late-occurring complications.

Statistical Analysis

After data collection, the data were encoded and analyzed using the Statistical Package for the Social Sciences (SPSS) version 21 (IBM SPSS Corp.; Armonk, NY, USA). The normal distribution of the data was determined by the Kolmogorov-Smirnov test. The chi-square and Fisher's exact were used for categorical variables, and the Mann-Whitney U test was used to compare the groups on baseline characteristics and to compare the outcome measures. Data are presented as mean, standard deviation (SD), or median (range). Statistical significance was defined as $P < .05$.

Results

All patients were treated at the same hospital and operated on by the same surgeons using a standardized approach via longitudinal laparotomy.

We operated a total of 33 adults. Twenty-two cases were female (66.7%). The common indication for surgery was IDO (54.6%) and NGB (33.3%), and low capacity and compliance bladder (12.1%) were in the next rank. Patients' characteristics, including detailed demographics, indications, and procedures performed per group, are listed in Table 1. Table 2 shows the comorbidities of included cases.

The Mann-Whitney U test results showed that the mean age of patients with NGB is statistically lower than in IDO groups ($P = .020$). The youngest patient in IDO group had 27 years, and

Table 1. Patient's Characteristics in Both Groups of IDO and NGB

Baseline Characteristics	Total (n = 33), N (%)	IDO (n = 22), N (%)	NGB (n = 11), N (%)	P-Value
Age (year)*	41.4 ± 13.8	44.4 ± 13.1	33.2 ± 14.0	.020**
Median (Minimum, Maximum)	35.0 (18.0, 67.0)	39.0 (29.0, 67.0)	32.0 (18.0, 58.0)	
Sex				.437 [†]
Male	11 (33.3)	6 (27.3)	5 (45.5)	
Female	22 (66.7)	16 (72.7)	6 (54.5)	
Diagnosis				
IDO	18 (54.6)	—	—	
NGB	11 (33.3)	—	—	
Low capacity and compliance	4 (12.1)	—	—	
Symptom Duration (Year)*	8.1 ± 6.9	8.8 ± 8.0	7.2 ± 4.0	.929**
Median (Minimum, Maximum)	6.5 (1.0, 30.0)	6.5 (1.0, 30.0)	6.5 (2.0, 15.0)	
Previous Intradetrusor Botulinumtoxin-A Injection (Times)				
0	2 (6.1)	1 (4.5)	1 (9.1)	.845 [‡]
1	17 (51.5)	11 (50.0)	6 (54.5)	
2 or more	14 (42.4)	10 (44.5)	4 (36.4)	

IDO: idiopathic detrusor overactivity; NGB: neurogenic bladder.

*Data are presented as mean (standard deviation).

**The Mann-Whitney U test.

[†]Chi-square test.

[‡]Fisher's exact test.

the oldest was 67. In the NGB group, they were 18 and 58 years old, respectively.

Most of the cases in the two groups were female. The mean ± SD of symptoms duration was 8.1 ± 6.9 years.

Symptoms Duration

In the IDO group, the minimum duration was 1 year, and one case reported the symptoms for 30 years. In the NGB group, the minimum duration of symptoms was two, and maximum was 15 years ($P = .929$).

Previous Medication

Ninety-four percent of the cases had a history of intradetrusor botulinum toxin-A injection. The used medications and patient's outcomes following surgery are presented in Table 3.

Bowel Function

Although during anesthesia, fentanyl, propofol, and midazolam were administered during surgery in some cases, it did not delay the return of bowel function, and bowel movement was established 1 day postoperation.

Generally, only 18.2% started a regular diet 1 day postoperation, and the others returned to a regular diet on the second day. Patients required neostigmine just for 1 day in 84.8%, and for the remained patients, we administered it for 2 days postoperation.

Early Mobilization

In the current study, all cases except paraplegic patients who had a disability following neurological disease had early mobilization 1 day postoperation.

Drain Function and Removal

The mean (SD) of drain function was 114.3 ± 51.7 mL daily. In the case with less than 50 mL, we removed the drain, and 2 days before discharge, it had removed too. The average ± SD time for drain removal was 5.5 ± 1.0 days. The median and range of drain removal in both groups are shown in Table 3.

Hospital Stay Duration

The mean (SD) duration of adults' hospital stay was 7.7 ± 1.5 days. Besides, the patients were discharged at 7.0 ± 0.9 days postsurgery.

Table 2. Comorbidities of Patients Underwent Augmentation Cystoplasty

Comorbidities	Frequency	Percent
Discopathy	3	9.7
Multiple sclerosis	2	6.5
Pelvic organ prolapse	2	6.5
Spinal cord injury	2	6.5
Vesicourethral reflux	2	6.5
Vesicovaginal fistula	2	6.5
End stage renal disease	1	3.2
Head trauma/seizure	1	3.2
Hypothyroidism	1	3.2
Meningocele/meningocele	1	3.2
Pneumatosis intestinalis	1	3.2
Urolithiasis	1	2.8
Bilateral hydronephrosis	1	3.2

Postoperative Medication

Metoclopramide was administered only for 24 hours after surgery. Postoperative fasting time was 8 hours, and their bowel function was returned 1 day postoperation. Postprocedure acetaminophen was needed in 33.3% of adults for 2 days, and the remained cases needed it only 24 hours. The fluid regimen was started on the first day postoperation.

Past Medical History

Discopathy, fistula, and trauma were the familiar underlying disease in patients. Before the procedure, one-third of adults had a positive urine culture. All of them were treated preoperation, and with negative urine culture, they underwent surgery.

Patient's Complications in Follow-Up Period

In the following period (range 1-5 years), the common AC complications such as urinary tract infection were observed in some cases, and one death due to an unrelated cause. In one case, we had persistent nonobstructive abdominal pain with a history of pneumatosis intestinalis managed by the gastrointestinal tract service and did not need our reintervention. We did not observe any case of need for reoperation, or obstruction or leakage from the operation site and peritonitis.

Discussion

Our findings revealed that adapted ERAS protocol could be safe, practical, and effective in adult AC even in low- and lower-middle-income countries. It accompanied by few com-

plications, reduced intestinal motility problems, and a short length of hospital stay.

Like ERAS, an adapted ERAS protocol increases early discharge rates, reduces overcrowding on the ward in hospitals, and decreases the costs for patients and health facilities.

There are different indications for AC, including congenital anomalies, acquired neurogenic or non-neurogenic, iatrogenic, and urinary undiversion.¹⁶ ERAS is a multimodal approach that focuses on stress response reduction by helping the patients return to the baseline status and social activities as soon as possible.²⁵

Over the past 20 years, ERAS programs lead to reduced hospital stay duration and complications in patients. The literature describes the implementation and outcomes of ERAS programs on pediatric AC.²⁶

This multidisciplinary work is accompanied by few postoperative complications and a short hospital stay.²⁵

In the present study, the patients who underwent the adapted ERAS protocol had a short time to stool and flatus. We noted few bowel-associated complications and a short hospital stay duration in our patients. Our results showed that the normal bowel function was achieved in more than two-thirds of patients on the first day following the procedure, and they received a normal regular diet on the second day postoperation. It has been shown that ERAS protocol reduces the average time of the first stool passage.²⁷ This is achieved by epidural perioperative analgesia,^{28,29} intraoperative fluid therapy optimization,³⁰ minimally invasive approach to surgery, early NGT removal/early oral intake,²⁷ and early mobilization.

Despite the use of opioids, which usually is accompanied by secondary side effects, including prolonged postsurgical recovery, delay hospital discharge, and return to the baseline condition, its administration for our patients did not delay their recovery. One way to prevent postsurgical complications is preoperative bowel preparation, which can be mechanical or in the form of antibiotics administration. However, bowel preparation has not been recommended for children for many years. But in adults, this approach is only used for radical cystectomy. Previous studies showed that adapted ERAS protocol could improve perioperative management of radical cystectomy. The results of a published meta-analysis of existing ERAS protocols for radical cystectomy showed that oral bowel preparation was omitted in 96%, optimized fluid management was administered in 88%, and early mobilization (postoperative day 1) in 84%. Gum chewing (46%), metoclopramide (44%), and

Table 3. The Used Medications and Patient's Outcome Following Surgery

Medications/Outcomes	Total (n = 33), N (%)	IDO (n = 22), N (%)	NGB (n = 11), N (%)	P-Value
Neostigmine Usage (Days)				0.194 ^u
1	28 (84.8)	17 (73.3)	11 (100.0)	
2	2 (6.1)	2 (9.1)	—	
3	3 (9.1)	3 (13.6)	—	
Drain Removal (days)*	5.5 ± 1.0	5.6 ± 0.9	5.5 ± 1.1	0.663**
Median (Minimum, Maximum)	5.0 (4.0, 8.0)	5.5 (4.0, 7.0)	5.0 (4.0, 8.0)	
Metoclopramide Usage (Days)				0.174 ^u
1	30 (90.1)	19 (86.4)	10 (90.9)	
2	3 (9.9)	3 (13.6)	1 (9.1)	
Drain function (cc)/daily*				0.031**
Median (Minimum, Maximum)	105.0 (0.0, 200.0)	140.0 (50.0, 200.0)	80.0 (0.0, 200.0)	
NPO Timing (Hours)*	8.8 ± 3.7	9.1 ± 3.6	8.3 ± 3.9	0.355**
Median (Minimum, Maximum)	8.0 (1.0, 24.0)	8.0 (8.0, 24.0)	8.0 (1.0, 18.0)	
Return of Bowel Function (Days)				0.391 ^u
1	27 (81.8)	18 (81.8)	8 (72.7)	
2	6 (18.2)	4 (18.2)	3 (27.3)	
Time to Regular Diet (Days)				0.129 ^u
1	6 (18.2)	6 (27.3)	2 (18.2)	
2	25 (75.8)	14 (63.6)	9 (81.8)	
3	2 (6.0)	2 (9.1)	0 (0.0)	
Acetaminophen Use Duration (Day)				0.721 ^y
1	22 (66.7)	17 (77.3)	8 (72.7)	
2	11 (33.3)	5 (22.7)	3 (27.3)	
Type of Augmentation Cystoplasty				0.355 ^y
Ileocystoplasty	32 (96.8)	22 (100.0)	10 (90.9)	
Ileocystoplasty+Mitrofanoff	1 (3.2)	0 (0.0)	1 (9.1)	
Concomitant Surgery				0.542 ^y
No	31 (93.9)	20 (90.9)	11 (100.0)	
Yes	2 (6.1)	2 (9.1)	0 (0.0)	
Hospital Stay Duration (Days)*	7.7 ± 1.5	7.8 ± 0.7	7.6 ± 2.4	0.676**
Median (Minimum, Maximum)	8.0 (1.0, 10.0)	8.0 (6.0, 9.0)	8.0 (1.0, 10.0)	
Hemoglobin (mg dL⁻¹)*	12.1 ± 1.1	12.1 ± 1.1	12.2 ± 1.0	0.929**
Creatinine (mg dL⁻¹)*	1.1 ± 0.7	1.2 ± 0.9	0.9 ± 0.3	0.671**
Sodium (mequiv. L⁻¹)*	135.7 ± 23.2	140.5 ± 4.0	126.2 ± 39.5	0.066*
Potassium (mequiv. L⁻¹)*	3.8 ± 0.6	3.9 ± 0.4	3.6 ± 0.9	0.454**

IDO: idiopathic detrusor overactivity; NGB: neurogenic bladder; NPO: nothing per oral.

*Data are presented as mean (standard deviation).

**The Mann-Whitney U test.

^uChi-square test.^yFisher's exact test.

alvimopan (24%) were the common measures to prevent post-operative ileus. Length of hospital stay, complications, and time to defecation outcomes were changed significantly following ERAS protocol.³¹

The other part includes using alvimopan. The peripherally acting μ -opioid antagonist alvimopan has been proven effective in published studies.²⁴ This μ -opioid receptor antagonist suppresses the narcotic medications-induced constipation effect and consequently protects the bowel by promoting bowel function and ileus prevention. Completed trials showed its efficacy in accelerating the recovery of gastrointestinal function after abdominal surgery.^{32,33} This agent's advantage of resuming a regular diet is demonstrated in a retrospective study of Hamilton et al.³⁴ on patients undergoing radical cystectomy, which the results were accompanied by a short average time of resuming a regular diet (5.3 vs 4.1 days, $P < .01$). In our center, we have not access to alvimopan, and we used an alternative agent and replaced it with neostigmine. Neostigmine has a parasympathomimetic effect on GI receptors and acts as a reversible acetylcholinesterase inhibitor. Clinically, it is used in patients with acute colonic pseudo-obstruction, postoperative ileus, urinary retention, and myasthenia gravis.³⁵ It has an important muscarinic effect on GI receptors and, by increasing the availability of acetylcholine, increases the GI motility.^{35,36} Since this agent's administration is accompanied by several side effects, including abdominal pain/cramping, bradycardia, an urologist assistant with controlling the vital signs, and cardiac monitoring injected it i.v., and similar to alvimopan, it reduced the time to return to a regular diet.

This protocol would ideally focus on optimization, available, and cost-effective medications (including antibiotics, regional anesthesia, multimodal pain management, and early postoperative mobilization).

AC is accompanied by some early complications that include thromboembolism and mortality, or long-term problems that include metabolic disturbance, bacteriuria, urolithiasis, urinary incontinence, perforation, or the need for intermittent self-catheterization and carcinoma.³⁷ However, in the following period (range 1-5 years) of our cases, the common AC complications such as urinary tract infection were observed in some cases, and we did not observe any reoperation indications, or obstruction or related complications.

The present study proposed an adapted ERAS protocol according to the presence or absence of some medications in our country. Approximately, all ERAS protocols were applied in our center: education of the patients, short fasting time, epidu-

ral perioperative analgesia, optimization of intraoperative fluid therapy, minimally invasive approach to surgery, early NGT removal with early oral intake, early mobilization, and reduce the length of hospital stay. However, our protocol's adapted elements were using neostigmine instead of alvimopan, which demonstrated a favorable effect on patient's recovery. Besides, we applied this protocol in adult AC. Based on our knowledge, this is the first study on adults that uses this protocol, and promising outcomes, including shorter hospital stay days, early recovery, and return to family social activity, have been demonstrated.

In a meta-analysis, ERAS pathway vs conventional care was associated with many benefits, including a decreased hospital stay duration by approximately 2-3 days, reductions in overall perioperative morbidity and complication rates,³⁸ quality of recovery better short-term quality of life (physical, emotional, cognitive, and social functioning), and patient satisfaction.³⁹ By minimizing hospital stay, the hospital care costs and potential health care expenditure are reduced too. One of our study limitations was the lack of a control arm, which led to researchers' inability to compare the outcomes between intervention and control groups.

Our findings revealed that adapted ERAS protocol could be safe, practical, and effective in adult AC even in low- and lower-middle-income countries. It accompanied by few complications, reduced intestinal motility problems, and a short length of hospital stay.

Similar to ERAS, an adapted ERAS protocol has the potential to increase early discharge rates and, hence, reduce overcrowding on the ward in hospitals, and decrease the costs for patients and health facilities. However, due to multiple underlying diagnoses in our patients, our findings should not be generalized, and well-designed controlled trials are recommended in this issue.

Ethics Committee Approval: Ethical committee approval was received from the Tabriz University of Medical Sciences (IR.TBZMED.REC.1397.1052).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - E.J., S.H.; Design - E.J., S.H.; Supervision - S.H.; Data Collection and/or Processing - E.J., M.Z.S., M.N.; Analysis and/or Interpretation - H.S.P.; Literature Search - F.S.; Writing Manuscript - H.S.P.; Critical Review - S.H.

Acknowledgments: The authors would like to thank the Research Center for Evidence-Based Medicine and Research Vice-Chancellor of Tabriz University of Medical Sciences for financial support.

Financial Disclosure: This study was supported by the Research Center for Evidence-Based Medicine and the Research Vice-chancellor of Tabriz University of Medical Sciences (Grant No. 59231).

References

- Vukovic N, Dinic L. Enhanced recovery after surgery protocols in major urologic surgery. *Front Med.* 2018;5:93. [\[CrossRef\]](#)
- Ljungqvist O, Scott M, Fearon KC. Enhanced recovery after surgery: A review. *JAMA Surg.* 2017;152(3):292-298. [\[CrossRef\]](#)
- Giannarini G, Crestani A, Ferrera A, et al. Impact of enhanced recovery after surgery protocols versus standard of care on perioperative outcomes of radical cystectomy: A systematic review and meta-analysis of comparative studies. *Minerva Urol Nefrol.* 2019;71(4):309-323. [\[CrossRef\]](#)
- McQueen K, Oudit R, Derewi M, Banguti P, Ljungqvist O. Enhanced recovery after surgery for low- and middle-income countries. *World J Surg.* 2018;42(4):950-952. [\[CrossRef\]](#)
- Melloul E, Hübner M, Scott M, et al. Guidelines for perioperative care for liver surgery: Enhanced recovery after surgery (ERAS) society recommendations. *World J Surg.* 2016;40(10):2425-2440. [\[CrossRef\]](#)
- Nelson G, Kalogeris E, Dowdy SC. Enhanced recovery pathways in gynecologic oncology. *Gynecol Oncol.* 2014;135(3):586-594. [\[CrossRef\]](#)
- Liu B, Domes T, Jana K. Evaluation of an enhanced recovery protocol on patients having radical cystectomy for bladder cancer. *Can Urol Assoc J.* 2018;12(12):421-426.
- Biers SM, Venn SN, Greenwell T. The past, present and future of augmentation cystoplasty. 2012;109(9):1280-1293.
- Duthie JB, Vincent M, Herbison GP, Wilson DI, Wilson DJCDoSR. Botulinum toxin injections for adults with overactive bladder syndrome. *Cochrane Database Syst Rev.* 2011;(12):CD005493.
- Herbison GP, Arnold E. Sacral neuromodulation with implanted devices for urinary storage and voiding dysfunction in adults. *Cochrane Database Syst Rev.* 2009;(2):CD004202.
- Madhuvarata P, Cody JD, Ellis G, et al. Which anticholinergic drug for overactive bladder symptoms in adults. *Cochrane Database Syst Rev.* 2012;1:CD005429.
- Khastgir J, Hamid R, Arya M, Shah N, Shah PJ. Surgical and patient reported outcomes of 'clam' augmentation ileocystoplasty in spinal cord injured patients. *Eur Urol.* 2003;43(3):263-269. [\[CrossRef\]](#)
- Surer I, Ferrer FA, Baker LA, Gearhart JP. Continent urinary diversion and the extrophy-epispadias complex. *J Urol.* 2003;169(3):1102-1105. [\[CrossRef\]](#)
- Bandi G, Al-Omar O, McLorie GA. Comparison of traditional enterocystoplasty and seromuscular colocystoplasty lined with urothelium. *J Pediatr Urol.* 2007;3(6):484-489. [\[CrossRef\]](#)
- Stone AR, Nanigian D. Augmentation cystoplasty for overactive bladder. In *The Overactive Bladder: Evaluation and Management.* London: Informa Healthcare, 2007:359-369.
- Wein AJ, Kavoussi LR, Novick AC, Partin AW, Peters CA. *Campbell-Walsh urology: Expert consult premium edition: Enhanced online features and print, 4-volume set.* Amsterdam: Elsevier Health Sciences, 2011.
- Patel HR, Cerantola Y, Valerio M, et al. Enhanced recovery after surgery: Are we ready, and can we afford not to implement these pathways for patients undergoing radical cystectomy? *Eur Urol.* 2014;65(2):263-266. [\[CrossRef\]](#)
- Law N-M, Bharucha AE, Undale AS, Zinsmeister AR. Cholinergic stimulation enhances colonic motor activity, transit, and sensation in humans. *Am J Physiol-Gastrointest Liver Physiol.* 2001;281(5):G1228-G1237. [\[CrossRef\]](#)
- Bucher P, Mermilliod B, Gervaz P, Morel P. Mechanical bowel preparation for elective colorectal surgery: A meta-analysis. *Arch Surg.* 2004;139(12):1359-1364. [\[CrossRef\]](#)
- Slim K, Vicaut E, Launay-Savary M-V, Contant C, Chipponi J. Updated systematic review and meta-analysis of randomized clinical trials on the role of mechanical bowel preparation before colorectal surgery. *Ann Surg.* 2009;249(2):203-209. [\[CrossRef\]](#)
- Belsey J, Epstein O, Heresbach D. Systematic review: Adverse event reports for oral sodium phosphate and polyethylene glycol. *Alimentary Pharmacol Ther.* 2009;29(1):15-28. [\[CrossRef\]](#)
- Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR, Committee HICPA. Guideline for prevention of surgical site infection, 1999. *Infect Control Hosp Epidemiol.* 1999;20(4):247-280. [\[CrossRef\]](#)
- Wolf JS, Bennett CJ, Dmochowski RR, Hollenbeck BK, Pearle MS, Schaeffer AJ. Best practice policy statement on urologic surgery antimicrobial prophylaxis. *J Urol.* 2008;179(4):1379-1390. [\[CrossRef\]](#)
- Lee CT, Chang SS, Kamat AM, et al. Alvimopan accelerates gastrointestinal recovery after radical cystectomy: A multicenter randomized placebo-controlled trial. *Eur Urol.* 2014;66(2):265-272. [\[CrossRef\]](#)
- Brown JK, Singh K, Dumitru R, Chan E, Kim MP. The benefits of enhanced recovery after surgery programs and their application in cardiothoracic surgery. *Methodist Debakey Cardiovasc J.* 2018;14(2):77-88. [\[CrossRef\]](#)
- Rove KO, Edney JC, Brockel MA. Enhanced recovery after surgery in children: Promising, evidence-based multidisciplinary care. *Pediatr Anaesth.* 2018;28(6):482-492. [\[CrossRef\]](#)
- Persson B, Carringer M, André O, Andersson SO, Carlsson J, Ljungqvist O. Initial experiences with the enhanced recovery after surgery (ERAS) protocol in open radical cystectomy. *Scand J Urol.* 2015;49(4):302-307. [\[CrossRef\]](#)
- Fitzgerald JE, Ahmed I. Systematic review and meta-analysis of chewing-gum therapy in the reduction of postoperative paralytic ileus following gastrointestinal surgery. *World J Surg.* 2009;33(12):2557-2566. [\[CrossRef\]](#)
- Mazul-Sunko B, Gilja I, Jelisavac M, et al. Thoracic epidural analgesia for radical cystectomy improves bowel function even in traditional perioperative care: A retrospective study in eighty-five patients. *Acta Clin Croat.* 2014;53(3):319-325.
- Pillai P, McElevy I, Gaughan M, et al. A double-blind randomized controlled clinical trial to assess the effect of Doppler optimized intraoperative fluid management on outcome following radical cystectomy. *J Urol.* 2011;186(6):2201-2206. [\[CrossRef\]](#)
- Wessels F, Lenhart M, Kowalewski KF, et al. Early recovery after surgery for radical cystectomy: Comprehensive assessment and meta-analysis of existing protocols. *World J Urol.* 2020;38:3139-3153. [\[CrossRef\]](#)
- Sultan S, Coles B, Dahm P. Alvimopan for recovery of bowel function after radical cystectomy. *Cochrane Database Syst Rev.* 2017;2017(5):Cd012111. [\[CrossRef\]](#)
- Alhasemi M, Hamad R, El-Kefraoui C, et al. The association of Alvimopan treatment with postoperative outcomes after abdominal surgery: A systematic review across different surgical procedures and contexts of perioperative care. *Surgery.* 2021;169(4):934-944. [\[CrossRef\]](#)

34. Hamilton Z, Parker W, Griffin J, et al. Alvimopan in an enhanced recovery program following radical cystectomy. *Bladder Cancer*. 2015;1(2):137-142. [\[CrossRef\]](#)
35. Kram B, Greenland M, Grant M, Campbell ME, Wells C, Sommer C. Efficacy and safety of subcutaneous neostigmine for ileus, acute colonic pseudo-obstruction, or refractory constipation. *Ann Pharmacother*. 2018;52(6):505-512. [\[CrossRef\]](#)
36. Claroni C, Covotta M, Torregiani G, et al. Recovery from anesthesia after robotic-assisted radical cystectomy: Two different reversals of neuromuscular blockade. *J Clin Med*. 2019;8(11):1774. [\[CrossRef\]](#)
37. Veeratterapillay R, Thorpe AC, Harding C. Augmentation cystoplasty: Contemporary indications, techniques and complications. *Indian J Urol*. 2013;29(4):322-327. [\[CrossRef\]](#)
38. Lv L, Shao Y-f, Zhou Y-b. The enhanced recovery after surgery (ERAS) pathway for patients undergoing colorectal surgery: An update of meta-analysis of randomized controlled trials. *Int J Colorectal Dis*. 2012;27(12):1549-1554. [\[CrossRef\]](#)
39. George JA, Koka R, Gan TJ, et al. Review of the enhanced recovery pathway for children: Perioperative anesthetic considerations. *Can J Anesth/J Can Anesth*. 2018;65(5):569-577. [\[CrossRef\]](#)