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Favorable Impact on Postoperative Abdominal Symptoms in Robot-assisted Radical Prostatectomy Using Enhanced Recovery After Surgery Protocol

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Abstract. *Background/Aim: This study aimed to examine the effectiveness of enhanced recovery after surgery (ERAS) protocols in robot-assisted radical prostatectomy (RARP). Moreover, this study focused on postoperative abdominal symptoms and compared the perioperative parameters between the ERAS and conventional groups in RARP patients. Patients and Methods: A retrospective analysis was performed on 37 consecutive prostate cancer patients who underwent RARP between January 2020 and September 2021. The ERAS and conventional protocols were received by 16 and 20 patients, respectively, excluding one patient with surgical complications. Results: The incidence and cumulative frequency of postoperative abdominal distention were significantly lower in the ERAS group (p=0.041 and p=0.039, respectively). Although not significant, the first flatus and defecation time tended to be shorter in the ERAS group (p=0.115 and p=0.074, respectively). Conclusion: The ERAS protocol contributes to the reduction in postoperative abdominal distension for patients undergoing RARP.*

The enhanced recovery after surgery (ERAS) protocol is a multimodal perioperative care pathway aimed to achieve early recovery after undergoing surgical procedures by maintaining postoperative physiological function and reducing surgical stress (1). Reducing fasting duration and implementing carbohydrate loading, multimodal analgesia, early oral nutrition, and early ambulation are the fundamental elements of the ERAS protocol (2). A group of European surgeons first conceived the ERAS protocol, and the first consensus document was produced for colonic surgery in 2005. The ERAS protocol has been shown in various studies to shorten hospital stays without increasing the incidence of complications and has been applied to surgeries in various fields (3, 4). Official guidelines from the ERAS Society exist only for radical cystectomy in the urology department. However, recent studies have also shown to shorten hospital stay and improve abdominal symptoms in patients who received robot-assisted radical prostatectomy (RARP) (5-7).

Whether the ERAS protocol reduces postoperative ileus is yet to be elucidated although previous studies found that it contributes to the stimulation of postoperative first flatus, defecation and reduction of nausea incidence in patients who underwent RARP. The number of patients included in previous studies was probably too small to lead to a statistically significant difference in ileus incidence because RARP is a minimally invasive operation with a lower risk of complications (8). However, the introduction of the ERAS protocol improves postoperative abdominal distension in patients who underwent RARP even if the complication is not severe enough to cause ileus.

Thus, the present study aimed to compare perioperative parameters, including abdominal distention, and short-term outcomes of patients who underwent RARP with ERAS protocol or conventional protocol.

Patients and Methods

The charts of all patients who underwent RARP between January 2020 to September 2021 at Ishikawa Prefectural Central Hospital were retrospectively analyzed. Preoperative evaluation included digital rectal examination, transrectal ultrasonography, serum prostate-specific antigen (PSA) level measurement, and systematic prostate biopsies of 12 cores for cancer detection. Cancer staging

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Table I. *Protocols of the conventional and ERAS groups.*

	Conventional group	ERAS group
Preoperative information	Information on only about RARP surgery	Detailed information on the ERAS protocol aside from RARP surgery
Preoperative bowel preparation	Mechanical bowel preparation with oral laxative and cleansing enema was performed before surgery	No mechanical bowel preparation
Preoperative fasting	No food and liquid intake for 12 and 9 h before surgery, respectively	No food and liquid intake for 12 and 2 h before surgery, respectively
Perioperative infusion	Approximately 2,000 ml per day for 4 days No fixed intraoperative infusion protocol	1,000-1,500 ml on POD 0 and stopped on the evening of that day if the patients can drink oral rehydration solution No fixed intraoperative infusion protocol
Postoperative analgesia	Use a PCEA with fentanyl on demand	Started regular oral NSAIDs on POD 1 in addition to PCEA with fentanyl
Postoperative mobilization	Based on the patient's desire	Started rehabilitation in a sitting position on POD 0, and were encouraged to ambulate on POD 1 if the patient's conditions allowed
Postoperative diet	Allow liquid intake on POD 1 after bowel sounds were assessed POD 2, semiliquid diet; POD 3 normal diet	Chewing gum was used on the evening of POD 0 and allowed liquid intake on that day A normal diet was resumed on POD 1

POD: Postoperative day: PCEA: patient-controlled epidural analgesia; NSAIDs: nonsteroidal anti-inflammatory drugs.

was performed using computerized tomography (CT), magnetic resonance imaging, and bone scintigraphy. Thus, all the included patients were diagnosed with localized prostate cancer. The ERAS or conventional protocols were chosen at the discretion of the attending physician before they were hospitalized, according to the patient's desire or surgery schedule.

The main principles of the ERAS and conventional protocols are shown in Table I. All the RARP surgeries were conducted by one experienced surgeon using the da Vinci Si Surgical System (Intuitive Surgical, Sunnyvale, CA, USA). Pelvic lymph node dissection was omitted in all patients following the guidelines of the European Association of Urology because they had low- or intermediate-risk disease according to the D'Amico risk classification; the estimated risk of lymph nodes metastasis did not exceed 5% (9, 10).

The collected medical data included age, body mass index (BMI), PSA level, the American Society of Anesthesiologists (ASA) classification score, Gleason score (GS) on biopsy, D'Amico risk classification, perioperative parameters, and short-term outcomes. Abdominal distention was defined as a visible increase in overall abdominal diameter and subjectively assessed by urologists or nurses compared to preoperative conditions. Ileus was defined by the combination of at least two of the following five criteria: nausea or vomiting for 12 h, inability to tolerate a solid or semisolid food for two meals, abdominal distension, lack of stool or gas for 24 h, and radiologic ileus images on CT scan (11). Other complications were classified following the extended Clavien–Dindo system (12). The present study was approved by the institutional review board of Ishikawa Prefectural Central Hospital and performed following the Declaration of Helsinki.

Preoperative information. Patients in the ERAS group were given detailed information on the ERAS protocol as well as on RARP surgery. Nutritionists instructed the patients to abstain from smoking and alcohol and evaluated their nutritional condition. In addition, the patients were also instructed on how to use oral rehydration solution and chewing gum in the perioperative period. In contrast, patients were only informed about the RARP surgery in the conventional group. Urinary incontinence after RARP surgery was explained to all patients, and the patients were instructed to train their pelvic floor muscles.

Preoperative bowel preparation and fasting. Patients in the ERAS group were restricted food intake for 12 h before operation. However, they were allowed to drink water until 2 h before operation. No mechanical bowel preparation was performed. In contrast, patients were restricted food and liquid intake for 12 and 9 h, respectively, before operation in the conventional group. They underwent preoperative bowel preparation with oral laxative and cleansing enema the night before and the morning of the day of the operation.

Perioperative infusion. The fluid infusion volume in the ERAS group was limited to 1,000-1,500 ml on postoperative day (POD) 0 and stopped on the evening of that day if the patients could drink water. In contrast, all patients were given approximately 2,000 ml of fluid per day for 4 days from the day of the operation in the conventional group. No fixed intraoperative infusion protocol was noted in both groups.

Postoperative analgesia. All patients used patient-controlled epidural analgesia (PCEA) with fentanyl for postoperative pain on

Table II. *Patient characteristics*.

	Conventional group (n=20)	ERAS group (n=16)	*p*-Value
Age (years)	71 (68.3-73)	68.5 (61.5-71)	0.084
BMI (kg/m^2)	24.6 (22.6-26.6)	22.6 (21.7-25)	0.156
PSA level at diagnosis (ng/ml)	5.33 (4.49-6.39)	6.39 (5.09-8.32)	0.089
ASA score			1.000
I	1 (5.0)	1 (6.25)	
II	19 (95.0)	15 (93.75)	
Biopsy GS			1.000
6	8 (40.0)	7 (43.75)	
7	12 (60.0)	9 (56.25)	
D'Amico risk classification			1.000
Low	8 (40.0)	6 (37.5)	
Intermediate	12 (60.0)	10 (62.5)	

Data are presented as median (interquartile range) or n (%). BMI: Body mass index; PSA: prostate-specific antigen; ASA: American Society of Anesthesiologists: GS: Gleason score.

Table III. *Comparison of intraoperative parameters*.

	Conventional group (n=20)	ERAS group (n=16)	*p*-Value
Operative time (min)	130.5 (109.5-142.8)	127.5 (114-152.5)	0.981
Console time (min)	100 (84-123)	86.5 (77.3-112.8)	0.429
Estimated blood loss (ml)	50 (42.5-112.5)	100 (20-262.5)	0.721
Nerve-sparing			0.347
None	6 (30.0)	8 (50.0)	
Unilateral	11 (55.0)	5 (31.25)	
Bilateral	3 (15.0)	3 (18.75)	

Data are presented as median (interquartile range) or n (%).

demand. Patients in the ERAS group started to take oral nonsteroidal anti-inflammatory drugs (NSAIDs). One tablet of loxoprofen sodium hydrate (60 mg) was given thrice a day after meals from POD 1. In contrast, no fixed protocol was noted for use of NSAIDs in the conventional group.

Postoperative mobilization. Patients in the ERAS group started rehabilitation in a sitting position on POD 0 and were encouraged to ambulate on POD 1 if the patient's conditions allowed. In contrast, patient ambulation was mainly based on the patient's own desire in the conventional group.

Postoperative diet. Chewing gum was taken on the evening of POD 0 in the ERAS group. Patients were then allowed to drink oral rehydration solution (Arginaid Water; Nestle Health Science Co., Tokyo, Japan) on the same day, and a normal diet was resumed on POD 1. In contrast, oral rehydration was administered to the patient on POD1 after confirming bowel sounds in the conventional group. A semiliquid diet was then given on POD 2 and the normal diet was resumed on POD 3.

Statistical analyses. Cumulative incidence of abdominal distention was calculated from the day of surgery to the event or 48 h after surgery as the censoring time, and estimated using the Kaplan–Meier method. In addition, the differences were compared using the log-rank test. Statistical analyses were performed using Prism software version 6.07 (GraphPad Software, San Diego, CA, USA). Continuous valuables are expressed as median (interquartile range) and were compared using Mann–Whitney's *U*-test. Categorical variables were compared using the Fisher's exact test or chi-square test. The significance threshold was set at 0.05 for all tests.

Results

RARP without pelvic lymph node dissection was performed in 37 patients during the study period. Of the 37 patients, one patient who chose the ERAS protocol was excluded from this study because the patient needed several days of fasting due to gastrointestinal injury which occurred during the operation. The ERAS and conventional groups comprised 16 and 20 patients, respectively. Table II shows the patient characteristics. No significant differences in age, BMI, PSA level, ASA, biopsy GS, and D'Amico risk classification were observed between the two groups (all $p>0.05$).

Table III shows the intraoperative parameters of the two groups. No significant differences were noted between the two

Table IV. *Comparison of postoperative parameters.*

	Conventional group (n=20)	ERAS group (n=16)	*p*-Value
Time to ambulation (day)	2 (2-2)	1 (1-1)	<0.001
Time to diet (day)	2 (2-2)	1 (1-1)	<0.001
Time to regular diet (day)	3 (3-3)	1 (1-1)	<0.001
Time to first flatus (day)	1 (1-1)	1 (1-1)	0.115
Time to defecation (day)	4 (3-4)	3 (2-4)	0.074
Abdominal distention	11 (55.0)	3 (18.75)	0.041
Ileus	1 (5.0)	0 (0)	1.000
Nausea	4 (20.0)	2 (10.0)	0.672
Urinary leakage	1 (5.0)	2 (10.0)	0.574
Urinary tract infection	1 (5.0)	0 (0)	1.000
Urinary catheter placement period (day)	4 (4-4)	4 (4-4)	0.581
Postoperative hospital stay (day)	6 (6-8)	6 (6-8)	0.875
Removed prostate volume (ml)	47.6 (31.2-57.5)	37.1 (33.3-42.4)	0.197

Data are presented as median (interquartile range) or n (%).

groups in operative time, console time, estimated blood loss, and proportion of patients who underwent nerve-sparing surgery. Table IV shows the postoperative outcomes and the details of complications of the two groups. No significant differences were noted between the volume of resected prostate, length of urinary catheter placement period, and length of hospital stay (all $p>0.05$). Interestingly, a significant difference in the incidence of abdominal distension was noted with three (18.8%) and 11 (55.0%) cases in the ERAS and conventional groups, respectively ($p=0.041$). Moreover, the cumulative frequency of abdominal distention was significantly lower in the ERAS group than in the conventional group ($p=0.039$; Figure 1). Incidentally, the appearance of abdominal distension was observed within 48 h after surgery in all patients. In contrast, patients in the ERAS group tended to have a shorter time to first flatus and defecation than those in the conventional group ($p=0.115$ and $p=0.074$, respectively). All the complications in both groups were minor complications classified as grade I or II following the Clavien–Dindo system, and no significant difference was noted in the incidence of complications between the two groups (data not shown).

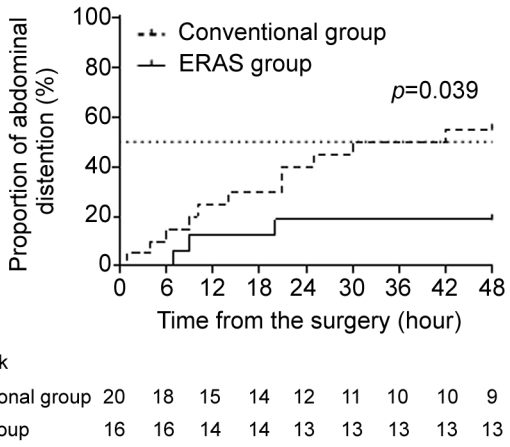

Figure 1. *Cumulative frequency of abdominal distention in the enhanced recovery after surgery (ERAS) and conventional groups.*

Discussion

The ERAS protocol, first introduced for colonic surgery in 2005, has been widely applied in patients undergoing breast, gastrointestinal, and urologic surgery, and proven to enhance postoperative abdominal recovery (1, 2). This study is believed to be the first to focus on postoperative abdominal distention for patients who underwent RARP with the ERAS protocol.

Previous studies revealed that the ERAS protocols can enhance the recovery of postoperative gastrointestinal dysmotility in patients who underwent RARP surgery even though several differences in bowel preparation, fasting, fluid infusion, mobilization, or analgesia protocols were noted because of the lack of official guidelines from the ERAS Society (13-16). Similar to previous studies, patients in the ERAS group in this study tend to have a shorter time to first flatus and defecation than those in the conventional group. In addition, the present study also found that the ERAS protocol was associated with a reduction of postoperative abdominal distention. The mechanism by which the ERAS protocol enhances abdominal recovery after surgery is multifactorial. First, mechanical bowel preparation with medication and fasting has been routinely performed in patients who undergo RARP surgery in case surgeons cause rectal injury during the procedure. However, recent studies have mentioned that mechanical bowel preparation causes dehydration and has

adverse physiologic effects on the intestinal mucosa, which is associated with prolonged ileus after colonic surgery (17, 18). Mechanical bowel preparation in the ERAS group was omitted based on these results. Second, early oral intake was traditionally considered to increase the incidence of intestinal complications; however, studies of patients who underwent gastrointestinal surgery have suggested that early oral intake enhances recovery of gastrointestinal function, prevents postoperative ileus, and reduces postoperative complications and length of hospital stay (19, 20). Thus, early oral intake is currently recommended as a key component of the ERAS protocol. Third, perioperative fluid management is indispensable to the ERAS protocol. Administering excessive fluid can lead to intestinal edema and increase interstitial lung water, which can also cause complications and adversely affect recovery (21). Thus, postoperative intravenous fluids should be minimized and discontinued at the earliest opportunity and the enteral administration should preferentially be used (22). Fourth, a study of patients with colon cancer indicated that postoperative exercise improves bowel motility after surgery (23). Moreover, early mobilization in this study is considered to improve abdominal symptoms in the ERAS group. Finally, narcotic use can lead to gut motility inhibition (24). The regular use of NSAIDs in the postoperative period may contribute to the reduction of the dose of opioids from PCEA and improve abdominal symptoms in the ERAS group. Although it is not possible to identify which factors contributed most to the improvement in abdominal symptoms (*e.g.*, preoperative bowel preparation, early oral intake, restricted fluid infusion, early mobilization, or use of NSAIDs), these elements are considered to enhance recovery of postoperative gastrointestinal dysmotility for patients who underwent RARP.

Previous studies showed that the ERAS protocol shortens the length of hospital stay (13-15, 25-27). However, no significant difference was noted between the ERAS and conventional protocols in this study because RARP was safely performed in the center of the current study before the introduction of the ERAS protocol. In addition, few perioperative problems (*e.g.*, the length of hospital stay in the conventional group) were sufficiently short compared with other studies (13). Another study in Japan reported that the length of hospital stay did not differ between the ERAS and conventional protocol (16), which was considered consistent with the present study. A possibility exists that the length of hospital stay will be shorter in the ERAS group if the criteria for discharge were set and the patients were urged to discharge.

This study has several limitations. First, it is a retrospective study in a single center and performed without randomization. Thus, it includes all the inherent biases present in the studies of this design. In addition, the sample size may be too small to determine the significant differences between groups. Second, the number of opioids consumed in the postoperative period was not controlled due to the limitation of the electronic medical record in recording PCEA usage. Finally, postoperative abdominal distention was subjectively evaluated by urologists or nurses, which may have led to differences between the assessments. Therefore, further studies with a randomized controlled design, larger sample size, and more than one center are required to assess the value of ERAS protocol for RARP.

In conclusion, the present study shows that the ERAS protocol for patients undergoing RARP contributes to a reduction in postoperative abdominal distension and may reduce postoperative abdominal symptoms.

Conflicts of Interest

The Authors declare no conflicts of interest in relation to this study.

Authors' Contributions

T.M. had full access to all the data and takes responsibility for the integrity and accuracy of the contents. Study concept and design: T.M. Acquisition, analysis, and interpretation of data: T.H. Drafting of the manuscript: T.H. and T.M. Critical revision of the manuscript: R.F., A.T., and S.U. Statistical analysis: T.M. Supervision: T.M.

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