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Original Article

Application value of enhanced recovery after surgery (ERAS) in laparoscopic nephron sparing surgery

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Abstract: *Backgrounds*: To investigated the application value of enhanced recovery after surgery (ERAS) in laparoscopic nephron sparing surgery (LNSS). *Methods*: As a retrospective case-control study, we retrospectively analyzed the clinical data of 147 patients whom suffered kidney cancer underwent LNSS between Jun, 2015 and Dec, 2016. The 69 patients who received ERAS management were allocated into the ERAS (enhanced recovery by optimizing perioperative management options) group and 88 patients who received traditional perioperative management were allocated into the control group. The post-operative recovery indicators, length of stay (LOS) and hospitalization expenses between the two groups were compared. *Results*: The time for the first water intake, first out of bed activity, first anal exhaust, catheter indwelling, pelvic drainage tube indwelling, LOS and hospitalization costs for the ERAS group were 2.5±0.6 h, 1.5±0.4 d, 8.6±1.9 h, 1.1±0.2 d, 2.4±0.3 d, 3.0±0.2 d, 31,000±2,000 RMB, while for the control group were 28.1±10.6 h, 7.4±0.6 d, 35.1±15.5 h, 7.0±0.6 d, 7.2±0.5 d, 8.2±0.6 d, 42,000±1,000 RMB. The differences between the two groups were statistically significant (t=-21.246, -69.253, -15.010, -76.464, -67.280, -58.727, -41.800, $P<0.05$). There was no significant difference in the overall postoperative complication rates (8.7%, 16.7%, $X^2=0.151$) or pain scores 2 h (0.75±0.67, 0.74±0.69, t=0.089) after surgery between the two groups ($P>0.05$). Pain scores after surgery in the time point of 24 h (1.65±0.72, 3.69±0.69, t=-17.486) and 48 h (2.20±0.76, 4.65±0.77, t=-19.391) were significant different between the ERAS group and the control group ($P<0.05$). Univariate regression analysis were conducted to match the groups on the aspect of recovery parameters respectively. All them have significant correlation ($P<0.05$) except General/Overall postoperative complications and Pain scores in the time point of 2 h have no significant correlation ($p=0.269/0.125/0.929$). *Conclusion*: The application of ERAS in perioperative management could enhance the patient's recovery after LNSS, relieve postoperative pain and reduce hospitalization time and costs, while not increasing the overall incidence of postoperative complications.

Keywords: Enhanced recovery after surgery, laparoscopic nephron sparing surgery, perioperative care

Background

Renal carcinoma is a common malignancy in the urinary system, which imposes a great threat to the patients. Radical nephrectomy is currently a generally accepted treatment method for possible cure of localized renal carcinoma [1, 2]. With the development in minimally invasive techniques, laparoscopy has now replaced open surgery to become the mainstream procedure for treating renal carcinoma due to smaller surgical trauma. For T1a stage renal carcinoma (tumor size ≤4 cm), the efficacy of laparoscopic nephron sparing surgery (LNSS) is comparable to radical nephrectomy, while preserving the function of residual kidney [3], which makes LNSS the recommended methods for treating renal carcinoma smaller than 4 cm [4]. However, LNSS normally requires absolute bedrest, leading to significantly longer length of stay (LOS) than radical nephrectomy. Enhanced recovery after surgery (ERAS) is a new surgical concept proposed by Kehlet [5] provides a good way in preserving the residual renal function while reducing LOS and accelerating patient's rehabilitation. In this study, we reported our experience of the application of ERAS protocol in LNSS patients and evaluated its effectiveness and safety.

Table 1. Comparison of the general Information between the ERAS and control group ($\bar{x}\pm s$)

Group	ERAS	Control	Statistic	*P* value
Age (years)	56.5±5.2	55.8±5.6	t=-0.718	0.474
Gender n (%)			X^2=1.541	0.214
Male	41 (59.4)	54 (69.2)		
Female	28 (40.6)	24 (30.8)		
BMI (kg/m^2)	21.1±1.3	21.6±1.6	t=-1.835	0.069
Kidney cancer location n (%)			X^2=0.717	0.397
Left	35 (50.7)	45 (55.6)		
Right	34 (49.3)	33 (42.3)		
Kidney cancer size (cm)	2.9±0.5	2.9±0.5	t=0.990	0.324
ASA grade n (%)			X^2=0.081	0.776
Grade I	63 (91.3)	69 (88.5)		
Grade II	6 (8.7)	9 (11.5)		

Methods

Clinical data

We retrospectively analyzed a cohort of 147 patients who received LNSS between June, 2015 and December, 2016. The inclusion criterion was receiving selective operation of LNSS. Exclusion criterion was with contraindications against ERAS, including old age, diabetes, serious hypertension or cardiovascular and cerebrovascular diseases. The 69 patients who adopted the ERAS protocol during perioperative period were allocated as the ERAS group, while the other 54 patients who used traditional perioperative treatment protocol were allocated as the control group. For all 145 patients the retroperitoneal LNSS surgery was performed by the same surgeon. Written informed consent was obtained from all patients and their close relatives for all procedures and for the use of clinical data in publication. This study was approved by the Ethics Committee of Yantai Yuhuangding Hospital. The patients age, gender, body mass index (BMI), tumor location, tumor size, TNM stage, ASA grading were comparable between the ERAS and control groups (P>0.05, **Table 1**).

Perioperative treatment

The perioperative treatment procedures were summarized in **Table 2**.

Postoperative pain scoring

Patient's postoperative pain was scored using the visual analog scale (VAS). 0 point: no distress; 1-3 points: tolerable slight pain; 4-6 points: tolerable pain affecting sleep; 7-10 points: unbearable increasing distress.

Observation parameters

The time for first water intake, first ambulation, first anal exhaust, ureteral catheter indwelling, pelvic drainage tube indwelling, gastrointestinal complications (Nausea & vomiting, Abdominal distention, Intestinal obstruction), general postoperative complications (infection, fever, Subcutaneous emphysema, hematoma, thrombus), length of stay (LOS), hospitalization costs and pain scores evaluate by VAS during 2 h, 24 h and 48 h post operation were compared between the ERAS and control groups.

Follow-up

Patients were followed by telephone or hospital revisit until 1st Dec, 2016. The follow-up content included postoperative urination, incision wound healing, renal function recovery and postoperative complications.

Statistical analysis

All of the data in the present study were analyzed with SPSS for Windows Version 19.0. Normally distributed data were expressed as mean±standard deviation and categorical data were expressed using expressed as number (n) and percentage (%). Parameters such as the time for first water intake, first ambulation, first anal exhaust, ureteral catheter indwelling, pelvic drainage tube indwelling, LOS and hospitalization costs were compared between the two groups using Student's *t*-test. The incidence of gastrointestinal complications and general postoperative complications were analysed using the χ^2 test. Pain scores were analysed using the Mann-Whitney U-test. Univariate regression analysis were conducted to match the groups on the aspect of recovery parameters respectively. All data with *P*<0.05 were considered statistically significant.

Results

In both groups the LNSS surgeries were successfully completed. The time for first water

Table 2. Perioperative treatment procedures for ERAS and control groups. b.o.: before operation

Procedures	ERAS group (n=69)	Control (n=78)
Preoperative		
Education	ERAS concept education	Conventional therapy education
Fast	No food intake 6 hr b.o.; no liquid intake 2 hr b.o. (Orally administrated 1000 mL 10% glucose 1 d b.o., 500 mL 2 h b.o)	No food or liquid intake 12 hr b.o.
Bowel preparation	No	Cleansing enema 1 night b.o. and on the morning of operation
Intraoperative		
Anesthesia	Total intravenous anesthesia+ epidural anesthesia+ incision local infiltration anesthesia	General anesthesia with endotracheal intubation
Warming	Yes	No
Venous transfusion	1000 mL Lactated Ringer's Solution	No limitation
Postoperative		
Food and water intake	Water intake on the day of operation, transitioning to liquid diet, then to normal diet	Water intake after anal exhaust, transitioning to liquid diet, then to normal diet
Off-bed activity	Encourage off-bed activity the day after operation	Bed rest for 1 week
Urethral catheter	Removed on the day after operation	Removed 1 week after operation
Drainage tube	Removed 2-3 day after surgery	Removed 1 week after operation
Venous transfusion	500 mL limitation	No limitation

Table 3. Comparison of the recovery parameters between the ERAS and control group ($\bar{x} \pm s$)

Parameters	ERAS group	Control group	Statistics	*P* value
First water intake (h)	2.5±0.6	28.1±10.6	-21.246	<0.001
First ambulation (d)	1.5±0.4	7.4±0.6	-69.253	<0.001
First anal exhaust (h)	8.6±1.9	35.1±15.5	-15.010	<0.001
Ureteral catheter indwelling (d)	1.1±0.2	7.0±0.6	-76.464	<0.001
Pelvic drainage tube indwelling (d)	2.4±0.3	7.2±0.5	-67.280	<0.001
LOS (d)	3.3±0.4	8.2±0.6	-58.727	<0.001
Hospitalization costs (thousand RMB)	31±2.0	42±13	-41.800	<0.001
Gastrointestinal complications n (%)	2 (2.9)	5 (6.4)	X^2=0.996	0.318
Nausea & vomiting	2 (2.9)	5 (6.4)		
Abdominal distention	2 (2.9)	5 (6.4)		
Intestinal obstruction	0	1 (1.3)		
General postoperative complications n (%)	4 (5.8)	8 (10.3)	X^2=0.971	0.324
Fever	3 (4.3)	6 (7.7)		
Pneumonia	0	1 (1.3)		
Urinary tract infection	2 (2.9)	4 (5.1)		
Deep venous thrombosis	0	1 (1.3)		
Others (subcutaneous emphysema/hematoma)	1 (1.4)	1 (1.3)		
Overall postoperative complications n (%)	6 (8.7)	13 (16.7)	X^2=2.067	0.151
Pain scores 2 h postoperative	0.75±0.67	0.74±0.69	0.089	0.929
Pain scores 24 h postoperative	1.65±0.72	3.69±0.69	-17.486	<0.001
Pain scores 48 h postoperative	2.20±0.76	4.65±0.77	-19.391	<0.001

intake, first ambulation, first anal exhaust, ureteral catheter removal and pelvic drainage tube removal times for the ERAS group were all significantly shorter (P<0.05) than the control group. Although incidences for gastrointestinal complications, general postoperative complications and overall incidence for postoperative complications in the ERAS group were reduced comparing to the control group, there was no statistically significant difference (P>0.05). In the ERAS group, 2 patients had abdominal distension with nausea and vomiting after surgery,

which were relieved following off-bed activities. In the control group, 1 patient had intestinal obstruction with nausea, vomiting, and abdominal distension, which was relieved after fasting, gastrointestinal decompression, correction of electrolyte imbalance and anti-emetic treatment. Four patients suffered nausea and vomiting and symptom was controlled anti-emetic treatment. In the ERAS group urinary tract infection with fever occurred in 2 patients, both of whom recovered after antibiotic treatment. There was one case of fever which was resolved by physical cooling, and 1 case of subcutaneous emphysema, in which the gas was spontaneously absorbed 3 days after. For the control group, there were 5 cases of postoperative infection with fever, all of whom were treated with antibiotics. There was one case of fever which was resolved by physical cooling, 1 case of deep venous thrombosis which was controlled by thrombolytic therapy, and 1 case of self-absorbed hematoma. There was no difference in pain scores between the two groups 2 h post operation. However the pain scores 24 h and 48 h post operation were significantly different ($P<0.05$, **Table 3**). The time for the first water intake, first out of bed activity, first anal exhaust, catheter indwelling, pelvic drainage tube indwelling, LOS, hospitalization costs and Pain scores in the time point of 24 h/48 h have significant correlation with the use of ERAS or not ($P<0.05$), which the adjusted R square were 0.732/0.969/0.577/0.973/0.967/0.959/0.925/0.676/0.720. The regression unstandardized coefficient and constant were (25.598/-23.054), (5.900/-4.422), (26.496/-17.901), (5.905/-4.804), (4.766/-2.345), (4.907/-1.653), (1.055/2.093), (2.040/-0.388), (2.451/-0.248) respectively. General/Overall postoperative complications and Pain scores in the time point of 2 h have no significant correlation ($p=0.269/0.125/0.929$). All patients were followed for 1-6 months (median 3 months) and no additional complications occurred in either group.

Discussion

With the improvement of imaging diagnostic techniques, the detection rate of asymptomatic renal cell carcinoma in the process of physical examination of patients rapidly increased [6], the majority of asymptomatic renal cell carcinoma is less than 4 cm in size limited renal cell carcinoma, for such renal cell carcinoma, LNSS can not only ensure the function and quality of life of residual kidneys, but also will not affect the postoperative survival rate, local recurrence rate and distant professional [4, 7, 8]. We found it would be better for patients if they were able to rehabilitate partially nephrectomized patients.

The concept of ERAS was first proposed by the Prof. Kehlet in 1997, which was a series of optimization in the comprehensive measures of perioperative treatment [5]. It is an evidence-based novel optimization of the perioperative treatment model and aims at reducing stress of surgical trauma, reducing occurrence of complications, accelerating patient rehabilitation and reducing LOS. The protocol of ERAS included three tiers: preoperative (preoperative propaganda and education to the patients, rejecting mechanical intestinal preparation and reducing the fasting time before operation), intraoperative (insulation, optimized anesthesia, and limiting venous transfusion) and postoperative (early oral diet and early off bed activities). See **Table 2** for details.

ERAS aims to reduce the postoperative complications, shorten the length of stay and reduce the cost of hospitalization under the premise of rapid recovery. Chughtai [9] reported that the application of ERAS in open partial nephrectomy can shorten the postoperative hospital stay without increasing the incidence of postoperative complications. In the present study, there was no significant difference in postoperative gastrointestinal-related complications, general complications and total postoperative complications between the ERAS group and the control group, but the morbidity of various complications was decreased in the ERAS group. It has been reported [10] that early removal of the catheter after thoracic and abdominal surgery can reduce the risk of developing urinary tract infection. In this study, the catheter was removed from the ERAS group after the next day's ambulation and the risk of urinary tract infection and fever is lower than that of the control group. ERAS program proposal to limit the amount of fluid to prevent excess fluid or inadequate blood volume caused by inadequate visceral perfusion, to avoid increasing the incidence of intestinal obstruction and postoperative hospital stay [11], which is consistent with the results of this study. Early postoperative oral feeding can stimulate the gastrointestinal

motility, reduce the first time of exhaust, without increasing the incidence of gastrointestinal complications such as intestinal obstruction [12], which is consistent with the results of this study. In this study, the first postoperative exhaust time was significantly earlier in the ERAS group than in the control group, and may be associated with early chewing gum [13]. In this study, no lower extremity venous thrombosis occurred in the ERAS group, which may be related to the prevention of wearing elastic stockings and LMWH, which is consistent with the literature [14].

In this study, the optimal anesthesia was used in the ERAS group. The optimal duration of epidural anesthesia during operation was between 48 and 72 h postoperatively [14]. After treatment with intravenous paracetamol and oral paracetamol. Therefore, postoperative pain control in ERAS group was better. There was no difference in ERAS group and control group at 2 h after operation, but significant difference was observed at 24 and 48 h after operation. The purpose of optimizing postoperative analgesia is to get out of bed early. In this study, the effective analgesic method of ERAS group prompts patients to get out of bed early after operation, which not only promotes the recovery of gastrointestinal function but also avoids the formation of venous thrombosis of the lower extremities and reduces the incidence of complications Occurrence of disease, accelerate postoperative recovery, shorten the hospital stay, reduce hospital costs. After the operation of various types of drainage tubes in ERAS and there is no uniform standard. in this study, drainage tube was removed when Drainage less than 20 ml, the average retention time of 2.4±0.3 d, less than the traditional retention time of 7.2±0.5 d. It not only convenient for patients to get out of bed activities, but also reduce the psychological burden, reduce stress response and promote patient rehabilitation. ERAS accelerated patients' recovery and reduced LOS without increase the incidence of long-term complications. In this study both groups of patients were followed for a median length of 3 months and no complication occurred.

Currently, with the development of minimally invasive techniques and precision medicine, urological surgery has evolved from open surgery to minimal invasion and even non-invasion. The core concept is reducing surgical trauma, reducing LOS and accelerating postoperative rehabilitation, which accorded with the aim of ERAS. Therefore, application of ERAS into urological surgery would promote the development of the overall technology.

In conclusion, in this study through analyzing a cohort of 147 LNSS patients we confirmed that ERAS could effectively reduce postoperative pain, accelerate patient rehabilitation, reduce LOS and hospitalization costs and not increase complication rate. ERAS is not only safe and effective to be applied in urological surgery, but also a major influence on the improvement in the therapeutic level of current urological surgery.

Disclosure of conflict of interest

None.

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