Original Article

Clinical application of 4N-enhanced recovery after surgery in retroperitoneal laparoscopic resection of adrenal tumors

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Background: Enhanced recovery after surgery (ERAS) has been widely applied in various surgical fields to improve postoperative recovery and reduce complications. However, its application in retroperitoneal laparoscopic resection of adrenal tumors remains limited. This study aimed to evaluate the effect and value of the 4N-ERAS protocol, which includes no Foley catheter, no drainage, no antibiotics, and "no pain" management for the postoperative recovery of patients undergoing retroperitoneal laparoscopic adrenal tumors resection.

Methods: We retrospectively analyzed data from 85 patients with adrenal tumors who were treated in the Urology Department of The University of Hong Kong-Shenzhen Hospital from January 2019 to December 2023. Of them, 42 patients were treated with the 4N-ERAS protocol (4N-ERAS group) and 43 patients received traditional treatment (control group). We compared clinical characteristics, such as sex, age, mean body mass index (BMI), preoperative diagnosis, tumor size, tumor location, and postoperative outcomes, including time to first flatus, time to first ambulation, time to Foley catheter removal, time to retroperitoneal drainage tube removal, postoperative pain score [Numeric Rating Scale (NRS)], length of hospital stay, total hospitalization costs, and postoperative complications between the two groups.

Results: There were no significant differences in terms of clinical characteristics between the two groups. Compared to the control group, the 4N-ERAS group exhibited shorter times for first flatus, first ambulation, Foley catheter removal, retroperitoneal drainage tube removal, lower postoperative pain scores (NRS), and shorter hospital stays ($P<0.05$). Furthermore, compared to the control group, the total hospitalization cost was significantly lower in the 4N-ERAS group ($P<0.05$). There were no significant differences in terms of postoperative complications between the two groups ($P=0.19$).

Conclusions: The 4N-ERAS protocol for retroperitoneal laparoscopic resection of adrenal tumors may expedite postoperative recovery, reduce pain, and lower overall hospital costs. This preliminary study demonstrated the safety and feasibility of the 4N-ERAS protocol for retroperitoneal laparoscopic resection of adrenal tumors, warranting future multicenter prospective, randomized, controlled trials in this field.

Keywords: Retroperitoneal laparoscopic surgery; adrenal tumor resection; 4N-enhanced recovery after surgery (4N-ERAS); hospitalization costs; postoperative complications

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Introduction

In 1997, enhanced recovery after surgery (ERAS) was first introduced for colorectal surgery by the Danish surgeon Kehlet. The final goal of the ERAS protocol is to use a multidisciplinary, patient-centered approach in the perioperative period to minimize surgical stress, optimize physiological function, expedite postoperative recovery, and minimize postoperative complications (1).

Highlight box

Key findings

- The 4N-enhanced recovery after surgery (4N-ERAS) protocol (no Foley catheter, no drainage, no antibiotics, and "no pain" management) significantly reduced the time to first flatus, time to first ambulation, time to Foley catheter removal, time to retroperitoneal drainage tube removal, postoperative pain scores [Numeric Rating Scale (NRS)], and length of hospital stay compared to the traditional treatment group ($P<0.05$) in patients undergoing retroperitoneal laparoscopic resection of adrenal tumors. Total hospitalization costs were significantly lower in the 4N-ERAS group compared to the control group ($P<0.05$). There were no significant differences in postoperative complications between the two groups ($P=0.19$).
- This study demonstrates that the 4N-ERAS protocol is safe and feasible for retroperitoneal laparoscopic adrenal tumor resection.

What is known and what is new?

- ERAS protocols have been widely applied in various surgical specialties to improve postoperative recovery and reduce complications.
- To evaluate the efficacy and value of the 4N-ERAS protocol, we introduced a novel approach—no Foley catheter, no drainage, no antibiotics, and "no pain" management. This protocol significantly accelerated postoperative recovery, reduced pain, and lowered hospitalization costs without increasing complications in patients undergoing retroperitoneal laparoscopic resection of adrenal tumors.

What is the implication, and what should change now?

- The 4N-ERAS protocol is a safe and effective approach for retroperitoneal laparoscopic adrenal tumor resection, providing faster recovery, reduced postoperative pain, and lower hospital costs without increasing complications.
- Future multicenter prospective studies are needed to further validate its efficacy and optimize perioperative care for patients undergoing this procedure.

In 2001, the Enhanced Recovery after Surgery Study Group was established in Europe to encourage the use of a multidisciplinary team collaboration model and a scientific, evidence-based approach to expedite postoperative recovery (2). Many studies have investigated the clinical value of ERAS in gastrointestinal surgery, colorectal surgery, hepatobiliary surgery, and other fields (3-6). Despite these positive results, data on the clinical application of ERAS in minimally invasive resection of adrenal tumors remain limited (7-9). In this context, our team adhered to the ERAS principles and proposed a 4N-ERAS (no Foley catheter, no drainage, no antibiotics, and "no pain") technical system for retroperitoneal laparoscopic adrenalectomy based on our clinical experience. This study aimed to investigate the feasibility and efficacy of the 4N-ERAS method compared to traditional methods among patients undergoing retroperitoneal laparoscopic adrenalectomy. We present this article in accordance with the STROBE reporting checklist (available at https://tau.amegroups.com/article/view/10.21037/tau-24-608/rc).

Methods

This study was a retrospective study. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and approved by the Research Ethics Committee of The University of Hong Kong-Shenzhen Hospital (No. [2024]225). Informed consent was obtained from all patients.

We retrospectively analyzed the clinical data of 85 patients with adrenal tumors who were treated in the Urology Department of The University of Hong Kong-Shenzhen Hospital from January 2019 to December 2023. Patients treated from January 2019 to December 2021 were included in the traditional treatment group (control group), whereas patients treated from January 2022 to December 2023 were included in the 4N-ERAS group. The 4N-ERAS group consisted of 15 males and 27 females with a mean age of 49.35±12.01 years. The mean diameter of adrenal tumors was 2.63±1.15 cm. The tumor was located on the right side in 20 cases and on the left side in 22 cases. The control group consisted of 22 males and 21 females with a mean age of 47.09±13.83 years. The diameter of the adrenal tumor

Table 1 Clinical data of the patients in both groups

Parameters	Control group (n=43)	4N-ERAS group (n=42)	P value
Age (years)	47.09±13.83	49.35±12.01	0.41
Gender			0.40
Male	22	15	
Female	21	27	
BMI (kg/m^2)	23.60±1.99	24.63±3.35	0.08
Diagnosis			
Pheochromocytoma	7	3	0.33
Primary aldosteronism	18	17	0.89
Cushing syndrome	2	7	0.14
Others	16	15	0.88
Tumor size (cm)	2.51±1.12	2.63±1.15	0.63
Tumor location			0.88
Left side	22	22	
Right side	21	20	

Data are presented as mean ± standard deviation or n; BMI, body mass index; ERAS, enhanced recovery after surgery.

was 2.51±1.12 cm. The tumor was located on the right side in 21 cases and on the left side in 22 cases (*Table 1*). There were no significant differences in clinical characteristics between the two groups (P>0.05).

Inclusion criteria were as follows: (I) age between 18 and 69 years; (II) non-functional adrenal tumors confirmed by endocrine examination with a diameter of <6 cm; (III) functional adrenal tumors confirmed by endocrine examination with a diameter of <6 cm; (IV) isolated adrenal metastasis with a diameter of <6 cm; (V) body mass index (BMI) <35 kg/m^2; and (VI) retroperitoneal laparoscopic surgery. Exclusion criteria were as follows: (I) adrenal tumors with a diameter of ≥6 cm; (II) history of retroperitoneal surgery; (III) severe cardiovascular and pulmonary diseases; (IV) coagulation disorders; (V) acute infectious diseases; (VI) organ dysfunction, such as severe hepatic or renal insufficiency; and (VII) BMI >35 kg/m^2.

Adequate medical preparation was performed for patients with a preoperative diagnosis of pheochromocytoma. In particular, medications, such as terazosin and metoprolol, were used to control blood pressure and volume expansion was done for 2 weeks to achieve the following standards: (I) blood pressure was stabilized at 120/80 mmHg and heart rate was controlled at 80–90 bpm; (II) the frequency of paroxysmal hypertension reduced, and palpitations, hyperhidrosis, and nasal congestion disappeared; (III) increased body weight, hematocrit <45%, warm extremities, and well-perfused nail beds; and (IV) improved glucose metabolism and other hypermetabolic syndromes. Patients diagnosed preoperatively with primary aldosteronism were treated preoperatively with potassium supplements and spironolactone to stabilize their electrolyte levels and blood pressure before retroperitoneal laparoscopic minimally invasive surgery. Patients diagnosed preoperatively with hypercortisolism received glucocorticoids intraoperatively and postoperatively to stabilize electrolyte levels, acid-base balance, and blood pressure.

Perioperative management

Preoperative preparation

The concept of 4N-ERAS was explained to patients in the 4N-ERAS group. They were instructed to fast for 6 hours and not to drink for 4 hours before surgery. No other specific bowel preparations were needed. Compression stockings were worn the day before surgery. In the control group, patients received routine preoperative education. They were instructed to fast for 8 hours and not to drink for 6 hours before surgery, following standard bowel preparation. No compression stockings were used in the

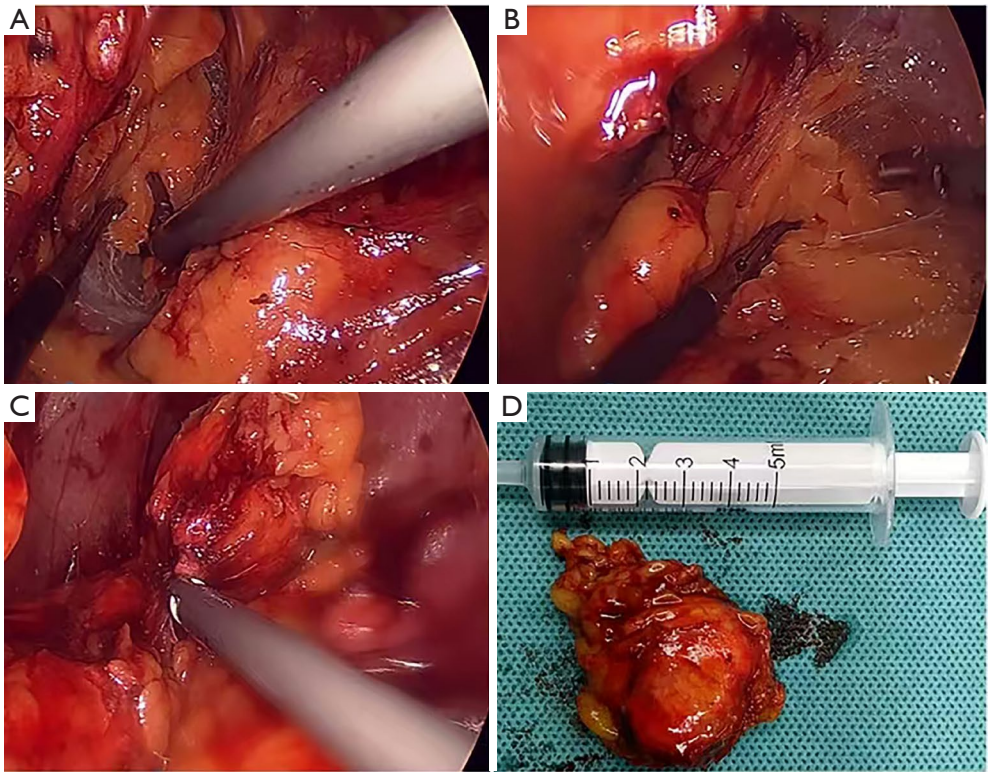

Figure 1 Surgical flowchart of laparoscopic resection of adrenal tumors. (A) The relative avascular space between the pararenal fat capsule over the kidney and the anterior layer was the first separated layer to expose the adrenal gland and adrenal tumor; (B) the relative avascular space was the second layer separated, and the lumbar large muscle was regarded as the anatomical landmark; (C) the layer between the upper surface of the renal pole and the bottom of the adrenal tumor was the third layer separated; (D) the removed adrenal gland and its size.

control group.

Intraoperative preparation

Retroperitoneal laparoscopic resection of adrenal tumors was conducted in the 4N-ERAS group without routine use of prophylactic antibiotics. No retroperitoneal drainage tube was left in place after surgery. The Foley catheter inserted intraoperatively was removed before the patient left the operation room. The surgical wound was closed with subcuticular sutures to resolve the need for postoperative suture removal. Local anesthesia with 1% lidocaine 10 mL was applied to the incision. A warming blanket was used during surgery. Retroperitoneal laparoscopic resection of adrenal tumors was conducted in the control group. A prophylactic dose of antibiotics was administered 30 minutes before surgery. A retroperitoneal drainage tube was left in place at the end of the surgery. A Foley catheter was placed when starting surgery and removed 2–4 days after surgery. The surgical wound was closed with standard sutures without administering local anesthesia, and the sutures were removed postoperatively. No warming blanket was used during surgery.

Anesthesia and surgical technique

Both groups underwent general anesthesia and endotracheal intubation. The same surgeon conducted all surgeries using the same approach and resection method: a three-port retroperitoneal approach was used to establish the surgical field. The adrenal tumor was resected using the three-layer dissection method (*Figure 1*): (I) in the first dissection layer, the relatively avascular space between the perirenal fat and the anterior layer of the renal fascia was separated, exposing the adrenal gland and tumor; (II) in the second dissection layer, the relatively avascular space between the perirenal fat sac and the posterior layer of the renal fascia was separated, using the psoas muscle as an anatomical landmark; (III) in the third level of dissection, the layer between the surface of the upper pole of the kidney and the base of the

adrenal tumor was separated, performing a partial or total adrenalectomy. The specimens were then collected and sent for pathological examination. Each layer of tissue was sutured in sequence and the incision was closed.

Postoperative preparation

In the 4N-ERAS group, patients returned to the ward without a retroperitoneal drainage tube and Foley catheter. The surgical wound was infiltrated with local anesthesia. Postoperative fluid replacement was limited to 500–1,000 mL. Patients were allowed to drink water 6 hours postoperatively. In addition, they were encouraged to ambulate 6 hours postoperatively. In the control group, patients were monitored for 24–48 hours postoperatively and the retroperitoneal drainage tube was removed when the drainage fluid was less than 20 mL. The Foley catheter was removed 24–48 hours after the surgery. The sutures were removed 5–7 days postoperatively. After the surgery, 1,000–2,000 mL fluid was given to patients. Patients were allowed to drink water 12 hours after the surgery and were encouraged to ambulate 12 hours postoperatively.

Observational indicators

We collected detailed records for all patients, including the time to first flatus, time to first ambulation, time to Foley catheter removal, time to retroperitoneal drainage tube removal, postoperative pain score, length of hospital stay, total hospitalization costs, and postoperative complications.

Statistical analysis

All statistical analyses were conducted using SPSS 25.0 software. Quantitative data were expressed as mean ± standard deviation. They were analyzed using Student's *t*-test. Categorical data were analyzed using Chi-squared test or Fisher's exact test. P values <0.05 were regarded as statistically significant.

Results

In total, 85 patients (42 in the 4N-ERAS group and 43 in the control group) were included in this study. The same experienced surgeon conducted all surgeries, using the same approach and resection method. The basic clinical data of the two groups showed no significant differences in terms of mean age (49.35±12.01 *vs.* 47.09±13.83 years; P=0.41). The mean BMI was 24.63±3.35 kg/m^2 in the 4N-ERAS group, showing no significant difference compared to the control group (P=0.08). In addition, there were no significant differences between the two groups in terms of surgical site, tumor type, tumor size, and tumor location (P>0.05). The clinical characteristics of patients are summarized in *Table 1*.

We compared the intraoperative and postoperative outcomes and complications of the two groups (*Table 2*). Compared to the control group, the 4N-ERAS group exhibited significantly shorter times to first flatus, first ambulation, Foley catheter removal, retroperitoneal drainage tube removal, and hospital stay (P<0.001). The total hospitalization costs were significantly lower in the 4N-ERAS group compared to the control group (P=0.03). The incidence of postoperative complications, including infectious complications, such as postoperative fever, wound infection, and pulmonary infection, were not significantly different between the two groups (P=0.19; *Table 3*). Postoperative pain scores [Numeric Rating Scale (NRS)] were significantly lower in the 4N-ERAS group compared to the control group (P<0.01; *Table 4*). All patients successfully underwent minimally invasive surgery with no major complications, no conversion to open surgery, and no mortality.

Discussion

Since Kehlet first introduced ERAS in the field of colorectal surgery in 1997, the ERAS protocol has been increasingly adopted in urologic surgery, including renal surgery, cystectomy, radical prostatectomy, and adrenalectomy (7-12). ERAS necessitates multidisciplinary team work, including cooperation between anesthesiologists, surgeons, and nurses, to reduce surgical stress, accelerate postoperative recovery, and prevent postoperative complications. Recent studies have shown that the ERAS protocol not only improves postoperative recovery and reduces patients' discomfort but also shortens the length of hospital stay, reduces hospital costs, improves patient satisfaction, and optimizes the use of medical resources.

There are few studies on the clinical application of the ERAS protocol in retroperitoneal laparoscopic resection of adrenal tumors (7-9). However, existing studies suggest that the ERAS protocol not only shortens postoperative hospital stays but also decreases total hospitalization costs, thereby reducing the financial burden on patients. We proposed the 4N approach to explore the feasibility of 4N-ERAS in retroperitoneal laparoscopic resection of adrenal tumors based on the principles of ERAS and our team's previous experience.

Table 2 Preoperative, intraoperative and postoperative management

Management stage	Control group (n=43)	4N-ERAS group (n=42)	P value
Pre-operative management			
4N-ERAS propaganda and education	No	Yes	NA
Bowel preparation	Yes	No	NA
Fasting before surgery (hours)	8	6	NA
Drinking before surgery (hours)	6	4	NA
Intraoperative management			
Surgical approach	Retroperitoneal approach (3-port)	Retroperitoneal approach (3-port)	NA
Prophylactic antibiotics	Yes	No	NA
Indwelling retroperitoneal drain tube	Yes	No	NA
Indwelling urinary catheter	Yes	No	NA
Intraoperative pressure antithrombotic therapy	No	Yes	NA
Postoperative management			
The first anal exhaust time after surgery (hours)	10.21±4.65	6.24±2.45	<0.001
The first leaving bedtime after surgery (hours)	13.32±6.65	8.35±4.81	<0.001
Retroperitoneal drainage tube removal (hours)	62.79±33.62	0	<0.001
Urinary catheter removal (hours)	22.32±20.98	0	<0.001
Length of hospital stay (days)	6.65±3.62	4.48±2.65	<0.001
Cost of hospitalization (thousand yuan)	23.2 (18.4–33.0)	20.6 (16.1–29.0)	0.03

Data are presented as mean ± standard deviation, n, or mean (range). One-way analysis of variance was used to analyze continuous variables. The Chi-squared test or Fisher's exact test was used for categorical variables. ERAS, enhanced recovery after surgery; NA, not applicable.

Table 3 Comparison of postoperative complications and inflammatory marks between the 4N-ERAS group and the control group

Results	Control group (n=43)	4N-ERAS group (n=42)	P value
Intraoperative prophylactic antibiotics for use	Yes	No	NA
Postoperative complications	11	6	0.19
Fever	3	2	
Infection of incisional wound	1	2	
Pulmonary infection	5	0	
Deep vein thrombosis in both lower limbs	1	2	
Others	1	0	
Inflammatory marker level before discharge			
White blood cell count (10^9/L)	9.09±2.72	9.21±3.05	0.85
C-reactive protein (mg/L)	22.34±36.58	16.48±14.47	0.34

Data are presented as mean ± standard deviation or n. ERAS, enhanced recovery after surgery; NA, not applicable.

Table 4 Postoperative pain scores (NRS) between the 4N-ERAS group and the control group

Results	Control group (n=43)	4N-ERAS group (n=42)	P value
Suturing method	Routine suture	Intradermic suture	NA
Stitches after surgery	Yes	No	NA
Local anesthetic was used during the intraoperative incision	Yes	No	NA
Postoperative incision pain score (NRS)	2.27±0.66	1.30±0.74	<0.01

Data are presented as mean ± standard deviation. ERAS, enhanced recovery after surgery; NA, not applicable; NRS, Numeric Rating Scale.

The 4N-ERAS concept encompasses the entire surgical process, from the pre-operative phase to the post-operative phase. Preoperatively, patients receive clear information and education about 4N-ERAS to control their anxiety and ensure patients' trust and cooperation. The 4N-ERAS protocol necessitates fasting for 6 hours and not drinking for 4 hours before surgery to avoid prolonged fasting, thereby preventing intraoperative hypoglycemia, insulin resistance, and fluctuations in blood pressure and reducing circulatory stimulation and intraoperative complications. In addition, preoperative bowel preparation is unnecessary, which can prevent fluid loss and rectal mucosal injury.

The 4N-ERAS protocol encourages patients to drink water and begin mobilizing 6 hours after surgery to promote gastrointestinal function recovery and prevent deep vein thrombosis in the lower extremities. Consistently, the 4N-ERAS group had significantly shorter times to first flatus (6.24±2.45 *vs.* 10.21±4.65 hours, P<0.001) and first ambulation (8.35±4.81 *vs.* 13.32±6.65 hours, P<0.001) compared to the control group. Intraoperatively, warming pads were used in the 4N-ERAS group to prevent hypothermia. They can affect the pharmacokinetics of drugs, prolong anesthetic recovery, increase myocardial oxygen consumption, and lead to arrhythmias and myocardial ischemia.

All of the 85 patients underwent anatomical laparoscopic resection of adrenal tumors through the retroperitoneal approach (13). Laparoscopic partial or total adrenalectomy was conducted based on the anatomical relationship between adrenal tumors and normal adrenal tissues and the qualitative diagnosis and classification of adrenal tumors.

Kosins *et al.* (14) indicated that omission of drainage tubes is safe and feasible in cesarean section, abdominal wounds, and hip and knee replacement. Lai *et al.* (15) reported that not using Foley catheters after lung cancer surgery is safe and feasible, lowering the risk of urinary tract infection but elevating the risk of urinary retention (8.3% *vs.* 5.8%, P=0.33). In our 4N-ERAS group, no retroperitoneal drainage tubes were placed after the surgery. We routinely conducted CT scans on the first postoperative day to assess the surgical field (*Figure 2*). In addition, the Foley catheter was removed immediately after surgery and patients were returned to the ward without a catheter. Compared to the control group, the 4N-ERAS group exhibited no increase in the risk of postoperative complications, such as wound infection, retroperitoneal infection, or urinary retention. The absence of a Foley catheter and retroperitoneal drainage tube helped early mobilization, expediting the recovery of gastrointestinal function and early flatus and bowel movements.

The volume of postoperative intravenous fluids was limited to 500–1,000 mL in the 4N-ERAS group, and patients were encouraged to drink water 6 hours after surgery. In this study, no antibiotics were administered in the 4N-ERAS group, and the risk of infectious complications did not increase compared to the control group. White blood cell count and the levels of inflammatory markers, such as C-reactive protein were checked before discharge, which exhibited no significant differences between the two groups. Subcuticular sutures were used for cosmetic closure in the 4N-ERAS group (*Figure 3*), resolving the need for suture removal. Local anesthesia was applied to the incision, significantly reducing postoperative pain scores (1.30±0.74 *vs.* 2.27±0.66, P<0.01).

Noba *et al.* (16) investigated the cost-benefit analysis, compliance, and clinical benefits of ERAS in pancreaticoduodenectomy. Ruiz *et al.* (17) assessed the impact of the ERAS protocol on colorectal cancer surgery outcomes. Their findings revealed that the protocol was associated with a significant reduction in postoperative infectious complications, including anastomotic dehiscence and surgical wound infections, as well as a shorter hospital stay. Moreover, the ERAS protocol demonstrated substantial cost-effectiveness, resulting in total savings of €37,673.44.

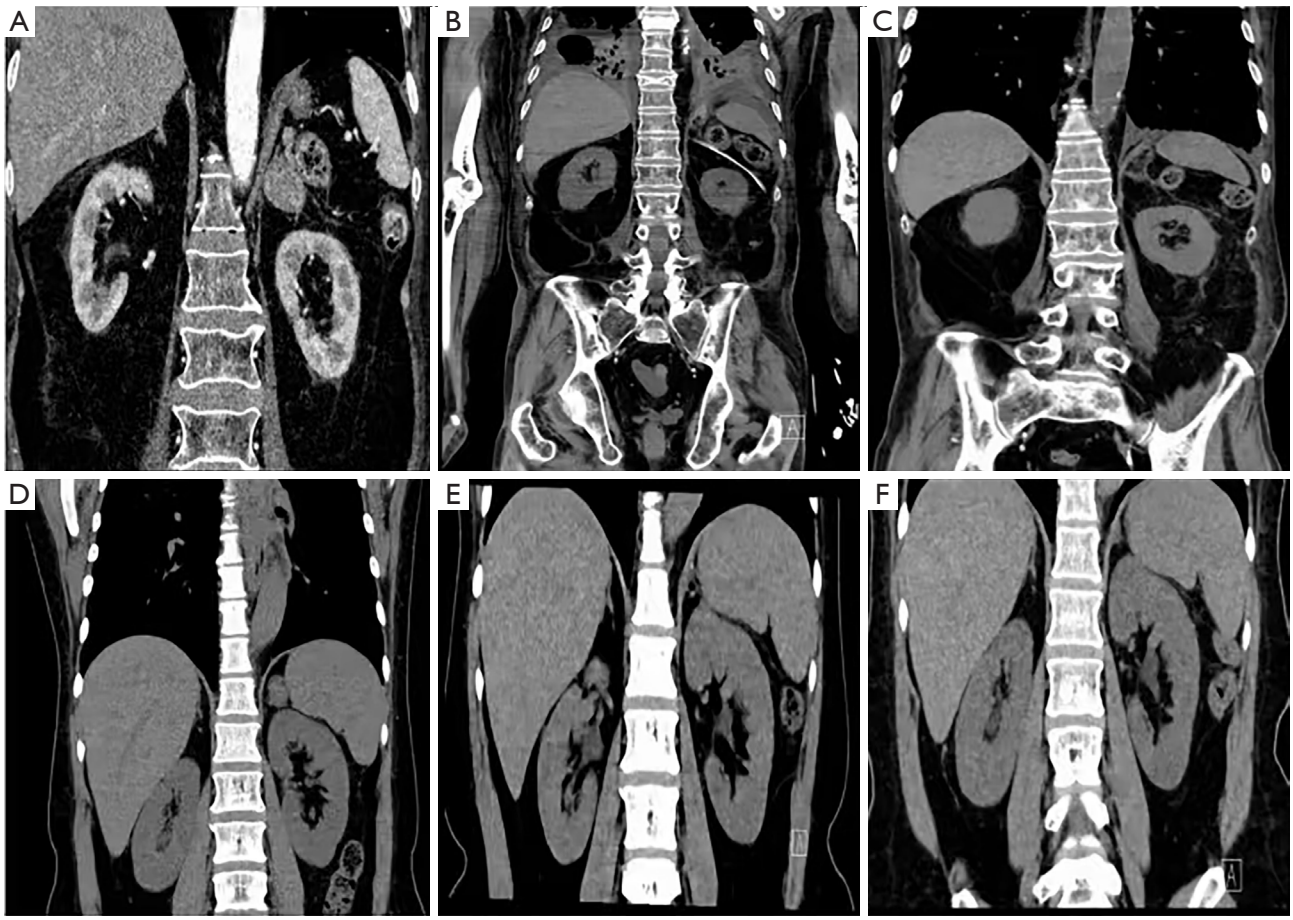

Figure 2 CT images before and after postoperative review of the control group (A-C) and the 4N-ERAS group (D-F). (A) CT image of adrenal glands, the location and size of the left adrenal tumor are shown; (B) adrenal CT images on the first day after surgery, showing no significant fluid accumulation after resecting the left adrenal tumor. The drainage tube is shown in this figure; (C) adrenal CT images at the third month after surgery, showing no abnormality in the surgical field after resecting the left adrenal tumor; (D) a CT image of the adrenal gland before surgery. The location and size of the left adrenal tumor are shown in this figure; (E) adrenal CT images on the first day after surgery, showing no fluid in the surgical field after resecting the left adrenal tumor (no drain); (F) review of adrenal CT images at the third month after surgery, showing the surgical field after resecting the left adrenal tumor with no abnormality. CT, computed tomography; ERAS, enhanced recovery after surgery.

However, there is limited data on the cost-effectiveness of the ERAS protocol in the laparoscopic resection of adrenal tumors in China (7-9). Yan *et al.* (7) reported that the ERAS protocol can reduce the use of disposable materials, drugs, and examination costs in laparoscopic adrenalectomy, saving an average of ¥8,326.00 per patient. The cost-effectiveness of the ERAS protocol encourages further application of ERAS in perioperative care.

Our study indicated that compared to the control group, the 4N-ERAS group had a shorter postoperative hospital stay (4.48±2.65 *vs.* 6.65±3.62 days, P<0.001) and lower total costs [¥20.6 (¥16.1–29.0) *vs.* ¥23.2 (¥18.4–33.0), P=0.03], reducing the financial burden on patients and demonstrating cost-effectiveness. Studies have shown that postoperative complications significantly affect surgical costs, especially in high-risk surgeries, where the severity of complications greatly increases the total cost (7,18). In our study, postoperative complications were mild in both groups, with no intensive care unit (ICU) admissions or deaths.

Figure 3 In the 4N-ERAS group, the incision was closed with local anesthesia, achieving the "no pain" state of the incision after surgery. ERAS, enhanced recovery after surgery.

Conclusions

The 4N-ERAS protocol for retroperitoneal laparoscopic resection of adrenal tumors is safe and feasible, improves perioperative outcomes, and reduces pain and cost. However, there are several limitations in this study. First, it was a retrospective study with a few patients; thus, further prospective randomized controlled trials are needed to assess clinical outcomes. Second, patients with different types of functional adrenal tumors were included in this study, which may differently affect preoperative preparation, postoperative recovery, and costs. Third, there are still challenges in the clinical application of 4N-ERAS, such as standardized implementation of postoperative recovery plans, optimization of 4N-ERAS strategies, and individualized perioperative management strategies. Future multicenter prospective studies are needed to validate the

safety and superiority of this system, encourage its clinical application, improve patients' outcomes, and save medical resources.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tau.amegroups.com/article/view/10.21037/tau-24-608/rc

Data Sharing Statement: Available at https://tau.amegroups.com/article/view/10.21037/tau-24-608/dss

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tau.amegroups.com/article/view/10.21037/tau-24-608/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work, ensuring that any questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by The University of Hong Kong-Shenzhen Hospital Research Ethics Committee (No. [2024]225), and informed consent was obtained from all patients.

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