

Original Article

Fast track surgery vs. conventional management in the perioperative care of retroperitoneal laparoscopic adrenalectomy

Chaopeng Tang, Zhenyu Xu, Xiaoming Yi, Ping Li, Haowei He, Zhengyu Zhang, Tianyi Shen, Xiang Liu, Yulin Zhou, Wenquan Zhou

Department of Urology, Jinling Hospital, Medical School of Nanjing University, 305# East Zhongshan Road, Nanjing 210002, China

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Abstract: Objective: It has been demonstrated that fast track (FT) surgery can accelerate the recovery of the patients in limited urologic procedures, but there are no reports regarding FT surgery within retroperitoneal laparoscopic adrenalectomy (RLA). This study aims at evaluating the impact of FT surgery on recovery after RLA. Methods: One hundred patients in our centre are randomly assigned to FT group and conventional group. The patients who have undergone RLA receive either conventional care or an FT recovery program. Surgical outcome, complications, gastrointestinal function, visual analogue scale (VAS) general state and VAS pain scores are compared between the two groups. In addition, white blood cell count, serum interleukin-6 and C-reactive protein levels are measured. Patients are discharged home when they meet discharge criteria. Results: Compared with the conventional group, the time of first flatus (18.97 ± 8.45 vs. 37.66 ± 17.17 h), initiation of normal diet (18.76 ± 4.94 vs. 53.15 ± 15.99 h), the time of first ambulation (19.64 ± 6.23 vs. 51.89 ± 18.19 h), length of post-operation hospital stay (2.35 ± 0.87 vs. 5.23 ± 1.62 d), duration of drainage (18.19 ± 5.19 vs. 68.10 ± 18.06 h) and catheter (17.19 ± 4.49 vs. 60.83 ± 25.53 h) are markedly shorter in FT group ($P < 0.01$). Post-operative coughing pain scores at 2 h (1.00 ± 0.61 vs. 1.42 ± 1.18), 12 h (0.96 ± 0.78 vs. 2.00 ± 1.40), 24 h (1.10 ± 0.97 vs. 4.22 ± 1.53) and resting pain scores at 12 h (0.64 ± 0.56 vs. 1.44 ± 0.91), 24 h (0.66 ± 0.63 vs. 1.22 ± 0.86) are consistently lower in the FT group. The level of CRP, IL-6 at 2 h and 24 h post-operation are lower than that of control group, and white blood cell count is lower than conventional group at 24 h after surgery ($P < 0.01$). FT patients have a overall higher level of post-operative VAS general state than conventional groups ($P < 0.01$). Age, sex, tumor size and side, BMI, ASA score, operation time, blood loss and complications are similar in both groups. Conclusions: FT surgery within RLA shortens the length of post-operative hospital stay without increasing the postoperative complication, lowers patients' VAS pain scores, and reduces inflammatory response intensity and improves the general state. Therefore, FT can be applied feasibly and safely in RLA.

Keywords: Fast track surgery, retroperitoneal laparoscopic adrenalectomy, urology, VAS pain scores, perioperative care

Introduction

Since the first successful laparoscopic adrenalectomy (LA) was performed by Michel Gagner and his colleagues in 1992 [1], subsequent studies have demonstrated the safety and advantages of LA over open approaches. LA, having now been proved to be associated with less morbidity, shorter hospital stay and earlier return to normal activity, has become the primary choice for the surgical management of many adrenal tumors. With clear benefits to the patients, some factors that preclude earlier discharge still exist, including major organ-system

dysfunction (i.e., atelectasis, ileus), postoperative pain, nausea, and generalized fatigue [2, 3].

In order to help improve postoperative outcomes and minimize morbidity of this procedure, the so-called FT concepts or enhanced recovery after surgery (ERAS) programs have been increasingly implemented into clinical practice in recent years. FT combines modern concepts of immediate postoperative feeding and ambulation as well as the use of well-tolerated surgical techniques and avoidance of drains, tubes and catheters to reduce patients'

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Table 1. Patient's descriptive data

	FT group	Conventional group	t/x ² /z	P value
Age (years)	49.34±10.18	47.70±10.95	0.776	0.440
Sex			0.040	0.841
Male	26	25		
Female	24	25		
BMI	21.73±4.13	22.77±4.00	-1.286	0.202
Tumor size (cm)	2.42±1.21	2.39±1.02	0.116	0.908
Tumor side			0.160	0.689
Right	27	25		
Left	23	25		
ASA score			-0.366	0.714
I	37	35		
II	11	14		
III	2	1		
Indications			-0.184	0.854
Aldosteronism	9	7		
Cushing's syndrome	3	4		
Pheochromocytoma	4	7		
Incidentaloma	34	32		
Histology			-1.090	0.276
Adenoma	36	31		
Aldosteronoma	3	4		
Pheochromocytoma	4	5		
Hyperplasia	5	6		
Myelolipoma	2	4		

perioperative stress response leading to reduced postoperative complication rates and length of hospital stay [4]. The implementation of FT surgery management has improved postoperative recovery in a variety of urologic surgical procedures [2, 5, 6]. However, similar perioperative protocols have not been evaluated in patients undergoing RLA. This study, therefore, aims at evaluating the effects of RLA within the FT surgery rehabilitation program.

Patients and methods

The study is approved by the Ethics Committee of Jinling Hospital, Medical School of Nanjing University, Nanjing, China. Written informed consent is obtained from all patients.

From December 2012 to December 2013, 100 patients undergoing RLA are randomly assigned by a computer-generated random-number sequence to receive either conventional perioperative management or a perioperative FT surgery management (50 patients per group). The patients' descriptive data are listed in **Table 1**.

FT surgery management includes preoperative, intra-operative and post-operative protocols, while patients in the conventional group are treated by an established standard procedure. The surgery is performed by a single surgeon at a single hospital.

The inclusion criteria are as follows: adrenal tumor <6 cm in diameter; no history of extensive operation on abdominal; American Society of Anesthesiology (ASA) score: degree I-III; no active gastrointestinal bleeding or peptic ulceration; and self-care function prior to hospitalization.

Exclusion criteria for study participation are as follows: having clinically significant cardiac, pulmonary, hepatic, or renal disease; abnormal renal function; extensive previous abdominal surgery; ASA score: degree IV; and refusal to participate in the study.

Criteria for hospital discharge include tolerance of regular diet, no pain in ambulation; and universal agreement with discharge

from hospital by medical assessment team, the patient and the family. In addition, drains and catheter are removed before discharge if not otherwise contraindicated. After discharge, patients return to outpatient setting for regular physical examination (including wound check, appetite) with their presentation of interval history.

Patients with pheochromocytoma receive phenoxybenzamine for periods up to 2 weeks and also require volume repletion three days before surgery to avoid post-operative hypotension. Patients with aldosteronoma are treated with potassium-sparing diuretics and potassium supplementation to keep their serum potassium >3.5 mmol/l. Patients with Cushing's disease require correction of electrolyte abnormalities and hyperglycemia prior to surgery.

Preoperative preparation

The protocol for the FT program includes preoperative patient education about FT surgery

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management, no bowel preparation, pre-operative liquids containing carbohydrates only until 2 h and solid food 6 h before operation. The traditional care program includes a routine bowel preparation with soapsuds, pre-operative fast solid food before 12 h and liquid food before 6 h.

Intraoperative preparation

General anesthesia and Foley catheter are used in all cases.

FT group: a F12 drain is placed in all cases, the skin wound is closed in a subcuticular (3-0 monocryl), intravenous fluid restricted to <30 ml/kg in order to avoid fluid overload.

Conventional group: a F28 drain is placed in all cases, the skin wound is closed with non-resorbable silk thread (3-0), and intravenous fluid ≥ 3000 ml.

Postoperative preparation

FT group: 40 mg parecoxib sodium (prizer) IV injection is administered immediately after surgery, then 20 mg parecoxib sodium parecoxib sodium (prizer) IV injection is administered at 12 h and 24 h after surgery. Postoperative feeding is served according to the patients' appetite. Patients are encouraged to ambulate as soon as possible after surgery. On day 1, the Foley catheter and drain are removed. Fluid infusion is withdrawn as soon as the patient is able to take oral nutrition.

Conventional group: Analgesia is not routinely administered, but if patient can't tolerate the pain, 40 mg parecoxib sodium (Prizer) IV injection is administered as a rescue medication. Oral intake is allowed after passage of gas. The drain is removed if the total drainage fluid is less than 10 ml in 24 h. The Foley catheter is removed when patients begin to take off-bed activities. Stitches are taken out in 7 days after surgery. The intravenous drip is stopped when patients meet the same criteria in FT group.

Surgical method

Patients are administered general anesthesia via tracheal intubation and are placed in a lateral position in order to elevate the kidney. A 1.5 cm mid-axillary line incision is made at two transverse fingers above the crista iliaca. A

10-mm trocar puncture is directed through the incision, pushing the peritoneum ventrally. A lactoprene balloon is placed, injected with 300 ml air (maintained 3 min), and then removed. Then, a laparoscope is inserted through the trocar, and the retroperitoneum is opened under direct vision. CO₂ is injected into the retroperitoneum to establish a retroperitoneal space (air pressure: 12 to 15 mmHg), then the 5-mm and 10-mm trocars are inserted in the subcostal incision on the anterior and posterior axillary lines, respectively. Then the corresponding surgical instruments are placed. In the pneumoperitoneum, the retroperitoneal fat should be pushed down and an incision made in the Gerota's fascia anterior to the psoas muscle to the diaphragm. Once the adrenal gland is exposed, adrenal vessels are identified, clipped, and divided. After resection, the specimen is placed into an extraction bag. Lastly, one drainage tube is inserted and the trocar sites are closed.

Clinical parameters

Tumor size is evaluated in cm using the widest dimensions from preoperative computed tomography (CT) or magnetic resonance imaging (MRI). The operative time is calculated from the initial skin incision until the skin closure. Estimated blood loss is measured from that collected in the suction device. The length of post-operative hospital stay is calculated from the day of operation (as day 0) to the day of hospital discharge. General and surgical complications are recorded.

Pain evaluation

The intensity of resting pain and coughing pain is assessed on the inpatient ward using a 10-point verbal analog scale (VAS), with 0= none to 10= maximal, at 2 h, 12 h and 24 h after surgery respectively. The interviewer is a member of the research team who is blinded to the patient's group assignment. The need for rescue analgesics is evaluated at the same time intervals by a personal interview.

VAS general state

The level of general state is evaluated using a 10-point VAS, with 0= very bad to 10= very satisfactory, on the pre-operative day, POD1 and POD2 respectively.

Table 2. Clinical parameters of outcome in the two groups

	FT group	Conventional group	t/	P value
Operation time (min)	30.22±10.18	30.14±9.50	0.041	0.968
Blood loss (ml)	21.22±14.78	20.00±12.81	0.441	0.660
Time of first flatus (h)	18.97±8.45	37.66±17.17	-6.907	0.000
Initiation of normal diet (h)	18.76±4.94	53.15±15.99	-14.582	0.000
Time of first ambulation (h)	19.64±6.23	51.89±18.195	-11.860	0.000
Duration of catheter (h)	17.19±4.49	60.83±25.53	-11.903	0.000
Duration of drainage (h)	18.19±5.19	68.10±18.06	-18.785	0.000
Length of hospital stay post-operation (days)	2.35±0.87	5.23±1.62	-11.081	0.000
Complication			1.0840	0.2978
Peritoneal injury	3 (6%)	2 (4%)		
Abdominal distension	3 (8%)	6 (12%)		
Vomiting	1 (2%)	3 (6%)		

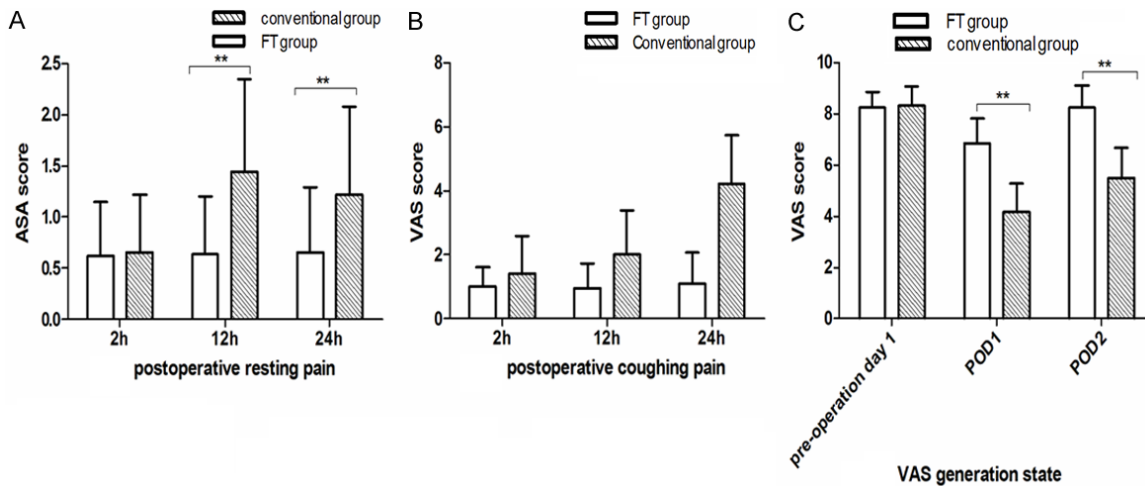


Figure 1. Pain score at different stages of operation. A: Resting pain score; B: Coughing pain score; C: General pain score.

Inflammatory parameters

Peripheral venous blood samples (about 4~5 ml) are drawn from the patients at 2 h, 12 h and 24 h respectively, 2 ml is measured for white blood cell count by an integrated system of automated analysis in cellular hematology (Sysmex HST-302, Japan), 3 ml subsequently centrifuged at 300×g for 15 min at 4°C, the serum samples are subsequently stored at -80°C until assayed for IL-6 and CRP. Circulating serum interleukin (IL)-6 levels are determined using a sandwich enzyme-linked immunosorbent assay (Tecan, Salzburg, Austria), as described by the manufacturer. C-reactive protein (CRP) is measured using an immunoturbidimetric method (Olympus, Tokyo, Japan).

Follow-up

Patients are reexamined at 1, 3, 6, and 12 months after surgery. Then, all cases are required to recheck once a year. The examination index includes clinical symptoms, routine blood, plasma adrenal hormone, plasma electrolytes and urine tests, chest radiograph and abdomen B ultrasonography and CT examination. Every patient after discharge is instructed for immediate consultation in case of pain, fever or any kind of clinical abnormality (e.g. vomiting, fatigue).

Statistical analysis

SPSS version 19.0 software is used for all statistical analyses. Data are expressed as mean

Table 3. Inflammatory parameters

	24 h before surgery	2 h after surgery	24 h after surgery
IL-6 (ng/L)			
FT group	5.84±0.74	74.11±13.13**	100.73±16.97**
Conventional group	5.59±0.93	89.94±13.97	135.91±22.19
WBC (×10 ⁹)			
FT group	5.92±1.26	12.23±3.17	8.80±2.11**
Conventional group	5.86±1.43	12.15±3.27	10.51±3.05
CRP (mg/L)			
FT group	0.63±0.47	3.58±2.21**	28.48±17.65**
Conventional group	0.64±0.37	14.14±9.50	50.88±24.45

**P<0.01.

± SD. Chi-square tests and Student's t tests are used for assessing differences between groups in categorical and continuous variables, respectively. Ordinal data are compared by the Mann-whitney rank-sum test. ANOVA is used to evaluate repeated measure data. P<0.05 is considered significant.

Results

The relevant patient characteristics are shown in **Table 1**, and no significant differences between the two groups exist with respect to age, gender, body mass index (BMI), ASA classification, tumor size and side.

All patients are successfully operated without conversion to open surgery. As shown in **Table 2**, the operative time, and estimated blood loss are similar in the two groups (P>0.05).

As compared with the conventional group, the time of first flatus, time of first ambulation, initiation of normal diet are markedly shortened in the FT group (P<0.01), so are duration of drainage, duration of catheter and length of post-operation hospital stay (P<0.01). There is no significant difference in the post-operative gastrointestinal complications (abdominal distension and vomiting). In the conventional group, there are 6 patients with abdominal distension, 3 patients with vomiting after surgery. In the FT group there are 4 patients with abdominal distension, 1 patient with vomiting. The reaction is relieved after symptomatic treatment and encouraged ambulation.

There are no pain complaints before surgery from the two groups. There is no significant dif-

ference with regard to resting pain between the two groups at 2 h after surgery (P>0.05), while the level of resting pain is lower than conventional group at 12 h and 24 h after surgery (P<0.01) (**Figure 1A**). FT group has a lower overall level of coughing pain at 2 h, 12 h and 24 h postoperatively (P<0.05) (**Figure 1B**). 5 patients in the conventional group cannot tolerate the pain after operation, thus 40 mg parecoxib sodium (Prizer) is intended as a rescue medication.

Concerning the VAS general state (**Figure 1C**), there are no significant differences between the two groups before operation. However, patients of the FT group have higher average levels in general state on POD1 and POD2 (P<0.05).

There are no significant differences in the pre-operative level of WBC, CRP and IL-6 between the FT group and conventional group (P>0.05). The post-operative levels of WBC, CRP and IL-6 are significantly higher in the patients of both two groups compared with the pre-operative conditions (**Table 3**). The levels of CRP, IL-6 at 2 h, 24 h after operation in the FT group are significantly lower than those in the conventional group (P<0.01). White blood cell count is lower than conventional group at 24 h after surgery (P<0.01), while the level of WBC at 2 h post-operative does not differ significantly (P>0.05).

Discussion

Since its first description in 1992, LA has replaced open adrenalectomy as the standard procedure for the treatment of most adrenal tumors. The benefits of this technique include decreased blood loss, less patient morbidity, shorter hospitalization, faster recovery, and cost-effectiveness when compared with open surgery [7]. However, surgical procedures inevitably disturb the physical integrity and cause a postoperative stress response of variable degrees depending on a number of factors, such as type of the surgical procedure, intra-operative complications, blood loss, length of procedure, and others [8]. The concept of FT surgery has recently aroused more interest. The FT surgical management mainly consists of modification of pain management, early ambu-

lation, and perioperative stimulation of intestinal function with the goal to shorten the convalescence phase. Previous studies have shown the beneficial effects of FT concepts for urologic procedures [6, 9], such as enhancing recovery, reducing complications, and shortening the length of hospital stay, but FT has not yet been applied in patients undergoing retroperitoneal laparoscopic adrenalectomy. For this reason, the main objective of this study is to determine whether FT within RLA can accelerate rehabilitation.

By now, mechanical bowel preparation (MBP) has been a standard procedure before RLA in China. However, MBP has been questioned during retroperitoneal laparoscopic surgery for the reason that such surgery has little impact on intestinal function. The disadvantages of MBP are patient discomfort, such as nausea, swelling, bloating, dehydration and electrolyte disturbances, and a higher social cost of the drugs for the treatment. In this study patients in the FT group undergo no bowel preparation, whereas the time of first flatus is shorter than conventional group.

Long time preoperative fasting can aggravate the psychological burden of patients and that the lack of energy consumption can produce post-operative insulin resistance [10]. It has been demonstrated that oral rehydration therapy until 2 h before surgery is safe and feasible in the low-risk surgical population [11]. Oral rehydration therapy can keep the balance of water and electrolytes in the body and to improve the patient's comfort. Therefore, patients in the FT group undergo 6 h of fasting and 2 h of water deprivation before surgery, whereas patients in the conventional group fast solid food 12 h and liquid food 6 h before surgery respectively.

Forced early feeding is usually initiated on the day of operation or the day after the operation in FT postoperative management, although its safety and feasibility have been demonstrated [6, 12, 13]. Enforced feeding may be difficult and unpleasant for patients without sufficient recovery of their appetite after the operation. Kawamura, Yutaka, et al. [14], find that appetite is one of the important vital signs that indicate recovery from surgical stress. Therefore, it is rational to start postoperative feeding

according to patients' appetite. In this study, water is allowed immediately after the operation for patients in FT group, a normal diet is served when they feel hungry. We find that most patients start normal diet on POD1. However, postoperative gastrointestinal complications including abdominal distension and vomiting are similar between the two groups, the reactions are relieved after symptomatic treatment and encouraged ambulation.

In this study, mean length of hospital stay after operation of RLA is reduced from 5.23 days to 2.35 days with an FT rehabilitation program, but an overall higher level of VAS general state compared with the conventional group. What is to be explained is that patients discharged home are arranged fully according to the criteria for hospital discharge. So there is no readmission in this study. This may be useful not only for the patients and their family but also for the increase of cost effectiveness. Our concern goes not only to patients' condition in hospital, but also to their condition after discharge to home. During follow-up, there are no postoperative hemorrhage, wound infection and no local recurrence or distant metastasis.

We provide sufficient information about the importance of postoperative ambulation pre-surgery for both two groups and encourage patients in FT group to make early postoperative ambulation, while we give patients in conventional group options to decide their off-bed time. It is seen from the result that the time of first ambulation for patients in FT group is earlier than patients in conventional group. FT patients have an overall shorter time of first flatus compared with the patients receiving conventional care. Early ambulation is believed to play a crucial part in the recovery of bowel function.

NSAIDs have become more popular in the management of pain associated with ambulatory surgery and proved to be safe in minimally invasive surgery [8, 15]. Early ambulation can only be achieved with sufficient pain management. RLA is a minimally invasive procedure (only 3 trocars sites) with fewer pain scores, so we choose Cox-2 inhibitor parecoxib as an analgetic other than opioid drugs which are known to cause nausea, vomiting, constipation, intestinal inactivity and urinary retention. We demonstrate the adequacy of postoperative pain con-

trol with Cox-2 inhibitor in FT group. Although the mean pain level is low to mid in conventional group, 7 patients cannot tolerate the post-operation pain. Pain relief after parecoxib sodium is intended as a rescue medication.

The inflammatory response may obviously be important for wound healing and resistance to infection, but on the other hand it may have undesirable effects by enhancing pain and leading to fatigue and sleep disturbances [16]. There are some techniques to reduce inflammatory responses, such as glucocorticoids, minimal invasive surgery and FT concept [17]. It is well established that minimal invasive surgery combined with FT surgery can reduce inflammatory responses [18]. It is found in our study that the post-operative levels of IL-6 and CRP in the FT group are significantly lower than those in the conventional group, demonstrating that RLA combined with FT surgery is less traumatic to patients. We ascribe reduced inflammation responses to the combined efforts, including laparoscopic surgery, no bowel preparation, short time starvation, adequate pain control, early enteral nutrition, and early ambulation etc.

Intravenous fluid therapy is an integral component of perioperative care in FT protocol. Perioperative fluid management traditionally has been liberal, but it is well established that either hypovolaemia or fluid excess post-operative may have detrimental effects on the cardiopulmonary system, tissue oxygenation and wound healing, postoperative ileus, renal function, and coagulation [19]. It has demonstrated that a pronounced reduction of morbidity and hospital stay in major abdominal surgery is observed by the so-called “goal-directed fluid therapy” or fluid restriction [19-21], but principles of perioperative fluid management within the concept of FT surgery are inconclusive, especially in urologic surgery. Kathrine Holte [19], recommended that fluids be controlled, with no more than 1 to 1.5 L of fluids applied in FT surgery, and intravenous fluid be administered in the least possible way for patients in FT group. Fluid balance can be adjusted by oral rehydration solution. That is why we encourage patients early enteral nutrition according to their appetite.

Conclusions

Patients undergoing RLA within the FT surgery rehabilitation program are discharged home

earlier with fewer complications and an overall higher satisfaction VAS of general state, earlier gastrointestinal function recovery, less postoperative pain, less intense inflammatory reactions compared with patients with conventional peri-operative care.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Wenquan Zhou, Department of Urology, Jinling Hospital, Medical School of Nanjing University, 305# East Zhongshan Road, Nanjing 210002, China. E-mail: wenquanvic@126.com

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