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A Comparative Study of Fast-Track Versus Conventional Surgery in Patients Undergoing Laparoscopic Radical Cystectomy and Ileal Conduit Diversion: Chinese Experience

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Fast-track surgery (FTS), which combines various techniques with evidence-based adjustments, is aimed to reduce postoperative morbidity, attenuate surgical stress response, thereby accelerating recovery and shortening length of stay. To further investigate the effectiveness of fast-track surgery, we compared the short-term outcomes of laparoscopic radical cystectomy and ileal conduit diversion for Chinese bladder cancer patients with FTS or with CS in our hospital. Patients with bladder cancer were included and divided into two consecutive groups: CS group and FTS group. Duration to first flatus and regular diet, postoperative hospital days, hospital expense, incidence of complications and postoperative surgical stress response were compared. There was no significant difference between the two groups in age, sex, BMI and postoperative TNM classification. Compared with the CS group, the FTS group had significantly shorter duration to first flatus, time to regular diet, postoperative hospital days and hospital expense, less complications, lower white blood count (WBC) and serum of C-reactive protein (CRP) on postoperative day 5 and 7. Our study indicates that FTS program is safe and efficacious for Chinese patients undergoing laparoscopic radical cystectomy and ileal conduit diversion. It can accelerate recovery, reduce stress action, shorten postoperative hospital days and reduce hospital expenses.

Bladder cancer is the second most frequent tumor of the genitourinary tract in Chinese adults. Radical cystectomy, which is usually followed by some form of intestinal urinary reconstruction, is recognized as the standard treatment for muscle-infiltrating bladder cancer and even high-risk, recurrent, non-invasive bladder cancer. With the widespread use of laparoscopic technique, laparoscopic radical cystectomy and intestinal urinary reconstruction is becoming more and more common.

Radical cystectomy with intestinal urinary reconstruction is thought to be a major operative procedure with potential for substantial morbidity and mortality¹⁻⁵. The incidence of the disease is still increasing and most of the patients with bladder cancer are elderly people, which means comorbid conditions is common⁶⁻⁹. Thus it is important for us to improve the perioperative management and reduce the morbidity of the procedure.

Fast-track surgery (FTS), also known as enhanced recovery after surgery, was first introduced by Kehlet in colorectal surgical practice¹⁰. It combines various techniques with evidence-based adjustments, for example, surgical, nursing, and preoperative, intraoperative and postoperative management to reduce postoperative morbidity, attenuate surgical stress response, thereby accelerating recovery and shortening length of stay. It has successfully been applied in hepatobiliary, vascular and colorectal operations¹¹⁻¹⁵. Besides, it has been showed to be effective in urologic operations, including radical cystectomy, radical prostatectomy and open partial nephrectomy in western populations¹⁶⁻¹⁹.

In our department, ileal conduit diversion is the main form of intestinal urinary reconstruction. To further investigate the effectiveness of fast-track surgery, we compared the short-term outcomes of laparoscopic radical cystectomy and ileal conduit diversion for Chinese bladder cancer patients with FTS or with CS in our department.



Result

The perioperative management was successfully carried out in two groups. There was no perioperative mortality or reoperation in the study. Demographic data of the two groups, i.e., FTS group and CS group is listed in Table 1. There were no significant difference between the two groups in age, sex, BMI and postoperative TNM classification (all $P > 0.05$). There were also no significant difference in estimated blood loss between the two groups ($P > 0.05$).

There were significantly more overall complications in the CS group than in the FTS group (17 versus 5, $P < 0.05$). All complications in two groups were minor complications (defined as Clavien grade 1 or 2) and all complications belonged to early complications (within 90 days after surgery). There were no major complications (Clavien grade 3 or higher).

Table 2 and 3 showed results related with operative outcomes. Compared with the CS group, the patients in the FTS group were discharged from hospital significantly earlier ($P < 0.05$). Duration time to first flatus, time to regular diet and hospital expenses were significantly shorter in the FTS group than the CS group (all $P < 0.05$).

White blood cell (WBC) counts and the levels of serum C-reactive protein (CRP), which reflect the surgical stress response, were measured. There were no significant difference in preoperative WBC count and level of serum CRP ($P > 0.05$). In POD 1, 3, there were no significant difference in two groups ($P > 0.05$). In POD 5 and 7, the mean \pm standard levels of WBC and CRP in the FTS group was significantly lower than the CS group (all $P < 0.05$).

Discussion

Perioperative management is of great importance and can bring beneficial effect including reduction in LOS, cost containment and improvement in quality of care. Radical cystectomy with intestinal urinary reconstruction is recognized as a major operative procedure with potential for substantial morbidity and mortality^{1–5}. In this case, perioperative management is a crucial factor for patients' total recovery. The FTS program has gained its popularity in hepatobiliary, vascular, colorectal and urologic operations^{11–19}. However, to date, application to radical cystectomy with intestinal urinary reconstruction is still limited, especially in laparoscopic radical cystectomy and ileal conduit diversion. In this study, we compared the short-term outcomes of laparoscopic radical cystectomy and ileal conduit diversion for Chinese bladder cancer patients with FTS or with CS in our hospital. The results indicated that the application of FTS program in patients undergoing laparoscopic radical cystectomy and ileal conduit diversion accelerated postoperative recovery with less complications and shortened postoperative days.

In the CS program, operation and medication are valued. However, in the FTS program, education plays a very important role. It is essential for patients to understand the diagnosis of the disease, knowledge regarding the operation, every detailed phase of the FTS program and the potential complications. This will help patients relieve their stress and better cooperate with doctors and nurses.

Traditionally, mechanical bowel preparation combined with medication and long-time fast has been routinely used in patients undergoing radical cystectomy and intestinal urinary diversion. However, the result of one study indicated that mechanical bowel preparation did not show beneficial effect²⁰. On the contrary, mechanical bowel preparation will increase the burden of patients, causing potential bad effects. In the FTS group, one-day bowel preparation program was introduced. Our result showed that in the FTS group postoperative complications did not increase while patients had a shorter duration to first flatus compared with that in the CS group.

Pain control is of great importance in perioperative management. Good pain control will not only relieve patient's stress, but also increase their satisfaction. It has been reported that opium analgesics have the potential to lead to nausea, fatigue and vomiting²¹. Therefore, celecoxib was used in the FTS group instead of opium analgesics.

In the FTS group, postoperative fluid infusion was contained. Too much fluid will delay the return of the function of bowel and increase the risk of heart failure. Under the premise of maintaining stable vital signs, reducing amount of fluid will not only relieve patient's pain, but also lower costs.

Postoperative stress response is an important factor for delayed recovery and affected organ function. Several measures were adopted to minimize the stress response, for example, the use of metoclopramide and celecoxib in the FTS group. We can evaluate the level of postoperative stress response by measuring WBC counts and CRP levels in the plasma. Our result showed that in POD 5 and 7, WBC count and CRP level in the FTS group was significantly lower than that in the CS group. This evidence indicated that patients in the FTS group had a quicker recovery.

Nausea and vomiting are common complications and preventing them effectively is important for early institution of an oral diet. The use of metoclopramide seemed to reduce rates of nausea and vomiting²². In our study, only 3 patients had nausea or vomiting in the FTS group. Using metoclopramide laid a solid foundation for early institution of an oral diet.

Early ambulation is an important step in the FTS program. Early ambulation can decrease the incidence of pulmonary and coagulation complications, enhance the recovery of bowel function, thus accelerate recovery. Most patients were elderly people who are afraid of ambulation. So it is especially important to encourage patients to mobilize out of bed as early as possible. In the FTS group, no patients had pneumonia or deep venous thrombosis (DVT). While in the CS group, 2 patients had pneumonia and 1 patient had DVT.

An early institution of oral diet is the most important component of the FTS program. Traditionally, patients undergoing laparoscopic radical cystectomy and intestinal urinary reconstruction were only allowed to consume liquid after flatus passed. However, in the FTS program, early institution of oral diet is encouraged. It has been reported that early institution of oral diet will stimulate bowel movement and enhance the recovery of bowel function²³. We found that early institution of oral diet has been successfully applied in our patients except those with nausea and vomiting. Besides, ileus and gastrointestinal dysfunction were not encountered. Based on the findings that gum-chewing can stimulate bowel movement and decrease the incidence of paralytic ileus after gastrointestinal surgery, we told patients to chew gum in POD 1^{24–25}. Gum-chewing is believed to enhance the recovery of bowel function through neurohumoral reflexes²⁴. It is a safe and inexpensive way. In POD 2, patients drunk clear liquids and in POD 4, regular diet was allowed to consume. Early institution of oral diet can meet patients' desire to eat, reduce the use of fluid infusion and most importantly, shorten patients' postoperative hospital days.

In the FTS group, time to first flatus was shorter than that in the CS group. In addition, our study shows a tendency to reduction in postoperative hospital days in the FTS group. By shortening post-

Table 1 | Demographic and clinical data of the patient cohort

	FTS group (n=60)	CS group (n=55)	P value
Male/female	53/7	49/6	0.898
Age(years)*	60.32 \pm 8.59(40–79)	59.95 \pm 8.86(40–78)	0.820
Mean BMI	23.63 \pm 2.2	23.49 \pm 2.05	0.717
TNM classification			
$T_2N_0M_0$	26(43.3%)	24(43.6%)	0.948
$T_3N_0M_0$	24(40.0%)	23(41.8%)	
$T_3N_1M_0$	10(16.7%)	8(14.5%)	

*Mean \pm SD(range); FTS: fast-track surgery, CS: conventional surgery; BMI: body mass index (calculated as Kg/m^2).



Table 2 | Operative details and outcomes

	FTS group(n=60)	CS group(n=55)	P value
EBL (ml)	204.5 ± 63.47	203.45 ± 71.83	P=0.934
Duration to first flatus (d)	2.92 ± 0.83	3.75 ± 0.78	P=0.000
Duration to regular diet (d)	4.43 ± 0.83	6.84 ± 0.92	P=0.000
Postoperative hospital days(d)	6.9 ± 1.1	10.0 ± 1.5	P<0.001
Hospital expense(10000 RMB)	4.87 ± 0.57	5.92 ± 0.52	P=0.000
Pain* (n)	4	28	P=0.000
Minor Complications(n)			
nausea	2	5	P=0.000
vomiting	1	4	
ileus	1	2	
pneumonia	0	2	
Wound infection	1	1	
UTI	0	2	
DVT	0	1	

*number of patients who needed opium analgesics; FTS: fast-track surgery, CS: conventional surgery; EBL: estimated blood loss; DVT: deep venous thrombosis; UTI: urinary tract infection.

operative hospital days, we can improve medical efficiency and utilization rate of health resources. After an introduction of FTS program, hospital expenses were reduced and patients were more satisfied.

This study had several limitations that may have influenced the results. Our sample size is small and duration time of follow-up is short. Randomized controlled trial may be needed to further compare FTS program with CS program. FTS program itself can also be improved. For example, 3D laparoscopic appears to enhance laparoscopic proficiency²⁶. Further studies may be focused on the use of 3D laparoscopic in radical cystectomy with intestinal urinary reconstruction.

In conclusion, The present study indicates that the FTS program can accelerate recovery, reduce stress action, shorten postoperative hospital days and reduce hospital expense. The FTS program is more safe and efficacious than CS program for Chinese patients undergoing laparoscopic radical cystectomy and ileal conduit diversion.

Methods

The methods were carried out in accordance with approved guidelines. The study was approved by the Ethics Review Board of Xiangya Hospital. The informed consent was obtained from all patients. From March 2011 to February 2012, 55 patients took laparoscopic radical cystectomy and ileal conduit diversion in the department of urology, Xiangya Hospital with curative intent. All of them received CS program. From March 2012 to February 2013, 60 patients took laparoscopic radical cystectomy and ileal conduit diversion in our department with curative intent. All of them received FTS program. Preoperative evaluation and inspection, including medical history, physical examination, imagine examination, ECG, cystoscopy with tissue biopsy, laboratory blood tests were performed in all patients before operations. All of them were diagnosed with muscle-infiltrating bladder cancer.

Laparoscopic radical cystectomy and ileal conduit diversion and the perioperative management were carried out by the same team of surgeons with rich experience. Postoperative results were reported by the same team of surgeons, too. The radical cystectomy is performed laparoscopically and the ileal conduit is carried out extra-corporeal. All patients in CS and FTS group took standard pelvic lymph node dissection. It involves the removal of all nodal tissue cranially up to, and including, the common iliac bifurcation, with the ureter being the medial border, and including the

internal iliac, presacral, obturator fossa and external iliac nodes. Criteria for hospital discharge included normal body temperature, satisfactory pain control, tolerance of regular diet, mobilization out of bed, patients' willingness to go home. Complications were defined using the Clavien system.

Preoperative education. In the FTS group, patients were given counseling regarding the FTS program as well as the knowledge about the operation. However, in the CS group, only information about the operation was given.

Preoperative bowel preparation. One-day bowel preparation program was adopted in the FTS group. Patients were allowed to consume clear liquid diet one day prior to the operation. In the afternoon prior to the operation, patients were given 139.12 g polyethylene glycol preparation mixed with 1 L of water. No mechanical bowel preparation was given. A mandatory overnight 12 h fast was kept pre-operatively. In the CS group, patients were given metronidazole (oral 0.4 g tid 3d) and gentamicin (oral 8wU tid 3d). On the third day before surgery, patients were allowed to consume semiliquid diets. On the second day before surgery, patients were allowed to consume clear liquid diet. On the first day before surgery, a 24 h fast were kept. A mechanical bowel preparation was given in the night before surgery.

Postoperative fluid infusion. In the FTS group, amount of fluid were reduced. Patients were given 1000–2000 ml fluid per day for 2–3 days after surgery. In the CS group, patients were given 3000–5000 ml fluid in the day of surgery. Then they were given about 3000 ml fluid per day in the next 4–5 days.

Postoperative pain control. Celecoxib (oral 200 mg bid) was used in the FTS group. In the CS group, patients were given opium analgesics, for instance, tramadol in the presence of intolerable pain.

Postoperative ambulation. Early ambulation was carried out in the FTS group. Patients were encouraged to mobilize out of bed at least four times per day in postoperative day (POD) 1. Ambulation was enforced in the rest of the postoperative days. In the CS group, patients' ambulation was based on their own desire.

Postoperative diet. In the FTS group, patients were given metoclopramide (10 mg im q8h) for 48 hours in order to prevent vomiting and nausea. In POD 1, chewing gum was initiated¹⁶. In POD 2, patients drunk clear liquids (200 ml q8h). In POD 3, patients drunk unrestricted clear liquid based on their need. In POD 4, regular diet was allowed to consume. In the CS group, patients were only allowed to consume liquid and diet after flatus passed. Details about FTS and CS program are listed in Table 4.

Table 3 | WBC and CRP in two groups

	WBC (×10 ⁹ /L)			CRP(mg/L)		
	FTS group	CS group	P value	FTS group	CS group	P value
Preoperative	6.17 ± 1.77	6.25 ± 1.78	P>0.05	2.11 ± 2.23	2.06 ± 1.65	P>0.05
POD1	15.14 ± 4.81	15.56 ± 3.66	P>0.05	74.55 ± 48.65	85.3 ± 41.29	P>0.05
POD3	13.19 ± 2.68	13.45 ± 2.58	P>0.05	57.47 ± 31.71	67.34 ± 37.63	P>0.05
POD5	8.76 ± 0.7	11.45 ± 1.2	P<0.05	13.03 ± 2.22	35.24 ± 7.42	P<0.05
POD7	6.66 ± 0.56	8.72 ± 1.15	P<0.05	6.35 ± 1.63	9.36 ± 2.59	P<0.05

WBC: white blood cell, CRP: c-reactive protein; FTS: fast-track surgery, CS: conventional surgery; POD: postoperative day.



Table 4 | FTS and CS program of patients undergoing laparoscopic radical cystectomy and ileal conduit diversion

	FTS group	CS group
Preoperative education	Counselling regarding the FTS program Knowledge about the operation.	Information about the operation
Preoperative bowel preparation	Clear liquid diet one day prior to the operation 139.12 g polyethylene glycol preparation mixed with 1 L of water in the afternoon prior to the operation A mandatory overnight 12h fast was kept pre-operatively No mechanical bowel preparation	Metronidazole (oral 0.4g tid 3d) and gentamicin (oral 8wU tid 3d) were taken Semiliquid diets on the third day before surgery Clear liquid diet on the second day before surgery A 24h fast were kept on the first day before surgery A mechanical bowel preparation were given in the night before surgery
Postoperative fluid infusion	I.V. infusion of 1000–2000ml per day for 2–3 days	I.V. infusion of 3000–5000ml in the day of surgery. I.V. infusion of 3000ml fluid per day in the next 4–5 days.
Postoperative pain control	Celecoxib (oral 200mg bid)	Opium analgesics were given in the presence of intolerable pain.
Postoperative ambulation	Patients were encouraged to mobilize out of bed	Patients' ambulation was based on their own desire
Postoperative diet	metoclopramide (10mg im q8h) for 48 hours in order to prevent vomiting and nausea POD 1: chewing gum POD 2: liquid (200mlq8h) POD 3: unrestricted liquid POD 4: regular diet	Patients were only allowed to consume liquid and diet after flatus passed.

FTS: fast-track surgery, CS: conventional surgery, POD: postoperative day.

Data collection. Duration to first flatus, time to regular diet, postoperative hospital stay (recorded as postoperative days) and hospital expenses were recorded. WBC counts, levels of CRP was measured from one day before surgery to POD 1, 3, 5 and 7. Number of complications were recorded. Surgical-related data such as estimated blood loss were also recorded.

Statistical analysis. For descriptive statistics, we presented our data as mean \pm standard deviations and counts or frequencies with percentages or proportions for categorical variables. Differences between two groups were made using a Student's t-test. Categorical measures were analyzed using chi-square analysis. A *P* value <0.05 was considered statistically significant. Data was made with SPSS version 15.0 for Windows (SPSS, Chicago IL).

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Author contributions

L.Q. conceived of the study, participated in the data collection and wrote the main manuscript. G.X., L.L.F. performed the statistical analysis, participated in the data collection and helped to write the manuscript. X.L., Y.L., M.F.C. participated in the data collection. X.B.Z., W.L. participated in its design. All authors reviewed and approved the final manuscript.

Additional information

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