"Fast-track" and "Minimally Invasive" Surgery for Gastric Cancer

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Abstract

Background: Enhanced recovery after surgery (ERAS) protocols or fast-track (FT) programs enable a shorter hospital stay and lower complication rate. Minimally invasive surgery (MIS) is associated with a lesser trauma and a quicker recovery in many elective abdominal surgeries. However, little is known of the safety and effectiveness made by ERAS protocols combined with MIS for gastric cancer. The purpose of this study was to evaluate the safety and effectiveness made by FT programs and MIS in combination or alone.

Methods: We summarized an 11-year experience on gastric cancer patients undergoing elective laparotomy or minimally invasive gastric resection in standard cares (SC) or FT programs during January 2004 to December 2014. A total of 984 patients were enrolled and assigned into four groups: open gastrectomies (OG) with SC (OG + SC group, n = 167); OG with FT programs (OG + FT group, n = 277); laparoscopic gastrectomies (LG) with FT programs (LG + FT group, n = 248); and robot-assisted gastrectomies (RG) with FT programs (RG + FT group, n = 292). Patients' data were collected to evaluate the clinical outcome. The primary end point was the length of postoperative hospital stay.

Results: The OG + SC group showed the longest postoperative hospital stay (mean: 12.3 days, median: 11 days, interquartile range [IQR]: 6–16 days), while OG + FT, LG + FT, and RG + FT groups recovered faster (mean: 7.4, 6.4, and 6.6 days, median: 6, 6, and 6 days, IQR: 3–9, 4–8, and 3–9 days, respectively, all P < 0.001). The postoperative rehabilitation parameters such as flatus time after surgery (4.7 ± 0.9, 3.1 ± 0.9, and 3.1 ± 0.9 days) followed the same manner. After 30 postoperative days' follow-up, the total incidence of complications was 9.6% in OG + SC group, 10.1% in OG + FT group, 8.1% in LG + FT group, and 10.3% in RG + FT group. The complications showed no significant differences between the four groups (all P > 0.05).

Conclusions: ERAS protocols alone could significantly bring fast recovery after surgery regardless of the surgical technique. MIS further reduces postoperative hospital stay. It is safe and effective to apply ERAS protocols combined with MIS for gastric cancer.

Key words: Enhanced Recovery after Surgery; Fast-track Surgery; Gastrectomy; Minimally Invasive Surgery; Optimized Care

INTRODUCTION

The introduction of multimodal rehabilitation for selective operations, which is also called enhanced recovery after surgery (ERAS) or fast-track (FT) programs,^[1,2] has significantly relieved postoperative stress, reduced perioperative complications, and accelerated recovery of postoperative bowel function and insulin sensitivity.^[3] The ERAS protocols, such as glucose load, short fasted time, early oral intake, no use of gastrointestinal (GI) tubes and drains, have been successfully applied to general,^[4,5] orthopedic,^[6] urological,^[7,8] gynecological,^[9] cardiovascular,^[10] thyroid,^[11] and thoracic^[12] surgeries.

Access this article online								
Quick Response Code:	Website: www.cmj.org							
	DOI: 10.4103/0366-6999.190659							

At the same time, the introduction of minimally invasive surgery (MIS) has led to decreased postoperative stress and short length of hospital stay across a variety of procedures. In gastric surgery, the laparoscopic approach has suggested rapid recovery, low morbidity, and decreased length of

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Received: 23-02-2016 Edited by: Ning-Ning Wang How to cite this article: Liu XX, Pan HF, Jiang ZW, Zhang S, Wang ZM, Chen P, Zhao Y, Wang G, Zhao K, Li JS. "Fast-track" and "Minimally Invasive" Surgery for Gastric Cancer. Chin Med J 2016;129:2294-300. hospital stay compared with open techniques.^[13,14] Recently, robotic surgery has been demonstrated to overcome the intrinsic limitations of a traditional laparoscopic approach where the anatomical and operative conditions are similar to those encountered during gastric resection.^[15,16] Several retrospective studies have reported that robotic surgery for the treatment of gastric cancer is feasible and can produce satisfying postoperative outcomes.^[17,18]

However, most of these prospective series and randomized studies were conducted in conventional perioperative cares. Only one study explored the effects of laparoscopic resection combined with ERAS protocols.^[19] Without control group, this prospective study of 32 consecutive patients drew the conclusion that minimally invasive gastrectomy with ERAS could result in a short hospital stay and low morbidity rate.^[19] It remains important, therefore, in the context of gastric surgery to understand the contributions made by optimized perioperative cares with the combination of minimally invasive approach.

To date, few studies have reported the application of ERAS in laparoscopic or robot-assisted gastrectomy for gastric cancer. Here, we summarized an 11-year experience on patients undergoing elective laparotomy, laparoscopic, and robot-assisted gastrectomy in standard care (SC) or FT programs. The purpose of this retrospective study was to evaluate the safety and effectiveness made by FT programs and MIS in combination or alone. Specifically, we were interested in determining whether the further reduction of postoperative hospital stay would follow in the context of FT programs when combined with MIS.

Methods

Patients and study design

This retrospective study reviewed the clinical records of patients receiving gastric cancer surgery in the Department of General Surgery, Jinling Hospital, Nanjing, China. From January 2004 to December 2014, 1044 gastric cancer patients with open, laparoscopic, and robot-assisted gastrectomies (RG) under the care of one surgeon (Zhi-Wei Jiang) in the institution were assessed for inclusion in the study. Informed consent of surgical procedure was obtained from the patients and their families before the surgery, and written paper forms were kept in medical record. The study was approved by the Research Ethics Committee of the Nanjing University. Patient records were anonymized prior to access for this study. All patients' hospitalization information were sorted and summarized by the patients' identification number. The patients' numerations for statistical data analysis were assigned according to the sequential order of hospital admission date.

SCs were applied during January 2004 and December 2006, and ERAS protocols or FT programs were applied from January 2007. From January 2008, our team began to perform laparoscopic gastrectomies (LG) with minimal

laparotomy anastomosis. From June 2010, our team began to perform RGs with minimal laparotomy anastomosis. Gastrectomies with D2 lymph node dissection were performed according to the rules of the Japanese Research Society for Gastric Cancer.^[20] Total gastrectomy and distal or proximal subtotal gastrectomies were performed according to the tumor location.

Nine hundred and eighty-four consecutive patients were assessed for entry into the study, and they were assigned into four groups: Open gastrectomies (OG) with SC between January 2004 and December 2006 (OG + SC group, n = 167); OG with FT programs between January 2007 and December 2014 (OG + FT group, n = 277); LG with FT programs between January 2008 and December 2014 (LG + FT group, n = 248); and RGs with FT programs between June 2010 and October 2014 (RG + FT group, n = 292).

The patients were followed from preoperative recruitment to 30 days postoperation. The postoperative recovery and complications were traced and summarized for analysis. The protocol for general anesthesia and postoperative pain relief was identical in all patients. To avoid possible analysis bias, those patients who converted from laparoscopic or robot-assisted surgeries to laparotomies were excluded from the study. Patients with contraindications to early postoperative discharge or optimized measures were also excluded from the study. These contraindications included reluctance to discharge early, presence of severe organ dysfunction, and abnormal clinical test results preoperatively. All patients followed the same discharge criteria: (1) bowel function returned and oral intake reached about 70% of the preoperative level; (2) no intravenous infusion; (3) no pain or well controlled with oral analgesics; (4) able to carry out normal daily activities and care for themselves; and (5) acceptance by the patients.

Fast-track programs

FT programs emphasize on minimizing unnecessary medical manipulation and reducing traumatic stress on the body. A series of optimized cares that involved preoperative, perioperative, and postoperative strategies (our previous study)[21] was implemented in the FT or ERAS group. Upon entry into the trial, the patients received both verbal and written information about the operation and the postoperative rehabilitation programs. The patients were allowed a normal diet up to 6 hours before operation and including the evening meal. A drink containing 100 g of glucose (glucose injection 10%) in 1000 ml of water was orally administered at 10 P.M. on the evening before the surgery, and a further 50 g of glucose in 500 ml of water was given 3-4 h preoperatively. Abdominal drains or nasogastric tubes were not placed unless required, such as in cases of possible abdominal contamination or confirmed gastric retention. The patients were allowed to orally intake fluids immediately on the day of surgery, and a diet was introduced as tolerated following a step-wise progression. A structured mobilization plan that involved active intervention by physiotherapists was adopted.

Standard cares

SCs, also called conventional cares, which took measures emphasized on prolonged rest for both the patients and the GI tract. These protocols were used daily in our center before January 2007 and are still routinely used in most of the other hospitals in China. Patients in SC received none of the optimized measures above.^[21] On the day before surgery, patients received GI preparation and were fasted from midnight. The lengths of incisions were determined according to the surgeon's preference (usually across the umbilicus). Nasogastric tubes were placed preoperatively and usually remained until flatus occurred and no gastric retention presented after operation. Intra-abdominal drains were placed during the surgery, and in most cases, they were maintained until the day before discharge to home. After the surgery, the patients were not allowed oral intake until bowel flatus or obvious GI movement occurred. The patients mobilized at their will and usually lay in bed for about 2 days after the surgery.^[21]

Study end points and definitions

The following variables were recorded: Age, gender, body mass index (BMI), presence of comorbidity, tumor characteristics, operation time, estimated blood loss, postoperative complications, and histological findings. The primary outcome of interest was postoperative hospital stay. Following discharge, the need for patient re-admission and any complaints were documented within 1 month. Postoperative complications were classified using the Clavien-Dindo classification,^[22] which categorizes surgical complications from Grades I to V based on the invasiveness of the treatment required. Grade I requires no treatment; Grade II requires medical therapy; Grade IIIa requires surgical, endoscopic, or radiologic intervention, but not general anesthesia; Grade IIIb requires general anesthesia; Grade IV represents life-threatening complications that require intensive care; and Grade V represents death of the patient. Complications were classified as Grade II or higher were recorded.

Statistical analysis

Categorical variables were presented as frequencies with percentages and compared utilizing the Chi-square statistics. Moreover, continuous variables were expressed as mean \pm standard deviation (SD) or median (interquartile range [IQR]) and compared by the independent samples *t*-test or the Mann-Whitney *U*-test. Statistical analysis was performed using SPSS version 20.0 software (IBM SPSS, Inc., Chicago, IL, USA). A *P* <0.05 was regarded as statistically significant.

RESULTS

Nine hundred and eighty-four patients were enrolled and analyzed (167 in the OG + SC group, 277 in the OG + FT group, 248 in the LG + FT group, and 292 in the RG + FT group). The relevant characteristics of patients and the types of surgery are summarized in Table 1. The average age is 56.9 ± 11.7 years in the OG + SC group, 57.8 ± 12.6 years in the OG + FT group, 56.6 ± 10.4 years in the LG + FT group, and 57.6 ± 10.4 years in the RG + FT group. The statistical analysis of age, gender, body weight, BMI, and American Society of Anesthesiologists status suggested similar characteristics between the groups (all P > 0.05). The ratios of distal, proximal, and total gastrectomy types were similar between the groups (all P > 0.05). According to postoperative pathological tumor staging, most cases were found at advanced stages, and there was no difference in TNM stage between the groups (all P > 0.05).

On postoperative day (POD) 3, nearly, all patients (88.8–95.2%) in FT program (OG + FT, LG + FT, and RG + FT group) and half patients (46.7%) in the SCs (OG + SC group) were able to walk [Table 2]. Flatus occurrence time was 4.7 ± 0.9 days in OG + SC group, 3.1 ± 0.8 days in OG + FT group, 3.0 ± 0.9 days in LG + FT group, and 3.1 ± 0.9 days in RG + FT group. The average postoperative hospital stay was 12.3 days (median: 11 days, IQR: 6–16 days) in OG + SC group, 7.4 days (median: 6 days, IQR 3-9 days) in OG + FT group, 6.4 days (median: 6 days, IQR 4-8 days) in LG + FT group, and 6.6 days (median: 6 days, IQR 3–9 days) in RG + FT group [Figure 1]. The postoperative hospital stay were significantly reduced in ERAS regardless of the minimally invasive technique (OG + SC vs. OG + FT, Z = -13.183, P = 0.000; OG + SC vs. LG + FT, Z = -14.881, P = 0.000; and OG + SCvs. RG + FT, Z = -14.505, P = 0.000). Further, a significant reduction of postoperative hospital stay could follow when combined with laparoscopic surgery or robot-assisted surgery in the context of FT programs (OG + FT vs. LG + FT, Z = 3.414, P = 0.001; OG + FT vs. RG + FT, Z =-3.703, P = 0.000). Postoperative hospital stay did not show significant differences between LG + FT group and RG + FT group (Z = -0.484, P = 0.629) [Table 2 and Figure 1].

After 30 POD follow-up, the total incidence of complications was 9.6% in OG + SC group, 10.1% in OG + FT group, 8.1% in LG + FT group, and 10.3% in RG + FT group. The total complications showed no significant differences between all the groups (all P > 0.05). Septic complication, such as incision poor healing and urinary, pulmonary, and abdominal infections, showed no difference between the four groups. Nonseptic complications, such as deep vein thrombosis, diarrhea and vomiting, ileus and bleeding, also showed no difference between all the groups. Anastomosis leakage occurred in three patients of OG + SC group, seven patients of OG + FT group, eight patients of LG + FT group, and six patients of RG + FT group. Most of the leakages were resolved by abdominocentesis or continual irrigation and drainage of double catheterization cannula. No patient died of anastomosis leakage. Three patients of OG + SC group, three patients of OG + FT group, four patients of LG + FT group, and four patients of OG + SC group were re-admitted. The main reason for re-admission to hospital was the complaints of dysphagia and failure to tolerate daily diet. One patient in OG + FT group and one patient in LG + FTgroup were re-admitted because of abdominal infection

Patient characteristics	0G + SC	OG + FT	LG + FT	RG + FT
	(<i>n</i> = 167)	(n = 277)	(n = 248)	(n = 292)
Age (years), mean \pm SD	56.9 ± 11.7	57.8 ± 12.6	56.6 ± 10.4	57.6 ± 10.4
Gender (male/female), n	127/40	198/79	186/62	219/73
BMI (kg/m ²), mean \pm SD	22.3 ± 4.6	22.6 ± 4.8	22.1 ± 4.5	22.2 ± 4.9
ASA status, <i>n</i>				
Ι	43	86	81	84
II	99	148	136	160
III	25	43	31	48
Gastrectomy type, n				
Proximal	40	36	30	42
Distal	59	102	93	105
Total	68	139	125	145
TNM stage, <i>n</i>				
Ι	20	21	25	30
II	51	75	72	90
III and IV	96	181	151	172

BMI: Body mass index; ASA: American Society of Anesthesiologists; OG: Open gastrectomies; LG: Laparoscopic gastrectomies; RG: Robot-assisted gastrectomies; SC: Standard cares; FT: Fast-track; SD: Standard deviation.

Table 2: Postoperative rehabilitation and hospital stay time of gastric cancer patients undergoing elective gastrectomies

Characteristics	0G + SC	0G + FT	LG + FT	RG + FT		
	(<i>n</i> = 167)	(n = 277)	(n = 248)	(n = 29)		
Mobilization time, <i>n</i> (%)						
Walk on POD1	0 (0)	62 (22.3)	96 (38.7)	112 (38.3)		
Walk on POD2	38 (22.7)	154 (55.5)	195 (78.6	225 (77.1)		
Walk on POD3	78 (46.7)	246 (88.8)	235 (94.7)	278 (95.2)		
Flatus time after surgery (day), mean \pm SD	4.7 ± 0.9	3.1 ± 0.8	3.0 ± 0.9	3.1 ± 0.9		
Postoperation hospital stay (days)						
Mean	12.3*	7.4^{\dagger}	6.4	6.6		
Median (IQR)	11 (6–16)	6 (3–9)	6 (4-8)	6 (3–9)		
Total hospital stay (days)						
Mean	17.4	12.6	10.6	10.3		
Median (IQR)	16 (8–24)	11 (6–16)	10 (6-14)	9 (4–14)		

*The postoperative hospital stay were significantly reduced in ERAS regardless of the minimally invasive technique (OG + SC vs. OG + FT, Z = -13.183, P = 0.000; OG + SC vs. LG + FT, Z = -14.881, P = 0.000; OG + SC vs. RG + FT, Z = -14.505, P = 0.000). [†]Further, a significant reduction of postoperative hospital stay could follow when combined with laparoscopic surgery or robot-assisted surgery in the context of fast-track programs (OG + FT vs. LG + FT, Z = 3.414, P = 0.001; OG + FT vs. RG + FT, Z = -3.703, P = 0.000). However, the postoperative hospital stay time between LG + FT and RG + FT showed no significant differences (Z = -0.484, P = 0.629). IQR: Inter-quartile range; OG: Open gastrectomies; LG: Laparoscopic gastrectomies; SC: Standard cares; FT: Fast-track; POD: Postoperative day; SD: Standard deviation; RG: Robot-assisted gastrectomies.

and abscess formation, respectively, after discharge. The details of postoperative complications with Clavien-Dindo classification are shown in Table 3.

DISCUSSION

FT programs were first initiated in 2001 by Professor Kehlet^[23,24] in Denmark, and it has been successfully used for the management of many diseases. Concepts to enhance recovery after different types of surgery, referred to as FT, ERAS, or multimodal rehabilitation, have been developed and evaluated.^[25] By targeting factors that delay postoperative recovery such as surgical stress and organ dysfunction, these FT programs have been shown to accelerate recovery and

reduce hospital stay, especially in patients undergoing colonic surgery with hospital stays of 2 days.^[26,27] Recently, robust data have shown that FT in D2 gastrectomy is safe and efficient,^[5,28] and it can also lessen postoperative stress, accelerate rehabilitation, shorten postoperative hospital stay, and hasten the return of gut function,^[5,28] which was also demonstrated in our previous study.^[21,29] In 2014, the consensus guidelines for enhanced recovery after gastrectomy have been established.^[30] The present evidence-based framework provides comprehensive advice on optimal perioperative care for the patients undergoing gastrectomy and facilitates multi-institutional prospective cohort registries and adequately powered randomized trials for further research.^[30] Through the organization of effective

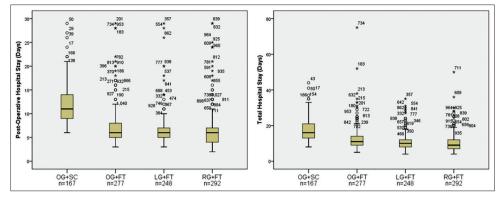


Figure 1: The OG + SC group with FT program showed the longest postoperative hospital stay and total hospital stay (OG + SC vs. OG + FT, LG + FT or RG + FT, all P < 0.01). MIS (laparoscopic or robot-assisted surgery) could further reduce postoperative hospital stay (OG + FT vs. LG + FT, or RG + FT, all P < 0.01). Boxes show the median with inter-quartile range; whiskers give the range. Circles and asterisks denote outliers and affiliated numeration for statistical data analysis. MIS: Minimally invasive surgery; OG: Open gastrectomies; SC: Standard cares; FT: Fast-track; LG: Laparoscopic gastrectomies; RG: Robot-assisted gastrectomies.

Table 3: Postoperative complications by Clavien-Dindo classification																				
Complications	0G + SC (n = 167)				OG + FT (n = 277)				LG + FT (n = 248)						RG + FT ($n = 292$)					
	П	Illa	IIIb	IV	V	П	Illa	IIIb	IV	V	Ш	Illa	IIIb	IV	V	II	Illa	IIIb	IV	V
Total, n	6	8	2	_	_	7	12	6	3	_	3	11	6	_	_	8	15	5	-	2
Anastomosis leakage	_	2	1	_	_	_	3	4	_	_	_	3	5	_	-	_	4	2	_	_
Other systems' nutrition status	_	_	_	_	_	2	_	_	_	_	1	_	_	_	_	1	_	_	_	1
Gastroplegia, prolonged ileus or intolerance, diarrhea, and alimentary tract obstruction	1	1	1	-	_	5	2	1	_	_	-	1	1	_	_	5	2	2	-	-
Alimentary tract hemorrhage and intra-abdominal bleeding	-	-	-	-	-	-	-	-	-	-	1	-	-	-	-	1	1	-	-	-
Incision of poor healing	1	2	_	_	_	_	3	1	_	_	_	1	_	_	_	_	2	_	_	_
Pulmonary or urinary infection	3	1	_	_	_	_	3	_	3	_	1	4	_	_	_	1	4	_	_	1
Abdominal infection or abscess	1	2	_	_	_	_	1	_	_	_	_	2	_	_	_	_	2	1	_	_
Vein thrombosis, cardio-cerebro-vascular events	-	_	_	-	-	-	_	-	-	-	-	-	-	-	-	-	-	-	-	-
Total complication cases/ patients (<i>n</i> / <i>N</i>)	16/167					28/277				20/248						30/292				
Complication ratio (%)	9.6						10.1						8.1			10.3				

The total complications showed no significant differences between any group (all P>0.05). Postoperative complications were classified by the Dindo-Clavien classification, which categorizes surgical complications from Grades I to V based on the invasiveness of the treatment required. Complications were classified as Grade II or higher were recorded. OG: Open gastrectomies; LG: Laparoscopic gastrectomies; SC: Standard cares; FT: Fast-track.

commitment and a multidisciplinary approach,^[31] our team led by Liu *et al.*^[21] and Jiang *et al.*^[29] began to implement FT in gastric cancer patients in January 2007. By now, we have over 8-year experience of "FT."

Although laparoscopic surgery, applied in the treatment of colorectal^[32,33] and gastric cancers,^[13,14] could significantly reduce trauma and speed up the rehabilitation of patients after surgery, almost all studies only compared open surgery with laparoscopic surgery in the context of conventional cares. Recently, several studies have reported the laparoscopic surgery in an enhanced recovery program.^[28,34,35] Those initial case series studies demonstrated that minimally invasive gastrectomy with ERAS could result in a short hospital stay, low morbidity rate,^[19] and immediate improvement of postoperative quality of life^[35] and nutritional status.^[28] The authors suggested that LG with FT is a safe,^[35] economic,

and feasible treatment for gastric cancer.^[28] However, there are still no comparison between LG and OG, with or without FT programs. Recently, robotic surgery has been demonstrated to overcome the intrinsic limitations of a traditional laparoscopic approach where the anatomical and operative conditions are similar to those encountered during gastric resection.^[15,36-38] Similarly, as for RG, a few studies adopted the FT or ERAS.

In the present study, we explored the safety and effectiveness made by ERAS protocol and MIS for gastrectomies. The postoperative hospital stay is 12.3 ± 4.4 days in OG + SC group, while 7.4 ± 4.1 , 6.4 ± 3.5 , and 6.6 ± 3.9 days in OG + FT, LG + FT, and RG + FT groups, respectively. Days until flatus after surgery followed the same manner. They are described as follows: OG + SC group is 4.7 ± 0.9 days, while OG + FT, LG + FT, and RG + FT are 3.1 ± 0.8 , 3.0 ± 1.3 , and 3.1 ± 1.2 days, respectively. The results showed that the postoperative recovery days were significantly reduced in ERAS protocols regardless of the minimally invasive surgical technique. When laparoscopic surgical technique is introduced, about 1-day shorter postoperative hospital stay (LG + FT 6.4 days, RG + FT 6.6 days vs. OG + FT 7.4 days) could be achieved. Further, a significant reduction of postoperative hospital stay did not follow in the context of FT when compared robot-assisted technique with laparoscopic surgery. Although the postoperative hospital stay was significantly reduced in the patients of FT groups, postoperative complication did not show any significant difference between the groups (P > 0.05) [Table 2].

The role of minimally invasive technique (laparoscopic or robot-assisted surgery) in diminishing surgical trauma and lessening postoperative stress was not as important as we thought before.^[28] Some scholars have pointed out that one reason for the insufficient demonstration of robot-assisted system's advantages was that full reconstruction of alimentary tract^[39] was not performed intra-abdominally. In our study, both laparoscopic and RGs underwent mini-laparotomy for anastomosis with the similar length of incisions. The similar traumatic stress between LG + FT and RG + FT patients may lead to no significant difference of postoperative hospital stay. Drawn from our present data, FT rehabilitation program played an important role in the recovery process after surgery, which could significantly accelerate the restoration of gastrointestinal function and shorten hospital stay time.

Although this study showed many benefits of clinical outcomes, limitations still existed. Due to the limitations of our retrospective study, we did not perform laparoscopic or robot-assisted technique with SCs. To compare the effect of FT or minimally invasive technique rigorously, LG + SC and RG + SC groups are required as a reference of LG + FT and RG + FT groups. Therefore, larger cases and prospective randomized studies are needed to focus on the potential influence of laparoscopic or robot-assisted surgery with or without FTs. Furthermore, laparoscopic and robotic group include cases in learning curve, thus may have some influence on result comparison.

Financial support and sponsorship

This study was supported by the grants from the National Natural Science Funding of China (No. 81300721), the Science and Technology Development Funding of Yangzhou City (No. YZ2014204), and the Social Development Fund of Jiangsu Province (No. BE2015687).

Conflicts of interest

There are no conflicts of interest.

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