

Title:

**Fast-track Surgery After Gynecological
Oncology Surgery**

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Fast-track surgery after gynecological oncology surgery: study protocol for a randomized controlled trial

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Abstract

Background

Fast-track surgery (FTS) pathway, also known as enhanced recovery after surgery (ERAS), FTS is a multidisciplinary approach aiming to accelerate recovery, reduce complications, minimise hospital stay without an increased readmission rate and reduce healthcare costs, all without compromising patient safety. The FTS pathway have been adopted by most surgical specialties worldwide, and it has been used successfully in non-malignant gynecological surgery, but it has been proven to be especially effective in elective colorectal surgery.

The advantages of fast-track principles that have been documented in connection with abdominal surgery most likely extend to the field of gynecology, but this is only an assumption, since fast-track in elective gynecological surgery has not been studied carefully so far. However, no consensus guideline has been developed for gynecological oncology surgery although surgeons have attempted to introduce slightly modified FTS programmes for patients undergoing such surgery. NO randomised controlled trials for now.

The advantages of fast-track most likely extend to gynecology, although so far have scarcely been reported. There is an existing research showed FTS in gynecological oncology provide early hospital discharge after gynaecological surgery meanwhile with high levels of patient satisfaction

The aim of this study is to identify patients following a FTS program who have been discharged earlier than anticipated after major gynaecological/gynaecological oncologic surgery and analyze the complication after surgery.

Methods/Design

Comparison of Fast-Track (FT) and traditional management protocols.

the **primary endpoints** is length of hospitalization post-operation (d, mean \pm SD). It was calculated by the difference between date of discharge and date of surgery. The **secondary endpoints** are complications in both groups are assessed during the first 21 days postoperatively. Including infection(wound infection, lung infection, intraperitoneal infection, operation space infection), postoperative nausea and vomiting (PONV) , ileus, postoperative hemorrhage, postoperative thrombosis and APACHE II score.

Discussion

The advantages of fast-track most likely extend to gynecology, although so far have scarcely been reported. NO randomised controlled trials for now. The aim of this study is to compare the LOS(Length of hospitalization post-operation) after the major gynaecological/gynaecological oncologic surgery and analyze the complication after surgery. This trial can show whether the FTS program can achieve early hospital discharge after gynaecological surgery meanwhile with low levels of complications.

Background

Fast-track surgery (FTS) pathway, also known as enhanced recovery after surgery (ERAS), was initiated in 1995 by Bardram et al [1]. FTS is a multidisciplinary approach aiming to accelerate recovery, reduce complications, minimize hospital stay without an increased readmission rate and reduce healthcare costs, all without compromising patient safety [2]. The FTS pathway have been adopted by most surgical specialties worldwide, and it has been used successfully in non-malignant gynecological surgery [3, 4], but it has been proven to be especially effective in elective colorectal surgery [5-7].

The speed of postoperative recovery is influenced by multiple factors such as occurrence of pain, postoperative nausea and vomiting (PONV), paralytic ileus, fatigue and sleep disturbances. A multimodal approach to prevent and minimize these factors is considered to be essential in order to enhance recovery [2, 5, 6, 8]. Fast-track principles include a series of elements such as providing the patient with thorough preoperative information and education concerning pre-, per- and postoperative care, the use of safe and short-acting anesthetics and optimal dynamic pain relief with minimal use of opioids, management of PONV, enteral nutrition and early mobilization, and use of minimal invasive surgery [9].

The advantages of fast-track principles that have been documented in connection with abdominal surgery most likely extend to the field of gynecology, but this is only an assumption, since fast-track in elective gynecological surgery has not been studied carefully so far. There is an existing research showed FTS in gynecological oncology provide early hospital discharge after gynaecological surgery meanwhile with high levels of patient satisfaction [10]. However, no consensus guideline has been developed for gynecological oncology surgery although surgeons have attempted to introduce slightly modified FTS programmes for patients undergoing such

surgery .NO randomised controlled trials for now[3, 11, 12].

In contemporary surgical care patients would often be admitted to hospital the day prior to planned surgery, undergo preoperative mechanical and antibiotic bowel preparation and have IV fluids running to keep them in fluid balance, prior to any surgical or anaesthetic insult. Intraoperatively patients were often volume loaded to maintain a filling pressure, as well as pelvic drains to prevent development of collections, then spent 2 - 3 days nil by mouth (NBM) until bowel sounds were heard before being commenced on a graduated diet of clear liquids, free fluids, light diet and finally commenced on a regular diet 5 - 7 days post surgery. Patients were then discharged, on average 5 - 7 days post surgery[13]. Fast Track Surgery (FTS) or Enhanced Surgical Recovery (ESR) programs have been developed and refined in many specialties with documented improved patient outcomes and as a consequence earlier discharge from hospital and reduced length of stay (LOS)[2, 14, 15].

The aim of this study is to identify patients following a FTS program who have been discharged earlier than anticipated after major gynaecological/gynaecological oncologic surgery and analyze the complication after surgery.

Methods/Design

Objectives and hypothesis

Comparison of Fast-Track (FT) and traditional management protocols.

The following hypotheses will be tested:

H0: The recovery and postoperative complications is equal in both groups.

H1: The recovery was enhanced and postoperative complications is different in both groups.

Study population and eligibility criteria

The trial is designed as a randomized, controlled, nonblinded and single-center trial.

The centre: Department of gynecological oncology of Si Chuan Cancer Hospital Chengdu, Sichuan, China

Detailed inclusion and exclusion criteria are described below.

Inclusion criteria

1. Patients scheduled for gynecological oncology surgery (including radical hysterectomy add lymphadenectomy, hysterectomy add lymphadenectomy and cytoreductive).
2. Aged 18 years or older
3. Signed informed consent provided

Exclusion criteria

1. Patients with a documented infection at the time of operation.
2. Aged 71 years or older.
3. Patients with ileus at the time of operation.
4. Patients with hypocoagulability.
5. Patients with psychosis, Alcohol dependence or drug abuse history;

6. Patients with primary nephrotic or hepatic disease;
7. Patients with severe hypertension systolic pressure ≥ 160 mmHg, diastolic pressure > 90 mmHg.

Sample size calculation

The sample size calculation is based on the Length of hospitalization post-operation. The standard deviation of length of hospitalization post-operation in the traditional group is 1.5 based on previous studies [16, 17].

We estimated the number of patients needed in a superiority trial with an effect size of 90 % and a margin of 10 (alpha 5 %, power 90 %). where $u_{\alpha} = 1.96$ and $u_{\beta} = 1.28$ and using the equation $n = [2(u_{\alpha} + u_{\beta}) \sigma / \delta]^2$, a sample size of 47 patients per group is necessary to detect a difference between the groups. With an expected dropout rate of 20%, we plan to enrol 120 patients into the study.

Postoperative data collection

A daily visit of the study patients will be made by clinical investigators or a delegated physician. All protocol-required information collected during the trial will be entered into the patient's record form. Data collected relate to 1) patient characteristics, 2) hospitalisation 3) post-operation and 4) complications. The patient characteristics collected were: age, weight, height, body mass index (BMI), medical insurance status and performance status. Hospitalization details included LOS (Length of hospitalization post-operation), the procedure performed, diagnosis, operating time, name of surgery, intraoperative estimated blood loss. Post-operation details included time to full tolerance of free fluids (days), time to full tolerance of solid food (days), time to drain removal (days). Complications details included infection (wound infection, lung infection, intraperitoneal infection, operation space infection), postoperative nausea and vomiting (PONV), ileus, postoperative hemorrhage, postoperative thrombosis and APACHE II score. (Table 1).

Primary and secondary endpoints

Primary endpoints

Length of hospitalization post-operation (d, mean \pm SD). It was calculated by the difference between date of discharge and date of surgery.

Secondary endpoints

Complications: complications in both groups are assessed during the first 21 days postoperatively. Including infection (wound infection, lung infection, intraperitoneal infection, operation space infection), postoperative nausea and vomiting (PONV), ileus, postoperative hemorrhage, postoperative thrombosis and APACHE II score. (Table 1).

Ethics, study registration and consent

This trial was approved by independent ethics committees at Sichuan Cancer Hospital and Research Institute

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The study procedures, risks, benefits and data management will be clarified with the patients before they are asked to give their informed consent to participate.

Study treatment

The surgical technique is standardized in The treatment team and the patients' families were not blinded to the study. In addition, the data collectors were not involved in the clinical management of patients to ensure statistical validity and reliability. All surgeries were performed by the same team of surgeons, and the patients were treated and nursed by the same treatment team during the peri-operative period. Post-operative complications were based on patient complaints and clinical symptoms.

Given there was no Fast-track surgery guideline in the field of gynecological oncology surgery , we refer to the guideline of gastrectomy, colorectal surgery and pancreaticoduodenectomy[18-20].(Table1)

Safety aspects

Gynecological oncology surgery is highly technically demanding procedure. In order to avoid bias based on the learning curve of the surgeons, every surgical procedure will be performed or supervised by a senior surgeon. And informed consent will be obtained from all participants,

Data collected relate to 1) patient characteristics, 2) hospitalisation 3) post-operation and 4)complications. The patient characteristics collected were: age, weight, height, body mass index (BMI), medical insurance status and per-formance status. Hospitalization details included LOS(Length of hospitalization post-operation), the procedure performed, diagnosis, operating time, name of surgery, intraoperative estimated blood loss. Post-operation details included time to full tolerance of free fluids (days), time to full tolerance of solid food (days), time to drain removal (days). Complications details included infection(wound infection, lung infection, intraperitoneal infection, operation space infection), ileus, postoperative hemorrhage, postoperative thrombosis and APACHE II score. (Table 2).

Methods for avoiding bias

Minimizing systemic bias

Patients will be randomized to one of the two groups after admitting diagnosis. Randomization will be accomplished using balanced permutation blocks by generation of random numbers in order to obtain homogeneity between groups. Opaque, sealed envelopes will be produced, labelled with the randomization number

and containing a sheet that states the group allocation for the patient. Randomization envelopes will be used in consecutive order. Basic characteristics of the patient and the day of randomization will be documented on a data sheet so that compliance to the randomization scheme may be checked retrospectively. If patients are excluded from the study after randomization, their numbers will not be reused. Obviously, operating surgeons, attending physicians and nursing staff and the patients and families cannot be blinded, as the procedure is different. However, outcome assessors will be blinded. The randomization process will follow the CONSORT guidelines (Figure 1)[21].

Minimizing treatment bias

gynecological oncology surgery (including radical hysterectomy add lymphadenectomy, hysterectomy add lymphadenectomy and cytoreductive) are standardized in both group, all surgeons participating in the study are familiar with them. common procedure performed on a routine basis, which eliminates a learning curve.

Minimizing measurement bias

Detection an length of hospitalization post-operation and postoperative complications, which are the primary and secondary endpoints, will be based on data in the patient's record form. Blinding is not necessary, because the length of hospitalization post-operation is an objective endpoint that cannot be influenced by the patient. Physician blinding is not possible, because they are involved during surgery.

Statistical methods

Each patient's allocation to the analysed population will be defined prior to the analysis and will be documented. In the full-analysis set, patients will be analysed as randomized according to the intention-to-treat principle. The intention-to-treat principle implies that the analysis includes all randomized patients. The per-protocol analysis set will include all the patients without major protocol deviation. Deviations from the protocol will be assessed as major or minor. Patients with major deviations from the protocol will be excluded from the per-protocol analysis. The safety analysis set will analyse patients according to the treatment.

The null hypothesis assumes that the length of hospitalization post-operation and postoperative complications is equal in both groups. A binary logistic regression will be applied in order to compare length of hospitalization post-operation in the groups adjusting for other factors.

Data were analyzed by SPSS19.0 (SPSS Inc Chicago, Illinois) and expressed as mean \pm SD. Length of hospitalization post-operation in the FTS and traditional groups were compared and analyzed by Mann-Whitney U-tests (non-normal distribution).

NRS2002 scores between the two groups were analyzed with the Wilcoxon test (nonnormal distribution) or with Student's t-tests (normal distribution). The chi-square test or Fisher's exact test will be used for analysis of categorical secondary endpoints (complications). A P-value <0.05 will be considered statistically significant. Statistical analyses will be performed using SPSS19.0 (SPSS Inc Chicago,

Illinois).

Discussion

Fast-track surgery (FTS) pathway have been adopted by most surgical specialties worldwide, but in gynecological malignant surgery is sparingly described[22] and there are currently no randomized controlled trials to support or refute employing this approach[11]. This needs to be explored right now.

However, no consensus guideline has been developed for gynecological oncology surgery although surgeons have attempted to introduce slightly modified FTS programmes for patients undergoing such surgery .NO randomised controlled trials for now[3, 11, 12].

Widespread education is needed to improve the rate of implementation of fast-track. There are several possible reasons for this, including lack of collaboration in the surgical team and lack of awareness of or failure to accept and adopt evidence-based findings[8, 9, 23]. Close cooperation between the surgical, anesthesiological and nursing staff is essential and the importance of cooperation cannot be overestimated as practice needed to achieve further development of surgical care and postoperative recovery[24, 25]. Fast-track regimens in general have been well evaluated regarding medical complications and they appear to be safe[26].

The aim of this study is to compare the LOS(Length of hospitalization post-operation) after the major gynaecological/gynaecological oncologic surgery and analyze the complication after surgery. This trial can show whether the FTS program can achieve early hospital discharge after gynaecological surgery meanwhile with low levels of complications.

Trial status

At the time of writing, we are about to enroll patients and the anticipated study completion date is April 2017.

Abbreviations

Abbreviations	Definition
FTS	Fast-track surgery
LOS	Length of hospitalization post-operation
PONY	postoperative nauseaand vomiting
APACHE II score	Acute Physiology and Chronic Health Evaluation II

Competing interests

The authors declare that they have no competing interests.

Author's contribution: Ling. Cui conceived of the study, design of the study and performed the statistical analysis and drafted the manuscript. Yu. Shi participated in the design of the study and performed the statistical analysis. Guonan Zhang participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.”

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Table 1 Procedure-specific management

	FTS management	Traditional management
Pre-operative	pre-operative assessment, counseling and FT management education	pre-operative fasting at least 8h
	Preoperative nutritional drink up to 4 h prior to surgery mechanical bowel preparation should not be used	Oral bowel preparation or mechanical bowel until liquid stool
	patients are not received mechanical bowel preparation, only oral intestinal cleaner 12 h pre-operation can be accepted, but no need of liquid stool	Antimicrobial prophylaxis and skin preparation
	Antimicrobial prophylaxis and	

	skin preparation	
	preoperative treatment with carbohydrates (patients without diabetes)	
Intraoperative	fast solid food before 6 h and liquid food Intake of clear fluids 2 h before anaesthesia	
	Avoiding hypothermia, keeping the intra-operative coretemperature at $36 \pm 0.5^{\circ}\text{C}$	$34.7 \pm 0.6^{\circ}\text{C}$
	Antiemetics at end of anaesthesia	
Post-operative	Postoperative glycaemic control	
	postoperative nausea and vomiting (PONV) control	
	Early postoperative diet(3-6 h after surgery, patients resumed a liquid diet, 12 h after surgery patients began to take solid diet)	6 h after surgery, patients resumed a liquid diet, patients began to take solid diet after anal exhaust
audit	Systematic audit improves compliance and clinical outcomes	

Table 2 Clinical parameters and postoperative complications for analysis

Parameters	Definitions
patient characteristics	age, weight, height, body mass index (BMI), medical insurance status and per-formance status.
hospitalisation	LOS(Length of hospitalization post-operation), the procedure performed, diagnosis, operating time, name of surgery, intraoperative estimated blood loss
Post-operation	time to full tolerance of free fluids (days), time to full tolerance of solid food (days), time to drain removal (days).
Complications	
infection	wound infection, lung infection, intraperitoneal infection, operation space infection
postoperative nausea and vomiting (PONV)	it was recognized that nausea and vomiting are common side effects of surgical recovery
Ileus	is a disruption of the normal propulsive ability of the gastrointestinal tract
Postoperative haemorrhage	Evidence of blood loss from drains or based on ultrasonography

Postoperative thrombosis	Evidence of blood thrombosis based on ultrasonography
APACHE II score	Acute Physiology and Chronic Health Evaluation II

Figure1 Study flow diagram

