

## Fast-track program vs traditional care in surgery for gastric cancer

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**Author contributions:** Chen ZX and Cen Y designed the study and wrote the manuscript; Chen ZX conducted the statistical analysis; Chen ZX, Liu AHJ and Cen Y wrote the manuscript.

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### Abstract

**AIM:** To systematically review the evidence for the effectiveness of fast-track program vs traditional care in laparoscopic or open surgery for gastric cancer.

**METHODS:** PubMed, Embase and the Cochrane library databases were electronically searched for published studies between January 1995 and April 2013, and only randomized trials were included. The references of relevant studies were manually searched for further studies that may have been missed. Search terms included "gastric cancer", "fast track" and "enhanced recovery". Five outcome variables were considered most suitable for analysis: postoperative hospital stay, medical cost, duration to first flatus, C-reactive protein (CRP) level and complications. Postoperative hospital stay was calculated from the date of operation to the date of discharge. Fixed effects model was used for meta-analysis.

**RESULTS:** Compared with traditional care, fast-track program could significantly decrease the postoperative hospital stay [weighted mean difference (WMD) = -1.19, 95%CI: -1.79--0.60,  $P = 0.0001$ , fixed model], duration to first flatus (WMD = -6.82,

95%CI: -11.51--2.13,  $P = 0.004$ ), medical costs (WMD = -2590, 95%CI: -4054--1126,  $P = 0.001$ ), and the level of CRP (WMD = -17.78, 95%CI: -32.22--3.35,  $P = 0.0001$ ) in laparoscopic surgery for gastric cancer. In open surgery for gastric cancer, fast-track program could also significantly decrease the postoperative hospital stay (WMD = -1.99, 95%CI: -2.09--1.89,  $P = 0.0001$ ), duration to first flatus (WMD = -12.0, 95%CI: -18.89--5.11,  $P = 0.001$ ), medical cost (WMD = -3674, 95%CI: -5025--2323,  $P = 0.0001$ ), and the level of CRP (WMD = -27.34, 95%CI: -35.42--19.26,  $P = 0.0001$ ). Furthermore, fast-track program did not significantly increase the incidence of complication (RR = 1.39, 95%CI: 0.77-2.51,  $P = 0.27$ , for laparoscopic surgery; and RR = 1.52, 95%CI: 0.90-2.56,  $P = 0.12$ , for open surgery).

**CONCLUSION:** Our overall results suggested that compared with traditional care, fast-track program could result in shorter postoperative hospital stay, less medical costs, and lower level of CRP, with no more complications occurring in both laparoscopic and open surgery for gastric cancer.

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**Key words:** Fast-track program; Traditional care; Gastric cancer; Meta-analysis; Laparoscopic and open surgery

**Core tip:** Our overall results suggested that compared with traditional care, fast-track program could result in shorter postoperative hospital stay, less medical cost, and lower level of C-reactive protein, with no more complications occurring in both laparoscopic and open surgery for gastric cancer.

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## INTRODUCTION

China, Japan, South America, Eastern Europe and parts of the Middle East are reported with the highest incidence of gastric cancer<sup>[1]</sup>. Over the past 20 years, there have been two important developments in elective major abdominal surgery; the introduction of laparoscopic surgery and the implementation of an enhanced recovery after surgery program, also referred to as “fast track” (FT) perioperative care, both focusing on accelerated recovery resulting in shorter hospital stay.

Laparoscopic surgery has definite advantages and has been used widely since its advent. And it is well known to be associated with less postoperative pain than open surgery and postoperative pain can be controlled without opioids<sup>[2]</sup>. In recent years, the advantages of laparoscopic surgery have been recognized in gastric cancer<sup>[3-6]</sup>.

FT surgery is an integrated application of various medical interventions that can enhance recovery after surgery. The FT perioperative care, or the enhanced recovery program after surgery, initiated by Bardram *et al*<sup>[7]</sup> in 1995, consists of a multidisciplinary approach, including preoperative counseling, no bowel preparation, perioperative high oxygen concentrations, active prevention of hypothermia, and no routine use of nasogastric tubes or drains. In recent years, FT surgery has been successfully applied to general<sup>[8]</sup>, urological<sup>[9]</sup>, cardiovascular<sup>[10]</sup>, gynecological<sup>[11]</sup>, orthopedic<sup>[12]</sup> and thoracic surgery<sup>[13]</sup>.

This study aims to systematically review the evidence for the effectiveness of FT program *vs* traditional care in surgery for gastric cancer.

## MATERIALS AND METHODS

### Search and selection strategies

PubMed, Embase and the Cochrane library databases were electronically searched for published studies between January 1995 and April 2013. The references of relevant studies were manually searched for further studies that may have been missed. Search terms included “gastric cancer,” “FT” and “enhanced recovery”. No language restriction was applied.

### Inclusion and exclusion criteria

Randomized controlled trials (RCTs) comparing FT program with traditional care in adult patients (aged > 18 years) undergoing laparoscopic or open surgery for gastric cancer were eligible for inclusion. Excluded studies (1) were not RCTs (such as nonrandomized, quasi-randomized, pseudorandomized, or controlled clinical trials or cohort or retrospective studies); (2) had no documentation of individual items of the FT programs; or (3) had no data available for the present meta-analysis.

### Methods of review

Each article was critically reviewed by two researchers

independently using the double-extraction method for eligibility. Any conflict was resolved before final analysis. Five outcome variables were considered most suitable for analysis: postoperative hospital stay, medical costs, duration to first flatus, C-reactive protein (CRP) level, and complications. Postoperative hospital stay was calculated from the date of operation to the date of discharge. The quality of the RCTs was assessed with the Jadad scoring system by two authors<sup>[14]</sup>.

### Statistical analysis

Weighted mean differences (WMDs) and their 95% CIs were used for analyzing continuous variables presented in the same scale (postoperative hospital stay, medical costs, duration to first flatus, and CRP level). Data reported as medians and ranges or medians and interquartile ranges were converted to means and standard deviation (SD)<sup>[15]</sup>. We calculated the lower and upper ends of the range by multiplying the difference between the median and upper and lower ends of the interquartile range by 2 and adding or subtracting the product from the median<sup>[16]</sup>. For dichotomous data (complications), relative risk (RR) with 95% CI was calculated. The effect measures were pooled using the fixed-effects model. Level of statistical significance was set at  $P < 0.05$ . Heterogeneity was quantified by calculating  $I^2$  where  $P < 0.10$  was deemed significant. Publication bias was not evaluated by a funnel plot, because the number of included trials in the present review was limited. All statistical analyses were executed using STATA version 11. Some outcomes were not analyzed but presented in a descriptive way.

## RESULTS

According to the searching strategy, three trials were included in our study. We divided the Chen's study into two comparisons, *i.e.*, FT program *vs* conventional care in laparoscopic surgery (Chen 2012), and FT program *vs* conventional care in open surgery [Chen 2012 (2)]. Two trials evaluated the effectiveness of FT program *vs* traditional care in laparoscopic surgery for gastric cancer<sup>[17,18]</sup>, while two trials assessed the effectiveness of FT program *vs* traditional care in open surgery for gastric cancer<sup>[17,19]</sup>. The sample size was small in all trials, ranging from 41 to 92. All studies were conducted in Asia, including China and Korea. Detailed characteristics of each trial are given in Table 1.

### Methodological assessment

No trials described the detailed methods of randomization, and allocation concealment was not performed in all trials. The incidence of withdrawal and dropouts was low, and the reasons were clearly reported. Blinding design was not applied in any trial. The methodological assessment by Jadad scale suggested that all trials were considered to be of moderate risk of bias.

### FT program in laparoscopic surgery for gastric cancer

In 2012, Chen *et al*<sup>[17]</sup> reported one RCT that evaluated the safety and effectiveness of FT program combined with

**Table 1** Main characteristics of included trials

Ref.	Location	Sample size	Age (yr)	BMI (kg/m <sup>2</sup> )	Intervention group	Control group	Follow-up (wk)	Jadad score
Chen <i>et al</i> <sup>[17]</sup>	China	19/22	59/63	22.9/22.9	FT + LADG	LADG	4	2
Kim <i>et al</i> <sup>[18]</sup>	South Korea	22/22	53/57	23.4/23.8	FT + LADG	LADG	2	2
Chen <i>et al</i> <sup>[17]</sup>	China	21/20	64/64	23.5/23.5	FT + ODG	ODG	4	2
Wang <i>et al</i> <sup>[19]</sup>	China	45/47	59/57	23.8/23.2	FT + OG	OG	4	2

BMI: Body mass index; FT: Fast-track.

**Table 2** Meta-analysis results

Gastric cancer	WMD/RR (95%CI)	P value	Heterogeneity	
			$\chi^2$ (P value)	I <sup>2</sup> (%)
Outcomes for laparoscopy surgery				
Postoperative hospital stay	WMD -1.19 (-1.79--0.60)	0.000	10.60 (0.001)	90.6
Medical cost	WMD -2590 (-4054--1126)	0.001	0.13 (0.72)	0.0
CRP	WMD -17.78 (-32.22--3.35)	0.016	0.51 (0.48)	0.0
Duration to first flatus	WMD -6.82 (-11.51--2.13)	0.004	0.29 (0.59)	0.0
Complication	RR 1.39 (0.77-2.51)	0.270	1.22 (0.27)	18.2
Outcomes for open surgery				
Postoperative hospital stay	WMD -1.99 (-2.09--1.89)	0.000	2.44 (0.12)	59.1
Medical cost	WMD -3674 (-5025--2323)	0.000	2.21 (0.14)	54.7
CRP	WMD -27.34 (-35.42--19.26)	0.000	5.10 (0.02)	80.4
Duration to first flatus	WMD -12.0 (-18.89--5.11)	0.001	-	-
Complication	RR 1.52 (0.90-2.56)	0.120	0.16 (0.69)	0.0

WMD: Weighted mean difference; CRP: C-reactive protein.

laparoscopy-assisted radical distal gastrectomy for gastric cancer. They found that combination of FT with laparoscopy in gastric cancer is safe, feasible, and efficient and can improve nutritional status, lessen postoperative stress, and accelerate postoperative rehabilitation. Meanwhile, Kim and colleagues published another trial which also evaluated the safety and efficacy of FT in laparoscopic distal gastrectomy. They also found that FT surgery could enhance postoperative recovery and improve immediate postoperative quality of life, and was safe in laparoscopic distal gastrectomy. We made a meta-analysis for the following outcomes in these two trials.

Our overall results showed that compared with traditional care, FT program could significantly decrease the postoperative hospital stay (WMD = -1.19, 95%CI: -1.79--0.60,  $P = 0.0001$ , Figure 1A), duration to first flatus (WMD = -6.82, 95%CI: -11.51--2.13,  $P = 0.004$ , Figure 1B), medical cost (WMD = -2590, 95% CI: -4054--1126,  $P = 0.001$ , Figure 1C), and the level of CRP (WMD = -17.78, 95%CI: -32.22--3.35,  $P = 0.0001$ , Figure 1D) in laparoscopic surgery for gastric cancer. Furthermore, FT did not significantly increase the incidence of complications (RR = 1.39, 95%CI: 0.77-2.51,  $P = 0.27$ , Figure 1E). Additionally, there was no significant difference between the two groups for length of operative time and intraoperative blood loss. Most of the heterogeneity tests for those outcomes did not detect significant heterogeneity, which is detailed in Table 2.

### FT program in open surgery for gastric cancer

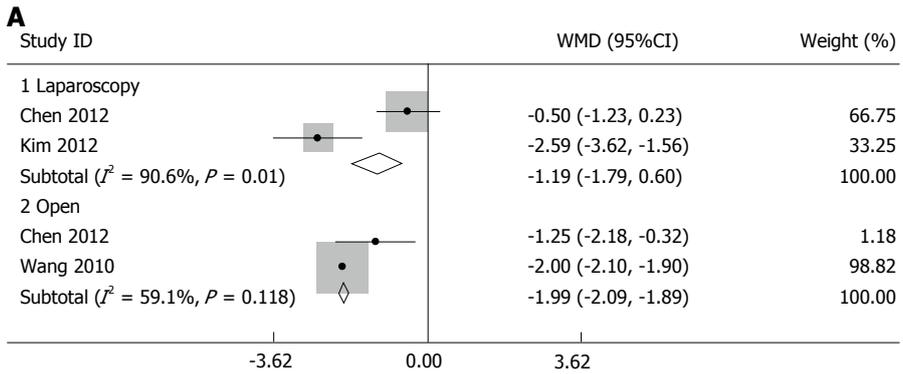
In 2010, Wang *et al*<sup>[19]</sup> reported a trial which evaluated the feasibility and safety of FT program in patients with

gastric cancer during the perioperative period. They suggested that FT open surgery could lessen postoperative stress reactions and accelerate rehabilitation in patients with gastric cancer. In 2012, Chen and colleagues also found that compared with conventional care in open distal gastrectomy, FT program could reduce postoperative stress and accelerate postoperative rehabilitation.

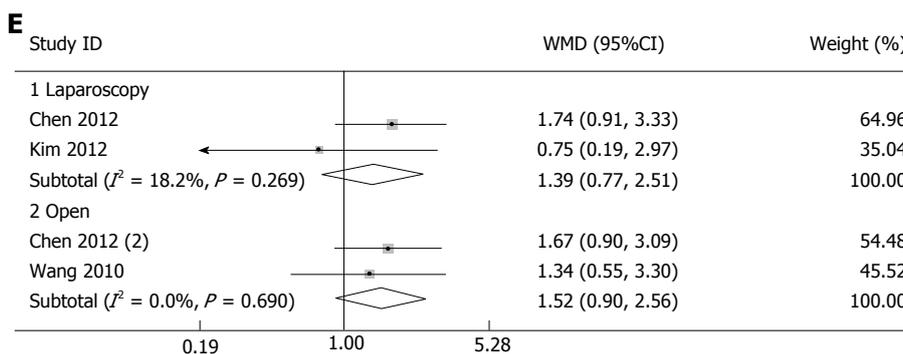
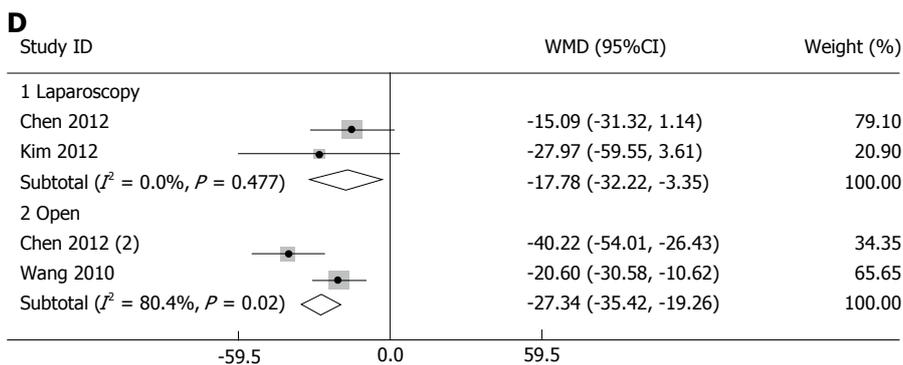
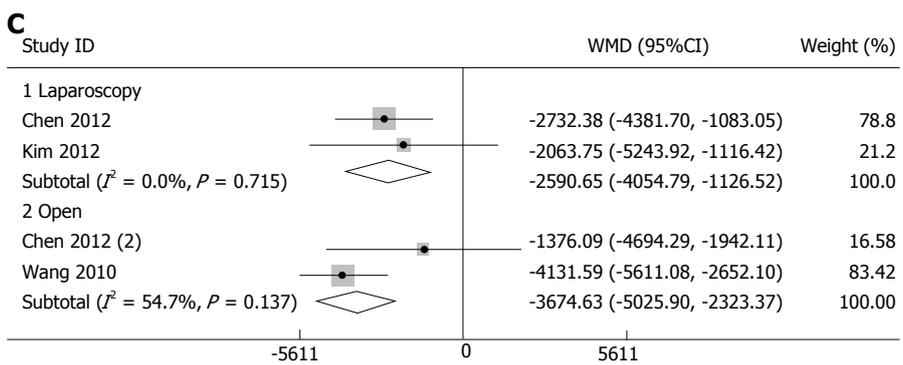
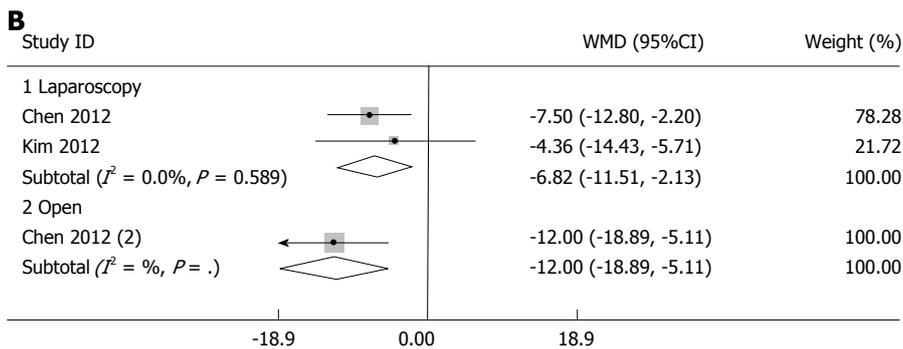
Our overall results found that compared with traditional care, FT program could significantly decrease the postoperative hospital stay (WMD = -1.99, 95%CI: -2.09--1.89,  $P = 0.0001$ , Figure 1A), duration to first flatus (WMD = -12.0, 95%CI: -18.89--5.11,  $P = 0.001$ , Figure 1B), medical cost (WMD = -3674, 95%CI: -5025--2323,  $P = 0.0001$ , Figure 1C), and the level of CRP (WMD = -27.34, 95%CI: -35.42--19.26,  $P = 0.0001$ , Figure 1D) in open surgery for gastric cancer. Furthermore, FT program did not increase the incidence of complications (RR = 1.52, 95%CI: 0.90-2.56,  $P = 0.12$ , Figure 1E). Additionally, there was no significant difference between the two groups for operative time and intraoperative blood loss. Most of the heterogeneity tests for those outcomes did not detect significant heterogeneity, which is detailed in Table 2.

## DISCUSSION

There have been a lot of studies and systematic reviews which evaluated the safety, feasibility, efficacy of FT program in colorectal surgery, and they found that compared with traditional care, FT program is safe and effective, justifying perioperative care in colorectal surgery<sup>[8,20-26]</sup>. However, until recently, only several trials evaluated the feasibility of FT program in surgery for gastric cancer.



**Figure 1 Meta-analysis.** A: Postoperative hospital day; B: Duration to first flatus; C: Medical cost; D: Level of C-reactive protein; E: Complications.



Our present work is to systematically review the evidence for the effectiveness of FT program vs traditional care in laparoscopic or open surgery for gastric cancer. Our results showed that compared with traditional care, FT program resulted in more rapid postoperative recovery, less medical cost, and earlier discharge from hospital, with no more complications occurring.

There was significant heterogeneity for the outcome of postoperative hospital stay between the two laparoscopy trials. FT program did not decrease the postoperative hospital stay in Chen's study. In contrast, Kim's study suggested that FT could significantly decrease the postoperative hospital stay. Causes of the heterogeneity may result from the differences in population, surgeon, sampling, FT program or traditional care. However, we could not be sure which factor was the main source of heterogeneity. The FT program in these two laparoscopy trials was similar in most items, such as normal diet in the preoperative stage, and no opioid analgesics by intramuscular injection or patient-controlled analgesia in the postoperative period. There was some difference in the surgery day. In Chen's study, there was no routine use of abdominal cavity drainage in the FT program, while in the Kim's study, routine use of abdominal cavity drainage were applied. Additionally, the necessary data of mean  $\pm$  SD in Chen's study were imputed according to the method described by Hozo *et al*<sup>[15]</sup>, and it could introduce some heterogeneity. No significant heterogeneity was found for the outcome of postoperative hospital stay between the two open trials.

The duration to first flatus in the FT program group was also found to be shorter, which implied that the bowel function recovered faster. The medical cost was significantly less in the FT program group, which may be explained by shorter postoperative hospital stay in this group. The incidence rate of complications was more frequent in Chen's study than in Kim's study, which can be explained by the fact that the duration of follow-up in Chen's study was longer. However, there was no significant difference in the incidence rate of complications between the FT program and traditional care. Several cytokines such as interleukin-6, tumor necrosis factor- $\alpha$ , and CRP have been demonstrated to be involved in the response to surgical stress and therefore considered useful serum markers for evaluating the severity of surgery-induced stress. CRP was chosen as a serum marker in our study, and the overall results showed that the level of CRP was significantly lower in the FT program group than in the traditional group.

Our work is the first systematic review to discuss the FT surgery for gastric cancer. However, there were several main limitations in our study. First, the sample size was relatively small. Second, the number of included studies was limited. Third, the methodological assessment showed that all trials were of moderate risk of bias, because no trial described the details of randomization and allocation concealment. Finally, all trials were single-center studies.

In conclusion, our overall results suggested that compared with traditional care, FT program could result in shorter postoperative hospital stay, less medical cost, and lower level of CRP, with no more complications in both laparoscopic and open surgery for gastric cancer. Future trials need to include more participants in multiple centers to assess the effect of FT surgery for gastric cancer.

## COMMENTS

### Background

Fast-track (FT) surgery is an integrated application of various medical interventions that can enhance recovery after surgery. It has been applied in the surgery for gastric cancer.

### Research frontiers

Several trials evaluated the effectiveness of FT program vs traditional care in surgery for gastric cancer.

### Innovations and breakthroughs

Authors' overall results suggested that compared with traditional care, FT program could result in shorter postoperative hospital stay, less medical cost, and lower level of C-reactive protein, with no more complications occurring in both laparoscopic and open surgery for gastric cancer.

### Applications

FT program can be applied in surgery for gastric cancer to enhance postoperative recovery.

### Peer review

The manuscript was well written and concise. The title and abstract explain the manuscript very well. Their results suggested that FT program can be used in surgery for gastric cancer.

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